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Credits and Introduction

To Helen, Laura and Esther
My precious wife and daughters
Thanks for your support and patience

To the Creative Genius behind the human body:
Did You have to make it quite so complicated?

This workbook collates all the study material lavished upon us in the 4th, 5th and 6th Year Medicine course taught at the Wellington School of Medicine. It is an attempt to organise and summarise the zillion and one things that of course you should know.

This third addition results from a substantial revision of the original 2002 notes, undertaken by Rhys Parry over 2010 – 2011 (thanks Rhys).

This document is intended to help you cram for exams. It is not intended as a clinical reference, and should not be used for making real life decisions. Find something more reliable. We have endeavoured to be as accurate as possible, but a patient on the end of a needle deserves better than the ravings of a 6th year student.

Sections whose headers are marked with an ‘*’ are sections compiled from books – these were not taught as discrete topics, but we thought they should be in here.

We are indebted to Matthew the many lecturers who taught us. Where we drew from substantial handouts, these are referenced.

We have also used the following books:


Feedback – especially any bloopers – would be most welcome. Email them to me at David.Tripp@xtra.co.nz.

Enjoy!

© David Tripp, March 2013
Patient Management

- This chapter contains aspects of history taking, examination, investigations and management that don’t sit neatly in another chapter. It therefore focuses on principles and general exam features, and covers some bits and pieces. For specific history taking or examination refer to the relevant chapter.

History Taking

Frameworks for consultation

- 4 tasks for consultation:
  - Management of presenting problems
  - Modification of help-seeking behaviour (did they come too soon/too late)
  - Management of continuing problems
  - Opportunistic health promotion

- Objective: integration of:
  - Doctor’s agenda: Correct diagnosis, preventative health care
  - Patient’s agenda: expectations, feelings, fears, understanding of illness experience

- Silverman and Kurtz: - five phases of the consultation:
  - Initiating the session: introduce yourself, why are you here, how can I help (not how are you)
  - Gathering information: start with open questions, physical exam
  - Building the relationship
  - Explanation and planning: what you’ll do, what you want the patient to do. Involve patient in planning.
    - Give them as many choices as possible
  - Closing the session: any more questions, check understanding, follow up, emergencies, etc

- Double Diamond model:
  - First phase: patient presents problems, doctor hones down
  - Second phase: diagnosis reached, expansive phase of explanation, management options, then brought to closure

- FIFE: Feelings, Ideas, Function/Dysfunction, Expectations

- Remember: listen, reassure

History Taking

- Always ask why they’ve come: and why that is a concern to them (what are they scared of?)

- Key skills:
  - Establishing rapport
  - Asking questions in a logical order
  - Observing non-verbal queues
  - Proper interpretation

- Record positive & negative findings. Always amplify positive findings:
  - Time course
  - How quickly did it come on (what were you doing then), pattern since then
  - Site and radiation
  - Character
  - Severity
  - Aggravating or relieving factors
  - Associated symptoms
  - Previous occurrences

- For each potential cause of a symptom think of:
  - Detail of the symptom
  - Other symptoms you would expect if that cause
  - Ask about risk factors of that cause

- See also Talking with Children, page 892 and Talking with Adolescents, page 1008

History Outline

- History:
  - Identifying data
- Presenting complaint (or complaints) eg Cough with green sputum 2 days, Dizziness 4 weeks
- History of presenting complaint
- Drug and medication use, including allergies, OTC drugs, herbal/alternative medicines
- Past medical and surgical history (including hospital admissions)
- Screen for hypertension, heart disease, asthma, diabetes, epilepsy, rheumatic fever, TB, bleeding tendency, hepatitis B
- Family history of illness (if genetic illness draw family tree)
- Social history: smoking, alcohol, job, living situation, social supports, overseas travel, functional history in the elderly or disabled
- If a child, then obstetric, neonatal, growth and development, immunisations
- Review of systems
- At end of history always ask ‘is there anything else you want to tell me’
- Note mental function and communication: dementia/delirium common

- Physical Exam:
  - Vital signs: temperature, respiratory rate, pulse, blood pressure
  - General observations: distress, pallor, hydration, cyanosis, weight
  - Relevant systems exams
- Formulation and problem list:
  - List of active problems or clusters of problems (always include smoking if they smoke)
  - List of inactive problems or clusters of problems
  - For each problem, list a set of differential diagnoses, investigations to establish which it is, immediate management, other management strategies
- Progress notes:
  - Changes in symptoms
  - Changes in physical exam or investigation
  - Assessment of what this means
  - Plan for what to do now

Cover-All Questions

- Always have **THYROID** (hypo or hyper) as a differential, especially with ‘tiredness’ stations

**General**
- How have your **energy** levels been?
- How has your **mood** been lately?
- Have you noticed in change in **appetite or weight**?
- Any recent **coughs/colds**?
- Any fevers or shaking or sweats?
- Skin rashes/changes?
- Sleeping OK?

**Endocrine**
- Have you noticed any **change in your weight**?
- How are you **sleeping**? How are your **energy levels**?
- Are you often **thirsty**? Are you going to the **toilet more frequently**?
- Do you have any problems with the **heat/cold**?
- Any diabetes?

**Haematology**
- Noticed any **bruising**?
- Problems with **stopping bleeding** (tooth extraction, surgery, cuts)?
- More **infections** than usual (coughs/colds/skin infections)?
- Mouth **ulcers**
- Lumps and bumps?
- Tiredness/fatigue? SOB/CP on exertion?

**Neuro**
- Have you had any **fits/faints/funny turns**? (CVS questions/aura/memory/incontinence/duration)
- Have you had any **headaches**? (SOCRATES/associated symptoms – fever, neck pain, photophobia, n & v, URTI)
• Have you noticed any **weakness** in limbs/*changes in sensation*? (time course/DM/distribution)
• Any changes in **vision**? **Hearing**?
• Any problems with your **balance**?
• Any previous **migraines**?

**CVS**
• Do you ever have any **chest pain**? **SOCRATES**
• Do you ever get **SOB**? At night? Sleep propped up?
• Do you ever have any **palpitations**/feel your heart racing?
• Do you ever feel **dizzy** or faint?
• Have you noticed any **ankle swelling**?
• Any pain in your buttocks/legs?
• How far can you walk? Up steps?
• Any heart attacks/angina/high blood pressure/high cholesterol/DM/smoking/FHx/rheumatic fever?

**Respiratory**
• Do you ever feel **SOB**? (SOCRATES)
• Do you ever have a **cough**? Productive? Blood?
• Do you ever notice a **wheeze**?
• Any **pain** during breathing?
• Any asthma/bronchitis/tuberculosis?

**GIT**
• Any problems with your teeth or ulcers in your mouth?
• Have you noticed a **change in your bowel habits**? Diarrhoea? Constipation?
• Have you noticed any **blood** in the toilet/on the toilet paper?
• Do you have any **nausea/vomiting**?
• Do you have any **pain**? **SOCRATES**
• Any troubles swallowing/any reflux/burning sensation behind chest?
• Any **yellowing** of your skin?
• Any crohn’s/celiac/bowel ca?

**Renal**
• Have you any **pain**? **SOCRATES**
• Do you have any **troubles with your waterworks**? (pain/colour/blood/odour/frequency/hesitancy/urgency)
• Have you had any flu-like illnesses/skin sores recently?
• Any kidney stones/UTIs?

**MSK**
• Have you had any **back/muscle/joint pains**? **SOCRATES**
• Any stiffness?
• Have you noticed any **swelling/redness**?
• Any arthritis?
• Any previous injuries?
• Any hx of diabetes, thyroid problems, eye problems, skin problems?

**Gynae**
• Have you had any **pain**? **SOCRATES**
• Have you needed to **pee more often**?
• Any discharge?
• Have you had a recent **smear**?

**Menstrual**
• When was your **last period**?
• Are your periods normally **regular**?
• Do you have much **pain**/are your periods **heavy**?

**Obstetric**
• Have you ever been **pregnant**?
If so, were there any complications? (bleeding/DM/pre-eclampsia) How were your previous babies delivered? Big babies?
Have you had any miscarriages/abortions?
When was your last period? Due date?
Have you had any bleeding or discharge?
Have you had any troubles with peeing? Frequency?

**Sexual**
- Are you sexually active?
- Do you have one partner?
- Do you use contraception? What?
- Have you ever had a UTI or an STI?
- Do you have any problems with sex? Any pain?

**Paediatrics**
- Any viral sounding illness: runny nose, pulling at ears, wheeze, cough, photophobia, stiff neck, rash, sleepy, feeling hot, shaking, vomiting, diarrhoea, sick contacts?
- Eating and drinking?
- PU? BO?
- PMHx: any previous hosp admissions? Surgeries?
- Birth: gestation, delivery, problems, preg probs/smoking, birth weight, inpt stay?
- Nutrition: breast/bottle fed, solids introduced?
- Imms: UTD?
- Development: tell me about ...’s dev, walking, talking, school, friends, vision, hearing?
- SHx: smoking at home/car? Access to car/phone?

**Psychiatry**
- CAMP SAND
- Cognition: any problems with your memory or your thoughts? Orientation to PPT
- Anxiety: any particular worries/stresses/panic symptoms?
- Mood: how has your mood been over the past little while?
- Psychosis: any odd thoughts people find strange? Any voices/visions/feelings others don’t experience?
- Suicide: any thoughts of hurting yourself or suicidal thoughts?
- A & D
- Neurobehavioural symptoms: sleep, appetite, concentration, energy, guilt?
- Development: any problems in childhood etc

**Examination**

**Rapid Screening Physical Examination**

**General Observation**
- Wash hands
- Introduce + gain permission
- Position at 45 degrees
- Patient looks well or ill, in any distress, breathing RA/O2, clues at the bedside

**The Hands and Arms**
- Nails for clubbing (resp/CVS/GIT) and stigmata of IE or chronic liver disease
- Nail changes of chronic renal disease (lindsay’s) or iron deficiency (koilonychia)
- Arthropathy (rheum/resp)
- Take pulse, measure RR
- Test for asterixis
- Inspect for brusing/scratch marks/jaundice/spider naevi
- Determine hydration
- BP
- Examine for lymphadenopathy
Face
- Eyes for jaundice, exophthalmos, pallor
- Face for vasculitic rash, other facies
- Mouth for mucosal ulcers, general hygiene
- Tongue for glossitis or cyanosis

Anterior Neck
- JVP
- Carotid pulses
- Trachea centrality

Anterior Chest
- Inspect for chest wall deformity, scars, skin changes, spider naevi, accessory muscle use, breath in for expansion
- Palpate for AB, thrills, heave, do chest expansion
- Percuss the chest
- Auscultate the heart and lungs

Posterior Chest and Neck
- Lymph nodes
- Inspect
- Chest expansion
- Percuss and auscultate the back of the chest
- Examine for a goitre
- Sacral oedema

Abdomen
- Lie pt down
- Inspect then palpate for organomegaly and other masses
- Percuss for shifting dullness if appropriate
- Auscultate
- Palpate for inguinal lymphadenopathy and herniae and testes in men

Legs
- Feel for peripheral pulses
- Look for peripheral oedema and leg ulcers
- Feel calves

Neurological Examination
- Do AMT (see neuro)
- Do CN examination
- Inspect for wasting + fasciculation in upper limbs
- Test tone, power, reflexes, coordination, sensation
- Inspect for wasting + fasciculation in lower limbs
- Test tone, power, reflexes, coordination, sensation
- Test gait: heel-toe walking
- Test ability to stand on the toes (S1) and heels (L4,5) and squatting (proximal muscles)
- Test for Romberg’s sign (posterior columns)

To Finish
- Observation chart
- Rectal and pelvic examination
- Urinalysis
- BMI

Purpose of Examination
- Aims to:
  - Confirm suspicion
Exclude other causes that mimic it
Measure severity

General
- Are the conditions OK to do an exam? Is the light in the room OK, is the patient positioned and exposed, etc
- ALWAYS OBSERVE FIRST: stand back and look.
- Distress, comfort, central or peripheral cyanosis, pallor, jaundice, dehydration, SOB, how sick or well
- Cachectic = severe loss of weight and muscle wasting. Usually malignancy, but also severe cardiac disease (due to anorexia from liver congestion and impaired absorption due to intestinal venous congestion)
- Facies: features of the face suggesting diagnoses: eg acromegaly, Cushing’s, Down’s, myxoedema, Parkinson’s, hair distribution in men and women, etc
- Weight, body habitus and posture, including deformities
- Include vital signs in general assessment: pulse, blood pressure, temperature, respiratory rate

Fever
- See also Fever in Children, page 950
- Taking a temperature:
  - Serial measurements the most useful
  - Also take pulse – if ↑temp should have ↑heart rate (except in typhoid)

<table>
<thead>
<tr>
<th>Normal Values</th>
<th>Low</th>
<th>High</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oral</td>
<td>36.6</td>
<td>37.2</td>
</tr>
<tr>
<td>In hot weather</td>
<td>+0.5</td>
<td>+0.5</td>
</tr>
<tr>
<td>Rectal</td>
<td>+0.2</td>
<td>+0.5</td>
</tr>
<tr>
<td>Axillary</td>
<td>-0.5</td>
<td>-0.5</td>
</tr>
</tbody>
</table>

- Children: the most common emergency presentation in paediatrics
  - Most common cause is viral infection, otitis media, pharyngitis, and tonsillitis
  - Also consider bladder infection, Rheumatic fever, Meningitis
  - Kids spike temperature easily
  - Febrile convulsions occur between 6 months and 6 years. At other ages investigate other causes
- Types of fever:
  - Continued: does not remit e.g. typhoid, drug fever
  - Intermittent: falls to normal each day – pyogenic infections, lymphomas
  - Relapsing: returns to normal for days then rises again – *Malaria*, *lymphoma*, pyogenic

Pyrexia/Fever of Unknown Origin (PUO/FUO)
- See also: Fever in Children, page 950
- Formal definition: > 38 C, > 3 weeks, no known cause (ie normal admission tests already done). However, often used to describe a temperature that you haven’t done any tests on yet
- Usually an unusual presentation of a common disease
- History, exam, investigations, time course, urgency and likely cause depend on setting

Classification of PUO
- Classic PUO:
  - Fever, higher than 38 on several occasions, persisting *without a dx* for at least 3/52, in spite of at least 2 outpatient visits or 3 days in hospital
  - Aetiologies: infections (most common), neoplasms, connective tissue disorders, miscellaneous, undiagnosed
  - Infective causes of classic PUO:
    - Imported infections = *malaria*, *dengue*, *enteric fever* (typhoid, paratyphoid fever); zoonoses (leptospirosis, toxoplasmosis, brucellosis, Q fever [coxiella burnetii])
    - Chronic infections = TB, endocarditis
    - Viral infections = CMV, EBV, acute HIV
    - Cryptic abscesses = psoas, perinephric, liver, spinal, dental
  - Non-infective causes:
    - Neoplasms = Hodgkin’s, other lymphoreticular malignancy, occult carcinoma (eg gastric)
    - Connective tissue disorders = still’s disease (JRA), SLE
    - Elderly: temporal arteritis, PMR
Clinical management:
- **Hx**: recent overseas travel, travel vax, weight loss, night sweats, back pain, HIV risk, recent AB therapy/other meds, occupation
- **Clinical findings**: documented fever, tachycardia, tachypnoea?
- **Ix**: FBC, CRP, U + E, LFTs, CXR, CT abdo, **blood cultures** (including TB BC bottle), **urine microscopy + culture**, **infectious disease serology** (dengue, CMV, EBV, HIV, leptospiira, toxoplasma), **blood film** for malaria, **mantoux**

- **Community acquired (Classic PUO)**
- **Nosocomial PUO** (ie hospital acquired):
  - Definition: fever, >38 for at least 3/7 and **not present on admission** to hospital
  - At risk groups = post-op pts, ICU, stroke pts
- **Immune-deficient PUO**:
  - Definition = fever, >38 for at least 3/7, with negative cultures for at least 48/24
  - Some causes of PUO in neutropenic pts who have not responded to broad spectrum ABs = **fungal infections** (45%), bacterial infections (10%), undefined (eg drug fever, 25%) etc
- **HIV-related PUO**:
  - Definition = fever >38 for more than 3/52 (outpatients), or >3/7 for inpatients with confirmed HIV
  - Some causes = Infections (eg DMAC, PCP, CMV, 85%), neoplasia (8%), miscellaneous (eg drug fever)

**Differential**

- **Neoplasm**: lymphoma, leukaemia (check lymph nodes), other (hepatic, renal, other)
- **Infection**:
  - **Bacterial**: TB, abscess (subphrenic, hepatic, pelvic, renal – look for ↑ neutrophils), **endocarditis** (any dental work?), pericarditis, osteomyelitis, cholangitis, pyelonephritis, PID, syphilis, cystitis
  - **Viral**: EBV, CMV, HBV, HCV, HIV, Varicella-Zoster
  - **Parasitic**: malaria, toxoplasmosis
  - **Fungal**
- **Connective Tissue**: RA, SLE, Vasculitis (eg polyarteritis nodosa – check for Raynaud’s phenomena)
- **Miscellaneous**: drug fever (especially penicillins, sulphonamides), Rheumatic fever, inflammatory bowel disease, granulomatous disease (eg Sarcoid), Factitious/Munchausen’s (eg injecting themselves with saliva)

- **Clues**:
  - Weight loss ⇒ chronic
  - Check eyes: iritis in connective tissue disease, jaundice, etc
  - Check tonsils, glands, ears for infection
- **History**:
  - **Travel** (eg malaria, did they have prophylaxis)
  - **Exposure** to others
  - **Sexual** history
  - Weight loss
  - Been to other doctors (had any antibiotics)
  - Occupational exposure (eg cows)
- **Exam**:
  - Lymph nodes
  - Heart murmurs
  - **Skin** for rashes
  - Abdominal exam
- **Possible investigations**:
  - Blood count
  - Blood cultures
  - Urine microscopy & culture
  - Liver function (eg hepatitis)
  - Viral serology
  - Malaria film
  - Chest X-ray

**Tiredness**

- **Differential**:
  - Sleep disturbance: eg anxiety, sleep apnoea, narcolepsy,
Depression
Anaemia
Endocrine: hypothyroidism, hypocortisolism (Addison’s), diabetes, hypercalcaemia (due to ↑PTH)
Infection (e.g. EBV)
Cancer
Drugs: alcohol intoxication, sedative drugs,
Head injury (e.g. subdural haematoma)
Post ictal states
Hypoglycaemia
Hepatic encephalopathy, Wernicke’s encephalopathy
Chronic heart failure
Malabsorption (e.g. coeliac disease)
Pregnancy

See also Sleep, page 128

Causes:
Lifestyle: stress, nutrition, sleep, exercise
Psychosocial: depression, anxiety
Physical: any illness, meds

Approach: define problem from patient’s viewpoint (what do you mean by tired? How does it affect your life? What do you think is going on?) → focused symptom review (look for red flags) → focused exam → focused lab tests

Lab Tests
Pt < 50 with no other risk factors: FBC + ferritin (looking for Fe def, macrocytosis, infection, leukaemia) + glucose if Maori/Pi/Asian over age of 40
Pt > 50 with tiredness > 1/12: FBC, electrolytes, ferritin, Fe sats, LFTs, Cr, TSH, glucose, Ca/PO, CRP, urinalysis
Pt < 50 with risk factors: specific tests as appropriate
FBC and ferritin are appropriate for most people with tiredness
TSH is investigation of choice for those at ↑ risk of thyroid dysfunction
Remember to consider UTI as a cause for tiredness (often non-specific symptoms)
Diagnostic testing for glandular fever unlikely to be helpful in those with tiredness only (do if glands up and fever)
Consider DM as a cause

Oedema
Include in exam of appropriate system
Need to retain 3 – 4 litres before pitting begins
Exam:
Where is it? Distribution
Is it pitting
Other signs of inflammation
Mechanisms:
↓ colloid osmotic pressure
↑ hydrostatic pressure
↑ permeability of wall

Localised Cause:
Inflammatory (e.g. infection, allergy - cytokine mediated, injury) → pain/heat/redness/swelling
Trauma
Venous occlusion by tumour or lymph nodes
Thrombus (e.g. DVT)

Generalised Cause:
Is it bilateral? Usually worse in the evenings
Heart Failure:
 Mechanism: ↑ preload → ↑ venous pressure + ↑ HSP, ↓ renal perfusion → ↑ renin → ↑ Na/H2O
 History: check SOB, orthopnoea, PND
 Signs/Tests: CXR, ECG, Echo
 Liver:
 Mechanism: liver failure/malnutrition → ↓ colloid pressure → ↓ renal flow → ↑ retention
 History: check alcohol, cholestasis, hepatitis, bleeding, bruising
• Signs/Tests: portal hypertension, enlarged liver, jaundice, bloods (Liver Function, INR)

➢ Renal:
  • Mechanism: nephrotic syndrome → ↓colloid pressure (have to lose 3.5 g protein a day to be nephrotic. NB nephritis is inflammation)
  • History: check change in urination, nocturia (due to diuresis), diabetes
  • Signs/tests: ↑BP, urine test, 24 hr urine, dipstick, urea/creatinine

➢ Drugs (eg vasodilators, like calcium channel blockers) can cause ankle oedema

➢ Gastrointestinal: Malabsorption → hypoalbuminaemia

• Non-pitting lower limb oedema:
  ➢ Lymphoedema (eg malignant invasion of lymphatics, allergy) doesn’t pit – push for 10 seconds
  ➢ Hypothyroidism

### Hands

• Nails:
  ➢ Takes ~ 6 months for fingernails to grow out
  ➢ Clubbing:
    • Respiratory: carcinoma, fibrosis, cystic fibrosis, TB, chronic suppuration (eg bronchiectasis), idiopathic pulmonary fibrosis, NOT asthma or COPD alone
    • Cardiovascular: infective endocarditis, cyanotic heart disease
  • Other (uncommon): cirrhosis, IBD, coeliac disease, thyrotoxicosis
  • Blue: cyanosis, Wilson’s disease
  • Red: Polycythaemia (red-blue), carbon monoxide poisoning (cherry red)
  • Pale nail bed: anaemia
  • Koilonychia: spoon shaped nails in Fe deficiency
  • Leuonychia: white nails in hypoalbuminaemia
  • Mee’s lines: single white transverse line in renal failure
  • Splinter haemorrhages: usually trauma (especially manual workers) or infective endocarditis, rarely vasulitis (eg in rheumatoid arthritis), polyarteritis nodosa, sepsis, blood malignancy or profound anaemia
  • Check capillary refill: squeeze nail and see how long it takes to return to red – sign of peripheral circulation. Normal < 2 sec

• Hands:
  ➢ Palmar erythema: pink spots on pale background – should be bilateral - Chronic liver disease, pregnancy, rheumatoid arthritis, polycythemia, thyrotoxicosis, SLE
  ➢ Skin: subcutaneous bleeding: petechiae small, purpura bigger, ecymosis – biggest. Petechiae caused by a platelet problem, not due to coagulopathy
  ➢ Dupuytren’s Contracture: extend fingers back – shortening of palmar aponeurosis – in alcoholic liver disease, epilepsy, manual workers and idiopathic
  ➢ Asterixis: metabolic flap – coarse, non-symmetrical – neural inhibition →encephalopathy in renal failure (↑urea), respiratory failure (↑CO2), liver failure (↑nitrogenous material), hypoglycaemia, barbiturate poisoning
  ➢ Raynaud’s Syndrome: intermittent attacks of ischaemia of fingers or toes due to intense arterial vasospasm, often precipitated by cold or emotional stimuli
  ➢ Tendon Xanthomata: lipid deposits in tendons of hands or arms in hyperlipidaemia

### Head

#### Headache

• See Headaches, page 209

### Eyes

• Jaundice: primary liver disease, liver congestion secondary to heart failure
• Anaemia: pale conjunctiva – especially anterior border just inside eye lid
• Sclera not affected by hypercarotenaemia
• Puffiness below eye: early nephritis (before feet oedema), myxoedema of hypothyroidism

### Mouth

• Mouth: Foetor hepaticus, ulceration, pigmentation, telangiectasia, gingivitis/hypertrophy, glossitis
• Ulcers: aphthous, drugs (e.g. gold), trauma, Crohn’s, infection (HVZ, HS)
• Pigmentation: heavy metals (lead, iron), drugs (anti-malarials), Addison’s, Melanoma, Kaposi’s sarcoma
• Snotty nose = coryza
Throat

<table>
<thead>
<tr>
<th>Bacterial</th>
<th>Viral</th>
</tr>
</thead>
<tbody>
<tr>
<td>High fever</td>
<td>Runny nose</td>
</tr>
<tr>
<td>Pus/exudate</td>
<td>Red raw throat</td>
</tr>
<tr>
<td>Productive cough (if any)</td>
<td>Persistent dry cough</td>
</tr>
</tbody>
</table>

- Whitish-yellow membrane over tonsils - ?EBV
- Patches of exudate on mucosa - candida
- Differential: Bacterial sore throat, viral URTI, glandular fever, rheumatic fever, quinsy (peri-tonsillar abscess, can lead to airway obstruction)
- See also Acute Pharyngitis, page 86

Lymph Nodes

- Occipital Nodes: scalp infections, bad nits, infected cradle cap, rubella
- Mastoid and posterior auricular
- Parotid: mumps
- Posterior sternomastoid
- Anterior sternomastoid: sore throat
- Jugulodigastric
- Submandibular and Submental: tooth infection, glandular fever
- Superior, deep and lateral cervical (internal jugular) nodes
- Supra & sub-clavicular: lung and lung surface infections, Tb, lung metastasis
- Enlarged lymph nodes and oral thrush →?AIDS

Investigations

CT and MRI Imaging

- CT:
  - Looks for density ⇒ bones are white (hyper-dense), air is black
  - If it is contrast enhanced then vessels will appear whitish
- MRI (=Magnetic Resonance Imaging):
  - Looks for H atoms
  - Very strong magnet lines up H atoms (effectively little dipoles), radio waves emitted which disturb net magnetic vector, then measure radio frequency emitted by atoms as they return to aligned state
  - Describe as hypo or hyper intense – as relates to signal intensity not density
  - Bones on both are black (no free fluid)
  - T1 weighting: simple fluid black (eg CSF, urine). Shows exquisite anatomy
  - T2 weighting: simple fluid turns white. Shows pathology, due to ↑ tissue hydration (eg infection, tumour). T2 shows H2O. Flowing blood is black

Blood Tests

Why Test

- Before ordering any test always ask yourself why you are ordering it. Labs confirm a diagnosis – don’t give it
- Diagnosis: to confirm diagnosis/exclude differential diagnosis from history & exam
- Prognosis: severity/progression
- Monitoring: Measure target of treatment rather than drug level (e.g. INR rather than warfarin)
- Screening: Only where test is reliable and you can do something about it

Parameters of a Test

- Normal range: either arbitrary (level which leads to ↓ risk) or statistical (what most people are)
- Should be reliable, sensitive, and specific
- Reliability:
  - Accuracy: mean of test results = real result
  - Precision: variability in results (i.e. want a small standard deviation). Important for serial monitoring. Only different if 2½ SDs from previous test
- Sensitivity: what rate of true positives does it pick up (are all positives found?)
- Specificity: false negative rate
• For further details on sensitivity, specificity, etc, see Sensitivity and Specificity, page 1047

Test Results

• Results may be:
  ➢ Real & require interpretation
  ➢ Erroneous: will always be some errors – there should be known rates of error for a lab and these should be within acceptable limits

• Artefact: affected by non-disease factors:
  ➢ Pre-analytical artefacts: mainly at time of collection
    o Incorrect labelling
    o Wrong tube/anticoagulant
    o Haemolysis
    o Delayed transport
    o Temperature effects e.g. refrigerating stuffs up electrolytes
    o Sample incorrectly taken (e.g. through or close to IV lines)
  ➢ Pre-analytical factors:
    o Not fasted/wrong time for sample
    o Medications interfere
    o Wrong reference range

Urgent Tests

• From Chemical Pathology lectures
• If the result may change the immediate management of a patient or if it plays a major role in ongoing assessment of a critically ill patient
• Routine ordering/screening not appropriate in A&E
• Emergency electrolytes:
  ➢ Frequently over-ordered
  ➢ Indications include:
    o D/V
    o Seizure of unknown cause
    o Muscle weakness
    o > 65
    o Known renal/diabetes disease
    o Hypertension/diuretics
    o Alcoholism
    o Clinical findings: oedema, volume depletion, ↑HR, ↓BP
    o Altered mental state

• Blood gases:
  ➢ Don’t need for uncomplicated asthma/MI, or if normal systemic perfusion and no dyspnoea/hyperventilation
  ➢ Indicated if: cyanosis, severe dyspnoea, hypotension, vasoconstricted and sweaty, septic shock, pneumonia, suspected PE, severe asthma/COPD in acute exacerbation

• Beware overdoses: people miscalculate/lie about consumption
  ➢ Timing important: test for paracetamol overdose after 4hrs to judge treatment required. LFT changes take 24hrs
  ➢ Ethanol levels: check in unconscious patient, for medicolegal reasons, or if intoxicated but potentially multiple problems

• Toxicology Testing:
  ➢ Serum levels for paracetamol, aspirin, ethanol, methanol, ethylene glycol, lithium, anticonvulsants, digoxin, iron, theophylline
  ➢ Urine screen for drugs of abuse (opiates, BZDs, cannabinoids, cocaine etc)
  ➢ Toxiclab screen: long and slow for about 400 therapeutic drugs. Qualitative only. Not done in Wellington any more

• Emergency use of cardiac markers: Laboratory Diagnosis, page 54

• Abdominal pain:
  ➢ Common to find no specific biochemical change; clinical signs, symptoms + hx are the most important indicator of dx
  ➢ Baseline Na, K, creatinine if D/V or surgery likely
  ➢ Amylase, glucose, HCG, LFT, calcium, cardiac enzymes
More rarely: urinary porphobilinogen, blood lead
Acute pancreatitis may not have ↑amylase, and ↑amylase can present in other conditions e.g. perforated/ischaemic bowel, ruptured ectopic pregnancy, diabetic ketoacidosis, renal failure

**Tests in Comatose Patients**
- Hx + exam are most important (+ resus: airway, ventilation, monitoring etc)
- Consider possible causes of coma:
  - Intracerebral: trauma, infection, bleeding, tumour
  - Intoxications: alcohol, opiates, CO, drugs
  - Metabolic: RF, endocrine, liver failure, porphyria
  - Miscellaneous: hypoxia, post seizure
- Should do:
  - Electrolytes
  - Osmolality
  - Cr
  - Glucose
  - ABGs
  - Blood alcohol levels
  - ?CSF
- Should consider special tests in + drug screens in individual cases

**Treatment**

**Differential Diagnosis**
- Always consider:
  - Autoimmune
  - Degenerative
  - Drugs
  - Doctors
  - Hereditary/congenital
  - Infective
  - Idiopathic
  - Mechanical
  - Metabolic
  - Nutritional
  - Neoplastic
  - Pregnancy
  - Psychiatric
  - Trauma
  - Vascular

**Formulating a Case**
- Differential diagnosis
- What are the risk factors
- Problem list
- Complications of problems and risk factors
- Prognosis: how does this impact on treatment decisions
- Investigations
- Treatment + management/monitoring of side effects
- Integration: stand back and think – am I missing something

**Treatment Checklist**
- Listen (therapeutic relationship)
- Education
- Lifestyle (diet, exercise, etc)
- Environment/social change
- Psychological
• Drugs
• Surgery
• Referral: to specialists, other health providers, support groups
• Family involvement
• Prevention
• Public Health measures

**Behavioural Change**

• Health Education is an attempt to achieve behavioural change
• See Parent and Adolescent Education, page 893

**Stages of Change Model**

• Stages of changes (Prochaska and Di Clemente 1982): Discussion must be tailored to the stage they're at:
  - Pre-contemplation
  - Contemplation
  - Planning/determination
  - Action
  - *Maintenance* (and maybe permanent exit)
  - *Relapse* (and maybe return to contemplation)

**Readiness to Change/Motivational Interviewing**

• Motivation = the probability that a person will enter into, continue and adhere to a specific change strategy. It fluctuates. It is a state not a trait. Measure motivation by what they say not what they do
• Motivational interviewing: goal is to get from the patient their reasons for concern and their arguments for change. Especially helpful in precontemplation/contemplative stages
• Confrontation tends to evoke resistance. Resistance ↓ the chance of change
• Approaches at each stage:
  - Pre-contemplation:
    - Lack of knowledge or inertia
    - Rebellion: try to provide choices
    - Resignation: given up – try to instill hope/explore barriers
  - Contemplation:
    - Not equivalent to commitment
    - Extra information may not make any difference
    - Work through ambivalence, anticipate barriers, ↓ desirability of present behaviour
  - Dealing with ambivalence:
    - “Yes, but...” is normal
    - Helping people resolve ambivalence is key to change
    - Good things and the bad things about behaviour
    - Further education may result in conflict or denial
    - Try to get the patient unstuck
    - Poor self-esteem, social context and values may make this difficult
    - Highlight discrepancy between personal goals and behaviour. Best if they can identify this discrepancy themselves, rather than feeling pressured
• Motivational Strategies (NB importance of empathy – understanding where the patient is at):
  - A – give Advice
  - B – remove Barriers
  - C – provide Choices
  - D – *decrease Desirability*: alter balance of perceived costs, barriers and rewards
  - E – practice Empathy. Accept and understand without agreeing
  - F – provide Feedback
  - G – clarify Goals
  - H – active Helping
• Counselling techniques:
  - *Open ended* questions
  - Reflective listening: voice what you think the patient means by what they are saying
  - Affirm: ↑ self esteem and support the patient
  - Summarise
Brief Interventions in General Practice

- Brief but repeated interventions avoid stigmatism, and are more effective than one long session
- Direct advice normally provokes resistance
- Opening lines:
  - “What are some good things about…? What are the less good things...”
  - Ask permission before giving information: “I wonder, would you be interested in knowing more about ....”.
  - When you’ve finished: “What do you make of all this?”
  - “What concerns do you have about ...”

Breaking Bad News

- Prepare patient for what is to come – give an honest explanation of why you’re doing investigations before you do them
- Think ahead – invite family members when results come back
- If there is no family, take a nurse (who has probably been preparing them anyway)
- Ask patient what they understand is happening or what they’re scared of – gives you a good intro
- It is the patient’s information – let them decide the pace and level of detail
- If the patient asks ‘have I got cancer’ then they will have been thinking about it and will have a reason for asking – this is helpful
- If the patient asks ‘What do you think’ then they’re likely to be anxious. Need to open up discussion and give them opportunity to express their fears
- Break up the information – ‘chunk and check’. Check understanding bit by bit
- ‘Denial’ can be shock, disbelief, or failure to understand. Denial is a longer-term pattern of behaviour. Whether denial is bad or not depends on the consequences
- **Document** your discussion and what you’ve said

Framework

- “SPIKES”
  - Setting:
    - Private and quiet
    - Allow enough time (give someone your pager)
    - Support person: “We’ve got some results we need to discuss, would you like anyone with you when we do that?”
    - Make sure of your facts: never give provisional results!
  - Perception:
    - What do they know/expect?
    - What have you been told so far? What do you think is happening?"
  - Invitation:
    - Try and allow the pt some sense of control
    - “Sounds like you’re not sure what’s going on, we’ve got some results that we need to discuss – is now a good time?”
  - Knowledge-giving:
    - Flag that you have bad news: “The ...(eg x-ray) is not normal and I’m concerned”
    - “Is it OK to go on?”
    - “We’ve found ... and we’re worried it could be ...”
  - Emotions:
    - Gauge the emotional temperature and respond appropriately: “It’s OK to feel...” “I can’t imagine what must be going through your mind right now...”
    - Some potential emotions: overwhelmed, disbelief, guilt, anger, grief
    - “Is there anything else going through your head?”
  - Strategise and summarise:
    - “We need to talk about where to from here...”

Pathology Basics

- Definitions:
  - **Metaplasia**: change from one adult cell type to another
  - **Dysplasia**: departure from normal; pre-cancerous architectural + cytologic alterations
Pathology Descriptions and Key Words

- Use key words to describe macroscopic + microscopic features:
  - Benign key words:
    - Bland
    - Regular
    - Circumscribed
    - No mitoses
    - Tissue architecture
  - Malignant key words:
    - Invasion
    - Desmoplasic reaction
    - Infiltrative
    - Destructive
    - Irregular
    - Cytological features of malignancy
    - Tissue architecture
  - Adeno- key words:
    - Glands
    - Papillae
    - Mucin
    - Crowding
  - Squam- key words:
    - Sheets
    - Keratin
    - Whorls

Inflammation

- Different patterns of inflammation often have different aetiologies
- Inflammation patterns:
  - Acute:
    - Vasodilatation (PG, histamine etc)
    - Increased vascular permeability (PG, BK, complement, LKT etc)
    - Entry of circulating neutrophils into tissue
  - Chronic:
    - Response to prolonged problems, orchestrated by T-helper lymphocytes
    - Features recruitment and activation of T- and B-lymphocytes, macrophages, eosinophils, and/or fibroblasts
    - Fibrosis
  - Granulomatous:
    - Aggregates of epithelioid histiocytes (macrophages & monocytes – phagocytosis to wall something off)
    - Giant cells often seen
    - Central necrosis often seen
  - Eosinophilic
- Abnormal accumulations of fluid:
  - A TRANSUDATE is protein-poor salt water squeezed through blood vessels by HSP ie it has sp gravity of ECF
  - An EXUDATE is an abnormal, protein-rich fluid that has leaked out of inflamed vessels
- Cardinal signs of inflammation:
  - Rubor
  - Dolor
  - Calor
  - Tumor
  - Functio laesa
Anatomy and Physiology

**Cardiac Output (CO):**
- \( CO = \frac{MAP}{TPR} \) (ie flow = pressure / resistance)
- \( CO = SV \times HR \)
- Normal adult at rest = 5L/min
- Can be measured with Doppler/echo

**Mean Arterial Pressure:**
- \( MAP = CO \times TPR \)
- \( MAP = DBP + \frac{1}{3}(PP) = \text{systolic-diastolic} \)

**Stroke volume:**
- \( SV = EDV - ESV \)
- Normal 60 – 80 ml

**Ejection fraction = ESV/EDV. Determined by:**
- **Preload** (=EDV): dependent on blood volume, venous tone, posture, intrathoracic pressure, peripheral muscle pump, and atrial contraction (20% of filling). Affects stroke volume through Starling’s Law:  
  \( \uparrow \text{myocardial fibre length (ie filling)} \rightarrow \uparrow SV \text{ until ventricle is over-stretched} \). Can be measured for the left ventricle using **pulmonary artery/capillary wedge pressure** (CAWP) and for the right using central venous pressure.
- **Force of Contraction** (Inotropy): shifts Starling Curve up and to the left. Increased by **sympathetic stimulation**, \( \uparrow \text{Ca}, \uparrow \text{thyroxine}, \uparrow \text{angiotensin}, \text{drugs, } \uparrow \text{temp}, \uparrow \text{HR} \). \( \downarrow \) by acidosis, hypoxaemia, \( \uparrow \text{K} \), drugs (general anaesthetics, Beta blockers).
- **Afterload = tension in the ventricular wall at the end of systole (essentially resistance).** Results from ventricular distension, elasticity of arterial walls and arterial network resistance. Measure with arterial catheter.

**Changes given certain shock states:**

<table>
<thead>
<tr>
<th>Cause</th>
<th>CVP</th>
<th>PAWP</th>
<th>BP</th>
<th>HR</th>
<th>Urine Output</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood Loss</td>
<td>↓</td>
<td>↓</td>
<td>↑</td>
<td>↓</td>
<td>↓</td>
</tr>
<tr>
<td>LVF</td>
<td>↑</td>
<td>↑</td>
<td>↑</td>
<td>↑</td>
<td>↓</td>
</tr>
<tr>
<td>RVF</td>
<td>↑</td>
<td>↓</td>
<td>↓</td>
<td>↑</td>
<td>↑</td>
</tr>
<tr>
<td>Fluid overload</td>
<td>↑</td>
<td>↑</td>
<td>↑</td>
<td>↑</td>
<td>↑</td>
</tr>
</tbody>
</table>

**Peripheral vascular resistance/TPR:**
- Resistance proportional to radius to the power of 4
- \( = (\text{Mean aortic pressure} - \text{right atrial pressure})/\text{cardiac output} \)

**Vascular Receptors**

<table>
<thead>
<tr>
<th>Receptor</th>
<th>Action</th>
<th>Where</th>
</tr>
</thead>
<tbody>
<tr>
<td>( \alpha ) receptors</td>
<td>Vasoconstrict</td>
<td>Peripheral, renal, coronary circulation</td>
</tr>
<tr>
<td>( \beta_1 ) receptors</td>
<td>Increase contractility, heart rate, and cardiac output</td>
<td>Heart</td>
</tr>
<tr>
<td>( \beta_2 ) receptors</td>
<td>Vasodilate</td>
<td>Peripheral and renal circulation</td>
</tr>
<tr>
<td>Dopamine (DA) receptors</td>
<td>Range of actions (see text)</td>
<td>Renal, mesenteric, coronary circulation</td>
</tr>
</tbody>
</table>

**Cardiac Anatomy**
- **Heart Valves:**
  - Mitral valve (left AV): anterior and posterior leaflets
Tricuspid valve: anterior, posterior and septal cusps
Aortic valve: left, right and posterior cusps
Pulmonary valve: left, right and anterior cusps

Blood supply:
- Left main stem (LMS) → LAD (anterior wall of LV and anterior 2/3 of septum) and Circumflex (lateral wall of left ventricle and most of the posterior wall of the LV).
- Right coronary artery → right atrium, right ventricle (except for left part of anterior wall), right posterior and inferior walls of LV and posterior 1/3rd of septum. Also supplies AV node, and SA node in 60%

Pericardial effusion: normal content of pericardial sac = 50 ml. Effusion can be serous, chylous or haemorrhagic. Sign of pericarditis but also accompanies MI

### Regional Blood Flow

<table>
<thead>
<tr>
<th>Organ (mass)</th>
<th>% Of Cardiac Output</th>
<th>O2 consumption (ml/100g/min)</th>
<th>Regulation of blood flow</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart – 300 g</td>
<td>5% - 250 ml/min</td>
<td>10</td>
<td>Metabolites (CO2, K, H, lactate, adenosine); α&amp;β adrenergics</td>
</tr>
<tr>
<td>Kidneys – 300 g</td>
<td>20-25% - 1000 ml/min</td>
<td>6</td>
<td>Myogenic autoregulation, angiotensin, α adrenergics, PGs, juxta-glomerular feedback</td>
</tr>
<tr>
<td>Brain – 1500 g</td>
<td>15% - 750 ml/min</td>
<td>3</td>
<td>H+; myogenic mechanisms</td>
</tr>
<tr>
<td>Liver – 2500 g</td>
<td>30% - 1500 ml/min</td>
<td>2</td>
<td>MAP, portal blood flow (local metabolites), adrenergics</td>
</tr>
<tr>
<td>Muscle – 35 kg</td>
<td>15% - 750 ml/min</td>
<td>0.2</td>
<td>α&amp;β adrenergics; local metabolites (K+)</td>
</tr>
<tr>
<td>Skin – 3500 g</td>
<td>10% - 500 ml/min</td>
<td>0.2</td>
<td>α adrenergics; kinins (thermoregulation); axonal reflex; sympathetic cholinergic</td>
</tr>
</tbody>
</table>

- Cerebral Perfusion:
  - Cerebral blood flow (CBF) = [MAP – ICP (or CVP, whichever is greatest)]/cerebral vascular resistance
  - Minimal desirable perfusion pressure is 60 mmHg. This is reduced by ↓arterial pressure, ↑venous pressure, constriction/spasm of cerebral vessels or ↑intra-cranial pressure (ICP)
  - Autoregulation keeps CBF at 50 ml/100g/min. Less than 15 → changes in electrical activity

- Coronary Perfusion:
  - Perfused during diastole
  - Coronary perfusion = (Mean diastolic pressure – VEDP)/Coronary Vascular Resistance
  - So treat poor perfusion with:
    - High diastolic pressure (eg systemic vasoconstrictor - α agonist)
    - Reducing end diastolic ventricular volume (prevent volume overload)
    - Decrease coronary vascular resistance (eg coronary vasodilator)
    - Slow heart rate → longer diastolic phase (eg beta blockers)
    - ↓Preload (nitrates and Ca channel blocker)
    - O2 therapy and maintain haemoglobin

- Renal Perfusion:
  - Normally autoregulated down to 80 mmHg systolic. When BP ↓, renal blood flow ↓↓→ renal failure and acute tubular necrosis
  - Treatment:
    - Colloid/saline → BP
    - Dopamine 2 – 5 mg/kg/min → renal vascular resistance

### History
- Major symptoms:
  - Chest pain/heaviness/discomfort
  - SOB (exertional, orthopnoea, PND)
  - Ankle swelling
  - Palpitations (due to ↑EDV, or do they mean arrhythmia — usually sudden onset – or tachycardia – usually gradual onset)
  - Syncope
  - Intermittent claudication (pain in legs on exertion due to ischaemia)
  - Fatigue
• Use SOCRATES for any symptom!
• Key differentials:
  ➢ Does it change with breathing? (⇒ respiratory cause OR pericarditis)
  ➢ Does it change with movement or localised pressure (⇒ musculoskeletal cause)
• Past history screen: rheumatic fever, STDs, recent dental work, thyroid disease, history of heart disease, drugs
• Social history: tobacco (ask ‘have you ever smoked’ not ‘do you smoke’ just in case they ‘gave up this morning’), alcohol, occupation
• Family history: early (<55yrs) ischaemic heart disease, valve disease, congenital disease, Marfan’s
• Risk factors for coronary artery disease: hyperlipidaemia, smoking, hypertension, family history, diabetes mellitus, obesity, ↓exercise, male, advanced age

Differentiating Chest Symptoms

Cough
• Due to non-specific irritation from pharynx to lungs
• Note duration:
  ➢ Short ⇒ Respiratory tract infection (especially if fever)
  ➢ Long ⇒ asthma, CHF
  ➢ Long + irritating and dry ⇒ ?reflux and aspiration
  ➢ Long + sputum ⇒ bronchiectasis
• Note time of day:
  ➢ Night ⇒ asthma, heart failure
  ➢ After food ⇒ reflux
• Infective respiratory causes:
  ➢ Yellow/green sputum ⇒ bronchitis, pneumonia
  ➢ Dark, fowl smelling sputum ⇒ anaerobic abscess
• Other potential causes:
  ➢ COPD
  ➢ Psychogenic
  ➢ ACE inhibitors
• Sputum:
  ➢ Yellow or green: lobar pneumonia or bronchiectasis
  ➢ Foul smelling and dark: anaerobic abscess
  ➢ Pink and frothy: not sputum but pulmonary oedema
• Haemoptysis (coughing blood) can be: bronchitis, cancer, bronchiectasis, cystic fibrosis, abscess, pneumonia, TB, foreign body, Goodpasture’s syndrome, rupture of a blood vessel after coughing, LV failure or mitral stenosis. Exclude nasal bleeding and haematemesis

Chest Pain
• Very common reason for ED attendance: but only a few have ST elevation MI
• Very localised pain (i.e. point to it with a finger) unlikely to be ischaemic
• History taking:
  ➢ SOCRATES
  ➢ Often a lot of denial
  ➢ Key question is time course (acute & on-going, episodic, persistence, etc)
  ➢ What causes it? If exertion, how far can you walk? Worse going up hill or into a cold wind? How long does it take to settle? What do you do to relieve it? Is the pain related to breathlessness
  ➢ Family history: not when did family die but when did it start – if patient young then looking for early onset in family
  ➢ Risk factors: smoking, hypertension, diabetes, hyperlipidaemia, obesity, homocystinaemia, age, sex (women better prior to menopause).
• Causes:
  ➢ Cardiac:
    o Myocardial ischaemia (narrowing of arteries, acute thrombosis, stenosis ⇒ ↓perfusion pressure, angina pectoralis) Gripping, crushing central chest pain. Pain may radiate. Provoked by exercise, relieved by rest. Should not be prolonged for hours unless MI
    o Myocardial infarction
Pericarditis (if infectious then severe inflammation, if secondary to MI then more mild. **ST elevation in all leads**). Pain changes with position/movement, respiration (ie pleuritic) & coughing. Sharp & severe central chest pain

- Aortic stenosis

**Vascular:**
- Aortic aneurysm: central chest pain radiating to the back. Can mimic MI pain
- **Pulmonary embolism** (PE): very sudden onset of SOB (if massive, may not be if submassive) – may ease gradually (as clot disperses). Several days later – pleuritic chest pain, may have high fever, haemoptysis
- **Dissection:** brachial pulse in each arm different, very sudden onset of very severe pain, can be described as tearing or be felt between the shoulder blades (c.f. MI has unstable angina phase first)
- Right ventricular strain

**Respiratory:**
- Pleuritis or **Pneumonia**
- Tracheobronchitis
- Pneumothorax
- Tumour
- Emphysema

**Gastrointestinal:**
- Oesophageal reflux
- Oesophageal spasm
- Mallory-Weiss tear
- **Peptic disease** (injury to oesophagus, ulcers, pancreatitis, biliary)
- Biliary disease
- Pancreatitis: do amylase to exclude

**Musculoskeletal** (localised – can point to it, will be palpable tenderness, pain on movement and maybe history of trauma)
- Cervical disk disease
- **Costochondritis** (Tietze’s syndrome)
- Arthritis of shoulder or spine
- Intercostal muscle cramps
- Subacromial bursitis

**Other:**
- Breast disorders
- Chest wall tumours
- Herpes Zoster prior to eruption
- Psychogenic causes

**Breathlessness**

- Normal around **16 breaths per minute**. 20-25 is high
- History questions should include:
  - Ask patient what they mean by breathless
  - How much exertion does it take to make them breathless (eg distance walked, stairs climbed)
  - Exclude obesity and lack of fitness
  - Chest pain: pleuritic is sharp and made worse by coughing and deep inspiration. Usually localised
  - **Occupational triggers**: e.g. asbestos, legionella, occupational allergens, hobbies, birds, animals
  - **Onset** (slow over years ⇒ ?fibrosis/COPD)
  - SOB on raising arms (eg reaching into a cupboard) → using accessory muscles to breath
  - Orthopnoea: breathless when lying down
  - Fever at night: consider TB, pneumonia, mesothelioma
  - **Sleep apnoea**: ask about snoring, daytime somnolence, chronic fatigue
  - Leg pain
  - Anxiety symptoms
  - Immune status (⇒ PCP or TB)
  - Medications for clues to condition and for possible side effects, eg PE from OC pill, cough from **ACE inhibitors**, cocaine
  - **SMOKING**
  - Check: cyanosis, can they complete a sentence, peak flow, consciousness level, pulse
  - Divide into:
Acute:
- PE
- Hyperventilation (tingling, strange pains – alkaloctic): anxiety
- HF/Acute LVF (no oedema c.f. CHF/MI
- Pneumothorax, lung collapse due to many causes
- Pneumonia
- Asthma

Chronic:
- COPD (asthma, bronchitis, emphysema)
- Interstitial lung disease
- HF
- Cancer
- Anaemia

- Asthma is fluctuating not progressive (i.e. ‘Do you have good days and bad days’)
- Obstructive: trouble breathing out
- Restrictive: trouble breathing in
- Think of systems: cardiac, respiratory, blood (anaemia, jaundice), hyperthyroidism, psychogenic, acidosis etc
- Paroxysmal Nocturnal Dyspnoea (PND):
  - Paroxysmal = sudden recurrence or intensification of symptoms
  - Heart failure: wake feeling like they’re suffocating, get out of bed and open window, may wheeze (cardiac asthma), may take ½ an hour to settle
  - Sleep apnoea: wakes feeling like they’re suffocating, panics, sits up, and settles very quickly. Get collaborative history
  - Asthma: wakes up coughing

Cyanosis
- Caused by > 50 g/L of reduced Hb (so if ↑Hb concentration and COPD then easy to be cyanosed → blue bloaters)
- < 66% saturation at normal HB (ie late sign)
- < 40% saturation in anaemia
- Causes:
  - Cardiac: shunts or congenital heart disease
  - Non-cardiac: e.g. hypoxia

Physical Exam
- Position patient at 45 degrees
- General appearance, including cachectic state, Marfan’s, Down’s or Turner’s Syndromes
- Dextrocardia = heart on right hand side (1 in 400??). Need right-sided heart leads

Examination of the Cardiovascular System – RP
- Wash your hands.
- Introduce yourself to the patient, and ask permission to examine them.
- Expose the patient, and position them at 45°.

**Inspection**

| Look around the bed | GTN spray (IHD), oxygen mask/nasal prongs, drips (eg IE), cigarettes |
| Look at the patient | Alert, comfortable at rest/in no distress, breathing RA, sweating, colour/cyanosis, breathless, syndromes (Marfan’s, Down’s), cachexia |
| Look at the hands | Capillary refill time, peripheral cyanosis, clubbing (look at toes also! congenital cyanotic heart disease, IE, atrial myxoma), splinter haemorrhages (IE), Osler’s nodes (IE), nicotine staining, pallor palmar creases (anaemia), Janeway lesions (IE), tendon xanthomata (hypercholesterolaemia). |
| Feel the radial pulse | Assess rate (over 15s) and rhythm (sinus, regularly irregular or irregularly irregular), assess for radioradial delay (coarctation of the aorta) |
| Check for collapsing pulse | Found in AR |
| Feel the brachial pulse | Assess character (slow rising [AS], bounding, pulsus alternans, pulsus bisferiens) and ask for BP (wide splitting, narrow splitting, pulsus paradoxus) in both arms + valsalva technique if indicated |
| Look at the neck | Assess the JVP + waveform (x vs y, outward bulges) + look for Kussmaul’s sign (lie pt down if |
cannot see); auscultate then feel the carotid pulse; mention that you’d like to assess abdominojugular reflux (can use this to determine JVP from carotid pulsation – push over liver and will see JVP rise)

| Look at the face | Look for signs of sweating, pain (IHD), Cushing’s (possible HTN), malar flush (mitral stenosis) |
| Look at the ears | Hairy ear canals, diagonal earlobe + pre-auricular creases |
| Look at the eyes | Xanthelasma, corneal arcus, anaemia, ophthalmoscopy (looking for Roth spots and hypertensive retinopathy) |
| Look in the mouth | High arch palate (Marfan’s), central cyanosis, telangiectasia, moist mucous membranes, dentition |
| Look at the chest | Chest wall deformity, scars (eg midline sternotomy for CABG, left axillary scar for mitral valve replacement), pacemaker boxes, pulsations |

Palpation

| Feel for the apex beat | Usually in the 5th intercostal space in the MCL (location, diameter, character, duration) |
| Feel for thrills and heaves | Along sternum with mid-palm; use 2 fingers in the pulmonary area; subxiphoid area for RV |

Auscultation

- Simultaneously listen and palpate a pulse (carotid – central pulse – to ↓ time delay) to time any murmur to the cardiac cycle
- Order: MTPA → carotid/axillae/back radiation → left lateral with bell (MS) → sitting forward (AR)

Listen at the left sternal edge in the 4th ICS (tricuspid area) + then the 3rd ICS (Erb’s point) WHILST TIMING CAROTID PULSE

Listen at the left sternal edge in the 2nd ICS (pulmonary area)

Listen at the right sternal edge in the 2nd ICS (aortic area)

RILE Listen in Inspiration to accentuate Right sided murmurs, listen in Expiration to accentuate Left sided murmurs

Listen over carotids

Listen over left axilla

Left decub position: listen over the apex beat (mitral area) with the bell, and then diaphragm

Ask patient to sit forward and listen at Erb’s point

Percuss and listen to the lung bases

Listen for heart sounds 1 and 2, systolic and diastolic murmurs.

Listen for heart sounds 1 and 2, systolic and diastolic murmurs.

Listen for heart sounds 1 and 2, systolic and diastolic murmurs.

Listen during insp + exp for splitting (timing, wide or narrow)

Listen for signs of pleural effusion (RVF) + pulmonary oedema (LVF)

Final manoeuvres

Palpate for sacral oedema

Palpate the liver

Palpate the spleen

Palpate for AAA

Palpate peripheral pulses

Examine for ankle oedema

Thank the patient and cover them up

I would complete my examination by....

- “I would like to look at the obs chart (temperature, sats), perform fundoscopy and dipstick the urine.”
- Link back to Examinations

Peripheral Exam

Hands

- Check for clubbing (congenital cyanotic heart disease), warmth (perfusion), capillary refill, anaemia (palmar creases), peripheral cyanosis, splinter haemorrhages

Pulse

- Radial pulse: assess rate, rhythm, and delay from radial to femoral pulse (radio-femoral delay)
- Brachial or Carotid pulse: Character and volume
- Rate:
  - Sinus Tachycardia:
Cardiology

- Sinus rhythm > 100 bpm. 120 bpm could be physiological, > 140 – 150 bpm more likely to be an aberrant rhythm
- Causes: fever, exercise, emotion, anxiety, pain, pregnancy, anaemia, hypoxia, thyrotoxicosis, HF, catecholamine excess, constrictive pericarditis, myocarditis, shock, MI, drugs, smoking, coffee, autonomic neuropathy (eg in DM), PE

- **Sinus bradycardia:**
  - = Sinus rhythm < 60 bpm
  - Causes: athlete, during sleep, drugs (β-blockers, digoxin, amiodarone), hypothyroidism, hypothermia, severe jaundice (due to bilirubin in conducting system), 3rd degree heart block, MI, paroxysmal bradycardia (eg vasovagal syncope)

- **Rhythm:**
  - Regular
  - Irregular:
    - Irregularly irregular: usually atrial fibrillation
    - Regularly irregular: Sinus arrhythmia (rate ↑ with respiration and ↓ with expiration) or 2nd degree heart block (Mobitz type 1)

- **Quality:**
  - If ‘thin’ then ↓ volume
  - Slow rising, low volume = aortic stenosis
  - Radial/femoral delay = aortic stricture e.g. coarctation,
  - Bounding pulse = a pronounced pulse – big difference between systolic and diastolic pressure (i.e. large pulse pressure). If bounding then always do a collapsing check
  - Collapsing pulse = bounding pulse + thumping pulse felt over wrist with palm of your hand when patient’s arm raised - aortic regurgitation (higher column of blood → ↑ regurgitation)

- Pulse deficit = difference between the radial pulse rate and heart rate. If rapid or irregular contraction then no time for ventricular filling ⇒ there may not be a corresponding radial pulse beat

**Measuring Blood Pressure**

- Ways of measuring blood pressure:
  - Mercury sphygmomanometer: listen for Korotkoff sounds
  - Oscillotonometer: detects arterial pulsations transmitted by the cuff. Tend to over-read very low pressures (oscillations diminish in amplitude)
  - Ultrasound sphygmomanometer: uses Doppler shift
  - Direct measurement: intra-arterial pressure with transducer

- How to measure with a sphygmomanometer:
  - Patient relaxed/seated for 5 minutes
  - Arm at heart level
  - Hold their hand under your right arm, straighten their arm and support under elbow. Use right thumb to feel brachial pulse as cuff is inflated (so you don’t over-inflate). Inflate to 30 mmHg above point where pulsation stops
  - Don’t push stethoscope diaphragm too hard (otherwise → bruit)
  - Start of Korotkoff sound 1 = systolic. Disappearance of Korotkoff sound 5 = diastolic
  - In obese people a normal width cuff will over-estimate blood pressure – must use a large one
  - Repeat several times, and on several occasions before deciding to treat

- Sources of operator error:
  - Wrong sized cuff
  - Poor positioning of the patient (including arm height)
  - Too rapid release of cuff pressure
  - Use of non-standard diastolic end points
  - Rounding to 5’s or 10’s

- Measurement problems:
  - Equipment problems and poor technique
  - Influences: caffeine, smoking, physical activity, white coat
  - Random variation throughout the day
  - Pseudohypertension (*failure of cuff to compress arterial wall* in oldies with stiff arteries)

- Watch for:
  - **Pulsus paradoxus**: Normally inspiration → ↓ systolic and diastolic blood pressure (more negative intrathoracic pressure → pooling in pulmonary vessels → ↓ filling). Pulsus paradoxus = this decrease is
Cardiology

exaggerated (ie fall of > 10 mmHg). Can occur in constrictive pericarditis, pericardial effusion, tamponade, tension pneumothorax or severe asthma

- **Postural hypotension:**
  - Fall of more than 20 mmHg systolic or 10 mmHg diastolic on standing (after 2 or 3 min)
  - Causes: hypovolaemia, drugs (vasodilators, antidepressants, diuretics), Addison’s disease, hypopituitarism, autonomic neuropathy
  - Risk factors: older age
  - Symptoms: presyncope (dizzy/woozy)
  - Pathophysiology: ↓ intravascular volume +/- inadequate CV compensation
  - If positive test → **Valsalva test +/- Tilt table test**
  - Pulse on standing. For vasovagal syncope pulse ↓
  - Management: review meds; get up slowly, pressure stockings, fludrocortisone

- See also Hypertension, page 47

**Face**

- **Eyes:**
  - Jaundice from liver congestion secondary to heart failure
  - Anaemia
  - Roth’s spots on retina: areas of retinal infarction and haemorrhage caused by septic emboli in bacterial endocarditis
- **Xanthelasma:** intracutaneous yellow cholesterol deposits around the eye. Normal variant or ?hyperlipidaemia
- **Mitral facies:** rose cheeks with dilated blue veins and cyanosed tongue. Due to pulmonary hypertension and ↓ cardiac output (eg as in severe mitral stenosis)
- **Mouth:** diseased teeth (cause of infective endocarditis), tongue for central cyanosis, and mucosa for petechiae

**Carotid Arteries**

- Never palpate both at once → occlude blood supply to brain
- Information about aorta and left ventricular function
- Pulse wave forms:

<table>
<thead>
<tr>
<th>Type</th>
<th>Causes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anacrotic: small volume, slow uptake</td>
<td>Aortic stenosis</td>
</tr>
<tr>
<td>Bisferiens: anacrotic and collapsing</td>
<td>Aortic stenosis and regurgitation</td>
</tr>
<tr>
<td>Collapsing</td>
<td>Aortic regurgitation, hyperdynamic circulation (eg exercise, fever), patent ductus arteriosus, atherosclerotic aorta</td>
</tr>
<tr>
<td>Small volume</td>
<td>Aortic stenosis, pericardial effusion</td>
</tr>
<tr>
<td>Alternans: alternating strong and weak beats</td>
<td>Left ventricular failure</td>
</tr>
<tr>
<td>Jerky</td>
<td>Hypertrophic cardiomyopathy</td>
</tr>
</tbody>
</table>

**Jugular Venous Pressure (JVP)**

- Information about right atrial and right ventricular function
- ↑ in RVF, volume overload, impaired RV filling, SVC syndrome
- Positioning:
  - Patient should be at 45 degrees
  - Internal jugular is **medial** to the superior end of sterno-mastoid then runs behind it as it descends
  - External is **lateral**, is easier to see, but is more tortuous and therefore less reliable
  - Sternal angle is the zero point – pulsations are visible above this point at 45 degrees (centre of the right atrium is 5 cm lower). Normal is pulsations just above the clavicle (<3 cm)
- Differentiating from carotid pulse. The JVP is:
  - Visible but **not palpable**
  - **Double impulse** with each cardiac cycle
  - Usually decreases with inspiration
  - Is **obliterated then filled from above** following light pressure at the base of the neck
  - Changes with **posture**
  - ↑ with abdominal pressure

Cardiology
Pressure waves in atria:

- **a wave**: atrial contraction at end of diastole $\rightarrow$ ↑ atrial pressure. Coincides with first heart sound and precedes carotid pulse. Closely followed by ...
- **c point**: bulging of AV valves into atria during systole $\rightarrow$ ↑ atrial pressure. Not usually visible
- **x descent**: ventricular contraction/atrial relaxation between S1 and S2
- **v wave**: end of atrial filling during systole – venous inflow into atria with AV valve closed $\rightarrow$ ↑ atrial pressure
- **y descent**: rapid ventricular filling following opening of the AV valve

**Height** (the easy bit):
- If $> 3$ cm above the zero point then right heart filling pressure is raised
- Rises with 10 seconds pressure on the liver (hepatojugular reflex). A rise is normal. If remains raised then ventricular failure
- Causes of ↑ height: RVF, tricuspid stenosis or regurgitation, pericardial effusion or constrictive pericarditis, SVC obstruction (no waves), fluid overload, hyperdynamic circulation
- Should normally fall on inspiration. If it rises then ?constrictive pericarditis. Investigate with echo

**Character** (the hard part):
- Causes of a dominant a wave: tricuspid stenosis (also causes a slow descent), pulmonary stenosis, pulmonary hypertension
- Causes of cannon a waves (↑↑ wave - right atrium contracts against closed tricuspid valve): intermittently in complete heart block (two chambers beating independently), retrograde conduction
- Cause of dominant v wave: tricuspid regurgitation (should never miss this, watch for movement of ear lobe)
- **x descent**: absent in AF, exaggerated in cardiac tamponade, constrictive pericarditis
- **y descent**: Sharp: severe tricuspid regurgitation, constrictive pericarditis, slow in tricuspid stenosis, right atrial myxoma

**Praecordium**

*Inspection of the Praecordium*

- **Scars**:
  - Median sternotomy: any surgery requiring cardiopulmonary bypass
  - Left lateral Thoracotomy: ?closed mitral valvotomy
- **Note structural abnormalities**: Pectus excavatum (sunken chest = funnel chest) or kyphoscoliosis may distort position of heart and vessels (ie shifting the apex beat). If severe then ↓ pulmonary function
- **Note presence of pacemaker**
- **Pulsations**: apex beat and others (eg over pulmonary artery in severe pulmonary hypertension)

*Palpation of the Praecordium*

- **Apex beat**:
  - Count down intercostal spaces (the 2nd space is the first one palpable, opposite the sternal angle). Find most lateral and inferior point at which pulsations are felt
  - Normal = 5th intercostal space, mid-clavicular line
  - If not palpable then thick chest wall, emphysema, pericardial effusion, shock (or rarely dextrocardia – inversion of heart and great vessels onto right side)
  - Pressure overloaded = systolic overloaded: Forceful, sustained, not displaced. Due to hypertension, aortic stenosis
  - Volume loaded = diastolic overloaded = hyperkinetic: displaced, unsustained, uncoordinated, large area.
    - Due to aortic or mitral regurgitation, dilation, LV dysfunction (eg anterior MI)
  - Double or triple impulse = hypertrophic cardiomyopathy
- **Parasternal impulse**: heel of hand rested just to the left of the sternum. Feel movement with systole in right ventricular enlargement or severe left atrial enlargement (right ventricle pushed anteriorly)
- Tap of pulmonary valve closure (P2) over pulmonary areas in pulmonary hypertension (+ ↑JVP)
Thrills = palpable murmurs. Apical thrills felt best with patient rolled onto left side. Pulmonary or Aortic thrills best felt with patient sitting up, leaning forward and on expiration. A thrill coinciding with the apex beat is a systolic thrill, otherwise a diastolic thrill.

**Heart Sounds**

- Stethoscope head:
  - **Bell**: good for low pitched sounds, eg diastolic murmur (*mitral stenosis*) or 3rd heart sound. Don't press too hard otherwise skin becomes a diaphragm.
  - **Diaphragm**: good for high pitched sounds, eg systolic murmur or 4th heart sound.

- Using stethoscope, auscultate:
  - Mitral area (5th intercostal space, left mid-clavicular line) with bell and diaphragm.
  - Tricuspid area (4th intercostal space, left sternal edge) with diaphragm.
  - Pulmonary area (second intercostal space, left sternal edge) with diaphragm.
  - Aortic area (second intercostal space, right sternal edge) with diaphragm.

- Heart sounds:
  - **First heart sound**: closure of mitral and tricuspid valves at beginning of systole. Mitral closes slightly before tricuspid but you won’t hear the difference.
  - **Second heart sounds**: closure of aortic and pulmonary valves. Lower pitch. End of systole. Aortic closes first (higher back pressure on valve) → splitting of heart sounds. But pulmonary closure is not heard over all the praecordium, so splitting best heard over pulmonary area. Inspiration → ↑venous return → later closure of pulmonary valve → enhanced splitting.
  - Use carotid pulsation to orientate to timing. This occurs during systole, between S1 and S2.

**Abnormal Heart Sounds**

| S1  | Loud | Mitral or tricuspid stenosis → limited ventricular filling → no easing of low at end of filling → valves snap shut. Also ↓diastolic filling (eg in tachycardia) |
|     | Soft | Prolonged filling (eg 1st degree heart block) or failure of leaflets to close properly (eg mitral regurgitation), delayed LV systolic (eg LBBB) |
|     | Splitting | Most often due to right bundle branch block |

| S2  | Loud | Aortic calcification or regurgitation → leaflets don’t close well |
|     | Soft | If abnormal ⇒ delay in right ventricular emptying, eg RBBB, pulmonary stenosis, pulmonary hypertension, ventricular septal defect (⇒ right ventricle filling). Also mitral regurgitation ⇒ earlier aortic valve closure |
|     | Increased splitting | Doesn’t change with respiration ⇒ atrial septal defect and both atria have equal volumes |
|     | Fixed splitting | Reversed splitting |

<table>
<thead>
<tr>
<th>Extra Heart Sounds</th>
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</thead>
<tbody>
<tr>
<td><strong>S3</strong></td>
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</table>

- Left Ventricular S3: Louder at apex than at sternal edge, and louder on expiration
- Right Ventricular S3: Louder at sternal edge than apex, and louder with inspiration

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*Cardiology* 31
**Late diastolic sound** (just before S1), higher pitched than S3. Can sound like a gallop rhythm

*Left ventricular S4*

Often during angina or MI

↓ *Left ventricle compliance: aortic stenosis*, acute mitral regurgitation, systemic hypertension, ischaemic heart disease, age

*Right ventricular S4*

↓ *Ventricular compliance: pulmonary stenosis or pulmonary hypertension*

*Summation Gallop*

If the heart rate > 120 bpm, S3 and S4 may be superimposed, and therefore more audible

Only implies ventricular stress if S3 or S3 persists when heart rate slows

---

**Miscellaneous Sounds**

- **Opening snap**: high-pitched sound after S2 in mitral stenosis, due to sudden opening of the mitral valve. Don’t confuse with widely split S2 (snap is higher pitched)
- **Systolic ejection click**: early systolic high-pitched sound over aortic or pulmonary areas. Is caused by pulmonary or aortic congenital stenosis and is followed by a systolic ejection murmur
- **Non-ejection systolic click**: high pitched systolic sound over the mitral area. Common. May be followed by systolic murmur. Due to mitral prolapse and atrial septal defects
- **Diastolic pericardial knock**: may occur if there is a sudden cessation of ventricular filling in constrictive pericardial disease

**Heart Murmurs**

**Timing of Murmurs**

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<tr>
<th>Murmur</th>
<th>Nature</th>
<th>Cause</th>
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<tr>
<td>Pansystolic</td>
<td>Pan-systolic: extend from S1 to S2, loudness and pitch vary during systole</td>
<td>Ventricular leakage:</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1. Mitral regurgitation</td>
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<tr>
<td></td>
<td></td>
<td>2. Tricuspid regurgitation</td>
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<td></td>
<td></td>
<td>3. Ventricular septal defect (can be mid-sys if small)</td>
</tr>
<tr>
<td>Ejection (mid) systolic</td>
<td>Intensity greatest in early to mid-systole then wanes</td>
<td>Turbulent flow through an orifice:</td>
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<tr>
<td></td>
<td></td>
<td>1. Aortic stenosis</td>
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<td>2. Pulmonary stenosis</td>
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<td></td>
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<td>3. HOCM</td>
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<td></td>
<td></td>
<td>4. Atrial septal defect</td>
</tr>
<tr>
<td>Late systolic</td>
<td>Noticeable gap between S1 and murmur, and continues to S2</td>
<td>1. Mitral valve prolapse</td>
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<tr>
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<td></td>
<td>2. Papillary muscle dysfunction</td>
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<tr>
<td>Early diastolic</td>
<td>Begins with S2 and fades (decrescendo). High pitched.</td>
<td>Regurgitation through a leaky valve:</td>
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<tr>
<td></td>
<td></td>
<td>1. Aortic regurgitation</td>
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<td></td>
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<td>2. Pulmonary regurgitation</td>
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<tr>
<td>Mid diastolic</td>
<td>Begin after S2, may extend to S1. Lower pitched.</td>
<td>Impaired flow during filling:</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1. Mitral stenosis</td>
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<tr>
<td></td>
<td></td>
<td>2. Tricuspid stenosis</td>
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<tr>
<td>Pre systolic</td>
<td>Just before S1</td>
<td>Atrial systole increases blood flow across the valve:</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1. Mitral stenosis</td>
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<tr>
<td></td>
<td></td>
<td>2. Tricuspid stenosis</td>
</tr>
<tr>
<td>Continuous murmurs</td>
<td>Through systole and diastole</td>
<td>Communication where there’s a permanent pressure gradient:</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1. Patent ductus arteriosus</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2. Numerous malformations or fistulas</td>
</tr>
<tr>
<td>Combined systolic and diastolic murmurs</td>
<td></td>
<td>Aortic stenosis and aortic regurgitation</td>
</tr>
<tr>
<td>Pericardial friction rub</td>
<td><strong>Superficial scratching sound at any time in the cycle. Intermittent. May vary with respiration and posture</strong></td>
<td>Pericarditis</td>
</tr>
</tbody>
</table>
Listening for Murmurs

- **Areas of greatest intensity:**
  - Mitral regurgitation is loudest over the apex and radiates into the axilla - but may be heard over the whole praecordium
  - Aortic murmurs radiate into the carotid arteries
- **Benign murmur of pregnancy – ejection systolic.** Pansystolic or diastolic murmurs are abnormal
- In general, systolic murmurs are easier to hear than diastolic murmurs
- **Loudness:** doesn’t always correlate with severity but a change is significant (eg after an MI).
  - For systolic:
    - Grade 1/6: very soft. Consultants only!
    - Grade 2/6: soft, detected immediately by an experienced operator
    - Grade 3/6: moderate but no thrill
    - Grade 4/6: loud, thrill just palpable
    - Grade 6/6: very loud, thrill easily palpable
  - For diastolic: Usually graded 1 to 4
- **Pitch:** low pitched → turbulent flow under pressure (eg mitral stenosis), high pitched ⇒ high velocity (eg mitral regurgitation)
- Clues can also be obtained from peripheral signs (eg tricuspid regurgitation → pulsatile liver, slow rising pulse → aortic stenosis)
- **Dynamic manoeuvre testing:**
  - **Respiration:** Right sided murmurs louder on Inspiration (due to ↑venous return). Left sided louder on Expiration (brings heart closer to the chest wall – especially for aortic regurgitation) – **RITE**
  - **Valsalva manoeuvre** (↓preload):
    - Hold nose, close mouth, breathe out hard to pop ears and hold
    - Listen over left sternal edge for changes in the systolic murmur of hypertrophic cardiomyopathy (↑intensity)
    - Listen over the apex for mitral valve prolapse.
    - Other murmurs will be quieter due to ↓left and right filling
  - **Squatting or leg raise** (↑preload): ↑venous return and ↑arterial resistance → most murmurs are louder
  - **Handgrip** (↑afterload): aortic stenosis quieter

| AS | 1. Mid-systolic ejection murmur – radiates to carotids  
2. **Pulsus tardus et parvus** (slow rising + low amplitude)  
3. ↓PP  
4. Prominent a waves on JVP (bernheim phenomenon – dilation of LV compressing RV w impaired filling) |
| MR | 1. Normal pulse or sharp upstroke due to rapid LV decompression, AF also common  
2. **AB is hyperdynamic + displaced down + laterally**  
3. Pansystolic (holosystolic) murmur – radiates to axilla  
4. Increased peripheral resistance (eg isometric handgrip) will increase murmur intensity |
| TR | 1. Pansystolic (holosystolic) murmur, high pitched , best heard over L lower sternal edge, louder on insp  
2. JVP = x descent obscured + large v wave seen (Lancisi’s sign)  
3. Signs of RH strain: likely a palpable P2 in L 2nd ICS + **RV impulse** (heave) + ↑JVP  
4. Positive abdominojugular reflux test w increased murmur intensity (Vitum sign)  
5. Pulsatile liver  
6. **Distended neck veins, peripheral oedema, ascites** |
| AR | 1. S1 soft + S2 loud – **decrecendo early diastolic murmur** best heard at Erb’s point, sitting forward in exp  
2. Increase in peripheral resistance (handgrip, squatting) increases murmur intensity  
3. Brisk upstroke + brisk downstroke of pulse – water hammer/Corrigan pulse with widened PP, may also see pulsus bisferiens  
4. AB displaced downwards + laterally + is hyperkinetic due to LV dilation |
| MS | 1. **Mid-late diastolic murmur** separated from S2, heard best at apex w bell lightly applied – low pitched, maybe ejection click  
2. Increased by dynamic manoeuvres  
3. Pulse + AB often low amplitude  
4. Prominent a wave in JVP in pts w PHTN |

**Lungs, Abdomen and Legs**
- Percuss and auscultate lung bases on the back for pulmonary oedema, then check for sacral oedema
- Abdomen:
  - Tender or enlarged liver $\Rightarrow$ ?heart failure
  - Pulsatile liver $\Rightarrow$ ?tricuspid regurgitation
  - Ascites $\Rightarrow$ ?heart failure
  - Splenomegaly $\Rightarrow$ ?infective endocarditis

- Legs:
  - Femoral artery pulses: palpate and auscultate for bruits
  - Popliteal pulse
  - Feel leg pulses both sides at once, standing at end of bed (gives you two chances to find them!):
    - Posterior tibial pulse: posterior to medial malleolus
    - Dorsalis pedis pulse: just lateral to the extensor hallucis longus tendon (seen when big toe dorsiflexed)
  - Palpate the distal shaft of the tibia for oedema – press for 15 seconds. If present, note upper level
  - Cyanosis and clubbing of the toes, pallor, cool, ↓capillary refill of toes

ECG Interpretation*

- 5 mm (one large square) = 0.2 secs $\Rightarrow$ 300 squares per minute

Leads

- Depolarisation:
  - R > S: depolarisation spreading toward lead
  - R < S: depolarisation spreading away from lead
  - R = S: depolarisation at right angles to lead

Axis

- Beware of leads on wrong arms!
- To check axis, look at I and II
- Normal is between aVL (-30) and aVF (90)
- Alternative: cardiac axis is at right angles to lead in which R & S are the same size (isometric)
- Right deviation: ?hypertrophy of RV or tall and thin
- Left deviation: ?hypertrophy of LV
- Extreme axis deviation $\rightarrow$ QRS are negative in both I + II $\rightarrow$ either leads round the wrong way (V1-V6 would be normal) or dextrocardia (V1-V6 all negative)
Nomenclature

QRS Complex in V Leads
- Should be < 0.12s
- Shape is determined by:
  - Septum is depolarised first, and the wave spreads from L to R in the septum:
    - V1 initially up as depolarisation in the septum (L → R) is towards the lead
    - V6 initially down as depolarisation in the septum is away from lead
  - Muscle mass: LV dominates so V1 is down and V6 is up.

Hypertrophy
- LVH: SV1 + RV5/6 = > 35mm
- RVH: RV1 + SV5/6 = > 11mm

Bundle Branch Block
- Delay in depolarisation of part of the muscle → widened QRS. If QRS > 3 small squares (0.12 secs) ⇒ slowed conduction ⇒ bundle block or ventricular ectopic beat
- RBBB:
  - V1/V2 are over the RV therefore will see split R’R” pattern in these leads
  - Can be benign. ?ASD
  - Left depolarises first, then right. May just be delay to the terminal end of QRS (especially in V5)
  - Have lost the RBB → rapid left-sided conduction with delayed muscle→muscle conduction from left to right, therefore will see narrow R wave (left conduction) + wide S wave (right muscle→muscle conduction)
  - V1-V3 STs are often depressed but can look at other leads for ST changes
  - Look at leads:
    - V1: small R wave then secondary R wave that is bigger and wider than the first
    - I: narrow R wave followed by larger/wider S wave
- LBBB:
  - V5/V6 are over the LV therefore will see wide notched R waves in these leads
  - Always pathological
  - RV depolarises, then wave spreads to LV
  - T wave inversion in anterior and lateral leads is common (I, aVL, V4 – V6)
  - Left bundle divides into the anterior and posterior fascicles. Failure of the anterior fascicle → left axis deviation (depolarisation is through the posterior fascicle)
  - Look at leads:
    - I: wide, upright QRS with downsloping, inverted T
    - V1-V2: deep QRS with overshoot ST segment + tall peaked T wave
  - If LBBB: ?aortic stenosis, ischaemic disease
  - LBBB prevents any further interpretation of the ECG i.e. cannot interpret ST segments
- To determine side of block: W in V1 and M in V6 is Left (WiLLiaM). M in V1 and W in V6 is Right (MaRRoW) – not always accurate
Reporting an ECG

- **ID**
- **Speed**
- **Check rate:** bradycardia or tachycardia? 300 → 150 → 100 → 75 → 60 → 50 → 43
- **Check rhythm:**
  - See also Arrhythmias, page 56
  - Regular or irregular
  - Sinus rhythm = one P wave per QRS complex = depolarisation begins in SA node
  - Sinus arrhythmia:
    - Bradycardia: athletes, fainting attacks, hypothermia, myxoedema, drugs
    - Tachycardia: exercise, fear, pain, shock, thyrotoxicosis
  - **Supraventricular arrhythmia:**
    - Sinus, atrial or junctional/nodal arrhythmia
    - **QRS is normal width** (unless also bundle block)
    - **Escape/ectopic beats** are atrial, nodal or ventricular pacemakers that fire if the SA node fails, as they have a slower intrinsic rate. Escape beats come late
      1. **Atrial escape:** abnormal P wave after SA node fails. Normal QRS
      2. **Junctional/nodal escape:** no P wave (either none or buried in normal QRS)
      3. **Ventricular escape** – not supraventricular: usually in complete heart block. Fast P waves. Slow wide QRS. Shape of QRS may vary
    - Extrasystole/ectopic beats come early – some part of the heart has depolarised prematurely
  - Distinguish VT and atrial tachycardia with BBB:
    - Both have wide QRS
    - But **atrial tachycardia has P waves** (check all leads). Compare QRS with normal QRS – if similar then bundle block
  - **Wolff-Parkinson-White Syndrome** (a type of ventricular pre-excitation): **accessory conducting bundle** (Bundle of Kent), usually to LV → short PR and QRS has abnormal slurred upstroke (delta wave), can → VF
  - **Treatments:**
    1. **Atrial Fibrillation:** digoxin/electrical cardioversion
    2. **Junctional Tachycardia:** carotid sinus pressure then adenosine
    3. **Atrial Flutter:** carotid sinus pressure, adenosine, flecainide, DC conversation
    4. **SVT:** vagal manoeuvres, adenosine
    5. **Ventricular Tachycardia:** amiodarone, DC conversion

- **Check Cardiac Axis**
- **Check P wave:** shape:
  - Normal is < 2 * 2 small squares
  - Right atrial hypertrophy (eg tricuspid stenosis) → peaked P (P pulmonale)
  - Left atrial hypertrophy (eg mitral stenosis) → broad, twin-peaked P, especially in II, III, aVF (P mitrale)
  - Potassium: ↓K → ↑P, ↑K → ↓P
- **Check conduction intervals** - PR interval:
  - From beginning of P wave to beginning of QRS = time for AP to spread from SA node to ventricular muscle.
  - Normal is 0.12 – 0.2 sec. (3 – 5 small squares)
- **Description of QRS Complex.** Width of QRS complex = time for AP to spread through ventricles:
  - Normal is <= 0.12 sec. (3 small squares)
- **Right Ventricular Hypertrophy:**
  - V1: R becomes higher (> 25 mm)
  - V6: S becomes deeper
  - Also look for:
    1. Right axis deviation
    2. Peaked P (right atrial hypertrophy)
    3. Inverted T in V1 – V3
  - This picture is similar to a PE (which also has a Q wave in III)

- **Left Ventricular Hypertrophy:**
  - V1: deep S wave
  - V6: Tall R wave (> 25 mm)
  - Inverted T wave in II, VL, V5 and V6
  - Left axis shift

- **Q waves:**
  - Negative wave at start of QRS
  - If > one small square wide and > 2 mm deep ⇒ patch of non-active muscle in the wall and the lead is ‘looking inside’ the heart, not at the wall ⇒ old MI. Usually permanent. Need to be seen in two leads of a contiguous lead grouping
  - Anterior/septal infarct ⇒ Q wave in V2, V3 and V4 (Left anterior descending artery)
  - Anterior-lateral infarct ⇒ Q waves in I, II, VL. V3 – V6 (Left circumflex)
  - Lateral infarct ⇒ Q wave in I, V5, V6
  - Inferior infarct ⇒ Q wave in II, III and VF (⇒ right coronary artery)
  - Inferior-lateral ⇒ Q wave in II, III, aVF, V5, V6

- **Bundle Branch Block**

- **Description of ST segments:**
  - Saddle shaped STE can be a normal variant (see right)
  - If raised ⇒ acute injury – recent MI or pericarditis. Anterior ⇒ V5, V6.
    - Inferior ⇒ II, III, aVF
  - Depression ⇒ ischaemia not infarction

- **T wave:**
  - Normally inverted in aVR and V1 as on the right side of the chest (also V1 → V3 in young people + dark skinned people)
  - Normal variant → seen in III
  - If not full thickness infarct ⇒ T wave inversion but no Q wave (no ‘window’ into heart) ⇒ non-Q wave infarction
  - If abnormal QRS ⇒ abnormal T of no significance (repolarisation also skewed)
  - Digoxin ⇒ T wave inversion and sloping depression of the ST segment
  - Electrolyte imbalances:
    - ↓K ⇒ T wave flattening
    - ↑K ⇒ tall, wide peaked T waves

- **QT interval**
  - Prolonged if QT segment is longer than ½ R-R segment
  - ↓Ca ⇒ ↑QT interval
  - ↑Ca ⇒ ↓QT interval

- **Progression following MI:**
  - Elevation of ST
  - Q waves appear
  - T becomes inverted – may be permanent
Locating an Infarct

- **Anterior** = V2 → V4 (LAD – Dx)
- **Septal** = V1, V2 (LAD – septal branch)
- **Inferior** = II, III, aVF (RCA – PDA)
- **Lateral** = aVL, I, V5, V6 (Cx)
- **Posterior** = ST depression (ie reciprocal changes) in V1 → V4 (Cx/PDA)

**ECG Abnormalities Due to Electrolyte Disturbances**

<table>
<thead>
<tr>
<th>Abnormality</th>
<th>Common Cause</th>
<th>ECG</th>
<th>Emergency Treatment</th>
</tr>
</thead>
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<tr>
<td>↑ Potassium</td>
<td>Renal failure</td>
<td>Peaked T</td>
<td>Calcium chloride</td>
</tr>
<tr>
<td></td>
<td>Addison’s disease</td>
<td>Prolonged PR</td>
<td>Bicarbonate</td>
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<td></td>
<td></td>
<td>Small P</td>
<td>Insulin/Glucose</td>
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<td></td>
<td></td>
<td>Wide QRS</td>
<td>Beta agonists</td>
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<td></td>
<td></td>
<td>VT, VF, asystole</td>
<td>Dialysis</td>
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<tr>
<td>↓ Potassium</td>
<td>Diuretics</td>
<td>Wide, flat or inverted T</td>
<td>Potassium</td>
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<td></td>
<td>Hyperaldosteronism</td>
<td>Depressed ST segment</td>
<td>Magnesium</td>
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<td>Vomiting</td>
<td>Small QRS</td>
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<td>Gastric aspiration</td>
<td>Prolonged PR</td>
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<td>Prominent U wave</td>
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<td>Large P wave</td>
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<tr>
<td>↑ Magnesium</td>
<td>Renal Failure</td>
<td>Bradycardia</td>
<td>Calcium Chloride</td>
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<td>AV block</td>
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<td></td>
<td></td>
<td>Asystole</td>
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<tr>
<td>↓ Magnesium</td>
<td>Alcoholism</td>
<td>Long QT</td>
<td>Magnesium</td>
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<td>Starvation</td>
<td>Short QT</td>
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<td>Urinary Loss</td>
<td>Broad T</td>
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<td></td>
<td>Diuretics</td>
<td>VF, VT, asystole</td>
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<td>GI loss</td>
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<td></td>
<td>Malabsorption</td>
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<tr>
<td>↓ Calcium</td>
<td>Hypoparathyroidism</td>
<td>Long QT</td>
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<td>Acute pancreatitis</td>
<td>Elevated ST</td>
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<td>Renal failure</td>
<td>Peaked or inverted T</td>
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<td>AV block</td>
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<tr>
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<td></td>
<td>Tachyarrhythmias</td>
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</tbody>
</table>

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Chest X-ray

- First check:
  - Is it the right patient
  - Is it the right date
  - Is it the right way round (ie L and R)
- Then ask what is their age (and therefore likely pathologies)
- How was the film taken:
  - Normal is PA erect, inspiratory:
    - PA as all Xray sensitive tissues are on the front (breasts, eyes, gonads, thyroid) – less exposure
    - Scapula off chest (in an AP then scapula projected onto chest)
  - Differences in Supine film:
    - Air collects on front of chest not top (important for pneumothorax)
    - Fluid distributes over back of pleura not in costophrenic angles
    - Normally more blood flow in lower zones, but in supine equal vascular markings at top
    - Better venous return in supine → distended great vessels
    - To tell if it’s supine where is gastric bubble: fundus = erect, body = supine
- Is the film good enough:
  - Is it rotated: medial ends of clavicle equidistant from spinous process
  - Is it a good exposure: can you see lung veins in periphery – if you can see the spine clearly then over exposed
  - Good inspiration: 5 – 7 anterior ribs on the right (hemidiaphragm is higher – must take a bigger breath to get it down) or 9 – 11 posterior ribs
- Key questions:
  - Is there any area that is lighter (↑opacity)
  - Is there any area that is darker (↑lucency)
  - Is there any abnormality of normally seen anatomy
- Normally seen anatomy/silhouettes:
  - Right Upper quadrant (above the right bronchi):
    - SVC: free edge abutting lung
    - Right paratracheal strip (lung abutting right side of trachea). If strip wider than 5 mm then lymph node enlargement
    - Arch of azygous in tracheal bronchial angle, just above carina. If enlarged think RH failure or IVC obstruction
  - Left Upper Quadrant (above the left bronchi):
    - Arch of aorta (aortic knuckle) and free edge of descending aorta behind heart
    - Pulmonary trunk
    - Between them is the aortic pulmonary window: should be concave, if convex then lymph node enlargement
  - Right lower quadrant (below right bronchi): Right atrium forming the border of the heart
  - Left lower quadrant (below left bronchi):
    - Border of heart = left ventricle + left auricle of atrium (NB its below the bronchi – a bulge above the bronchi must be something else)
    - Left hemidiaphragm (lower than the right)
  - Lateral view:
    - Spine should get blacker as you go down
    - Retrosternal and retrocardiac areas should be the same density
    - Left hemi-diaphragm is the one that the heart sits on
- Heart size:
Enlargement: greatest transverse diameter = largest horizontal distance from midline to right border + largest horizontal distance from midline to left border. If this is > 50% of greatest internal diameter then the heart is enlarged.

Signs of left atrial enlargement:
- 2nd heart border parallel and medial to RH border (atrium bulging around behind the RA)
- ↑Density medial to this 2nd border
- A prominent left atrial appendage
- Elevation of the left main bronchus

Right atrial enlargement: bulges into right lung and elevation of right main bronchus

Right ventricle enlargement: Apex tilts upwards. On the lateral film, ↑area of contact between the heart and the sternum

Left ventricle enlargement: Elongates along its long axis →apex shifts down and out. Posterior bulge on the lateral film

Causes of global heart enlargement:
- Sack like dilatation: due to pericardial effusion, cardiomyopathy or multi-valvular disease
- Multi-valvular disease
- Hypertrophic cardiomyopathy
- Pericardial effusion

Progression of pulmonary oedema:
- ↑Prominence of upper zone vessels due to redistribution of blood to upper zones
- Leakage →interstitial changes: peribronchial cuffing, Kerley B lines, effusion
- Flooding of the airspaces →'Bats wing' appearance
- With treatment, resolves in the reverse order

Ribs:
- Posterior of rib connects with midline, anterior doesn’t as it turns to cartilage which isn’t calcified (but maybe in old person)
- If 1st and 2nd ribs fractured, this takes massive force, consider concurrent damage to great vessels
- If sternum fractured, consider cardiac contusion – do cardiac enzymes
- If 11th and 12th ribs fractured, consider damage to kidney’s, liver, spleen
- If multiple fractures: flaccid chest →Paradoxical Breathing (segment of chest moves in on inspiration)

Lobes:
- Upper: apical, posterior, anterior
- Medial: superior, inferior
- Lower lobe: Anterior, posterior, lateral, medial, apical

Pathology to look out for:
- Pulmonary contusion: Opacity in parenchyma = bleeding. Should clear in 3 – 6 days (cf consolidation which may take 6 weeks to clear). May resolve leaving clots filling cavities created from shearing forces
- Pneumothorax: must see visceral pleural edge AND no vascular markings lateral to this edge. Edge alone might be other things
- ARDS: soft and fluffy over all the lung parenchyma
- Aspiration: won’t be symmetrical. If it’s global is it the ‘bats wing’ appearance of pulmonary oedema?
- Is it effusion or pneumonia: Pleura is 2 cells thick. If pleural cavity fills up lose sharp edge. If unsure, take another film lying on side (De Cubitus view) and see if fluid level shifts. If the opacity is heterogeneous (eg polka-dots) then pneumonia, if homogenous (a smear) then effusion
- Miliary pattern: occurs in Tb, fungi, Thyroid cancer, pneumoconiosis, rarely Sarcoid
- Cysts ⇒ cystic bronchiectasis. Especially in Cystic Fibrosis and Staph.
- Enlarged hilum can be:
  - Enlarged vessels
  - Lymph node enlargement (like bunches of grapes): sarcoid, Tb, lymphoma
  - Cancer – usually unilateral

Differential if CXR is normal:

Cardiology 40
Airflow obstruction: asthma, COPD
PE
Pneumothorax (look again...)
Hidden pneumonia: check apices, angles and behind both sides of the heart (can you see the diaphragm below the heart or the ribs behind the heart?)

• Chest X-ray checklist:
  ➢ A – airway – midline
  ➢ B – bones and soft tissue. Check for gaps in bones →?bony metastases
  ➢ C – cardiac size and silhouette. Should be < 50% of maximal internal chest width
  ➢ D – diaphragm – right higher than left, angles sharp, contract with lung sharp
  ➢ E – equal volume, density symmetrical
  ➢ F – fine detail (pleura & lung parenchyma)
    o Is upper darker than lower
    o Pronounced/wider vessels in upper lobes → pulmonary venous congestion
    o Interstitial/pulmonary oedema → fine diffuse shadowing
    o Kerley B lines → oedematous interlobular septa
    o Fluff extending from hilum (bat’s wing appearance): alveolar pulmonary oedema
    o Atelectasis: dense, short, usually peripheral horizontal lines. If large then collapsed lung
    o Are L & R main bronchus < 75 degrees at carina
    o If there are dots, are they hollow (if so then likely to be blood vessels end on)
  ➢ G – gastric bubble
  ➢ H – hilum – left higher than right, no larger than thumb + Hardware
• Don’t make pathological diagnoses – say an opacity consistent with consolidation
• Treat the patient not the x-ray

Cardiovascular Risk Factors

• Framework:
  ➢ Collect information on risk factors
  ➢ Estimate prognosis
  ➢ Decide on Treatment based on assessment of benefits and risks:
• Risk factors:
  ➢ Constitutional: age, sex, family hx
  ➢ Medical: DM, HTN, dyslipidaemia
  ➢ Lifestyle: smoking, diet, exercise
• Protective factors = daily fruit + veg, alcohol in moderation, physical exercise
• Risk marker vs risk factor:
  ➢ Risk marker → if you remove it (eg diagonal earlobe creases), it does not affect risk ie is not causal
  ➢ Risk factor → if removed, it does affect risk (ie ↓) ie is causal
• ~80% of ↓ in coronary artery death since the 1960s is thought to be attributable to the control of smoking, lipids, and HTN
• DM + obesity are areas of concern (ie on the ↑)
• Important things to cover in discussions post a CV event (ie secondary prevention):
  ➢ Admission time
  ➢ Rehabilitation schedule (eg when back to work, physical activity, driving [2/52 min], sex)
  ➢ Long-term lifestyle advice: diet, exercise
  ➢ What to do with recurrent symptoms
  ➢ Drug therapy
  ➢ Further investigations/intervention?
• The hierarchy of efficacy in secondary prevention = medication > lifestyle change > PCI

Assessment of Risk

• Absolute risk of cardiovascular disease depends on the combination of all risk factors. Treatment decisions should be based on assessment of total risk – not one factor in isolation (eg raised blood pressure or cholesterol)
• Absolute risk is usually stated as the risk of a cardiovascular event in the next 5 years (Based on the Framingham Study):
  ➢ Very high risk: > 20% risk in next 5 years. Includes by definition people with:
Proven cardiovascular disease (past MI, positive treadmill, stroke, claudication, etc) automatically qualifies you as having a 20% risk of another CV even in the next 5 years → can add this to other risk factors to give a total risk (according to the risk charts)

- Familial hypercholesterolaemia and familial combined hyperlipidaemia
- Established diabetic nephropathy (albumin excretion > 300 mg/day)
  - High risk: 15 – 20% risk in next 5 years
  - Moderate risk: 10 – 15% risk in next 5 years
  - Mild risk: < 10% in next 5 years
  - Over age 70, risk for all individuals is very high, and age effect dominates

- Risk factors in the Framingham tables are age, gender, blood pressure, TC:HDL, smoking and diabetes/IGT
- Risk factors not included in the tables are: family history of coronary disease, physical inactivity, obesity (especially BMI > 27), LVH, fibrinogen, lipoprotein (a). The presence of these should bias treatment decisions towards treatment at any level of risk
**Dyslipidaemia**

- Levels:
  - TC < 4
  - LDL < 2
  - TG < 1.7
  - HDL > 1
  - TC:HDL < 4

- High levels of LDL (‘bad’ cholesterol), low levels of HDL (‘good’ cholesterol): *normal ratio* < 4
LDL reflects heredity, diet (both high cholesterol & high saturated fat) and exercise

↑ TAG and ↓ HDL may be related to insulin resistance, without total cholesterol being appreciably raised

Raised triglyceride levels are closely related to low HDL levels \(\Rightarrow\) hard to separate their independent effects on risk

Secondary causes: DM, obesity, alcohol abuse, hypothyroidism, renal disease, corticosteroids, exogenous sex hormones, pregnancy

Levels should be measured in early adulthood, especially if other risk factors or significant family history of heart disease

Fasting lipids best measure of TAGs (from which LDL can be inferred – more accurate than total cholesterol)

Within 24 hours of an MI, and up to 3 months later, total cholesterol ↓ and HDL ↑, so measurements over this period are not reliable

Treatment:
- Crudely, a statin ↓ RR by 20-30% (ie, if absolute risk of an event was 10%, with a statin, is now 7-8%) after a CV event
- A 10% relative reduction in TC reduces relative risk (risk of an event relative to exposure) by 15 – 20% over 5 years
- Treatment goal: total cholesterol <5 , HDL > 1, TAG < 2. TC: HDL < 4.5. Realistic goal is 25% reduction in total cholesterol through diet and drugs
- Thresholds for drug treatment following dietary treatment:
  - For very high risk: treat if TC or TC:HDL > 5.5
  - For high risk: treat if TC or TC:HDL > 6.5
  - For moderate risk: treat if TC or TC:HDL > 7.5
  - For mild risk: treat if TC or TC:HDL > 8.0
- Dietary advice: reduce saturated and trans unsaturated fats + exercise
- For drugs, see Lipid Lowering Drugs, page 74

Other Specific Risks

- Hypertension: Blood pressure > 160/95 has 5 times risk. Vibrational stress damages intima. Pressure wave tears the intima and this heals by scarring. Large pulse pressure also significant. Atheroma occurs most commonly at vascular bifurcations. See Hypertension, page 47
- Cigarette smoking: 2 times risk. Intimal microulceration (a complication to a plaque) predisposes to thrombosis. Tobacco oxidises LDL → poorly digested form that accumulates in the intima
- Diabetes: 2 times risk factor → advanced glycosylation end-products (non-enzymatically glycosylated proteins) bind to endothelium → permeable, causes cells to produce fibrous tissue

Vessel Pathology

- Arteries:
  - 3 layers:
    - Intima: thin, includes endothelium, underlying thin layer of connective tissue containing smooth muscle, and internal elastic lamina – elastic fibre layer
    - Media: thick, smooth muscle and collagen. Large arteries have elastic fibres as well
    - Adventitia: thin layer containing elastic fibres in loose connective tissue
  - 3 sizes: large (elastic), medium (muscular), small
- Veins: thin wall, large lumen, IEL intact only in large vessels, scant media, contain valves
- Arteriosclerosis = loss of elasticity of artery walls; is an umbrella term including atherosclerosis, monckeberg medial calcific sclerosis, arteriolosclerosis etc
- Arteriosclerosis:
  - = Thickening and loss of elasticity of arterial walls. Seen in chronic hypertension, and to a lesser degree with ageing
  - Hyaline arteriosclerosis: blood vessel takes on glassy ‘hyaline’ appearance. Reflects mild or ‘benign’ hypertension. Particularly seen in kidneys
  - Hyperplastic arteriosclerosis: concentric rings of increased connective tissue and smooth muscle give arteries an onion skin appearance. Signifies acceleration/malignancy of the hypertension

**ARTERIOSCLEROSIS**

<table>
<thead>
<tr>
<th>Atherosclerosis (large + medium arteries)</th>
<th>Intimal atheromas – fibrofatty plaques</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Gross = yellow/white streaks esp around ostia/branchings, may see sclerotic firm surfaces or ulceration +/- thrombosis</td>
</tr>
</tbody>
</table>
Atherosclerosis

Epidemiology
- Causes 50% of all deaths in US – including coronary, cerebral and peripheral vascular disease
- A disease of Western civilisation. Absent in certain 3rd world ethnic groups

Aetiology
- Multifactorial
- Endothelial damage (HTN, smoking etc – mechanical injury) \(\rightarrow\) inflammation \(\rightarrow\) LDL uptake (lipid metabolism) \(\rightarrow\) macrophage foam cells \(\rightarrow\) cytokines (inflammatory mediators) \(\rightarrow\) smooth muscle proliferation \(\rightarrow\) neovascularisation \(\rightarrow\) sclerosis and thrombosis

Gross Morphology
- Lesions appear in childhood as fatty streaks
- Adult plaques: discrete, yellow white random elevations, more prominent around ostia of large branches
- Plaques may have sclerotic firm surfaces or ulcerate exposing soft cholesterol-laden material
- Severity increases with age

Microscopic Morphology
- Plaque: intimal lesion – deposition of cholesterol esters, necrotic debris, smooth muscle and foam cells. Chronic fibrotic inflammatory response forming a superficial fibrous cap
- Complications are ulcers with thrombi, haemorrhage into plaque, embolisation, calcifications, atrophy of media \(\rightarrow\) aneurysms
- Reduplication of internal elastic lamina: shows with Elastin Van Geesen (EVG) stain
- Adventitial fibrosis and chronic inflammation

Complications
- Complicated plaques = ulceration, haemorrhage, aneurysm, thrombosis, calcification
- Calcification: \(\rightarrow\) rigid pipe \(\rightarrow\) ↑pulse pressure \(\rightarrow\) distal atherosclerosis. (NB Calcium laid down in two ways: dystrophic calcification – Ca laid down in necrotic tissue – and metastatic calcification - ↑serum Ca \(\rightarrow\) Ca laid down abnormally
- Ulceration: fibrous cap cracks – debris discharged into lumen \(\rightarrow\) embolisation/thrombus
- Thrombus: can embolise, or occlude artery. Cause of majority of myocardial infarcts and cases of unstable angina pectoris. If collateral circulation, can recannalise thrombus
- Haemorrhage: a weak little new artery in the plaque bursts \(\rightarrow\) pushes plaque against opposite wall

Aortic Aneurysm

Aneurysm Pathology
- True aneurysm = all layers involved
- False aneurysm = intimal or full thickness tear, wall does not remain intact
- Dissecting aneurysm = blood between TI & TM; as blood tracks proximally – aortic valve insufficiency, tamponade, coronary artery involvement
- Aneurysm causes = atherosclerosis, infection, HTN, CMN, post traumatic etc
- Aneurysm complications = thrombosis, embolism, erosion of adjacent structures, rupture

Aetiology
- Atherosclerosis \(\rightarrow\) media weakening \(\rightarrow\) as intraluminal P \(\propto\) r (LaPlace), increased P causes evolving aneurysm
- 20% familial incidence \(\rightarrow\) defect in connective tissue component (?type III procollagen)
- Syphilis and other bacterial infections

Cardiology 45
Cystic medial necrosis \(\rightarrow\) denudation of elastic layer

Trauma

Common in Marfan's syndrome (eg Abraham Lincoln). Long ulnar, femur, weak aorta, and high arched palate

Clinical

- 75% occur in abdominal aorta. Easy to repair cf thoracic and thoraco-abdominal cases
- Often asymptomatic \(\rightarrow\) incidental finding
- Can cause back pain (due to retroperitoneal blood). Differential \(\rightarrow\) pancreatitis
- 44% of symptomatic aneurysms rupture. ↑Distension \(\rightarrow\) inevitable rupture (Law of Laplace)

Pathogenesis

- Arteriosclerosis \(\rightarrow\) gradual destruction of media \(\rightarrow\) focal weakening of wall \(\rightarrow\)↑distensibility \(\rightarrow\)↓w + ↑r  
  \(\rightarrow\)↑tension + ↓blood velocity \((T \propto Pr/W)\)
- ↑Pressure \(\rightarrow\)↑radius \(\rightarrow\)↑tension \(\rightarrow\)↑radius, etc

Gross Description

- Fusiform dilatation of severely atherosclerotic aorta with sharp superior and inferior margins
- Typically abdominal aorta, from just below ostia of renal arteries to bifurcation of aorta
- Larger aneurysms contain thick old laminated thrombus reducing patent luminal size
- Aneurysmal thrombus does not organise due to the paucity of functioning vasa vasorum in fibrotic wall

Microscopic Description

- Aneurysm wall: barely identifiable media, fibrotic lesions with focal aggregates of mononuclear cells
- Adventitia is fibrotic with chronic inflammation

Complications

- Thrombus \(\rightarrow\) distal gangrene, calcification, bacterial infection (salmonella, shigella), rupture, dissection, fistula (eg aorta-vena cava)

Dissecting Aneurysms

- Usually involves the aorta
- Fatal in 75 – 90% of cases
- Causes: atherosclerosis, also hypertension, Marfan’s syndrome, trauma, inflammation of media
- Pathogenesis:
  - Cystic medial necrosis: mucoid cysts in the media, elastic fragmentation and fibrosis
  - With ageing, degenerative changes lead to breakdown of the collagen, elastin, and smooth muscle and ↑ground substance = CMN \(\rightarrow\) defect in mucopolysaccharide synthesis (atherosclerosis, HTN, marfan’s)
  - Atherosclerosis that causes occlusion of the vasa vasorum also produces this
  - CMN is the hallmark histologic change associated with dissection in those with Marfan syndrome
  - Media weakening (see cysts, loss of cells, elastic fragmentation + fibrosis)
  - Commences as a transverse intimal tear, 90% in ascending aorta
  - Splits the media between the mid and outer 1/3
  - Proceeds down occluding branches
- Split in aortic wall, blood flows into false lumen b/w intima + media (can involve media too)
- Type a = involves ascending aorta
- Type b = involves desc aorta
- Causes end-organ ischaemia (eg gut, kidneys, heart etc), can extend + cause tamponade, can rupture etc
- Outcomes:
  - Acute perforation \(\rightarrow\) sudden death
  - Subacute progression \(\rightarrow\) perforation in several days
  - Chronic \(\rightarrow\) rupture back into the lumen \(\rightarrow\) double barrel aorta

Arteritis

- Diverse group of diseases classified by aetiology, vessel size or histologic changes

Infectious Arteritis

- Wide range of organisms, pyogenic, TB, parasites, viruses, fungi, syphilis
- Vessel infected by septic emboli (→ lodges and forms mycotic aneurysm) or direct extension from adjacent abscesses
- Histology: oedema, fibrin, dense neutrophilic infiltrate
- Outcome: scarring, obliteration of lumen → distal infarction
- Syphilis: occludes vasa vasorum → ischaemic damage to artery, small vessel occlusion → obliterative end arteritis, perivascular lymphocyte and plasma cell cuffing. Famous for causing proximal aortic aneurysms

**Physical/Chemical Agents**
- Irradiation, trauma, vascular toxins, sulphonamides, penicillin

**Arteritis Syndromes**
- See Vasculitis, page 444

**Other Vessel Abnormalities**
- **Fibromuscular dysplasia**: non-inflammatory thickening of large and medium sized muscular arteries causing stenosis. Most significant in renal arteries → secondary hypertension
- **Thrombophlebitis**: inflammation and secondary thrombosis of veins, usually small veins as part of a local reaction to bacterial infection
- **Varicose veins**: enlarged, dilated, tortuous blood veins and incompetent venous valves – mainly in legs. Predisposing factors include older age, female, heredity, posture and obesity. Varicose veins at other sites include haemorrhoids (rectal), oesophageal varices and varicocele (scrotum)
- **Vasculitis**: inflammation and necrosis of blood vessels – including arteries, veins and capillaries. May be due to infection, trauma, radiation, toxins or immune (eg disposition of immune complexes)
- Leukocytoclastic vasculitis: a form of hypersensitivity angiitis in the skin presenting as purpura

**Ischaemic Heart Disease**
- Most common cause of death in Western countries
- Incidence peaked in NZ in 1968 at 320 deaths /100,000. Now 200/100,000
- In NZ, 4,500 acute MI per year, 3,200 CIHD per year (=25% of all deaths)
- Risks factors:
  - Cigarette smoking 5.2 x
  - Hypertension 3.3 x
  - Dyslipidaemia 3.7 x
  - Diabetes mellitus
  - Male gender
  - Family history
- Pathogenesis:
  - Myocardial blood flow < metabolic demand of myocardium
  - Coronary perfusion related to:
    - Atherosclerosis occluding coronary arteries (fixed coronary stenosis), acute plaque changes (eg rupture), thrombosis, vasoconstriction
    - Differential between ostia (aortic diastolic pressure) and coronary sinus (right atrial pressure)
    - Compression of intramuscular arteries during contraction → myocardium perfused in diastole
    - Decreased coronary blood flow also due to ↑intraventricular pressure & myocardial contraction, aortic valve stenosis/regurgitation, ↑right atrial pressure
  - Cross sectional area of major vessels must be reduced by 75% to significantly affect perfusion

**Pathology of Smoking**
- Smoking →
  - Endothelial damage
  - Intimal ulceration
  - Altered lipid metabolism (oxidised LDL)

**Hypertension**
- See Measuring Blood Pressure, page 28, for measurement
- Is a risk factor not a disease
- **Systolic BP best predicts CV risk** (ie SBP carries the risk)
- Rise in risk is continuous from 115mmHg up
Definition:
- No dividing line between normal and high blood pressure. There are arbitrary levels set based on the risk of complications (the main ones being stroke, MI, heart failure and renal failure).
- In determining whether the blood pressure is ‘bad’, take into account the systolic and diastolic pressure, age, sex, other diseases (eg DM, hyperlipidaemia), smoking. Older age is the greatest risk factor (ie risk if you have HTN depends on age): treat high blood pressure in an older person regardless of other risk factors.
- WHO definitions:

<table>
<thead>
<tr>
<th>Category</th>
<th>Systolic</th>
<th>Diastolic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>&lt; 130</td>
<td>&lt; 85</td>
</tr>
<tr>
<td>High Normal</td>
<td>130 - 139</td>
<td>85 – 90</td>
</tr>
<tr>
<td>Hypertension</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stage 1 (mild)</td>
<td>140 – 159</td>
<td>90 – 99</td>
</tr>
<tr>
<td>Stage 2 (moderate)</td>
<td>160 – 179</td>
<td>100 – 109</td>
</tr>
<tr>
<td>Stage 3 (severe)</td>
<td>180 – 209</td>
<td>110 – 119</td>
</tr>
<tr>
<td>Stage 4 (very severe)</td>
<td>&gt; 210</td>
<td>&gt; 120</td>
</tr>
</tbody>
</table>

- Also classified according to retinopathy, see Hypertensive Retinopathy, page 220.
- Classified as:
  - Primary/essential (what most people have – but a diagnosis of exclusion): contributing factors include hereditary, obesity, alcohol intake, salt intake (60% of patients respond to ↓salt intake – but compliance difficult).

<table>
<thead>
<tr>
<th>Essential hypertension</th>
<th>Isolated systolic hypertension</th>
</tr>
</thead>
<tbody>
<tr>
<td>↑ peripheral resistance (↑ SBP + DBP) → ↑ MAP</td>
<td>↑ large artery stiffness (normal ageing process)</td>
</tr>
<tr>
<td>Seen in younger pts</td>
<td>Similar MAP to normal: ↑SBP ↓DBP</td>
</tr>
<tr>
<td>Mainly ↑ TPR</td>
<td>Mainly &gt; 55yrs</td>
</tr>
<tr>
<td>Easy to treat</td>
<td>Difficult to treat</td>
</tr>
<tr>
<td>DBP a reasonable marker</td>
<td>SBP + PP are markers</td>
</tr>
</tbody>
</table>

- Secondary causes: renal disease (eg renal artery stenosis, diabetic kidney disease, etc), endocrine (eg ↑cortisol, ↑aldosterone, acromegaly, oral contraceptives), neurogenic (eg psychogenic), sleep apnoea (major changes in baroreceptor reflexes).

Epidemiology:
- Prevalence ↑ with age. Older people at greater risk at any given blood pressure compared with young.
- Strong risk factor for stroke, congestive heart failure, coronary artery disease and renal failure.
- Probably 10 – 20% of older adults require treatment (ie have essential hypertension with diastolic pressure > 95 mmHg).
- Treatment reduces related complications. Stroke risk reduces in line with BP, MI risk doesn’t reduce as much for a given drop in BP.

History:
- How accurate is the diagnosis?
- Usually symptomless
- Possibly related symptoms: palpitation, flushing, headache
- Related risk factors: history of renal, cardiac or neurological disease
- Asthma, diabetes, gout, renal disease: complications with drug treatment
- Occupational
- Diet: salt, fat
- Smoking and alcohol
- Family History

Detection and assessment:
- Blood pressure more labile in older adults ⇒ measure 2 to 3 times (in same arm). Measure standing and sitting.
- In primary hypertension usually ↑ on standing. In secondary hypertension, usually ↓ on standing.
- Basic workup:
  - Urine for protein, blood and glucose ⇒ DM, renal disease
  - FBC for polycythaemia, renal disease, alcohol
  - Electrolytes (especially K): exclude odd endocrine causes
  - ECG: any end organ damage
  - Ophthalmology
- Additional tests if indicated.
Microscopic analysis of urine (for casts)
- Plasma lipids
- Blood glucose: need to modify drug treatment
- Serum Ca, PO4, uric acid (gout – associated with hypertension, may also ↑ due to drugs)
- Echocardiogram or CXR
- Special tests for secondary causes if indicated: eg renal imaging, 24 hour urine for catecholamine metabolites (pheochromocytoma)

Pathology
- **Vibratory stress damages endothelium** especially at bifurcations → fibrosis and lipid infiltration
- Affects small arteries + arterioles
- Pathophysiology: poorly understood. Older people have ↓ renin, and are more responsive to Na depletion. ‘Hardening’ of arteries → ↑ systolic pressure. ↓ Responsiveness to β-mediated vascular relaxation
- Leads to **hypertensive heart disease**: LVH → relative myocardial ischaemia. Aortic valvular disease also → LVH
- Malignant hypertension (accelerated hypertension): hypertension leading to rapidly progressive vascular compromise. Blood vessels show fibrinoid necrosis or concentric hyperplasia (‘onion skin’ changes)

Complications:
- Accelerated atherosclerosis
- Haematological CVA (ruptured charcot-bouchard microaneurysms)
- Hypertensive HF – LVH
- Aortic dissection
- Nephrosclerosis
- Retinopathy
- Sudden death

Non-Drug Treatment
- Remove/substitute drugs: eg NSAIDs, OCP, Prednisone
- Always attempt lifestyle changes first:
  - Stop smoking (little effect on BP, but biggest impact on risk factors)
  - Weight loss
  - ↓ alcohol (max 2 drinks per day)
  - ↓ salt intake (max 70 mmol/day)
  - ↑ exercise
  - ↓ saturated fats

Drug Treatment
- When to treat:
  - Given it is such a strong risk factor, consider hypertension above systolic 140 mmHg
  - Always treat > 170 systolic or > 110 diastolic
  - Hardly ever treat < 140 and < 90 diastolic
  - In between, controversial. **Consider other risks.** If over 65 no other risk factors needed (eg diabetes, etc).
  - Give considerable attention to non-pharmacological approaches for 3 – 6 months. Long term follow up necessary
  - Treat 72 older adults for 5 years to prevent 1 death, treat 43 for 5 years to prevent one cerebrovascular event
  - Aim of treatment: diastolic < 90

- Rules of thumb:
  - **Use low doses of several agents**, rather than ↑ doses of one drug (especially thiazides)
  - First line: *thiazides* (with or without a potassium sparing agent) *and/or β-blocker* (atenolol most used in trials). If tolerate them both then add them together
  - **ACE inhibitors**: not so effective but rated best quality of life
  - Don’t take diuretic, ACE inhibitor and NSAIDS together (renal side effects)
  - Introduce slowly, monitor for symptoms and postural hypotension
  - **Aim for 140/90**, and then attempt back titration 3 monthly
- **ABCD = ACEi, β-blocker, CCB, diuretic** (eg thiazide)
- Best **substitutions** are made by going horizontally, best **combinations** by going vertically
Angina Pectoris

- **Symptom complex characterised by attacks of chest pain, causing ischaemia but not infarction**
- **Patterns:**
  - **Stable** angina (typical): *pain on exertion, relieved by rest or vasodilators*. Subendocardial ischaemia with ST depression
  - **Unstable** angina: variable, prolonged pain, *pain at rest or worsening of pain in stable angina*. ST depression – but may be elevated. Most common complication: arrhythmias (especially VF). Within 3 months 4% will have sudden death and 15% a myocardial infarct
  - **Variant or Prinzmetal’s angina**: classically occurs at rest. Caused by *reversible spasm* in normal to severely atherosclerotic coronary arteries. Can see ST-segment elevation or depression
  - **Sudden cardiac death**: Usually within an hour of a cardiac event or without symptoms. Usually high-grade stenosis. Usually associated with arrhythmias, especially ventricular ectopic beats and subsequent VF

**Treatment Options for Stable Angina**

- **Nitrates**: short & long acting
- **β-blockers** (↓myocardial O2 consumption)
- Ca antagonists
- Aspirin

**Unstable Angina**

- Is one form of Acute Coronary Syndrome (ACS)
- **Investigations:**
  - **ECG**: serial or continuous if high risk
  - **Bloods**: troponin (repeat after 3-6 hours), FBC, Cr, electrolytes, CK, blood glucose. Want to test lipids/cholesterol – but false positives following an acute coronary event. Do later.
  - **CXR**: cardiomegaly? Pulmonary oedema? Dissection?
  - **ETT**
- **Medical therapy:**
  - Aspirin: reduces progression to MI. Neither warfarin nor heparin confers further benefit. Use heparin if high risk.
  - β-blockers: reduce progression to MI
  - iv nitroglycerine for symptomatic relief
  - Maybe calcium channel blockers that reduce the heart rate
- **Low risk:**

**Best drug choices:**

<table>
<thead>
<tr>
<th>Condition</th>
<th>Implication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atrial Fibrillation</td>
<td>Some Ca channel blockers and β-blockers may help (but not together!). Watch for drug interactions with digoxin</td>
</tr>
<tr>
<td>COPD/Asthma</td>
<td>Avoid β-blockers, care with ACEi (cough)</td>
</tr>
<tr>
<td>CHF</td>
<td>ACE inhibitors improve the CHF. If diastolic dysfunction is prominent then β-blockers or Ca antagonists</td>
</tr>
<tr>
<td>Diabetes Mellitus</td>
<td>ACE inhibitors delay renal failure. Thiazides worsen diabetic control. β-blockers may mask hypoglycaemic symptoms</td>
</tr>
<tr>
<td>Gout</td>
<td>Thiazides may worsen hyperuricaemia</td>
</tr>
<tr>
<td>Ischaemic Heart Disease</td>
<td>Consider β-blockers</td>
</tr>
<tr>
<td>Renal Failure</td>
<td>↑half life of some drugs (eg atenolol)</td>
</tr>
<tr>
<td>Voiding Dysfunction</td>
<td>In men with ↓urine flow, consider α-blockers (eg terazosin)</td>
</tr>
<tr>
<td>History of IHD, stroke or DM</td>
<td>Aspirin</td>
</tr>
</tbody>
</table>
Normal ECG and no detectable troponin despite ↑angina frequency or severity
Management: discharge for outpatient assessment

High risk:
- If even a minor degree of ST depression or a significant elevation of troponin (would then = NSTEMI) → minor myocardial damage so now is the time to act
- Overlap between high risk ACS and non-STEMI
- Management: admit for coronary angiography and, if positive, early percutaneous coronary intervention (ie more aggressive treatment than previously)

Long Term Management
- ↓Obesity, diabetes, smoking, ↑exercise
- Referral to a cardiac rehabilitation programme
- Statins
- ACE inhibitors if hypertension or diabetes

Myocardial Infarction (MI)

Definition and Classification
- Old WHO definition: two out of three of: chest discomfort for > 30 minutes, enzyme rise and typical pattern of ECG involving the development of Q waves (ie normal ECG does not rule out infarction)
- New definition: blood levels of sensitive and specific markers with at least one value above the 99th centile of the upper reference limit with at least one of the following (ie ↑importance of biochemical tests)
  1. Symptoms of ischaemia
  2. ECG changes suggestive of new ischaemia
  3. Development of pathological Q waves
  4. Imaging of new loss of viable myocardium or regional wall motion abnormality

- 2 classifications:
  STEMI and NSTEMI. Often ST elevation progresses to Q wave
  Q wave verses none (older classification) → transmural or not

Epidemiology
- Same risk factors as for atherosclerosis
- 5% occur under age 40, 45% over age 65
- Oestrogen protective in women pre-menopause
- 30% mortality with 20% dying before admission

Symptoms
- Crushing chest pain (absent in 15% of cases). But < 25% with chest pain have an MI (relatively sensitive but not specific)
- Can also present as epigastric, arm, wrist, or jaw discomfort with exertion or at rest ie beware of atypical presentations!
- May be associated with dyspnoea, sweating, nausea, vomiting, weakness, dizziness, fainting

Acute Coronary Syndrome
- Either:
  1. Unstable angina: essentially rest pain with no TnT ↑
  2. NSTEMI
    - Due to microcirculation embolization (as cf STEMI → complete vessel occlusion)
    - TnT ↑ (by 3-12 hours; NB TnT determinable between 3-12hrs post infarct, peaks at 18-24hrs, prolonged for up to 10d)
    - NSTEMI = chest pain syndrome + positive TnT +/- ECG changes (but not STE)
  3. STEMI: Complete vessel occlusion
  4. SCD

Pathology
- Ischaemia = diminished perfusion relative to demand; compromised O2 and glucose delivery etc and metabolite removal
- Infarction = tissue death:
  - Arterial (blockage – thrombosis/embolism); arterial = white
  - Venous (mechanical compression); venous = red
- MI reversible injury = **20-60 minutes** – reperfusion leads to restoration of function – time is muscle
- Reperfusion injury = can cause ischaemic cells to die more quickly – abundant haemorrhage
- Myocardial rupture = **3-7d post MI**
  - Rupture of: 1. free wall (tamponade) or 2. septum (shunt) or 3. papillary muscle (valve regurg)
- Granulation tissue = fibroblasts + angiogenesis
- Coagulation necrosis:
  - Haemorrhage
  - Wavy myocytes without nuclei
  - **Hypereosinophilia** (take up stain – redder the deader)
  - Scant neuts
- Virchow’s triad:
  - Hypercoagulability/altered blood composition (dyslipidemia, DM, bed rest, ca., obesity, smoking, factor V leiden etc);
  - Endothelial damage (smoking, trauma, vasculitis, HTN etc);
  - Altered blood flow (bifurcations, HTN etc)
- Post-mortem clot = **yellow fatty clot (no circulating RBC) cf embolus** = laminations of red/brown/black = **true clot**

**Pathogenesis**
- Irreversible damage in 20 – 40 minutes
- Essentially: disruption of an atherosclerotic plaque → platelet activation, adhesion + aggregation leading to ACS
- Occlusive intracoronary thrombus, overlying ulcerated or stenotic plaque:
  - Causes 90% of transmural acute MIs.
  - For blood to clot need: abnormal flow, damage to vessel wall and clotting factors
  - Thrombus formation: activated platelets adhere to exposed collagen of damaged endothelium → release thromboxane A2 → expanding platelet mass + coagulation
- Vasospasm: with or without atherosclerosis. Postulate where no findings at post-mortem (10%) – but many of these will be thrombi that have lysed
- Emboli: from left sided mural thrombosis, vegetative endocarditis
- Arteritis: polyarteritis nodosa, Kawasaki disease
- Other: dissecting aneurysm occluding coronary ostia, ↓O2 supply (anaemia, CO, cyanide), ↑O2 demand (hyperthyroidism, fever)

**Gross Morphology**

<table>
<thead>
<tr>
<th>MI Morphology</th>
<th>Macroscopic</th>
<th>Microscopic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 1</td>
<td>Subtle changes – congestion – dark. Maybe pallor</td>
<td>Coagulation necrosis: wavy myocytes, haemorrhage, scant neuts</td>
</tr>
<tr>
<td>Day 2</td>
<td>Mottled, tan infarct centre</td>
<td>Coagulation necrosis + neuts ++</td>
</tr>
<tr>
<td>1 Week</td>
<td>Hyperaemic (blood engorged) border + central tan area</td>
<td>Disintegration of necrotic myofibres, dying neuts, macrophages</td>
</tr>
<tr>
<td>2 Weeks</td>
<td>Yellow, tan and soft</td>
<td>Phagocytosis, granulation tissue, early fibrosis</td>
</tr>
<tr>
<td>2 Months</td>
<td>White scarring</td>
<td>Dense collagenous – fibrous scarring</td>
</tr>
</tbody>
</table>

A, 1 day old MI showing coagulative necrosis and wavy fibers, oedema and scattered neuts.
B, 3 to 4 days’ duration: dense neuts.
C, 1 week: removal of necrotic myocytes by phagocytosis.
D, gran tissue characterized by collagen and capillaries.
E, Well-healed MI with replacement of necrotic fibres by dense collagenous scar.
Transmural infarct: entire thickness of wall from endocardium to epicardium. Usually Anterior wall (50%) or posterior free wall/septum in 15 – 30%. Q wave

Subendocardial infarct: multifocal necrosis confined to inner 1/3 to 1/2 of left ventricle wall. More commonly associated with temporary hypoperfusion (e.g., shock). No Q wave

Occlusion:
- LAD: 40 – 50%
- RCA: 30 – 40%
- LCA: 15 – 20%

Gross changes over time:
- 18 – 24 hours: Pallor of myocardium – anaemic, grey brown (cf normal brown-red)
- 24 – 72 hours: Pallor (yellow/brown) with ↑ly defined hyperaemia border
- 3 – 7 days: Hyperaemic border (darker brick red) with central yellowing, haemorrhagic areas
- 10 – 21 days: Maximally yellow and soft with vascular margins (red edge – granulation tissue moves in)

7 weeks: White fibrosis

Microscopic Appearance
- 1 – 3 hours: Wavy myocardial fibres
- 2 – 3 hours: Staining defect with tetrazolium
- 4 – 12 hours: Coagulative necrosis with loss of cross striations, oedema, haemorrhage, early neutrophil infiltrate (WBCs with multilobed nuclei), loss of myocardial striations
- 18 – 24 hours: Continuing coagulation necrosis, pyknosis (margination) of nuclei (healthy myocardial nuclei are usually central)
- 24 – 72 hours: Total loss of nuclei and striations, heavy neutrophilic infiltrate
- 3 – 7 days: Macrophage and mononuclear infiltration, fibrovascular response begins (starts at edges), myocardium at its weakest
- 10 – 21 days: Prominent granulation tissue: fibroblasts and neovascularisation, macrophages (tissue scavengers – high fat content → yellow, high iron → brown), plasma cells

7 weeks: Fibrosis

Images
Laboratory Diagnosis of Acute Coronary Syndrome

- The best use of trop in the primary care setting is in the stable pt who may have had atypical symptoms who is presenting late

- **Troponins:**
  - Is specific to cardiac muscle; is more sensitive + has a longer time course of elevation cf CKMB
  - Is a complex of 3 protein subunits bound to muscle filaments; involved in regulation of muscle contraction
  - Trop T + I from cardiac muscle are immunologically distinct from T + I in skeletal muscle + therefore is specific (as cf Trop C)
  - **Highly specific** for MI injury – but not synonymous with MI or ischaemia; probably indicates irreversible injury
  - Increases above the 99th percentile are significant (lower than previously)
  - Prognosis related to degree of elevation
  - Rises no faster than CK (ie starts to rise within 3 – 12 hours) and more expensive but substantial rise after MI (400 fold)
  - Causes besides MI:
    - Subendocardial injury from wall stress in left ventricular hypertrophy (eg heart failure)
    - Right ventricular injury in severe PE
    - Direct trauma (eg contusion)
    - Toxic injury by drugs or in septic shock
    - Myocarditis
    - Post-cardioversion
  - New Highly Sensitive Test:
    - New sensitive troponin testing caused \( \uparrow \) numbers of pts w CP to be diagnosed with MI rather than UA
    - There will be impact on epidemiological data, indications for treatment + f/u, pt’s perceptions + resources
    - The 2007 universal definition of MI required the ability to measure trop at the level of the 99th centile of a reference population with no more than 10% coefficient of variation (refers to the reproducibility of a test: if measured the same sample 20 times would we always obtain results that are very close to the true result?)
    - 99th centile of upper reference limit is the value above which only 1% of the normal population will lie
    - The improved sensitivity of the new test allows more secure rule out of MI in late presenting case cf the old test ie a result of <14ng/L more than 9hrs after symptoms essentially rules MI out
    - As sensitivity \( \uparrow \), specificity \( \downarrow \)
  - **Troponin T:**
    - Wellington hospital uses high sensitivity TnT = hsTnT
    - RR = 0-13; diagnosis of MI requires a setting of ischaemia [symptoms or ECG changes] and hs-TnT \( \geq 14ng/L \) with a rise and/or fall of: 50% if hs-TnT is 14-50ng/L; 20% if hs-TnT is >50ng
    - TnT determinable between 3-12hrs post infarct, peaks at 18-24hrs, prolonged for up to 10d
    - Increases in renal failure due to ↓clearance (⇒ false positive)
  - **Troponin I:**
    - Everyone else’s test. Normal value depends on which assay is used
    - I remains elevated for 5 – 9 days and T for 2 weeks. Better marker for recent MI than LDH. Harder to interpret in re-infarct – don’t know whether it’s the 1st or 2nd infarct
    - Test on admission to either see if already raised (poor prognosis) or to establish baseline
• Older tests:
  ➢ CK – total: not specific to myocardial injury. Do baseline and use to check for reinfarction (Troponins not so good for this)
  ➢ CK – MB fraction:
    ➢ MM fraction is in both skeletal and myocardial muscle. But 15 – 40% of cardiac CK is MB, compared with 2% skeletal. BB found in brain, bowel and bladder. The MB fraction is therefore very specific
    ➢ MB fraction rises within 2 – 8 hours. Dissipates within 1 – 3 days. So also a good marker of reinfarction
    ➢ CK – MB isoforms: Ratio of isoform 2 to isoform 1 > 1.5 ⇒ early acute MI (changes before CK- MB elevated). Requires electrophoresis, so labour intensive. False positives with heart failure
  ➢ Myoglobin: Oxygen binding protein in skeletal and cardiac muscle. Elevated before CK-MB, but is not specific to cardiac muscle. Negative myoglobin can help rule out MI
  ➢ LDH: supplanted by other tests. Rises later (24 – 48 hours) and elevated for 7 – 14 days. Isoenzyme measurement of LDH 1 and 2 necessary for cardiac specificity
  ➢ AST and ALT: intermediate timing but rather non-specific
• Other Investigations: CXR, echo, ABG, FBC, ?perfusion scan, ?amylase
• ETT: “Bruce protocol”: dx 2/3 of pts with CAD if target HR achieved (85% of max); done in 3 minute stages (according to speed/slope). Monitor HR, ECG, BP and for Sx; stop if ischaemic changes/pain

Management
• Exclude differentials:
  ➢ Aortic dissection
  ➢ Pericarditis
  ➢ PE or other causes of pleuritic chest pain
  ➢ Pneumothorax
  ➢ Peptic ulcer
  ➢ MSK injury
• Investigations as for Unstable Angina, see page 50
• They will be frightened. Reassure. > 90% survival if low risk (< 60, no diabetes, no past history, pulse < 100)
• MONA: morphine, O2, nitrates, aspirin
• O2 (unless CO2 retaining)
• Morphine 5 – 15 mg iv at < 1 mg/min (+ antiemetic eg metoclopramide 5 – 10 mg iv). Effects: analgesic, anxiolytic, anti-arrhythmic, venodilatory
• Restoring/Maintaining vessel patency: Aspirin 300 mg (unless contra-indicated, ongoing)
• STEMI:
  ➢ Complete vessel occlusion
  ➢ if:
    o ST elevation > 1mm in 2 limb leads or
    o ST elevation > 2mm in 2 chest leads or
    o New Left Bundle Branch Block (LBBB)
  ➢ AND ongoing ischaemic chest pain for less than 12 hours (preferably less than 6 hours)
  ➢ Best within 60 mins
• Treatment is either:
  o PAMI (if readily available) or
  o Fibrinolysis Contraindications:
    1. General bleeding tendency: warfarin, haemophilia, severe liver disease, thrombocytopenia
    2. Local bleeding risk: Past haemorrhagic stroke or recent surgery, prolonged resuscitation (⇒rib fractures, contusion, etc), peptic ulcer, GI bleeding, pregnancy, cavitating Tb
    3. Severe hypertension (systolic > 200, diastolic > 120) ⇒ risk of ICH
    4. Pre-existing thrombus that might embolise (eg endocarditis, aortic aneurysm)
  ➢ Options:
    1. Streptokinase: restores perfusion in 30%
    2. TPA: restores perfusion in 54%. Expensive. Use tPA if previous reaction to SK, or if SK has been used between 1 year and 5 days ago
  ➢ Complications: 1% risk of stroke
  ➢ Watch this space for platelet receptor blocking drugs (eg IIb/IIIa inhibitors)
  ➢ Streptokinase: in elderly due to tPA’s slightly ↑ risk of intracranial haemorrhage
  ➢ tPA: more expensive but slightly more effective
Contraindications = recent major surgery/bleed, previous streptokinase (CI for streptokinase due to Ab production), bleeding condition, hypertension (risk of intracranial haemorrhage)

Post successful fibrinolysis → exercise treadmill test → if positive → angiography

Management of preload, afterload and heart rate and rhythm:

- Glyceryl trinitrate
- ACE inhibitor + β-blocker (unless contra-indicated)
- Bed rest

Other Pharmacological treatment:

- Clopidogrel (maybe)
- Aspirin (ongoing)
- Statin (ongoing)

Monitor ECG, BP, cardiac enzymes, ABGs

Stop smoking

Early stress/treadmill test

Prognosis

Good prognostic indicators:

- No pre-existing hypertension
- Normal heart size
- No post MI pulmonary oedema
- No significant arrhythmias after day 1
- No post-MI angina

If good prognosis, discharge on aspirin, statin and β-blocker. Add an ACE inhibitor if ↓LV fx (or if you’re Phil Matsis)

Complications

- 35% die within one year, 10% per year thereafter. NZ overall hospital mortality 19%
- Arrhythmias and conduction defects: eg premature ventricular beats, sinus bradycardia, VT, VF, heart block
- Extension of infarction, re-infarction
- Congestive heart failure (pulmonary oedema): everyone who’s had a significant MI will have some degree of this
- Cardiogenic shock: if more than 40% of the left ventricle is infarcted. 70 – 90% die
- Pericarditis: fibrinous adhesions in the pericardium overlying the infarct
  - Dressler’s syndrome – autoimmune adherent pericarditis – occurring 2 – 6 weeks post MI or cardiac surgery
  - Treatment = steroids
- Mural thrombosis → embolisation
- Myocardial rupture → tamponade. Maximum incidence day 5 - 7. Can include rupture of interventricular septum
- Papillary muscle rupture or infarct → mitral incompetence
- Ventricular aneurysm formation: 12 – 20% of cases
- Ischaemic cardiomyopathy: severe atherosclerosis involving all major branches → inadequate vascular supply → myocyte loss and interstitial fibrosis → ↓compliance & dilation → compensation by myocyte hypertrophy → slow progressive heart failure and ↑heart size (up to 2 to 3 times normal)

Time to complications:

- 0 – 3 days: arrhythmia, CHF, pericarditis
- 5 – 7 days: rupture
- Later: recurrent MI, angina, embolism from mural thrombosis, mitral regurgitation, Dressler’s syndrome (Post MI syndrome), aneurysm

Arrhythmias

- For cardiac arrest rhythms (VT, VF, Torsade and asystole) see Cardiac Arrest Rhythms, page 792

Atrial Fibrillation

- = a type of supra-ventricular arrhythmia
- Mechanism:
  - Most AF originates from small foci of muscle; paroxysmal from small bits of muscle within the pulmonary veins (can ablate)
Wave of depolarisation circulates in atria at much faster rate than the discharge from the SA node
Disorders changing the conduction characteristics of the AV node + predispose to AF:
- ↑atrial size
- Fibrosis, inflammation
- Thyrotoxicosis
- Ischaemia
- Others: altered autonomic tone, alcohol use, after bypass surgery (30%), after valve replacement surgery (50%)
AV node receives irregular impulses at a rate of 250 – 400 per minute. Conducted through the node at a frequency dependent on the pathway’s refractory period
Typical ventricular rate is 120 per minute: but this may ↑ if sympathetic stimulation (→↓refractory period) or alternative conducting path to the AV node (eg Wolff-Parkinson-White syndrome) or can be slower

- Epidemiology: most common cardiac arrhythmia. M > F. 5% of over 70s
- Causes:
  - IHD: especially post MI
  - Mitral valve disease (→ ↑atrial size)
  - Alcohol
  - Thyroid disease
  - Idiopathic
- Potential implications:
  - Thromboembolism: especially cerebral (also mesenteric arteries or lower limbs). If no other risk factors then 1% per year. 5% if one other risk factor (age over 65, ↑BP, heart failure, diabetes, IHD, previous embolism, RF). If RF and AF then 20% annual rate
  - Reduced cardiac output: ↓ventricular filling → ↓cardiac output → heart failure or ↓exercise tolerance. Also high ventricular rate → ↓filling time → ↓CO
  - Other symptoms: palpitations (25%) and dizziness or syncope (20%)
- Diagnosis:
  - Should always be confirmed by ECG. Ventricular rhythm in AF can be deceptively regular, and not all irregular rhythms are AF (eg variable AV block, ventricular or atrial ectopics)
  - More prominent atrial waves in V1 as directly over RA
- Assessment:
  - Hx and exam
  - Exclude thyrotoxicosis
  - Manage contributing MI, respiratory disease or alcohol abuse
  - Check electrolytes
  - Assess cardiovascular risk factors: eg glucose, lipids
  - Echocardiogram to assess atrial size or abnormal ventricles (eg valvular heart disease). These are harder to cardiovert (also have a higher risk of embolism). Transthoracic echocardiogram is poor at detecting thrombus (transoesophageal echocardiogram is better)

Management
- Electrical cardioversion:
  - Indicated if onset is < 48 hours (chemical or electrical; if >48hrs, anticoagulate for 3-4/52 and bring them back for chem/elec CV) and no other risk factors (eg no atrial enlargement or ventricular abnormality)
  - Involves general anaesthetic and synchronised DC shock at 100 then 200J. Successful in about 85%.
  - May need anticoagulation for cardioversion (thrombi may get dislodged if normal rhythm returns)
- Chemical cardioversion:
  - Flecainide or
  - Amiodarone
  - Successful in 60 – 90%. (Digoxin does not cardiovert)
- > 50% revert in one year if no ongoing drug treatment
- Drug treatment:
  - 1. Rate control: β-blocker
  - 2. Rhythm control: consider digoxin (increases heart block → slows ventricle → improved pump action), flecainide (in those without structural heart disease), amiodarone (extensive toxicity issues) or sotalol
  - 3. Antithrombotic therapy: reduces annual risk in those at risk from 5% to 1.5% (60% relative risk reduction), with 1% having material anti-coagulant side effects. Use warfarin with a goal of an INR from 2 to 3. Use aspirin if warfarin contra-indicated (only 10 – 15% relative risk reduction)
<table>
<thead>
<tr>
<th>Agent</th>
<th>Action</th>
<th>Adverse effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amiodarone</td>
<td><strong>Prolongs action potential via Na/K/ATPase blocking</strong>, (\beta)-blocker activity: ↓HR. Class III. Hepatic metabolism, active metabolites. T½ of weeks.</td>
<td><strong>Pulmonary fibrosis</strong>, thyroid and hepatic dysfunction (do baseline bloods), muscle weakness, peripheral neuropathy, skin discoloration</td>
</tr>
<tr>
<td>Digoxin</td>
<td>↑vagal tone, renal elimination, T½ = 36 hours. Blocks Na/K/ATPase (\rightarrow) Ca (\rightarrow) <strong>Positive inotrope + prolonged AP</strong></td>
<td>Nausea, vomiting and confusion. ↓K (eg diuretics) (\rightarrow) ↑toxicity. Diltiazem, amiodarone and flecainide (\rightarrow) ↑digoxin concentration.</td>
</tr>
<tr>
<td>Diltiazem</td>
<td><strong>Ca channel blocker</strong>. Hepatic elimination. T½ = 4 hours.</td>
<td>Hypotension, headache, bradycardia, oedema, heart failure. ↑Digoxin levels.</td>
</tr>
<tr>
<td>Flecainide</td>
<td><strong>Na channel blocker</strong>. Renal and hepatic metabolism. T½ = 10 – 17 hours</td>
<td>Sudden cardiac death in those with structural heart disease, CHF or heart block</td>
</tr>
<tr>
<td>Metoprolol</td>
<td>(\beta)-blocker. Hepatic metabolism. T½ = 4 hours. High first pass metabolism</td>
<td><strong>Hypotension, heart block</strong>, worsening of heart failure if larger doses, <strong>asthma</strong></td>
</tr>
<tr>
<td>Sotalol</td>
<td>(\beta)-blocker, <strong>prolongs action potential</strong>. Renal elimination. T½ = 8 hours</td>
<td>Ventricular arrhythmia, hypotension, heart block, worsening of heart failure, asthma</td>
</tr>
</tbody>
</table>

**Atrial Flutter**
- Probably due to atrial re-entrant pathway around tricuspid valve orifice
- Atrial rate of 300
- Regular atrial saw tooth pattern with ventricular beat every 2:1, 3:1 or 4:1
- Will not respond to vagal manoeuvres or adenosine, needs electrical CV
- If unstable eg hypotension, synchronised counter-shock at 50J (treat as for AF)

**Wolff-Parkinson-White Syndrome**
- WPW has an accessory pathway – when the two waves collide they create the delta wave (see below)
- If AF occurs in WPW, can see VF/VT as the accessory pathway does not ↓ the rate of conduction of the atrial ectopic foci as the AVN does
- Delta wave seen as rapid conduction through the bundle of Kent (abnormal connection) and depolarisation of ventricular muscle; AVN then catches up + activates the rest of the ventricle:

![Image](Image)

**Sinus Arrhythmia**
- Normal sinus rhythm: rate 60 to 100 per minute, P wave upright in leads I, II and AVF
- **Sinus tachycardia:**
  - ↑discharge of sinus node. Rate is > 100/minute and regular
  - P wave is upright in leads I, II, AVF. Treat underlying cause
- **Sinus bradycardia:**
  - Constant and normal PR interval
- **< 60 bpm**: but this is relative. An athlete may normal at 40, and a hypovolaemic patient bradycardic at 65 bpm
- **Causes**: SA node disease, ↑parasympathetic tone, drug effect
- **Treat if hypotension or ventricular escape beats present**
- **Treatment**: atropine (0.6 mg) unless MI, trans-thoracic pacing, dopamine or adrenaline

**Sick sinus syndrome:**
- Common in elderly
- Bradycontin +/- arrest, AV block, or SVT alternating with bradycardia/asystole (Tachy-Brady Syndrome)
- Pace if symptomatic

### Tachycardias

- **Sinus** (as above): p waves + narrow QRS
- **Atrial tachycardia** (paroxysmal atrial tachycardia):
  - P waves with **different morphology** to normal
  - **Narrow QRS** complex (always exclude atrial flutter with 2:1 block)
  - Often abrupt onset, last for seconds to many hours, then abrupt offset
  - Rate is usually 160 – 200/min
  - Therapy: *vagal stimulation* (carotid massage, one side at a time), **adenosine**, amiodarone, beta-blockers or **digoxin**. If LV failure, chest pain or HR > 220 bpm then synchronised counter-shock

- **Supraventricular tachycardia**:
  - No p wave
  - Narrow QRS
  - Treat with *vagal manoeuvre* or **adenosine**

- **Ventricular tachycardia** (see cardiac arrest rhythms): wide QRS; treat with **amiodarone**/electrical cardioversion

### Ectopic Beats

- **Premature Atrial Complexes** (PAC): atrial ectopic beats. Small spike before premature but normal width QRS

- **Junctional escape**: “passive protective beat from a subsidiary pacemaker cell that occurs when the primary PM slows, pauses or is blocked” → no p wave but narrow QRS

- **Premature Ventricular Complexes** (PVC’s): bizarre, wide QRS complexes triggered by an **ectopic ventricular focus**. Most common post-MI rhythm. Unifocal PVC’s (each complex looks the same) or multifocal (each complex looks different from others)

- **R on T wave ectopic**: PVC landing on a T wave → can lead to VT/VF; tends to happen for the first couple of days post an MI

### Other Abnormal Rhythms

- **Junctional or Nodal rhythm**:
  - Originating from AVN
  - **Regular** rhythm, HR usually between 40-60 bpm but can have accelerated junctional rhythm (as below; between 60-130bpm)
  - **No detectable P wave** (due to retrograde firing into atrium) or inverted P-wave with short PR interval. P wave may be buried in QRS complex. Reduction in atrial filling. Treatment often not indicated

- **Idioventricular rhythm**: wide complex, no P waves, seen in reperfusion

### Heart Block

- **Atrioventricular block/Heart Block**: Delay or interruption in conduction between atrium and ventricle
First degree (partial block): PR interval prolonged beyond 0.2 secs (5 small squares). Often seen in normal people. Acute MI or Rheumatic Fever. No urgent action needed.

Second degree AV block (partial block): some impulses are conducted and some not ⇒ Heart disease. Often seen in acute MI:
  - Mobitz type 1 (Wenckebach): progressive prolongation of PR interval before an impulse is completely blocked – then sequence starts over. Usually transient and prognosis is good
  - Mobitz type 2: PR interval does not lengthen but some beats are not conducted. May lead to bundle branch block (→ wide QRS), transvenous pacing may be required
  - 2:1 block (every second beat gets through). Also 3:1 block. May need pacing if ventricular rate too slow.

Third degree (complete heart block): no conduction – either at AV, bundle of His or bundle branch level. More often fibrosis than ischaemia:
  - P waves firing regularly as are QRS complexes, however completely dissociated
  - At level of AV node: junctional escape pacemaker will fire at 40 – 60 bpm with normal QRS. Prognosis favourable. Due to ↑parasympathetic tone from inferior MI or drug effect
  - At infranodal level: Implies extensive disease of both bundles. Associated with anterior MI. Distal escape rhythm, slow rate (<40) plus wide QRS, possibly asystole. Management: transvenous or transthoracic pacing, dopamine or adrenaline, pacemaker

Anti-Arrhythmics

### Drugs for Acute, Life Threatening Arrhythmias

**Ventricular Tachycardia**

- Amiodarone
- **Lignocaine**: dose 1 – 1.5 mg/kg by slow iv bolus, followed by infusion of 1 – 4 mg/min. Reduce dose in heart failure, shock, > 70 years, β blockade & hepatic disease. Side effects include convulsions. Action on sodium channels reduces myocardial excitability, especially in ischaemic myocardium. Raises threshold for VF, and suppresses VT and ventricular ectopy. Should be considered in VF after 3 defibrillatory loops. No evidence of usefulness in converting VF but may prevent return to VF. Reduces blood pressure and slows the heart rate
- Bretyllium: anti-adrenergic, although initially causes adrenergic stimulation (for 20 minutes), raises VF threshold. Use if lignocaine fails
- Procainamide: powerful antiarrhythmic and strong negative inotropic agent, but slow to act. Use where lignocaine has failed to suppress recurrent ventricular tachycardia
- Magnesium: prevention and treatment of refractory ventricular arrhythmias

**SVT**

- **Adenosine**: slows sinus rate and AV conduction. Use for SVT due to re-entry. Very short T½
- Verapamil: Ca blocker. Suppresses pacemaker activity in SA and AV nodes. For SVT where adenosine has failed
- Amiodarone: delays repolarisation with less cardiac depression than other antiarrhythmics. Good for SVT, less so for ventricular arrhythmias. Via central line, long T½
- β-blockers: useful in treatment of hypertension, supraventricular arrhythmias and recurrent VT where LV function is not severely impaired. E.g. propranolol (unselective), atenolol (β1 selective), metoprolol (relatively β selective), labetalol (α&β selective, short acting, for acute hypertensive crises), sotalol (non-selective β blocker + antiarrhythmic), esmolol (ultra-short acting β block)

**Other Arrhythmias**

- **Digoxin**: ↑force of contraction and ↓AV conduction – for heart failure and supraventricular arrhythmias (particular AF). Avoid in recent MI, heart block, renal impairment, and hypokalaemia

Cardiology 60
• Dopamine: for treatment complete heart block. A catecholamine (sympathomimetic: dopamine, adrenaline, NA). Infuse at 5 – 20 μg/kg/min. Adjust to keep heart rate at 60 beats per minute. ↑renal blood flow (→↑renal output) through renal vasodilator and due to ↑CO and perfusion generally

Bradycardias
• Atropine: Competitive anticholinergic at muscarinic nerve endings. Enhances SA discharge and AV conduction. Use in bradycardia or AV block. Care in MI – may increase HR → extension of ischaemia
• Isoprenaline: β agonist - use for significant bradycardia refractory to atropine. Use dopamine or adrenaline first

Others
• Inotropes: dopamine and dobutamine (β1-agonists) – for supporting blood pressure once cardiac output has been established. Useful in cardiac failure secondary to ischaemia.
• Noradrenaline: intense vasoconstrictor – use for restoring MAP where vasodilation induced hypotension
• GTN: venous vasodilator - ↓blood pressure and improve artery blood flow. Preload and afterload reduced
• Diuretics: frusemide – also causes venodilation (→↓preload)
• Antihistamines: H1 antagonists (promethazine / Phenergan), H2 antagonists (ranitidine)

Emergency Cardiac Pacing
• Complete heart block most common indication. Also for non-response bradycardias and asystole with P waves
• Transcutaneous/transthoracic pacing: Electrodes over apex and sternum. Sedation + analgesia required. Temporary measure only
• Transvenous pacing: via arm or neck vein into right atrium or ventricle

Valvular Heart Disease
• = Stenosis, insufficiency/regurgitation or mixed
• Insufficiency may be due to diseased cusp or supporting structures (valve ring, cordae tendinae, papillary muscles, ventricular wall). Can be acute or chronic
• Stenosis: disease of valve cusps, usually always chronic
• See Heart Murmurs, page 32 for clinical descriptions

Aortic Stenosis
• Compared with regurgitation/incompetence:
  - Have different effects on the LV (can’t have severe stenosis and severe regurgitation together):
    - Stenosis: ↑pressure but no ↑ in volume. LV tolerates pressure loads less well than volume loads → stenosis is the worse of the two
    - Regurgitation: ↑volume but no ↑ in pressure. However, some ↑ in afterload due to ↑stroke volume
• Causes of aortic stenosis:
  - Post inflammatory scarring (eg rheumatic fever): 10%
  - Degenerative (senile) aortic stenosis: commonest, in 8th – 9th decade
  - Calcification of deformed valve in 6th – 7th decade (associated with coarctation ⇒ check for radio-femoral delay)
  - Congenital stenosis/bicuspid valve
  - Infective
• Pathophysiology:
  - LV outflow obstruction ⇒ gradient between the LV + ascending aorta
  - LV has to work harder to eject blood ⇒ LVH
  - ↓coronary flow ⇒ exertional ischaemic chest pain
• Symptoms: Occur late
  - 1. Exertional dyspnoea and chest tightness
  - 2. Exertional syncope: due to inability to increase CO and transient ventricular arrhythmias
  - 3. Angina/MI, fibrosis, ventricular arrhythmia and sudden death due to impact on myocardial O2 supply and demand:
    - ↑↑ O2 demand due to ↑pressure and LV mass (↑LV workload ⇒ concentric hypertrophy)
    - ↓down coronary blood flow due to ↓diastolic aortic pressure ↑coronary vascular resistance and ↑systole compared with diastole ↓time for perfusion
    - ⇒ ischaemia
  - No pulmonary oedema unless eg mitral problems secondary to LV hypertrophy, etc
• **Signs:**
  - **Sounds:**
    - *Harsh systolic ejection murmur* (unless in severe LV failure) +/- *systolic ejection click* and a short aortic diastolic murmur. Heard in base, apex and carotids
    - May have paradoxical (reversed) splitting of S2 if severe stenosis or LBBB. 3rd and 4th sounds common
  - **↓ Pulse pressure and low blood pressure**
  - **Pulsus parvus et tardus** (slow rising + low amplitude)
  - **LV hypertrophy** on ECG or x-ray and heave on examination. Palpable LV hypertrophy with a dynamic quality is more related to incompetence – the ventricular impulse reflects stroke volume more than pressure
  - **LV failure:** progression from LV hypertrophy to LV dilation in late stages
    - **AF** in 10%
  - **Diagnosis:**
    - Often a discrepancy between symptoms and severity. Pre-symptomatic progression is highly variable
    - Usually at least some regurgitation as well
    - **ECG:** LVH, occasionally left or right BBB
    - **ECHO:** pressure differential with Doppler → estimate valve area
      - Pressure gradient of > 40mmHg = < 1cm² aortic valve area = severe AS
      - ↓ valve area → ↑ velocity (use Doppler)
    - **CXR**
    - **Cardiac cath:** prior to surgery to assess coronary artery disease and valve gradient
  - **Gross:**
    - Look for commissural fusion (rheumatic)
    - Heaped up calcified masses in leaflets. Beginning at the base ⇒ senile, beginning at the edge ⇒ abnormal valve
  - **Management:**
    - If mild/moderate then monitor + medical therapy
    - If symptomatic + ↓LV function or abnormal stress echo → surgery (mechanical valve requires warfarin, therefore use freestyle if possible) or balloon valvuloplasty (in non-surgical candidates due to CVA risk)
    - Fix/replace valve **before** LV failure
    - **Medical management:** treat underlying coronary artery disease, hypertension, dyslipidemia, stop smoking
  - **Complications:**
    - Sudden death
    - LVF
    - Conduction defects
    - Infective endocarditis
    - Embolisation
  - **Differential:**
    - Can rarely be due to supraventricular or subvalvular lesions, with no problem with the valve
    - Left ventricular failure
    - Hypertrophic obstructive cardiomyopathy: pulse is jerky and upstroke rapid. Longer, harsher murmur **best heard at the left sternal edge**
    - Hard to confuse with mitral regurgitation (!!!): Pansystolic murmur and rapid upstroke
    - Coarctation
  - **DDx of a collapse:**
    - Arrhythmia
    - Vasovagal
    - Neuro cause eg seizure
    - MI
    - LVOT obstruction (AS, HOCM)
    - Drugs eg anti-hypertensives

### Aortic Regurgitation

• **Causes:**
  - Intrinsic valvular disease:
    - Acute lesions: *rheumatic fever, infective endocarditis* (have high index of suspicion), traumatic rupture, *aortic dissection* (may also have dissected coronary arteries → MI)
Chronic lesions: congenital lesions, **rheumatic heart disease**, arteritis, aortic aneurysm, **collagen diseases**, **ankylosing spondylitis** and Reiter’s Syndrome (may be secondary to aortitis)

- **Aortic root disease:**
  - Degenerative aortic dilatation
  - Syphilitic aortitis, ankylosing spondylitis, rheumatoid arthritis, Marfan’s syndrome

### Key features:
- LV hypertrophy
- Large aorta
- ↑ stroke volume
- **Wide pulse pressure** eg 140/50 (↑ systolic due to extra work of the heart, ↓ diastolic due to back flow)

### Symptoms:
- Generally well tolerated if chronic
- Acute: *dyspnoea* – often paroxysmal, orthopnea, pink frothy sputum. Chest pain, sudden death, etc. If sub-acute, possibly embolisation
- Chronic: symptoms unrelated to severity. Either awareness of ↑ force of contraction (palpitations) or LV disease/failure

### Signs:
- Prominent pulsations in the neck (**Corrigan’s Sign**)
- Collapsing peripheral pulses (water-hammer)
- ↑ PP
- Prominent apex beat over a wide area
- High-pitched, blowing early diastolic murmur beginning immediately after S2. The more severe the longer it lasts. Systolic flow murmur. Described as the absence of silence after S2 (lub dup-haa)
- Quinke’s sign: Pulsatile blanching of the nail bed

### Pathogenesis:
- **Acute:**
  - ↑ LV blood volume → ↑ left atrial and pulmonary pressure → oedema
  - ↑ Pressure inside a non-compliant pericardium → ↑ RH pressures
  - ↓ **Myocardial flow due to ↓ aortic diastolic pressure** and constricted pericardium → ischaemia, further dysfunction, etc
- **Chronic/Gradual:**
  - SV ↑ but CO ↓ → ↑ volume and pressure load systemically → LV dilatation + hypertrophy + ↑ afterload to ↑ BP
  - → eccentric hypertrophy with low filling pressure. ↑ SV → ↑ systolic pressure → baroreceptor reflex → peripheral vasodilation → further widening of the pulse pressure. Copes with tachycardia better than stenosis: ↓ proportion of cycle in diastole → ↓ proportion of blood flowing back into the ventricle. However, ↑ peripheral resistance (eg cold, iso- tonic exercise, sympathetic nervous stimulation) → ↑ pressure load on the heart

### Complications:
- LV failure + myocardial fibrosis (secondary to hypertrophy, ischaemia, etc) late in the progression
- Infective endocarditis
- Conduction defects less common
- No pulmonary oedema unless LV hypertrophy

### Treatment:
- ↓ afterload with CCBs/ACEi
- Need AVR: timing of surgery is key → if aortic dissection → urgent repair. Aim is to have surgery prior to LV damage from volume overload

### Differential diagnosis:
- Pulmonary regurgitation + pulmonary hypertension
- Other causes of rapid run-off: patent ductus, arterio-venous fistula

### Aortic Dissection
- Medical emergency
- Risk factors = hypertension, Marfan’s, Ehlers-Danlos
- Symptoms = tearing sensation, back/chest pain, breathlessness
- Signs:
  - **BP different between arms** (subclavian artery involvement)
  - Ischaemic changes in II, III, aVF if dissection into RCA
• Ix: CT, CXR, TOE (best for ascending aorta)
• Treatment:
  ➢ Analgesia
  ➢ Aggressively lower BP (with eg labetalol)
  ➢ If type A dissection (ie involving ascending aorta) → urgent surgical repair
  ➢ If type B (descending aorta) → medical management in the first instance

Mitral Stenosis
• Causes: *rheumatic heart disease* (most common), congenital, infection (less common than aortic) → fusion of the leaflets
• Symptoms:
  ➢ Dyspnoea, PND
  ➢ Fatigue
  ➢ Chest pain
  ➢ Haemoptysis secondary to *pulmonary oedema*
  ➢ Arrhythmia (→ palpitations)
  ➢ RH signs if pulmonary hypertension
• Pathophysiology:
  ➢ Diastolic gradient between LA + LV → ↑LA size + ↑ flow into PA
• Signs:
  ➢ *Loud S1*, opening snap after S2 (loudest at apex)
  ➢ *Long, loud diastolic murmur accentuated just before S1* (atrial systole – not if AF). Loudest with **bell** at apex + left lateral side
  ➢ *Pulmonary oedema* is worse than in other causes (eg mitral regurgitation)
  ➢ AF
  ➢ Hypoxia due to alveoli being full of fluid
  ➢ If pulmonary hypertension then low cardiac output failure → thin patient, peripheral cyanosis, cool extremities, small pulse volume
  ➢ Dilated veins and cyanosis of cheeks = **mitral facies**
• Leads to:
  ➢ LA enlargement:
    o → *pulmonary hypertension* (> 7.5 mmHg/L/min; >25mmHg mean) and pulmonary oedema
    o → AF
  ➢ Non-infectious bronchitis
• Investigations:
  ➢ ECG: **broad P wave**, RVH (NB – LV enlargement is not typical – key differential with mitral regurgitation)
  ➢ CXR: LA enlargement, RH enlargement
  ➢ ECHO: good at imaging the mitral valve
  ➢ Differential: Left atrial myxoma (much less common)
• Treatment:
  ➢ Prophylaxis for RF (till 20) and infective endocarditis (eg dental work)
  ➢ Surgery: valvotomy (valve repair), balloon valvuloplasty, replacement
  ➢ *Medical management*: diuretics, **warfarin** (if AF)
  ➢ Treat AF: cardiovert (chemical/DC with anticoagulation), control rate (eg digoxin)

Pulmonary Hypertension
• >25mmHg mean pressure
• Causes = MS/LVH/COPD/interstitial lung disease/chronic PEs/idiopathic/autoimmune
• Treat with **sildenafil** (fix underlying cause if possible)

Mitral Regurgitation (MR)
• Causes:
  ➢ Abnormalities of leaflets:
    o *Rheumatic heart disease* → post inflammatory scarring
    o Infective endocarditis
    o Degenerative change
- Mitral valve prolapse. Immaterial haemodynamic changes (\(\Rightarrow\) normal heart size, etc). Common - 75-10% of young women. Mid/late systolic murmur +/- mid/late systolic click. Complications (3% of affected) are infective endocarditis, mitral regurgitation, and embolism of leaflet thrombi
  - Congenital
  - SLE can cause Libman-Sacks endocarditis: sterile immune mediated endocarditis mainly affecting underside of mitral valve (cf other vegetative endocarditis on top)

- Abnormalities of tensor apparatus:
  - Acute MI: ruptured papillary muscle
  - Previous MI: fibrosis or rupture of papillary muscle

- Abnormalities of LV cavity or valve ring:
  - Calcification of mitral ring (annulus; especially elderly women)
  - LV enlargement (whole ventricle expands). Dilatation of the mitral annulus and lateral displacement of the papillary muscles
  - Hypertrophic cardiomyopathy (thickening in parts of wall – e.g. enlarged septum disrupts flow to aortic valve). Anterior displacement of the anterior leaflet

- Existing MR – begets MR. Enlargement of LV pulls posterior leaflet away from the mitral orifice

- Pathophysiology:
  - Systole: antegrade ejection + regurgitant volume \(\rightarrow\) dilated LV \(\rightarrow\) myocardial damage \(\rightarrow\) CHF
  - CHF \(\rightarrow\) loss of contractility \(\rightarrow\) more dilatation \(\rightarrow\) valve pulled further open \(\rightarrow\) more regurgitation

- Signs:
  - Pansystolic murmur: regurgitation throughout the whole of systole. Loudest at apex. Radiates over precordium and into axilla. No S1. No opening snap unless concurrent stenosis. Early diastolic flow murmur
  - In severe MR, Aortic valve closes prematurely \(\rightarrow\) split S2
  - S3 caused by sudden tensing of papillary muscles, cordae tendiniae and valve leaflets
  - Small volume pulse
  - Maybe AF

- Significant difference between acute and chronic presentations:
  - Pulmonary oedema + RV overload much more significant if acute. In chronic, enlargement of LA \(\downarrow\) pulmonary ‘back flow’
  - AF better tolerated than in mitral stenosis
  - RHF rare unless acute presentation or LVF

- Diagnosis:
  - ECHO: look at jet colour
  - ECG: LVH
  - CXR: cardiomegaly
  - Cardiac cath: right + left heart pressures + assessment of coronary arteries

- Treatment:
  - Surgery depending on symptoms + LV function
  - Medical management: vasodilators eg ACEi

- Leads to:
  - Eventually leads to LV and LA hypertrophy (may take decades)
  - AF common – mostly correlated with age
  - Infective endocarditis (in 20%)
  - Systemic embolisation
  - Pulmonary hypertension (but much later compared with mitral stenosis)

- Differential:
  - Hypertrophic cardiomyopathy: both long systolic murmurs, but MR radiates to the axilla, hypertrophic cardiomyopathy radiates centrally
  - VSD

Tricuspid Regurgitation

- Commonest cause is RHF/enlargement secondary to left ventricular failure. Left atrium is also likely to be enlarged \(\rightarrow\) AF common too

Infective Endocarditis

- = Infection of mural endothelium or heart valves. May also include the proximal aorta
- See also Rheumatic Fever, page 934
Classification

- Now all called infective endocarditis
- Acute bacterial endocarditis (ABE):
  - < 6 weeks duration
  - Virulent organisms eg staph
  - Normal valves (eg IVDU)
  - Bulky friable vegetations: may extend to adjoining endocardium and cordae tendinae. Destructive (directly proportional to virulence of organism). Much more destructive than Rheumatic Fever. Microscopically vegetations show a suppurative exudate, fibrinous thrombi, and large bacterial colonies destroying valve substance
- Sub-acute bacterial endocarditis (SBE)
  - > 6 weeks duration
  - Avirulent organisms: normal flora eg strep viridans (normal oral commensal)
  - Abnormal valves
  - Evolution slower, gradual valvular dysfunction, flatter vegetations with deeper chronic inflammatory component including a vascular fibrous tissue healing response

Predisposing Factors

- 1950s: rheumatic heart disease (most cases) – affect 15 – 35 year olds
- 1990s: degenerative, rheumatic, congenital (low pressure side of a septal defect gets infected), prosthetic valves – affects 50 year olds
- Circulatory factors:
  - Regurgitant blood stream (incompotent valve)
  - Large pressure gradient across valve (i.e. rarely right heart except IVDU)

Anatomic Sites of Infection

- Nearly always where there’s a pre-existing abnormality
- Usually on the top of the valve
- Incompetent mitral and aortic valves: 40% mitral, 40% mitral and aortic valve
- Calcific aortic stenosis
- Prosthetic heart valves
- Congenital septal or valve defects
- Also in Intra-venous drug users (IVDU) with normal hearts (Right side commonly affected).

Causal Organisms

- In theory: any organism (including fungi and chlamydiae)
- In practice:
  - Native valves:
    - Streptococci: 70%
    - Staph: 20 – 25%
    - Miscellaneous (including enterococci) 5%
    - Culture negative 5%
  - Prosthetic valves:
    - < 3 months (early PVE): staphylococci > streptococci
    - > 3 months: staph = streptococci
- Streptococcal causes of endocarditis:
  - Oral Commensals: Viridans Strep – more in younger people, good at sticking, don’t cause much infection elsewhere: S. sanguis, s. salivarius, s. mitis, s. milleri, s. mutans
  - Faecal: called enterococcal
- Staphylococcal causes:
  - S. aureus: coag +ve – 60% mortality (common in intravenous drug user)
  - S. epidermidis + 20 others: coag –ive – 40% mortality
- Miscellaneous causes: Haemophilus, Actinobacillus, Cadriobacterium/Candida Albicans (↑ in prosthetic valves, mortality 100%), Eikenella, Kingella

Pathology

- Endocarditis = thrombus formation on valve cusps:
  - Mirant (sterile due to hypercoag state)
  - Auto-immune (eg Libman-Sacks due to SLE)
Rheumatic
Infective

Bacterial endocarditis:
- See vegetations + thrombus + bacteria
- Acute (virulent MO, normal valve), can see regurg
- Subacute (low virulence MO, abnormal valve), can see regurg

Pathogenesis of Infection
- Abnormal valve → NBTE (non-bacterial thrombotic endocarditis) – little blood clots – we all have them but ↑ risk on a deformed valve → transient bacteraemia from possibly trivial infection → adherence of bacteria → acute inflammatory reaction – WBCs, fibrin & platelets laid down → mature vegetation – sheds bacteria

Diagnosis
- Existing immunosuppression, neutropenia, diabetes, and alcohol increases risk
- Symptoms:
  - Always a differential in pyrexia of unknown origin
  - Malaise, weakness
  - SOB
- Signs:
  - Heart murmur, isolated petechiae (eg nail beds, retinal) and splenomegaly significant
  - Janeway lesions (rare as hen’s teeth), Osler’s nodes (less rare but still rare), splinter haemorrhages, Roth’s spots
- Ix:
  - Blood culture: 3 times – organism load in blood may be low. ALWAYS do before ABs → very hard to treat, and need to ID correct organism to target therapy
  - FBC: anaemia of chronic disease (if chronic), ↑ WCC
  - ↑CRP/ESR
  - ECHO (although may miss flat vegetations, therefore use TOE)

Complications
- Valvular insufficiency or stenosis (aortic stenosis → LV hypertrophy → coronary artery insufficiency)
- Local extension: down septum, into wall of aorta, perforated valve, suppurative pericarditis, ring abscesses
- Embolism: small infarcts (e.g. in kidney cortex) or abscess (each emboli has bacteria in it) eg in lungs (do not anticoagulate as can → reperfusion injury)
- Mycotic aneurysms, focal and diffuse glomerulonephritis
- Septicaemia
- Antigenaemia: antigen/antibody complexes → skin lesions, clogged up kidneys

Treatment
- Identify causal organism with antibody sensitive tests (MIC & MBC)
- Treat with 2-4/52 tailored IVABs
- If non-responsive or embolization or valve regurgitation → surgery
- Empiric antibiotic therapy - regimes:
  - Staphylococcal: flucloxacillin (or vancomycin) 2g iv 4 hourly for 2 weeks, then 1 g orally 6 hourly for 4 weeks
  - Streptococcal: penicillin + gentamycin or amoxycillin + gentamycin iv for 2 weeks, then 4 weeks oral

Heart Failure

Background
- = at normal filling pressures, the heart is unable to pump sufficient blood to meet the metabolic demands of the body’s tissues
- = Pump function is inadequate to maintain body homeostasis → Na and H2O retention
- ↑ Left atrial pressure above 25 mmHg → transudate of ECF into alveoli → pulmonary oedema
- 20% have infarcts without knowing it
- Strong association with old age. A common diagnosis amongst the most disabled elderly
- Normal EF = 55%-75%
- Preload = filling
- Afterload = resistance
Preload/afterload analogy: setting = room full of people, fire alarm rings. Preload = the number of people in the room, the afterload is the size of the door or the number of people in the corridor outside the room

Most HF is diastolic dysfunction

Symptoms may be non-specific: ↓energy, nausea, poor appetite, poor mobility, confusion, ↓sleep etc

**Classification**

- Classify as:
  - **High output failure**: due to ↑O2 requirements and heart can’t keep up. Happens quicker if pre-existing heart disease. Eg anaemia, pregnancy, hyperthyroidism, Paget’s disease. Initial features of RH failure. Progresses to LH failure
  - **Low output failure**: inadequate output (ejection fraction < 0.35 – 0.40) or only adequate with high filling pressure:
    - Excessive preload: eg mitral regurgitation or fluid overload
    - Pump failure due to heart muscle disease, restricted filling, inadequate heart rate (eg heart block, post MI)
    - Chronic excessive afterload (eg aortic stenosis, hypertension)

- Can also classify as:
  - **Diastolic dysfunction**: normal EF (>40%) eg poor filling due to, for example, tamponade or restrictive cardiomyopathy
    - Result of impairment in heart's ability to relax → is an increase in the ventricular diastolic pressure at any given diastolic volume. The heart doesn’t let blood in well
    - Causes include restrictive and hypertrophic cardiomyopathies, ischaemic states, hypertension
    - S & S: SOB, wheeze (due to bronchial constriction as bronchiole wall fills with fluid), pleural effusion, creps
  - **Systolic dysfunction**: abnormal EF (<40%) eg poor contraction due to a large floppy heart
    - Result of an impaired inotropic state; this is failure of the heart's actual pumping capacity → it can’t get blood out
    - Causes include idiopathic dilated cardiomyopathy, or myocardial infarction that damages the muscle
    - S & S: skeletal muscle fatigue, cool peripheries (SNS), tachycardia, weak pulse, peripheral cyanosis

- **LHF → pulmonary oedema**: Pathophysiology: ↓EF → banking up of fluid in LV → ↑LA P → ↑PV P ↑ capillary P → ↑interstitial fluid:
  - ↓ gas exchange (as ↑ fluid in interstitium) → cyanosis
  - Pulmonary oedema (fluid pushed from interstitium into alveoli)
  - Pleural effusion (fluid pushed out of lung and into pleural space)

- Contractile failure, caused by:
  - Ischaemic heart disease
  - Hypertension
  - Aortic and mitral valve disease (aortic stenosis/rheumatic heart disease)
  - Myocardial disease
  - Hypertrophied L ventricle → secondary atrial enlargement → atrial fibrillation

- Leads to:
  - Renal flow/GFR → renin release → ATII →
    - Vasconstriction + ↑TPR
  - ↑SNS drive + ↑TPR/HR
  - aldosterone + Na and H2O retention → oedema
  - Pulmonary hypertension → pulmonary oedema and bronchospasm
  - LVF leads to LV dilatation → this is useful initially but the shape change leads to ineffective contraction + the MV annulus gets pulled apart, leading to MR

- Symptoms:
  - Exertional dyspnoea
  - Orthopnoea, PND
  - Wheeze (‘cardiac asthma’)
  - Cough + pink froth, haemoptysis
  - Fatigue

- Signs:
  - Tachypnoea, tachycardia
  - End-inspiratory basal crackles
  - Dullness to percussion over lung bases eg pleural effusion
  - S3, cardiomegaly
  - Cyanosis
• RHF → peripheral oedema:
  ➢ Due to:
    o LHF → pulmonary hypertension → RV failure
    o Cor pulmonale (R ventricle ↑ pressure due to disease of lung or pulmonary vasculature)
    o Constrictive pericarditis
  ➢ Symptoms: fatigue, abdominal pain, oedema, anorexia, wasting, weight gain
  ➢ Signs:
    o Enlargement of liver, spleen, kidneys, subcutaneous tissues and brain
    o ↑JVP, pulsatile liver, hepatomegaly, pitting oedema, ascites, RV heave, palpable P2
• Congestive HF: both sides, but really implies RH involvement

Aetiology
• Age associated changes:
  ➢ Reduction in β adrenergic responsiveness → ↓inotropic response and ↓vasodilation
  ➢ Increased arterial stiffness → ↓compliance → ↑afterload
  ➢ Alterations in cardiac filling: ↑connective tissue content of myocardium → stiffer ventricle → filling more dependent on atrial contraction → ↑pressure and size of left atrium → predisposes to AF (→ further filling problems)
  ➢ Failure of reserve capacity of mitochondria
• Age associated diseases:
  ➢ Hypertension → risk factor for atherosclerosis, and ↑size and stiffness of left ventricle. By the time they have heart failure, may no longer have hypertension as they can’t sustain the cardiac output necessary to be hypertensive
  ➢ Coronary artery disease
  ➢ Also ↓respiratory function and ↓renal function
• Precipitating factors unmask the subsequent reduced cardiac reserve, eg arrhythmia, infarction, AF, infection, thyroid disease, anaemia, PE, COPD → hypoxia, DRUGS, etc
• Decreased perfusion due to decreased pump action → ↓kidney perfusion → ↑renin/aldosterone → ↑blood volume to try and increase pre-load and push heart up the starling curve (however, they’re often into negative marginal gain from increased volume). However, ↑ BP also raises after-load and increases work of the heart → ↑ischaemia
• Cardiac dysfunction due to:
  ➢ Disruption of circulatory system
  ➢ Disorders of conduction
  ➢ Lesion preventing valve opening
  ➢ Pump failure (contraction/dilation) → ↓SV and ↑EDV → ↓CO
• Beriberi = heart failure due to deficiency of Vitamin B1 (Thiamine): bradycardia, premature ventricular beats, VF, AF, and heart block

Differential
• Must be able to prove the heart is the problem
• Otherwise consider:
  ➢ Renal failure (eg nephritic syndrome) → oedema
  ➢ Liver disease or malnutrition → ↓albumin → oedema

Investigations
• Bloods: FBC, Cr, electrolytes, Trop T, BNP, U&E, glucose, TFTs, LFTs, Cholesterol, ?ABG
• ECG
• CXR:
  ➢ Dilated upper lobe vessels
  ➢ Cardiomegaly
  ➢ Pulmonary oedema: Kerley B lines
  ➢ Pleural effusions
  ➢ Although concomitant COPD may obscure changes in heart size and pulmonary vasculature
• Echocardiogram:
  ➢ LV hypertrophy (normal thickness 1 cm), valve regurgitation or stenosis (check rate of flow), areas of hypokinetic myocardium
Normal velocity of blood through the heart = 1 m/sec. If aortic valve narrowed then faster flow then > 3 m/sec (same amount of blood through smaller space). Velocity between ventricles and aorta is proportional the change in pressure

Angiography

Treatment

Principles:
- If possible, reverse underlying process (e.g., thyrotoxicosis)
- Halt progression
- Alleviate symptoms

Acutely:
- Treat cause if any: hyperthyroid, hypertension, anaemia, alcohol, valve lesions
- Symptomatic treatment:
  - Sitting position → ↓ venous return
  - O2 therapy (care with CO2 retainers)
- Frusemide 40 – 80 mg iv (if not already on it) → ↓ afterload, vasodilation (↓ preload and ↓ ECF volume).
  - Watch for ↓ K+
  - Don’t worry about whether pt is hypotensive – frusemide will not ↓ BP significantly (fluid will move from interstitium back into vasculature)
- Morphine 5 – 10 mg iv: (as long as not low BP) a potent vasodilator (↓ preload → ↓ work of heart and ↓ pulmonary capillary pressure), bradycardic and sedative effects
- Also consider:
  - Aminophylline 250 mg over 5 – 10 min (+ive inotrope, mild diuretic, ↓ bronchospasm. iv form of theophylline)
  - Blood pressure control: Nitrates, Oral ACE inhibitors (↓ preload and afterload, and ↑ heart remodelling)
  - Arrhythmia control: Digoxin, amiodarone
  - Inotropes: dopamine, dobutamine
  - DVT prevention
  - Not β-blocker acutely, but ↑ use in chronic management
- Intensive treatment:
  - Mechanical ventilation with positive end-respiratory pressure (CPAP) → ↓ preload and ↑ intra-alveolar pressure
  - Aortic balloon pump:
    - Inflates during diastole, deflates during systole – acts as an auxiliary ventricle
    - ↑ coronary artery flow as blood is pushed back and into coronary arteries (requires competent aortic valve)
    - ↑ renal (and peripheral) flow as blood is pushed forward
    - ↓ afterload
  - Heart transplant
  - Monitoring: weight, fluid balance, telemetry and U&Es (e.g., ↓ K)

Chronic:
- Balancing act, especially in elderly: eg risks of polypharmacy, comorbid disease, what is the goal of treatment, postural hypotension if over-treated → falls, etc
- Non-drug treatment:
  - Stop smoking
  - Control of blood pressure, DM, ↓ alcohol
  - Exercise within ability to tolerate it (prevent further deterioration and problems of immobility)
  - Dietary advice: ↓ weight, ↓ Na and H2O depending on weight (ie educate patient about illness and to monitor weight daily), low fat, high calorie
  - Physio: mobilisation and breathing control
  - Vaccination against influenza and pneumococcus
- Principles of pharmacological management:
  - ↓ the effects of ATII:
    1. Use ACEI or ARBs
    2. Treat HR with β-blockers (seems counter-intuitive to ↓ the force of contraction but in HF, SNS is thought to get a bit confused and goes into overdrive, therefore there is a need to calm it down; aim to get rid of fluid first, and then add β-blockers slowly)
    3. Treat fluid overload with diuretics (frusemide/spironolactone)
    4. Treat AF if present with digoxin
‘Core’ drugs:
- **β-blockers**, used cautiously, are now proven:
  - If ↑sympathetic drive is causing a relative tachycardia then β-blockers will help (will get worse on β-blockers if reliant on sympathetic drive to maintain CO)
  - Criteria: chronic, stable, LV systolic impairment (ejection fraction < 45%), resting HR > 50 bpm, no contraindications (eg asthma, AV block). Not if very low ejection fraction
  - Start at low dose, titrate up as outpatient with carvedilol (α + β blocker) or metoprolol
  - Clear instructions to patient of symptoms of deterioration
- **ACE Inhibitors**: ↓dyspnoea, ↑exercise tolerance, ↓mortality, ↓admissions. Even if low BP
- **Diuretics**: for all people with volume overload and CHF. In elderly, effect of loop diuretics may be delayed through poor absorption, and ↓elimination → ↑effect. Accumulation can → deafness. Limited if poor renal perfusion. May exacerbate urinary incontinence. Low dose spironolactone may be useful (if high dose and ACE inhibitor → ↑K and ↓renal function)
- Aspirin

**Second line drug treatment for systolic dysfunction:**
- Spironolactone
- Other vasodilators (e.g. nitrates, calcium channel blockers): ↓work of heart, ↑efficiency of heart, peripheral redistribution of blood. But problems with postural hypotension (especially if already volume depleted – check for hyponatraemia)
- Inotropic agents if low BP, eg digoxin. Controversial in heart failure, main role is in AF
- Limited role for anti-arrhythmic agents

**Drug treatment for diastolic dysfunction (ie normal ejection fraction):**
- Avoid over diuresis
- Tolerate AF poorly
- Aspirin
- β-blockers

**Statins if cholesterol > 4 mmol/l**

---

**Myocarditis**
- = Inflammation of the myocardium, excluding IHD
- Suppurative myocarditis: focal necrosis, pyogenic abscesses or diffuse spreading infection. Neutrophil infiltrate

**Interstitial myocarditis:**
- Characteristic of viral myocarditis
- Occurs mainly in children and young women
- Most have benign, self limiting course
- Microscopic appearance: oedema, chronic inflammatory cells
- Parenchymatous myocarditis: diffuse, patchy destruction of muscle cells. Associated with diphtheria, typhoid, some β haemolytic streptococci, protozoa and parasitic infections
- Miscellaneous: Idiopathic (giant cell, Fiedler’s). Also autoimmune disease or hypersensitivity to drugs

---

**Cardiovascular Pharmacology**

- For Anti-coagulation, see Anticoagulant Treatment, page 103

*Idiot’s Guide*

- Always push non-drug treatment: lifestyle, smoking, etc
- Hypertension:
  - ABCD
  - Thiazides (not diabetics or gout)
  - β-blockers (not COPD/asthma)
  - Maybe ACE inhibitors or CCBs
- Angina:
  - β-blockers
  - Aspirin
  - Nitrates
  - Maybe CCBs (↓HR), statins, ACE (if hypertension/diabetes)
- Post MI:
  - Aspirin
- β-blockers
- ACEi if ↓LVF (or Phil Matsis)
- Statin
- Clopidogrel for varying length of time depending on intervention

- Heart failure:
  - ACEi
  - Diuretic
  - Aspirin
  - Maybe β-blockers, spironolactone, other vasodilators, statins, digoxin, etc

- Atrial fibrillation:
  - Rate control with β-blockers
  - Rhythm control with digoxin
  - Antithrombotic therapy with warfarin

**ACE Inhibitors**

- Block the formation of angiotensin II →diuretic, ↓peripheral vascular resistance, and better tissue remodelling/healing of damaged myocardium. But 30% of hypertensives are non-responders
- Eg Captopril, quinapril
- Many patients (especially the elderly) don’t respond on its own. Synergistic effect with diuretic (ie shifts ACE inhibitor dose-response curve to the left). If it’s not working, add in a low dose diuretic

- Adverse effects:
  - Metabolic taste, hypotension (especially with first few doses), hyperkalaemia, angioedema, neutropenia, proteinuria.
  - ↓Renal function, especially if existing renal impairment (↑efferent flow →↓glomerular filtration)
  - Dry cough (due to ↑bradykinins). If cough a problem, then use an angiotensin II receptor antagonist (eg Losartan)
  - Rash: may be long time after starting, especially captopril due to sulphur group

- Interactions:
  - Diuretics: hypotension + ↓renal function
  - NSAIDs: renal failure, hyperkalaemia

- Contra-indications:
  - Bilateral renal artery stenosis
  - Pregnancy, breast feeding
  - LV outflow obstruction (eg Aortic Stenosis)
  - Marked hypotension
  - Other drugs: K supplements, Li, NSAIDs

- Monitor for: ↓Na, ↑K, Cr > 200, rare neutropenia

**Diuretics**

- Common types:
  - Thiazides eg bendrofluazide. Flat dose response curve so ↑dose only ↑side effects. No ↑effect from a dose above 2.5 mg. Effect: mainly vasodilation, also inhibit Na/K co-transport in distal convoluted tubule →salt and water loss. VERY cheap. Take 6 – 8 weeks to work
  - Frusemide: blocks Na/K/Cl transport in Loop of Henle. No role in lowering blood pressure

- Interactions:
  - General: NSAIDs, lithium, digoxin, ACE inhibitors, corticosteroids
  - Loop: antibiotics
  - Thiazides: calcium supplements

- Adverse drug reactions are dose dependent (⇒ use in low dose):
  - General: dehydration, electrolytes, lipids, endocrine, skin
  - Loop: ototoxicity, ↓K, ↓Ca. Frusemide →water rush. Difficult if you’re out and about →↓compliance
  - Thiazide:↓K, ↑Ca, ↓Mg, ↑urate (+/- gout), ↑lipids, progressive glucose rise over years, thrombocytopenia, impotence in high doses

- Spironolactone:
  - Acts at distal renal tubule as an aldosterone antagonist
  - Adverse effects: hyperkalaemia, diarrhoea, gynaecomastia
  - Interactions: ACE inhibitors, digoxin
\textbf{\(\beta\)-blockers}

- Action (effect takes 2 – 4 weeks):
  - Renal effect (↓renin)
  - Pre-synaptic \(\beta\)-receptor blocker
  - ↓Cardiac output due to ↓rate and strength of myocardial contraction (→↓O2 consumption). Acutely →↑TPR (so not if peripheral vascular disease otherwise ↑ischaemia). ↓CO resolves over time
  - ?Central action

- Use in angina, hypertension, heart failure

- Classified by:
  - Lipid vs H2O soluble
  - \(\beta\)-receptor selectivity
  - \(\alpha\)-blocking activity (eg labetalol →prone to postural hypotension)

- Contraindications:
  - Arrhythmias: bradycardia and AV block
  - Asthma
  - Peripheral vascular disease: lead to unopposed \(\alpha\)-1 stimulation
  - Diabetes: block the symptoms of hypoglycaemia, potentiate effects of insulin and oral hypoglycaemics
  - Overt cardiac failure: negative inotropes – but still OK in heart failure at low dose

- Adverse effects (generally dose dependent):
  - Common: Lethargy, heavy legs (slowed up feeling due to ↓CO), cold extremities, ↑lipids, headaches, nightmares (in lipid soluble propranolol, not water soluble atenolol)
  - Less common: GI disturbances and rashes
  - Rapid withdrawal →angina, arrhythmias due to \(\beta\)-1 up-regulation

- Interactions with:
  - CCBs eg verapamil: severe bradycardia
  - Cimitidine: inhibits metabolism →potentiates effect

- Consider \(\alpha\)-blockers for hypertension – but not as first line agents (may exacerbate heart failure). Dilate peripheral arterioles (modern ones don’t cause reflex tachycardia), less arterial dilation. Start low to avoid profound hypotension (especially elderly). Good for lipids

\textit{Ca Channel Blockers}

- Uses: Angina, dysrhythmias, hypertension, NOT heart failure

- Hypertension: only in isolated systolic hypertension (eg due to hardened arteries)

- Not better than diuretics or \(\beta\)-blockers for hypertension, but additive effect

- Action: ↓myocardial work, decrease afterload, vasodilate coronary arteries
  - Verapamil (originally an anti-arrhythmic, derivative of theophylline, less effect on vasodilation but ↑bradycardia) and Diltiazem: slow conduction at the AV node and cause coronary vasodilation
  - Nifedipine: vasodilator ⇒ good for coronary artery spasm, but may also cause reflex tachycardia so may use with a \(\beta\)-blocker

- Adverse effects:
  - All cause headache, flushing, dizziness, hypotension, ↓LV function
  - Verapamil: constipation
  - Verapamil and diltiazem: ↑heart block
  - Nifedipine and verapamil: ↑blood sugar

- Interactions:
  - ↑ plasma digoxin levels
  - Enzyme inhibitors →↑plasma levels of carbamazepine and cyclosporin
  - Don’t use verapamil with \(\beta\)-blockers: bradycardia + LVF

- Also consider long acting nitrates

\textbf{Vasoactive Drugs}

- See Vascular Receptors

- An inotrope is an agent that increases myocardial contractility (acts on \(\beta\)-1-R)

- A vasopressor causes vasoconstriction (acts on \(\alpha\)-R)

- A vasoactive drug is a term used for either an inotrope or a vasopressor

\begin{table}[h]
\centering
\begin{tabular}{|l|c|c|c|c|}
\hline
\textbf{Table 2 Inotrope actions} & \textbf{\(\alpha\)} & \textbf{\(\beta_1\)} & \textbf{\(\beta_2\)} & \textbf{Dopamine} \\
\hline
Dobutamine & +++ & ++ & & \\
Adrenaline & + to +++ & +++ & ++ & \\
Noradrenaline & +++ & + & & \\
Dopamine: & & & & \\
\quad Low dose & & & & \\
\quad Medium dose & & & & \\
\quad High dose & & & & \\
\quad Dopexamine & & & & \\
\quad + to +++ increasing affinity for receptor & & & & \\
\hline
\end{tabular}
\end{table}
• All vasoactive drugs are short acting and are given by infusion into a central vein. They act on adrenoreceptors in the circulation via cyclic AMP
• The most commonly used vasoactive drugs are dobutamine, adrenaline, noradrenaline, and dopamine
• **Dobutamine** has predominantly \( \beta \)-effects, so it increases heart rate and contractility and hence cardiac output. It also has \( \beta \)-effects which cause vasodilatation. This has the effect of reducing afterload—that is, the work required to contract. It is commonly used in ischaemic heart disease because it makes the heart work harder, but also makes it easier for the heart to do so. If cardiac output is increased but TPR is reduced, blood pressure may not rise. This may not matter, but some vital organs—the kidneys, brain, and coronary arteries—depend on a critical pressure not a critical flow.
• If the blood pressure is critically low, it may need to be raised by other means—for example, drugs with \( \alpha \) effects or intra-aortic balloon pumping in the case of cardiogenic shock
• **Adrenaline** is a \( \beta_1 \), \( \beta_2 \), and \( \alpha \) agonist. At lower doses, \( \beta \)-effects predominate and \( \alpha \) effects become marked with increasing doses. It is used in low cardiac output states with severe hypotension
• **Noradrenaline** is a potent \( \alpha \) agonist, so it raises blood pressure by vasoconstriction. This would be damaging in patients who have not been properly filled with fluid first. It is used in septic shock where hypotension is caused by vasodilatation
• **Dopamine** is a complex inotrope. This is because it has a range of actions throughout its dose range. At lower doses, dopamine receptors are stimulated, at medium doses \( \beta \)-receptors are stimulated, and at higher doses, \( \alpha \) receptors are stimulated. It is sometimes used in high doses in septic shock. The problem is that there is wide interpatient plasma clearance of dopamine in critically ill people so a dose range does not correlate with effect. You may have heard of “renal dose” dopamine—low dose dopamine used for acute renal failure. Several trials have shown it has no effect whatsoever on improving kidney function, and it is no longer used

### Positive Inotropes

- **Digoxin**: only oral inotrope. Slows AV conduction and increases contractility
  - Use: in AF, slows rate →↑output. But **poor for rate control** – still ↑HR in response to standing up
  - Orally takes a week to reach steady state (T½ is 36 – 40 hours)
  - Shortens QT interval → causes digitalis effect on ST interval (not a sign of toxicity)
  - **Low therapeutic index** (although wide therapeutic range) → **toxicity** common:
    - CV: any **arrhythmia**, arrest, worsening heart failure
    - GI: anorexia, nausea, vomiting, diarrhoea, abdominal pain, gynaecomastia
    - CNS: headache, drowsiness, unsteadiness, blurred/yellow vision, **confusion**
    - Worse if:
      - **Electrolyte disturbance**: hypokalaemia, hypercalcaemia, alkalosis
      - Potassium sparing diuretics, steroids, verapamil, amiodarone, spironolactone
      - Disease: hypothyroidism, hypoxia, renal failure
      - Old age
    - Management: stop digoxin, check plasma level and K, treat arrhythmias, antidote (Digibind)
- **Dopamine** *(precursor of nor-adrenaline)*
  - In low doses → renal vasodilation and improved renal function
  - In higher doses → acts on cardiac \( \beta_1 \) receptors → inotropic effects
- **Dobutamine**: acts on cardiac \( \beta_1 \) receptors → inotropic effects

### Lipid Lowering Drugs

- See Dyslipidaemia, page 43
- **Lipids**:
  - Cholesterol is most concentrated in LDL
  - HDL is beneficial
  - VLDL carries TAGs
- **Hypercholesterolaemia**:
  - Primary: Hepatic overproduction of VLDL →↑VLDL/LDL/Remnant lipoproteins
  - Secondary: Obesity, diabetes, hypothyroidism, nephrotic syndrome, alcohol, drugs (oestrogen, Retinoids, \( \beta \)-blockers, thiazides...)
- **Drug groups**:

<table>
<thead>
<tr>
<th>Drug groups</th>
<th>Action</th>
<th>Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>HMG Co-A Reductase Inhibitors</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Statins</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Simvastatin, Pravastatin, Atorvastatin</td>
<td>↓Cholesterol synthesis</td>
<td>LDL ↓ 20 – 40%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>HDL ↑ 5 – 15%</td>
</tr>
</tbody>
</table>

*Cardiology* 74
Cardiology

**Fibric-acid derivatives:**

- Benzafibrate, Gemfibrozil
  - ↑Lipoprotein lipase activity.
  - ↓release of FFA from periphery
  - LDL ↓10 – 15 %
  - HDL ↑10 – 15 %
  - TAG ↓20 – 50%

**Bile Acid Sequestrants:**

- Cholestyramine, Colestipol
  - Non-specific binding of bile acids
  - LDL ↓15 – 30%
  - HDL ↑3 – 5%
  - TAG: no affect (but can rise)

**Nicotinic acid derivatives:**

- Acipimox
  - ↓VLDL.
  - ↓FFA from periphery
  - LDL ↓10 – 25
  - HDL ↑15 – 35
  - TAG ↓20 - 50

- Commencement of treatment depends on HDL:cholesterol ratio plus other risk factors
- HMG-CoA Reductase Inhibitors (Statins):
  - Treatment: Requires health benefits approval (it’s expensive) and is always accompanied by diet
  - More effect in lowering plasma concentrations of LDL and total cholesterol →↓mortality in hypercholesterolaemia + angina
  - SE: rare. GI, headaches, ↑LFTs, myopathy from ↑CK. Potentiates warfarin
- Fibrates: ↑HDL and ↓TAGs
- Bile-acid sequestrants: Indicated for children and women of childbearing age. SE: constipation, skin rashes. Bind fat soluble vitamins and other drugs (eg warfarin, give two hours before or 4 hours after)

**Cardiomyopathy**

- = Primary or idiopathic diseases involving the myocardium
- Diagnosis by exclusion of other more common causes of heart failure: IHD, hypertension, rheumatic fever, and infectious myocarditis

**Pathology Overview**

- = Abnormal myocardial structure + function not caused by ischaemia or HTN (in practice however, CM also used when MI or HTN the cause - 1°)
  - Dilated (dilatation and enlargement – systolic/contractile dysfunction)
    - See interstitial fibrosis, hypertrophic myocytes
    - 2° cause = ETOH, preg, haemochromatosis, infections
  - Hypertrophic (mutations in sarcomeric proteins, diastolic dysfunction)
    - See ventricular outflow tract obstruction, septal hypertrophy; myocyte disarray, interstitial fibrosis
  - Restrictive (usually secondary, diastolic dysfunction)
    - Usually a 2° cause (radiation, sarcoid, amyloid, mets)
    - See thickened myocardium, atria dilated

**Primary Cardiomyopathy**

**Congestive-Dilated Cardiomyopathy**

- Presents as congestive heart failure at any age
- Dilatation and enlargement → systolic/contractile dysfunction
- Men twice as common as women
- Exclude pre-existing hypertension and alcoholism
- Macroscopic appearance: greatly dilated ventricles, heart weighs 500 – 1000g (normal is 300g female, 350 g male)
- Microscopic appearance: patchy interstitial fibrosis, ↑interstitial oedema, hypertrophy of remaining fibres
- Complications: arrhythmia, mural thrombus, mitral and tricuspid insufficiency
- Prognosis: progressive disease, no cure
- 2° causes = ETOH, pregnancy, haemachromotosis, infections
Hypertrophic Cardiomyopathy

- Disproportionate hypertrophy of the interventricular septum → ventricular outflow obstruction
- Mutations in sarcomeric proteins → hypertrophy → diastolic dysfunction
- Familial and non-familial forms
- Signs: ejection systolic murmur (LVOT obstruction) loudest at LSE
- Macroscopic appearance: heart weighs 600 – 1300g. Septum thicker than free wall of left ventricle
- Microscopic appearance: diffuse hypertrophy of tangled myocytes. Interstitial collagen
- Prognosis: poor, 1/3 die from outlet obstruction (can be precipitated by digoxin); can die from arrhythmias (common in young adults)

Restrictive Cardiomyopathy

- Usually secondary cause (radiation, sarcoid, amyloid, mets) → diastolic dysfunction
- Endocardial fibroelastosis: cartilage-like thickening of the left sided endocardium. Most common < 2
- Endomyocardial fibrosis: Only tropical Africa. Fibrosis → thickening of cordae tendiniae and aortic valve leaflets

Secondary Cardiomyopathy

- Alcohol, cobalt, sarcoid (infiltrative granulomatous), amyloid (accumulation of insoluble β pleated proteins derived from immunoglobulins in elderly patients), metastatic carcinoma, storage diseases (eg haemochromatosis), ischaemia
- Effect of alcohol on the heart:
  - Binge drinking (also exercise and caffeine) → AF a day later lasting for a day
  - Fibrotic cardiomyopathy
  - Arrhythmia

Neoplasia of the Heart and Blood Vessels

- Haemangioma:
  - Common congenital vascular lesions usually occurring in the skin
  - Haemangioendothelioma: endothelial vascular tumour, intermediate between haemangioma and frankly malignant angiosarcomas
  - Multiple Haemangiomatous syndromes: angiomatoses lesions present in two or more tissues
  - Kaposi’s sarcoma: malignant tumour of endothelial cells. Associated with AIDS. Painful purple to brown lesions
- Myxoma: most common primary benign tumour of the heart. Jelly like appearance, typically located on the atrial side of the mitral valve
- Rhabdomyoma: primary benign striated muscle cell tumour of the myocardium, typically found in children
Respiratory Physiology

- For acid-base disturbances, see Acid-Base balance, page 169

Blood Gases

- Normal Values:
  - **PaO₂**: 75 – 100 mmHg. Determinants of this:
    - Dependent on ventilation/perfusion balance (A-a gradient)
    - **Inspired O2 (FiO2)** concentration
    - **PCO₂**
  - **O2 saturation**: 95 – 100%
  - **PaCO₂**: 36 – 46 mmHg. If high then hypoventilation, if low then hyperventilation. Measured with capnograph
  - **pH** falls by 0.1 for every rise of 10 CO₂
  - Plasma **HCO₃⁻ (arterial)**: 22 – 26 mmol/L
  - **PAO₂** is lower than inspired PO₂ because:
    - It becomes saturated with water vapour
    - It is diluted by expired CO₂
    - **O2** is absorbed into the blood

Calculating the A-a Gradient

- **PIO₂** = (PB – PH₂O) * FIO₂ = (760-47) x 21% = 150 mmHg
- **PAO₂** = PIO₂  – **PaCO₂**/R, essentially = PAO₂ = 150 – **PaCO₂**/0.8
- A-a gradient = **PAO₂** – **PaO₂**. Normal is 5 – 15

Factors Affecting the A-a Gradient

- Normally 5 mmHg at FiO₂ of 21%, may be up to 100 at 100%
- Diffusion
- Ventilation/Perfusion balance (V/Q):
  - Most common cause of a fall
  - Responds well to O₂ therapy
  - The term used when the ventilation and the perfusion of a gas exchanging unit are not matched
  - Can be either **V > Q** or **Q > V**
- Shunts:
  - Can be pathological or anatomical
  - **Shunts exist when there is perfusion but no ventilation**
  - Eg collapse, consolidation, obstruction
  - **Cannot** be corrected by O₂ therapy
- Dead space:
  - No perfusion in the presence of ventilation
  - Eg PE
- At the extremes of V/Q mismatch, an **area of lung receiving no perfusion** will have a V/Q ratio of (infinity) and is referred to as **alveolar dead-space**, which together with the anatomical dead-space makes up the **physiological dead-space**
- In contrast an **area of lung receiving no ventilation**, owing to airway closure or blockage, its V/Q ratio will be zero and the area is designated as **shunt**. Blood will emerge from an area of shunt with a PO₂ unchanged from the venous level (40mmHg) and produce marked arterial hypoxaemia. **This hypoxaemia cannot be corrected by increasing the FiO₂**, even to 1.0, as the area of shunt receives no ventilation at all. The well-ventilated parts of the lung cannot compensate for the area of shunt because Hb is fully saturated at a normal PO₂. Increasing the PO₂ of this blood will not increase the oxygen content substantially.
ABG Examples

<table>
<thead>
<tr>
<th></th>
<th>Normal</th>
<th>Acute RAI</th>
<th>Acute RA</th>
<th>Acute MA</th>
<th>Acute MA</th>
<th>Chronic RA</th>
<th>Acute on chronic RA</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>pH</strong></td>
<td>7.4</td>
<td>7.55</td>
<td>7.1</td>
<td>7.1</td>
<td>7.2</td>
<td>7.4</td>
<td>7.3</td>
</tr>
<tr>
<td><strong>PCO2</strong></td>
<td>40</td>
<td>24</td>
<td>80</td>
<td>24</td>
<td>12</td>
<td>48</td>
<td>56</td>
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<tr>
<td><strong>PO2</strong></td>
<td>95</td>
<td>70</td>
<td>45</td>
<td>115</td>
<td>80</td>
<td>70</td>
<td>50</td>
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<tr>
<td><strong>HCO3</strong></td>
<td>24</td>
<td>24</td>
<td>24</td>
<td>5</td>
<td>10</td>
<td>32</td>
<td>32</td>
</tr>
<tr>
<td><strong>O2Sats</strong></td>
<td>99%</td>
<td>95%</td>
<td>70%</td>
<td>100%</td>
<td>95%</td>
<td>80%</td>
<td></td>
</tr>
<tr>
<td>A-a g</td>
<td>5</td>
<td>50 (i.e. VQ mismatch)</td>
<td>5 (no VQ mismatch)</td>
<td>5</td>
<td>55</td>
<td>20 (VQ mismatch)</td>
<td>30</td>
</tr>
<tr>
<td><strong>Example</strong></td>
<td>PE/pneumonia/ asthma with hyperventilation</td>
<td>1st resp depression eg opiate OD</td>
<td>DKA (hyperventilating to blow off CO2)</td>
<td>Pneumonia causing DKA</td>
<td>Fully compensated RA eg COPD w some CO2 retention</td>
<td>Is left case ie COPD w superimposed pneumonia</td>
<td></td>
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</tbody>
</table>

- NB. In the acute RAI example above for example: if pCO2 ↑ to 40 (eg sleep/morphine) but still with same VQ mismatch (ie A-a g doesn’t change), pO2 will ↓ to 50 (rearranging A-a g formula)

**Oxygen Saturation**

- **Saturation** = % of haemoglobin that is fully bound. Determined by PO2 and shape of dissociation curve.
- Oxyhaemoglobin dissociation curve
  - Shifted right by ↑ blood temp, CO2, H+, 2,3BPG [at same PO2, sats are lower]
  - A rightward shift indicates that Hb has a ↓ affinity for oxygen. This makes it more difficult for Hb to bind to oxygen (requiring a higher partial pressure of oxygen to achieve the same oxygen saturation), but it makes it easier for the Hb to release oxygen bound to it.
  - Factors that move the oxygen dissociation curve to the right are those physiological states where tissues need more oxygen. For example during exercise, muscles have a higher metabolic rate, and consequently need more oxygen, produce more carbon dioxide and lactic acid, and their temperature rises.
  - Shifted left by ↓ blood temp, CO2, H+, 2,3BPG [at same PO2, sats are higher]
- O2 available to tissues (Oxygen flux) depends on:
  - O2 saturation
  - Hb concentration
  - Blood flow
  - Normal flux is 1000 ml/min. If flux falls below 250 then hypoxia
- **Cyanosis**
  - Peripheral cyanosis: capillary de-oxy Hb > 50 g/litre. Eg cold + vasoconstricted
  - Central cyanosis: due to ↓ saturation and de-oxy Hb > 50 g/litre eg in mouth and tongue

**Pulmonary Function Tests**

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</table>

- Definitions:
  - PEFR = peak expiratory flow rate
  - FEV1.0 = maximum volume of air that can be exhaled during the first second of a Forced Vital Capacity (FVC= maximum expired volume = FV). May use SVC if it’s higher
    - Normally 80% of FVC
    - < 70% ⇒ obstructive lung disease
    - > 70% ⇒ restrictive lung disease, eg lung fibrosis, neuro-muscular disease, chronic PEs (→ scarring) and HF
    - But this can lead you astray. Eg if bronchodilator ⇒ ↑ FVC by more than FEV, then the ratio drops
  - FEV 25-75%: Mean forced expiratory flow from 25 to 75% of vital capacity = Mean Mid-expiratory Flow (MMEF). Gets rid of peak flow which is very effort dependent → more reliable measure
  - VC = vital capacity:
    - FVC: forced vital capacity
- SVC: slow vital capacity
- FIF50%: Forced inspiratory flow at 50% of vital capacity
- FRC: Functional residual capacity (the relaxed end expiratory volume) (NB. ↑ stiffness will ↓ FRC + vice versa)
- IC: Inspiratory capacity (TLC – FRC)
- RV: Residual volume (TLC – VC)
- ERV: Expiratory reserve volume (FRC – RV)
- PIFR: Peak inspiratory flow rate
- DLCO: Diffusing capacity of the lung for Carbon Monoxide
  - Needs adjustment for Hb – eg anaemia, polycythaemia
  - If DLCO is ↓ but FEV1 etc are all normal, must be a problem with blood flow eg chronic PE, pulmonary HTN, anaemia
- Dl/VA: rate at which CO diffuses across lung parenchyma
- KCO: rate of uptake of carbon monoxide (synonym of Dl/VA)
- VA: alveolar volume which is the single-breath estimate of the TLC
- “Airflow obstruction” = if FEV1/FVC ratio < 0.7 i.e. obstructive
- “Gas trapping” = if RV ↑ (i.e. lost elastic recoil → cannot expire all inspired air e.g. emphysema)
- Patterns:

<table>
<thead>
<tr>
<th></th>
<th>Obstructive</th>
<th>Restrictive</th>
</tr>
</thead>
<tbody>
<tr>
<td>FEV1</td>
<td>↓ ↓</td>
<td>↓ ↓</td>
</tr>
<tr>
<td>FVC</td>
<td>↓ ↓</td>
<td></td>
</tr>
<tr>
<td>FEV1/FVC</td>
<td>↓ ↓</td>
<td></td>
</tr>
<tr>
<td>TLC</td>
<td></td>
<td>↓ ↓</td>
</tr>
<tr>
<td>RV</td>
<td>↑ ↓</td>
<td></td>
</tr>
<tr>
<td>DLCO</td>
<td>↓ [emphysema, normal in bronchitis/asthma]</td>
<td>↓</td>
</tr>
</tbody>
</table>

- PV = pulmonary vascular disorders
- CW = chest wall
- NM = neuromuscular
- CB = chronic bronchitis

- Fick’s law of diffusion:
  - Amount of gas that diffuses across a sheet of tissue (i.e. lung) is:
    - Directly proportional to the surface area of the sheet (↓ in emphysema)
    - Indirectly proportional to the thickness of the sheet (↑ in fibrosis etc)

- Performing Lung Function Tests:
  - Requires at least 3 manoeuvres, the best 2 having FEV1.0’s & FVCs within 5% of each other
  - Biggest problems with serial reproducibility are obtaining maximum inspiration first, and getting maximum effort
  - All are reported at BTPS (body temperature, saturated)
  - If assessing bronchodilator responsiveness, should have no inhaler for 2 hours beforehand. Maximum responsiveness usually 20 minutes after dosing
  - Predicted values are based on age, height and sex. Different racial groups and people with varying proportions (eg long legs/short torso) may be very poorly approximated by predicted values
Flow-volume loop gives very valuable information. Eg in emphysema, ↓↓ expiratory flows but inspiratory flows normal.

Flow-volume Characteristics of Acceptable and Unacceptable Spirometry

- Patterns of disease:
  - Obstruction:
    - ↓ airflow
    - A disproportionate reduction of maximal airflow from the lung in relation to the maximal volume
    - Characterised by a low FEV1/FVC ratio (<0.7)
  - Restrictive:
    - ↓ volume
    - Characterised by a reduction in TLC below the 5th percentile of the predicted value, and normal FEV1/FVC ratio (or ↑)
  - Mixed:
    - Characterised by the coexistence of obstruction and restriction, and is defined physiologically when both FEV1/FVC and TLC are below 5th percentiles of the predicted value

- Other lung function tests:
  - Asthma provocation: for pilots, divers, police, etc
  - Cardiopulmonary exercise testing – finds how much of shortness of breath is due to pulmonary causes and how much to cardiac causes

- Important PFTs (according to Dr Perrin):
  - FEV1 (tells how severe airflow obstruction is, if present)
  - FVC
  - FEV1/FVC (airflow obstruction or not)
  - TLC
  - RV (gas trapping or not)
  - DLCO (tells how good gas transfer is)

**Bronchodilator Reversibility**

- An integrated physiological response involving airway epithelium, nerves, mediators and bronchial smooth muscle
- >12% AND 200mL in either FEV1 OR FVC cf. baseline during a single testing session suggests “significant” bronchodilation
- NB. BDR response may not be seen after a single LFT session (i.e. ↑ inflammation at the time) therefore need to re-test after inhaled corticosteroids (~6/52)

**Respiratory Cytology**

- Can use either sputum, bronchial cytology (washings, brushings) or FNA

**Respiratory Failure**

- Ventilatory failure: when bellows function inadequate to excrete CO2 produced (ie above 60 mmHg)
- Signs of hypoxia: cyanosis, ↑RR, tachycardia, confusion
- Signs of hypercapnia: plethora, asterixis etc
- Respiratory Failure: (PaO2 < 60 mmHg)
- Perfusion and ventilation must be matched (normal VA ~ 5L/min; normal CO ~ 5L/min)
Type I: Hypoxemic
- \( \text{PaO}_2 < 60 \text{mmHg} \)
- \( \text{PaCO}_2 < 50 \text{mmHg} \) (normal or low) → VQ mismatch plus other causes (e.g. heart failure).
- Hypoxia due to diseases affecting lung gas exchange
- Commonly seen in cardiogenic or noncardiogenic pulmonary edema, pneumonia, and pulmonary hemorrhage
- Treat with oxygenation (aim for >91%)
- Hypoxic respiratory failure (type I) is characterized by a \( \text{PaO}_2 \) of less than 60 mm Hg with a normal or low \( \text{PaCO}_2 \). This is the most common form of respiratory failure, and it can be associated with virtually all acute diseases of the lung, which generally involve fluid filling or collapse of alveolar units. Some examples of type I respiratory failure are cardiogenic or noncardiogenic pulmonary edema, pneumonia, and pulmonary hemorrhage.

Type II: Hypercapnic
- \( \text{PaCO}_2 < 60 \text{mmHg} \)
- \( \text{PaCO}_2 > 49 \text{mmHg} \) + PC→ hypoventilation – both gases are affected reciprocally.
- Hypoxia and hypercapnia due to disease affecting ventilation (therefore CO2↑)
- Commonly seen in: drug overdose, neuromuscular disease, chest wall abnormalities, and severe airway disorders (e.g., respiratory fatigue in asthma, chronic obstructive pulmonary disease [COPD])
- Treat with ventilatory support
- Hypercapnic respiratory failure (type II) is characterized by a \( \text{PaCO}_2 \) of more than 50 mm Hg. Hypoxemia is common in patients with hypercapnic respiratory failure who are breathing room air. The pH depends on the level of bicarbonate, which, in turn, is dependent on the duration of hypercapnia. Common etiologies include drug overdose, neuromuscular disease, chest wall abnormalities, and severe airway disorders (e.g., asthma, COPD)

Aetiology
- What can fail:
  - Pump mechanism:
    - Brain: drugs, metabolic, vascular, trauma
    - SC + nerves: polio, motor neuron disease, trauma, guillain-barre
    - Muscles: muscular dystrophy, myasthenia, poisons
    - Chest wall: trauma (flail chest), skeletal abnormalities, obesity
    - Pump failure is a failure of ventilation → produces ↑ in CO2 (type II) and therefore ↓pH
  - Airways:
    - Asthma, COPD
    - Airway disease effectively is a failure of ventilation → produces ↑ in CO2 (eventually) and therefore ↓pH
  - Lung parenchyma:
    - Alveoli + interstitial space
    - Acute: pneumonia, pulmonary edema, ARDS, alveolitis
    - Chronic: interstitial or infiltrative lung disease
    - See shunting (as ↓ventilation) + V/Q mismatch → hypoxia
    - CO2 will be normal or low because of ↑ ventilatory drive (until late stage of muscle exhaustion)
- Respiratory Failure can be due to:
  - Central respiratory depression:
    - Drugs: opiates, alcohol, barbiturates
    - Brain stem: CVA, coning
    - If A-a gradient normal but patient hypoventilating → central depression. If young then ?OD
  - Sleep Apnoea syndromes
  - Lung Pump Failure: neuromuscular disease, chest wall, lung disease. E.g. diaphragm dysfunction:
    - Unilateral paralysis may be asymptomatic
    - Bilateral paralysis: neurological (e.g. polio, motor neuron, Guillain-Barre) or myopathic (e.g. hypothyroid)
    - Signs: orthopnoea, morning headache (hypercapnia over night), paradoxical breathing (chest wall and abdomen go in opposite directions when breathing), lung function worse when lying down
    - Treatment: treat cause, positive pressure ventilation systems
- Key indicators of respiratory emergency = ↑HR, ↑RR, ↓sats, confusion, ↓BP
Oxygen Therapy

- Ensure PO2 is on plateau of O2 saturation curve (ie PaO2 > 70 mmHg)
- Shunt (normal perfusion but no ventilation) is resistant to O2 therapy, whereas a diffusion abnormality + V/Q mismatch respond well
- Complications of O2 therapy:
  1. Reduced respiratory drive in COPD. Consider if ↑PCO2 but pH not as low as you’d expect. Don’t give too much O2 otherwise ↓respiratory drive → ↑CO2. Aim for saturation of ~ 90% (88-92)
  2. Loss of nitrogen splint, etc
  3. O2 is a vasoconstrictor + can cause free radical damage → ie it can be toxic (is a drug). Can ↓ coronary artery flow by 20% therefore do not use high flow O2 unless low O2 sats!
- O2 therapy options: NP → Hudson mask → HM with reservoir/high-flow NP (humidified; can deliver high concentration O2) → CPAP/BiPAP → intubation
- Levels of O2 therapy:
  1. 21%: room air
  2. 24%: nasal prongs at 1 litre
  3. 28%: nasal prongs at 2 litres
  4. 32%: nasal prongs at 3 litres (need Hudson mask to deliver higher %)
  5. 35%: Hudson mask at 6L/min
  6. 40%: Hudson mask at 8L/min. Maximum level obtainable with a mask (inspiratory flow > flow from wall)
  7. 50-60%: Hudson mask with rebreather bag
- Aim is to titrate % therapy (ie how many litres/method of delivery) to achieve sats between 93-97%
- If sats still low after Hudson mask with rebreather → use CPAP or BiPAP (see below) → if still low → intubate
- Types of ventilation:
  1. CPAP: Continuous positive airways pressure – splints airways open at end of respiration. Always a positive P in airways and alveoli therefore do not have to overcome surface tension when inspiring (as airways normally collapse during expiration). Allows ↑ time for gas exchange
  2. BiPAP: Positive pressure for inspiration + less P during expiration. Good if CO2 retention – makes it easier to blow off CO2 as less pressure during expiration
  3.IPPV: intermittent positive pressure ventilation: complete control
  4. PEEP: positive end expiratory pressure ventilation: splints collapsed or fluid filled alveoli
- Complications of ventilation:
  1. Application of pressure to lungs → rupture, ↑thoracic pressure → ↓venous return
  2. Artificial airway → obstruction, trauma to teeth, pharynx, ciliary damage, infection
  3. Ventilation mismanagement → inappropriate ventilation, hypoxic gas mixture, equipment failure

Respiratory History

- See Differentiating Chest Symptoms, page 24

Respiratory Exam – RP

- Wash your hands.
- Introduce yourself to the patient, and ask permission to examine them.
- Expose the patient, and position them at 45°.

**Inspection**

<table>
<thead>
<tr>
<th>Look around the bed</th>
<th>Oxygen mask, sputum pot, PEFR, inhalers, nebuliser, cigarettes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Look at the patient</td>
<td>Comfortable at rest, cyanosis, breathlessness, use of accessory muscles; listen</td>
</tr>
<tr>
<td>Look at the hands</td>
<td>Clubbing (CF, bronchiectasis, bronchogenic ca – but not small cell), peripheral cyanosis, nicotine staining, muscle wasting – pancoast tumour, tremor (β2-agonists)</td>
</tr>
<tr>
<td>Feel the wrists</td>
<td>Asterixis (CO₂ retention flap); painful wrists in hypertrophic osteoarthropathy</td>
</tr>
<tr>
<td>Feel the radial pulse</td>
<td>Assess rate</td>
</tr>
<tr>
<td>Count RR</td>
<td>Whilst feeling pulse</td>
</tr>
<tr>
<td>Ask for blood pressure</td>
<td>Enquire about pulsus paradoxus (severe asthma + tamponade)</td>
</tr>
<tr>
<td>Look at the neck</td>
<td>Examine JVP (raised in cor pulmonale – RVH and tension pneumothorax), tracheal tug</td>
</tr>
<tr>
<td>Check trachea is central</td>
<td>Including the laryngeal height (from thyroid notch to sternal notch, &lt;4cm indicates COPD)</td>
</tr>
<tr>
<td>Check lymphadenopathy</td>
<td>Do this from behind when examining the posterior chest</td>
</tr>
</tbody>
</table>
Respiratory Exam - DT

**Inspection, Palpation and Percussion**

- **Inspection:**
  - Count respiratory rate (at rest should be < 14 per minute)
  - Chronic airways disease \(\rightarrow\) barrel (expanded chest) \(\rightarrow\) can’t find apex beat
  - Look for use of accessory muscles. Are intercostals depressed (ie being used a lot)? Look for paradoxical breathing of the abdomen
  - Cyanosis (eg tongue)
- Ask patient to cough. Listen for wheeze, gurgling, etc
- Inspect sputum
- Listen for stridor or hoarseness (laryngitis, cancer affecting left recurrent nerve or larynx)
- **Hands:**
  - Clubbing (and maybe Hypertrophic Pulmonary Osteoarthropathy – ‘swollen’ metacarpals and elsewhere, eg in lung cancers). See Hands, page 15 for causes of clubbing
  - Staining from cigarettes
  - Wasting (Pancoast tumour)
  - Pulse rate: tachycardia
  - Flapping tremor: late and unreliable sign of severe CO2 retention
- The face:
  - Eyes for Horner’s syndrome (constricted pupil, partial ptosis)
  - Tenderness over sinuses \(\rightarrow\) sinusitis
  - Nose: check for polyps (associated with asthma), deviated septum (nasal obstruction), etc

- **Do the FET**
  - Auscultate over trachea – exp fast + complete. >6s = FEV1/FVC <0.4

- **Look at the face**
  - SVC obstruction

- **Look in the eyes**
  - Anaemia, ptosis, miosis and anhydrosis (Horner’s)

- **Look at the nose**
  - Flaring, polyps, septal deviation, mucosa

- **Look in the mouth**
  - Central cyanosis (look under the tongue), pursed lips, tonsils, hoarse voice, stridor

- **Look at the chest**
  - Scars, costal/sternal retraction, subcostal recession, acc muscle use, asymmetry, deformity, hyperexpansion (Barrel chest), pectus carinatum, pectus excavatum, kyphoscoliosis, cachexia, radiotherapy marks, chest drain, Hoover’s sign

- **Assess chest expansion**
  - Without palpation – “big breath in” and observe

- **Palpate for rib tenderness**
  - Also for pleural friction rubs

- **Feel for the apex beat**
  - May be displaced, eg in pneumothorax or effusion or hyperinflation

- **Tactile vocal fremitus**
  - ‘99’ – best done after auscultation should an area of interest be found

- **Palpate liver/spleen**
  - For ptosis in hyperinflation

- **Percuss anteriorly**
  - Compare L with R, include axillae + supraclavicular regions. Resonant, hyperresonant, dull or stony dull

- **Auscultate anteriorly, breathing through mouth**
  - Compare L with R, listening for air entry, crackles, wheeze and bronchial breathing. Don’t forget the supraclavicular regions and axillae

- **Assess vocal resonance, asking pt to say ‘e’**
  - Compare L with R, listening for e to a change (consolidation) – best done if an area of interest found on auscultation

Repeat chest expansion (looking over shoulders then palpatory method), TVF, percussion (percuss Kronig’s isthmus) and auscultation posteriorly, with the patient’s arms crossed in front of them. Also good to assess lymph nodes from behind.

- **Final manoeuvres**
  - Examine for ankle and sacral oedema
  - Thank the patient and cover them up

*I would complete my examination by....*

“I would like to take a blood pressure, examine the sputum pot, look at the obs chart (temperature, sats) and perform a peak flow measurement”.

- **Link back to Examinations**

---

Respiratory 83
Throat for URTI
Check lymph nodes

Trachea:
Check for displacement
Tracheal Tug: trachea moves inferiorly with inspiration, due to over expansion of the lung in airflow obstruction

Chest:
Inspect:
Shape and symmetry, including funnel chest (= pectus excavatum or sunken sternum), kyphosis (forward curvature) and scoliosis (lateral bowing)
Scars, signs of radiotherapy
Subcutaneous emphysema – crackling under the skin due to air from pneumothorax
Prominent veins in SVC obstruction
Movement when breathing in and out – better from behind. Look for uni-lateral or bi-lateral reduction in movement

Palpation:
Check expansion: the affected side dose NOT expand – regardless of pathology
Apex beat: if not found then → hyper-expanded. Maybe displaced by pathology (pneumothorax, fibrosis, etc)
Vocal fremitus: Feel with hand while patient says 99, each side font and back
Compress sternum to spine → pain if fracture or bone tumour

Percussion:
Ask patient to move elbows forward to move scapula off the lungs
Around lung and also directly on the clavicle
Normal lung is resonant, pneumothorax is hyper-resonant, liver is dull, consolidation is dull, effusion is stony dull

Chest Sounds
When auscultating, ask patient to breathe through mouth – not to take deep breaths

<table>
<thead>
<tr>
<th>Vesicular breath sounds (= normal)</th>
<th>Bronchial breathing</th>
<th>Diagram</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Length</strong></td>
<td>Inspiration &gt; expiration (3:1) inspiration requires work, expiration is elastic recoil – snaps back)</td>
<td>Inspiration = expiration (1:1) takes longer for air to get passively squeezed out through reduced bronchioles)</td>
</tr>
<tr>
<td><strong>Relative Volume</strong></td>
<td>Inspiration louder</td>
<td>Equal (sounds like Darth Vader)</td>
</tr>
<tr>
<td><strong>Gap between in + out</strong></td>
<td>No</td>
<td>Yes</td>
</tr>
</tbody>
</table>

Crackle:
= Crepitations, rales
Coarse or fine (like hair rubbing)
Short, discontinuous, non-musical sounds heard mostly during inspiration
Fine (high pitched) are from distal air-spaces, coarse (low pitched) are proximal air spaces
Produced when there is fluid inside a bronchus with collapse of the distal airways and alveoli

<table>
<thead>
<tr>
<th>Disease</th>
<th>Early Crackle</th>
<th>Late Crackle</th>
</tr>
</thead>
<tbody>
<tr>
<td>Congestive Heart Failure</td>
<td>Very Common</td>
<td>Common</td>
</tr>
<tr>
<td>Obstructive Lung Disease</td>
<td>Present</td>
<td>Absent</td>
</tr>
<tr>
<td>Interstitial fibrosis</td>
<td>Absent</td>
<td>Present</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>Absent</td>
<td>Present</td>
</tr>
<tr>
<td>Bronchitis</td>
<td>Present</td>
<td>Absent</td>
</tr>
</tbody>
</table>

Wheeze:
Continuous musical sounds heard mostly during expiration
Produced by airflow through narrowed bronchi
Narrowing may be due to swelling, secretions, spasm, tumour, or a foreign body

Rhonchi are lower pitched, “snoring”-like noises heard over obstruction (mucous/FB etc)

Pleural Rub:
Grating sound like Velcro ripping or walking on snow on inspiration and expiration
Produced by motion of roughened or thickened pleura
Caused by inflammatory or neoplastic cells or fibrin deposits

Differentiating Consolidation from Pleural Effusion:

- **Consolidation** = exudate in alveoli. Signs are:
  - Expansion: reduced on affected side
  - Percussion: dull but not stony dull
  - Breath Sounds: *increased volume* and *bronchial* not vesicular (ie will hear coarse breath sounds like over the trachea)
  - Additional Sounds: *inspiratory crackles* (as pneumonia resolves)
  - Vocal Resonance/TVF: *increased*
  - Plural Rub: may be present

- **Effusion** = fluid in pleural space (but not blood – that’s haemothorax, and not pus – that’s empyema).
  - Signs of effusion are:
    - Displaced trachea if massive effusion
    - Expansion: reduced on affected side
    - Percussion: stony dullness over effusion
    - Breath Sounds: *reduced* or absent
    - Vocal Resonance/TVF: *reduced*

  The key differences are therefore:

<table>
<thead>
<tr>
<th></th>
<th>Consolidation</th>
<th>Effusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Percussion</td>
<td>Dull</td>
<td>Stony Dull</td>
</tr>
<tr>
<td>Breath Sounds</td>
<td>Bronchial</td>
<td>Reduced</td>
</tr>
<tr>
<td>Vocal Resonance/TVF</td>
<td>Increased</td>
<td>Reduced</td>
</tr>
<tr>
<td>Crackles</td>
<td>Sometimes</td>
<td>No</td>
</tr>
<tr>
<td>Expansion</td>
<td>↓</td>
<td>↓</td>
</tr>
</tbody>
</table>

**Common presentations:**

- **Expansion**
  - **Consolidation**: ↓
  - **Effusion**: or ↓

<table>
<thead>
<tr>
<th></th>
<th>Percussion</th>
<th>Breath sounds</th>
<th>VR</th>
<th>Trachea</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Consolidation</strong></td>
<td>Dull</td>
<td>↑, bronchial</td>
<td>↑</td>
<td>-</td>
</tr>
<tr>
<td><strong>Effusion</strong></td>
<td>or ↓, Stony dull</td>
<td>↓</td>
<td>↓</td>
<td>-</td>
</tr>
<tr>
<td><strong>COPD</strong></td>
<td>Hyperexpanded lungs</td>
<td>Hyper resonant</td>
<td>↓</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>Hyper-expanded lungs / ↓ chest expansion</td>
<td>↓ / - wheeze</td>
<td>↓</td>
<td>-</td>
</tr>
<tr>
<td><strong>Pneumothorax</strong></td>
<td>- or ↓, Hyper resonant</td>
<td>↓</td>
<td>↓</td>
<td>Deviated (push) if tension</td>
</tr>
<tr>
<td><strong>PE</strong></td>
<td>-</td>
<td>- (unless effusion)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td><strong>Fibrosis</strong></td>
<td>↓ - or dull</td>
<td>Crackles</td>
<td>↑</td>
<td>Depends</td>
</tr>
<tr>
<td><strong>LV Failure</strong></td>
<td>↓</td>
<td>Dull</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td><strong>Collapse</strong></td>
<td>↓</td>
<td>Dull</td>
<td>↓</td>
<td>Deviated (pull)</td>
</tr>
</tbody>
</table>

*Other Systems*

- Check JVP for right heart failure
- Listen to **P2** of second heart sound, at 2nd intercostal space on the left. If louder → pulmonary hypertension
- Check liver for tumour 2nd to lung cancer, and for ‘ptosis’ – displaced downwards in emphysema
- **Pemberton’s sign**: SVC obstruction – hold arms over head → facial plethora, inspiratory stridor and ↑ JVP
- Feet: check for oedema (pulmonary hypertension) and DVT

**Upper Respiratory Tract**

- See also URTI in Respiratory Tract Infections in Children, page 937

**Nasal & Sinus**

- For Nasal neoplasms, see Cancer of the Nasal Cavity and Paranasal Sinuses, page 121
- **Warms, cleans and humidifies** inspired air. By back of nose air is 98% humidified & 35C
- Anatomy: maxillary, ethmoid, frontal and sphenoid sinuses. Concha and turbinate bones

**Nasal Obstruction**

- Mechanical:
  - Defect in cartilage or bone
Septal deviation. Over time → paradoxical obstruction – hypertrophy of turbinate on other side → bilateral obstruction. Treatment: septoplasty

- Mucosal:
  - Blocked nose, mucoid discharge, ↓smell
  - Vasomotor rhinitis (VMR): there is normally a cycle between one nostril blocked and other cleared. This cycle upset. Treatment: cauterise turbinates → reduce venous congestion
  - Allergic rhinitis
  - Polyps: sessile or pedunculated. Usually inflammatory – related to asthma and aspirin sensitivity. Can be idiopathic or secondary to infective sinusitis
  - Treatment: topical steroids (↓allergy, ↓primary polyps, ↓VMR), antihistamines, mast cell stabilisers

**Epistaxis**

- Adults: From further back – septal or lateral wall. In elderly, mortality from severe epistaxis 1% - from secondary effects eg stroke (aspirin common cofactor → ↑bleeding)

**Sinusitis**

- See also Acute Sinusitis, page 940
- Face pain after cold
- Maxillary most common presentation, although ethmoid more commonly infected
- Causes: Strep pneumoniae, Strep pyogenes, H. influenzae, B. catarrhalis
- Treatment: Amoxicillin
- Complications:
  - Orbital cellulitis via orbital periosteum → optic nerve compression → compression of ophthalmic artery → retinal blindness. Need to drain pus and iv antibiotics
  - Sphenoidal and frontal sinusitis can → cerebral complications (eg cavernous thrombosis)
- Chronic sinusitis: pus, ↓smell, no pain. Can be from dental infection

**Allergic Rhinitis**

- See also Allergy and Hypersensitivity Disorders, page 496
- Symptoms: recurrent or acute
  - Sneezing, blocked or runny nose, itchy, watery or puffy eyes, itchy throat
  - May also be epistaxis, snoring, mouth breathing
- Examination: look at anterior nares for nasal patency, polyps (chronic rhinitis), secretions, oedema
- Two types:
  - Seasonal Allergic Rhinitis = hay fever. Allergy to birch or grass pollen etc especially rye grass
  - Perennial Allergic Rhinitis: allergy to dust mites, cat dander, moulds, etc
- Non-drug treatment:
  - Avoid allergen
  - Avoid other irritants: perfume, temperature change, other smoke
- Drug treatment:
  - Antihistamines: eg cetirizine once daily
  - Decongestants: vasoconstrictors. Can have stimulant effects (including ↑BP). Overuse → rebound congestion therefore use for 1-2d only
  - Mast cell stabilisers: Nasal spray. Slow onset. Not used very often
  - Topical nasal steroids: slow onset. Can cause mucosal atrophy → nose bleeds
  - Desensitisation: injections of ↑ doses of allergen. Expense and takes time (eg up to two years)

**Acute Pharyngitis**

- See also Pharyngitis, page 940
- Clinical signs: fever, respiratory distress, cervical lymphadenopathy, pharyngeal erythema, pharyngeal exudates

**Causal Organisms**

- Viral causes (commonest):

<table>
<thead>
<tr>
<th>Agent</th>
<th>Disease</th>
<th>Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rhinovirus, coronavirus</td>
<td>Common Cold</td>
<td>Common cold. Fever uncommon except in kids</td>
</tr>
</tbody>
</table>
Influenza (A & B)  ‘Flu  As for common cold + fever, headache, generalised myalgia
Parainfluenza virus 1-3  Croup = Laryngotracheobronchitis  Initial: sore throat, rhinorrhea, mild cough
                                      Leading to: severe cough (seals bark), hoarseness, inspiratory stridor (subglottic inflammation)
Adenovirus  Pharyngo-conjunctival fever  Sore throat (often erythema and exudate – even though virus), fever, headache, myalgia, conjunctivitis
Herpes Simplex  Mild: indistinguishable from other viral URTI. Severe: pharyngeal exudate/erythema, shallow ulcers, vascular rash on lips
Epstein Barr Virus  Infectious Mononucleosis – Glandular fever (See Epstein Barr Virus, page 820)  Usually adolescents/young adults. Sore throat (erythema/exudate in 50%), fatigue, malaise, fever, headache, cervical lymphadenopathy, atypical mononucleosis on blood film, splenomegaly

**Bacterial Causes:**

<table>
<thead>
<tr>
<th>Agent</th>
<th>Disease</th>
<th>Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Streptococcus Pyogenes (Lancefield Gp A) &amp; Strep Group C</td>
<td>Pharyngitis/Tonsillitis</td>
<td>Marked variation: Mild: indistinguishable from viral URTI, minimal erythema. Severe: Marked pharyngeal erythema &amp; florid tonsillar exudate, high fever, cervical lymphadenopathy, leucocytosis on blood film. Type M strains →Rheumatic fever.</td>
</tr>
<tr>
<td>Mixed anaerobes</td>
<td>Gingivitis/Pharyngitis</td>
<td>Polymicrobial infection, due to poor dental hygiene, bad breath</td>
</tr>
<tr>
<td>Corynebacterium diphtheriae</td>
<td>Diphtheria</td>
<td>Pharyngeal diphtheria rare. Range from mild non-specific illness to severe. Sore throat/fever, pain on swallowing, headache, vomiting. Characteristic greyish-green membranous exudate on pharynx</td>
</tr>
<tr>
<td>Neisseria gonorrhoeae</td>
<td>Pharyngitis</td>
<td>Mostly asymptomatic. Mild pharyngitis. Pain/difficulty swallowing</td>
</tr>
</tbody>
</table>

**Fungal causes:**

<table>
<thead>
<tr>
<th>Agent</th>
<th>Disease</th>
<th>Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Candida Albicans</td>
<td>Thrush</td>
<td>Usually immunocompromised. Creamy white plaques on tongue/mucosa. Complication of asthma steroids and long-term antibiotics</td>
</tr>
</tbody>
</table>

**Diagnosis**

- **Throat swabs:**
  - For routine bacterial culture: especially to confirm/exclude Strep Pyogenes
  - Low sensitivity (730%) and specificity (775%)
  - 40 – 50% of people with sore throats have bacteria isolated
  - Lots of variability: swab-taking technique, delays in transport, etc
Worth it for $18?

- Nasopharyngeal washings (kids): Antigen detection by immunofluorescence for RSV, Influenza A & B, Parainfluenza 1 – 3 and adenovirus

**Other URTIs**

<table>
<thead>
<tr>
<th>Infection</th>
<th>Common causative organisms</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Acute Otitis Media</em></td>
<td>Strep pneumoniae, H influenzae, Branhamella catarrhalis. See Acute Otitis Media, page 938</td>
</tr>
<tr>
<td><em>Acute Sinusitis</em></td>
<td>Strep pneumoniae, H influenzae</td>
</tr>
<tr>
<td><em>Acute Epiglottitis</em></td>
<td>H influenzae type B. See Epiglottitis, page 941</td>
</tr>
<tr>
<td><em>Chronic Bronchitis (acute infectious exacerbations)</em></td>
<td>Strep pneumoniae, H influenzae, Branhamella catarrhalis</td>
</tr>
<tr>
<td><em>Bronchiolitis</em></td>
<td>Respiratory Syncytial Virus. See Bronchiolitis, page 942</td>
</tr>
</tbody>
</table>

**Antibiotic Treatment of URTI**

- See also Acute Otitis Media, page 938
- Treatment for Strep Pharyngitis (Path lecture):
  - **Oral Penicillin:**
    - On empty stomach (before food)
    - 500 mg (200 for kids) 8 hourly for 10 days (adults)
    - If compliance in doubt, IM benzathine penicillin G (single dose)
  - Allergic to Penicillin: Erythromycin 500 mg (200 for kids) 8 hourly for 10 days
- **Antibiotic treatment (source - ‘Just Say No’, Thomas and Arroll, NZMJ, 14 July 2000):**
  - No benefits in patients with colds
  - Trivial benefit in patients with acute bronchitis
  - Trivial benefit in all but a minority of patients with acute exacerbations of COPD
  - Modest benefit in sinusitis
  - But, in real life, antibiotics are prescribed for a majority of patients with URTI
- **Antibiotic treatment (Cochrane review):**
  - Absolute benefits modest
  - Preventing complications can only be achieved by treating many who will derive no benefit
  - Symptoms: reduced duration by about half a day, especially at 3 days (although 50% of untreated had also settled by then)
  - Non-suppurative complications: Reduces rheumatic fever to less than one third. Possible protection against acute glomerulonephritis (although rare)
  - Suppurative complications: Reduces rate of otitis media to a quarter (NNT = 29), acute sinusitis to about one half and reduced incidence of quinsy
- No risk of delaying antibiotic treatment for possible Strep Pyogenes pharyngitis until culture results received. Late treatment as effective as early treatment
- Risks of ‘over treatment’ with antibiotics: Penicillin resistance – 2 to 9 times, ↑ risk of subsequent otitis media, pneumonia, bacteraemia or meningitis being caused by resistant S. Pneumoniae. ‘Cherish your normal flora and don’t assault it with antibiotics’
- Delayed/contingent prescription can allow ↓ antibiotics without ↑ morbidity. Eg antibiotics dispensed for sore throat dropped from 99% to 31% with wait of 2 days
- For Treatment of Otitis Media, see Acute Otitis Media, page 938

**Larynx**

- See also Tumours of the Larynx, page 122
- Function: protect airway from saliva and food, voice production
- Vocal cords shut during coughing, straining, lifting → maximal splinting from thoracic muscles
- Anatomy:
  - **Recurrent laryngeal nerve:** maintains open vocal cords via abductor muscle. If damaged → stridor. Rest of muscles supplied by superior laryngeal nerve
  - Pharynx: superior, middle and inferior constrictor muscles attach on the cervical spine at medium raphae
- Paediatric problems:
  - See also Neonatal Acute Airway Problems, page 924 and Respiratory Illness, page 936
Signs: stridor, feeding difficulties
Failure of canalisation → severe (normally dies)
Laryngomalacia: Supraglottic structures floppy → collapse on inspiration → inspiratory stridor. Improves with ↑muscle tone/innervation
Subglottic stenosis: congenital or trauma (eg too big a ventilation tube)
Croup:
- = Laryngo-tracheo bronchitis.
- Inspiratory and expiratory stridor, barking cough
- If frequent, may have anatomical narrowing
- Usually viral infection. If severe, steroids → ↓inflammation
Obstructive sleep apnoea:
- Very different to adults: usually due to enlarged adenoids/tonsils – snore loudly
- → Failure to thrive, behavioural problems, etc
- Obstructive apnoea up to age 7 → take adenoids out
Epiglottitis:
- Symptoms: obstruction, sore throat, drooling, toxic/septicaemia, no cough
- Cause: bacterial infection (eg H. Influenzae)
- Medical emergency: can deteriorate quickly. Don’t examine throat – may cause spasm and obstruct
- Emergency treatment: Geudal airway and ambubag. If unsuccessful get a very experienced person to intubate. If unsuccessful cricothyroidotomy with 14 gauge needle
Tonsillitis:
- Tonsils are not normal lymph nodes: don’t have capsule or afferent vessels
- Bulk of lymphoid tissue is in base of tongue
- Decrease in size with age. At 40 half the size as when 15
Foreign bodies:
- Can’t eat or drink.
- In kids: 10-cent pieces, inhaled peanuts. Differential: asthma (cough and wheeze). If < 2 years old, do CXR and look for collapse distal to obstruction
- In elderly with dentures: can’t chew or feel unwell
- Must take out: if stuck in gullet, will perforate within 7 days. Can linger for months in lung
Vocal cords:
- Papillomas: usually solitary. Very low incidence of malignant change. Laser them (usually repeatedly)
- Nodules: usually bilateral. Keratinised lesions from cords banging together. Treatment: vocal rest, correct voice abuse
- Polyps: usually unilateral. Granulation tissue/inflammatory
- Reincher’s disease: in middle aged female smokers. Degenerative, gelatinous polyps of surrounding mucosa → hoarse voice, obstruction. Cause unknown
Recurrent Laryngeal Palsy:
- Usually left nerve: longer. Right only goes round subclavian
- 40% idiopathic
- Exclude: bronchogenic cancer, mediastinal lymph nodes (eg lung or breast Ca), Ca of larynx, mononeuropathic infection
Voice disorders (Dysphonia, Aphonia):
- Obstruction to vocal cord closure: vocal cord thickening/oedema, nodules, papilloma, ulcers, polyps
- Larynx growths: leukoplakia, hyperkeratosis
- Trauma: intubation, external
- Paralysis: superior or recurrent laryngeal nerve
- Vocal hyperfunction: spastic dysphonia, tension due to voice abuse (singers, teachers)
- Presbyphonia: in the elderly
- Other: chronic laryngitis → mucosal atrophy, Parkinson’s, Motor neuron disease, following laryngectomy
- In all cases refer to speech-language therapy for assessment/management

**Adult Pneumonia**

- = Inflammation and consolidation of the pulmonary parenchyma

**Classifications**

- Community acquired vs. hospital acquired (probably most useful)
- Microbiological: typical vs. atypical organisms
• Radiological: lobar vs. diffuse/non-lobar/bronchopneumonia (although no clinical relevance as it doesn’t tell you which bug)
• Ventilator associated
• Normal vs. immunocompromised
• Severe or not
• Includes: bronchopneumonia, lobar pneumonia, interstitial pneumonia, and infectious granulomas

**History**

• Previous pneumonia, asthma, bronchitis
• Aspiration risk eg alcohol
• SHx: *smoking, alcohol, occupational or hobby exposure* (birds, dust, healthcare worker, etc)
• Infectious: overseas travel, recent arrival
• **TB History**: race, previous history, family history, exposure, living situation, BCG status
• History of *immunosuppression*: transplant, cancer, high dose steroids, HIV risk (sexual, weight loss, night sweats)
• Rigors and drenching sweats

**Epidemiology**

• 10% of hospitalisations
• At risk:
  ➢ Infants and children: more frequent exposure, immature immune system, narrower bronchial tree
  ➢ Elderly
  ➢ Altered level of consciousness: post-operative, CVA, fits, drugs/alcohol, diabetic coma: diminished cough reflex
  ➢ Smokers
  ➢ Patients with pulmonary oedema
  ➢ Immune deficiencies: leukaemia, lymphoma, renal transplant patients, cytotoxic drugs
  ➢ AIDS (80% of patients die of respiratory failure: 60% of these will have a pulmonary infection)

**Pathology**

• Pneumonia = inflammation of lung parenchyma with necrosis causing consolidation
• Bronchogenic pneumonia = extension of pre-existing bronchitis; patchy consolidation around small airways
• Lobar pneumonia = congestion, red hepatisation, grey hepatisation, resolution

**Complications**

• **Fibrosis rather than resolution;** organising pneumonia; polyps of granulation tissue in alveoli (*masson bodies*)
• Parapneumonic effusion
• **Pleuritis** – inflammation extends to pleura – pleuritic pain; starts as effusion then fibrosis
• *Empyema* = pus collection in the pleural cavity, heals by fibrosis
• *Abscess* = *dead neuts + bact*; necrosis of lung tissue *surrounded by fibrosis*; associated w staph aureus + klebsiella pneumoniae
• *Haematogenous seeding* = dissemination; bacteraemia, septicaemia; bact endocarditis, meningitis, pyelonephritis
• Death

**Types of Infectious Pneumonia**

*Bronchopneumonia*

• **Patchy consolidation of the lung.** Infection centred on a bronchus or bronchiole, involving immediately adjacent alveoli. Pleura not usually involved. Can overlap with lobar pneumonia
• Infection is spread through the airways
• **Macroscopic appearance:** patchy consolidation – firm, raised, nodular, red to grey-white. Colour varies with the amount of necrosis and haemorrhage, and due to stage. May involve one or more lobes
• **Microscopic appearance:**
  ➢ Bronchocentric lesions
  ➢ Early: congestion and oedema
  ➢ Progresses to: neutrophils + proteinaceous (fibrinous) exudate + RBCs fill distal airways and alveoli
Resolution: airways clear but may organise into fibrous tufts. Parenchymal destruction depending on organism

- **Causative organisms:**
  - Depends on whether community or hospital acquired, depressed pulmonary defences, etc
  - G +ive cocci (staphs and streps) and G –ive H Influenza, Pseudomonas, E Coli and Klebsiella
  - S. Aureus and G -ives more common in hospital acquired (eg in ICU) – also more destructive
  - Pseudomonas aeruginosa: can infect lung haematogenously → infection of vascular walls → haemorrhagic pneumonia. Common in burn, immunocompromised and cystic fibrosis patients. Usually fulminant course

- **Legionella pneumonia** (Legionnaire’s disease):
  - Characteristic morphology is acute fibrino-purulent exudative pneumonia – neutrophils + macrophages within a fibrinous exudates
  - Inflammatory response spares alveolar walls, so no necrosis or haemorrhage
  - **Mild and self-limiting**, except in elderly and smokers
  - 10 – 20% mortality in immunocompromised
  - Rumoured to have prominent GI symptoms *(diarrhoea and vomiting)* – but ?any difference in incidence to other agents
  - Characteristic in **air conditioning** (ie plumbers, office workers, etc) and carriage in **potting mix** (ie gardeners)
  - **Relatively normal WCC** seen (suggesting *atypical pneumonia*) and **hyponatremia** often

**Lobar Pneumonia**

- Involves whole lobe uniformly, often with reactive fibrinous pleuritis
- 95% of cases are Strep pneumoniea
- **Pathogenesis:** **bacteria inhaled → profuse fluid exudate** (good growth medium) → infection spreads through interalveolar pores throughout lobe
- **Macroscopic and Microscopic appearance**: 4 stages based on macroscopic appearance:
  - **Congestion**: 12 – 24 hours, **oedema**
  - Red hepatisation: 2 – 3 days. Redness due to *congestion and haemorrhage*. **Fibrinous neutrophilic exudate**, consistency of liver
  - Grey hepatisation: 3 – 4 days, grey due to ↑WBCs and fibrin, and ↓blood due to compression of capillaries
  - **Resolution**: 2 – 5 days, **macrophage phagocytosis and clearance**. Pulmonary architecture usually maintained, or fibrous tufts fill distal airways and alveoli and are then incorporated in the interstitium → interstitial fibrosis
- Complications: 20 – 30% get bacteraemia → meningitis, endocarditis, arthritis, etc.
- **Presentation**: fever, chills, productive cough with sputum from watery to rusty as the disease advances. ↓Functional parenchyma → SOB and cyanotic. Pleural rub.

### Pneumonia stage

<table>
<thead>
<tr>
<th>Macro</th>
<th>Micro</th>
</tr>
</thead>
</table>
| **Congestion** | Enlarged, heavy, red | Air spaces filled with:  
  - Fibrinogen  
  - RBC  
  - Neuts  
  - Bacteria |
| **Red hepatisation** | Looks like liver (solid, dense) | **Fibrinogen has clotted**  
  - Neuts ++  
  - Bacteria ++ |
### Lung Abscesses
- Can occur secondary to pneumonia or independently. There are two patterns:
  - Multiple abscesses: haematogenous spread or bronchopneumonia from a virulent organism that causes necrosis
  - Solitary abscess: usually due to anaerobic organism – e.g. following aspiration in alcoholic with depressed reflexes

### Infectious Granulomas
- Four possibilities for a granuloma:
  - **Tb**: no neutrophil infiltrate in granuloma → caseating necrosis
  - **Fungal**: causes abscess ⇒ neutrophils/pus in the middle
  - **Sarcoidosis**: non-necrotising (non-infectious)
  - **FB**
- Mainly Mycobacterial Tuberculosis: can infect any organ but commonly the lung
- Immune cells in granulomas:
  - Histiocyte = epithelioid cell = activated macrophage (‘eating phase’ as opposed to circulating in blood [= monocyte])
  - Bigger and more cytoplasm than a lymphocyte
  - If cytoplasm fuses → giant cell with multiple nuclei

### Tuberculosis
- See also Mycobacteria, page 817
- Usually Mycobacterium Tuberculosis. In AIDS/immunosuppression, may be M. avium-intracellulare. M. bovis causes GI Tb in 3rd world from contaminated milk
- Epidemiology:
  - Affects 33% of world’s population and causes 3 million deaths a year.
  - In first world, improved sanitation has reduced incidence – but is climbing again due to AIDS and antibiotic resistance
  - NZ: 300 notifications per year: European < Maori < PI < Other
- Clinical:
  - Non-specific fever and weight loss (due to macrophage cytokines), coughing, blood-tinged sputum. If in GI, can present with obstruction
  - Takes 6 weeks to 3 months before Tb sensitivity develops (ie Mantoux positive)
  - Predisposing host factors: malnutrition, alcohol, diabetes, age, immune suppression (diseases or drugs), background population prevalence
- Progression:
  - **Primary infection**: initial exposure is self-limiting → formation of a solitary granuloma (Ghon focus), often with granulomas along lymphatic drainage and in hilar lymph nodes (Ghon Complex). Lesions usually asymptomatic and undergo fibrosis and calcification
  - **Spontaneous recovery**: may still have bacilli on board
  - **Progressive primary infection**: rare, primary lesion erodes into airways or vasculature → airway spread or miliary spread → fulminant bronchopneumonia
  - **Post-primary pulmonary Tb**: fibro-caseous pulmonary TB. Infection in host with T cell memory (ie previously exposed). See a granulomatous response (nodules on CXR). Granulomas coalesce → consolidation evident on X-ray → cavity ruptures into a bronchus → productive cough, fever, sweating, haemoptysis (and infectious)
  - **Secondary infection**: in small percentage of those who had primary infection. Reactivation of latent mycobacteria. Usually in lung apices (higher O2 tension). Can become progressive. Can have isolated involvement of the intestine or adrenals (⇒ acute Addison’s Disease). Cell mediated immunity or delayed type hypersensitivity contributes to tissue destruction

<table>
<thead>
<tr>
<th>Grey hepatisation</th>
<th>Loss of red colour but still solid + dense</th>
<th>Neuts ++</th>
<th>Macrophages</th>
<th>Decreased cap congestion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Resolution</td>
<td>Liquefaction of exudates - expectorated</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
• **Respiratory**

**Diagnosis:**
- **Samples:** sputum, bronchial wash, gastric lavage in the morning, bronchoscopy, pleural tap
- **Culture** (6 weeks), **ZN stain**, **PCR** (not very sensitive or specific for serious disease but used to look for genes conferring resistance)
- **CXR**
- **Biopsy** (LN or pleura)
- **Tests of T cell memory for mycobacterium Ag:** Mantoux, **Quantiferon gold test:** IFN-γ (released when T cell encounters TB)

**Treatment:**
- Combinations always required for a long duration
- **Drugs:**
  - **Rifampicin:** Destroys rapidly dividing bacilli quickly (⇒ good for fulminant disease). SE: *enzyme induction, orange secretions*, rash, flu like illness, purpura, interference with OCP
  - **Isoniazid:** best and cheapest. Bactericidal. Side effects: rash, *peripheral neuropathy*, *hepatotoxicity*
  - **Pyrazinamide:** bactericidal, works intra-cellularly (ie bacilli inside macrophages). SE rash, *hepatotoxicity, gout*
  - **Ethambutol:** until sensitivities known. SE *optic neuritis*. In kids too young to monitor visual acuity, use streptomycin
  - **Pyridoxine:** vit B6 – counteracts isoniazid’s effect on vit B12 and therefore ↓ chance of peripheral neuropathy
- **Regime:** 2 months of isoniazid + rifampicin + pyrazinamide (+ethambutol until sensitivities are known) + 4 months of just isoniazid and rifampicin
- Compliance a major issue (⇒ direct observed therapy. Is cost effective compared to self-administered therapy. Treatment completion rates up to 90% are possible), also toxicity
- May need steroids (in addition to antibiotics) if adrenal suppression, miliary Tb or pleural effusion

**Pathology:**
- **Primary** pulmonary TB: **ghon complex** (*sub pleural lesion: Ghon focus + enlarged caseous hilar LNs = parenchymal lesion + nodal involvement*)
- **Post primary** pulmonary TB: reactivation; lesions in apex (O2 tension)
- **Progressive** pulmonary TB: cavitation; miliary spread; tuberculous bronchopneumonia (rapid spread throughout lung parenchyma)
- **TB histology:**
  - Granulomas: *epithelioid histiocytes; giant cells* (langerhan’s – immune type)
  - Central caseous necrosis
- Granulomatous inflammation:
  - Chronic, activated macrophage (epithelioid histiocyte) is the predominant cell
  - Caseating necrosis seen sometimes
  - Seen in TB, FBs, fungal infection, sarcoidosis (non-caseating)
- **Granuloma** = activated macrophages (epithelioid histiocytes) +/- giant cells; **lymphocytes** + plasma cells
- Bacterium is ingested by macrophages, but resists lysis due to waxy coat. Multiplies inside macrophage. Immune response forms granuloma through unknown mechanisms
- Macroscopic appearance: lesions in any organ – but mainly in lungs and lymph nodes. Initially small focus of consolidation < 3cm with central caseation, which cavitates if it communicates with a bronchiole. Resolution → fibrocalcific scarring puckering the pleural surface. Large nodules have extensive cavitation and necrosis, and are lined with a ragged white material containing millions of mycobacteria
- Microscopic appearance: granulomas composed of epitheliod cells surrounded by fibroblasts and lymphocytes, containing giant cells and Langhans cells (nuclei around the edge). Central caseous necrosis. Acid-fast bacilli with ZN stain

**Fungal Pneumonias**
- Second most common cause of **infectious granulomas**
- Often form necrotising granulomas with **central cavitation** similar to Tb
- Uncommon in NZ: but query in returned travellers or immunosuppressed
- Causative agents:
  - **Candida:** includes yeast and pseudohyphae. Oral commensal → multiple scattered lesion in the lung
  - **Aspergillus:**

---

Bottom L is central necrosis

Ghon complex - subpleural lesion mid-R; small hilar lesion in middle

Branching septate hyphae
- A saprophytic hyaline mould causing bronchopneumonia, possibly with vascular invasion and dissemination \(\Rightarrow\) haemorrhage and necrosis
- Most common in immunocompromised – especially **acute leukaemia**
- See **branching septate hyphae**
- Types:
  1. **Allergic bronchopulmonary aspergillosis** (*allergic rx in asthmatic pts; sputum = eosinophils, charcot-leyden crystals*)
  2. **Aspergilloma** (*fungus ball occurring in existing cavity – see fungal hyphae*)
  3. **Invasive pulmonary aspergillosis** (*in immunocompromised; hyphae invade parenchyma + blood vessels*)

  - **Mucormycosis** (*Zygomycosis*): 2 infectious types: Rhizopus and Mucor. Tendency to invade blood vessels and cause haemorrhagic pneumonia
  - **Cryptococcus neoformans**: pleomorphic round to oval 4 – 10 micron yeast with thick mucinous capsule. Found in bird (pigeon) droppings. Most common infection is **meningitis**. Stains with **Indian Ink**
  - Others: histoplasma capsulatum, coccidioides immitis and blastomycosis dermatitidis

**Viral Pneumonias**

- Usually acquired through inhalation
- Typically result in **diffuse interstitial oedema and lymphocytic cellular infiltrates in the septae**. Lungs tend to be heavy and diffusely firm without focal lesions. If severe \(\Rightarrow\) microvascular injury \(\Rightarrow\) pneumocyte necrosis and leakage of proteinaceous fluid into alveoli \(\Rightarrow\) hyaline membrane formation
- Most due to **influenza** viruses (elderly), **respiratory syncytial virus** (kids) and **rhinovirus** (kids)
- Viruses of note:
  - **Cytomegalovirus**: Herpes virus causing cytomegaly or enlargement of infected cells. May have multiple small **cytoplasmic inclusions** that are purple and PAS-positive. Subclinical infection unless immunocompromised. Commonest viral pneumonia in **immunosuppressed**. Focal or diffuse interstitial pneumonia. **CMV** primary infects epithelial and endothelial cells
  - **Herpes Simplex Virus** types I and II. Have characteristic nuclear inclusions in epithelial cells. Two patterns of spread: Necrotising Tracheobronchitis mechanism (spread by contiguity through necrotic mucosa) or Haematogenous dissemination (more random distribution through lung)
  - **Varicella Zoster**: Lung involvement similar to **H. Simplex**
  - **Measles**: RNA virus, infection leads to multinucleate giant cells, interstitial pneumonia, and focal bronchiolar necrosis. Mainly in immunocompromised kids with measles
  - **Adenovirus**: DNA virus mainly causing mild upper RTI. Clinical disease in transplant patients (eg bone marrow). Necrotising bronchitis and bronchiolitis. Smudge cells seen (large cells with dense mass filling the nucleus)
  - **Influenza**: RNA virus seen in older adults
  - **Respiratory Syncytial Virus**: RNA virus causing RTI in the young. Causes bronchiolitis, sometimes necrotising, and less frequently interstitial pneumonia

- Mainly **Influenza A** or **B**, **Adenovirus** or **RSV**

**Other Pneumonias**

<table>
<thead>
<tr>
<th>Pneumonia</th>
<th>Features</th>
<th>Pathology</th>
</tr>
</thead>
</table>
| **Viral pneumonia** | Influenza A + B, CMV | **Interstitial inflammation**  
|               |                           | **Lymphocytic infiltrate**                     |
| **CMV pneumonia** | Newborns + immunocompromised | **Chronic interstitial pneumonitis**  
|               |                           | **Intranuclear + cytoplasmic inclusions**     |
**Pneumocystis pneumonia**
- Pneumocystis carinii (fungus)
- Alveolar space filled with foamy amorphous material
- Silver stain = numerous round cysts

**Lipoid pneumonia**
- Due to obstruction of airway (eg FB or tumour)
- Lipid within surfactant builds up in macrophages
- Macro = yellow consolidation
- Micro = alveoli filled with macrophages containing lipid in cytoplasm

**Aspiration**
- Affects dependent parts (apical lower lobe, basal lower lobe) in a bronchopneumonia pattern
- URT normal microflora responsible
- Peribronchial consolidation
- Undigested food particles
- FB giant cells

- **Mycoplasma** pneumonia: Common cause of URTI. Smallest free-living organism. 15% of all pneumonias in general population. **Benign and self-limiting** with few complications. Peak incidence is 5 – 15 years. Causes a bronchiolar lesion with neutrophil rich exudate, and bronchiolar metaplasia
- Pneumocystis Carinii Pneumonia: Extracellular protozoan parasite almost exclusively infects the lung. Selective attachment to type I pneumocytes → injury. Usually in AIDs. Microscopic appearance: interstitial infiltrate of lymphocytes and plasma cells, and foamy intra-alveolar exudate containing the organism. Stain with silver (GMS). Occurs as cysts, excysted forms and trophozoites. Ground glass appearance on X-ray
- Lipoid Pneumonia: Exogenous lipid pneumonia – aspirated mineral oil being taken by the elderly for constipation → segmental opacification (whiting-out) of the lung and granulomatous fibrous reaction. Endogenous lipid pneumonia occurs distal to an obstruction (eg cancer) due to coalescing lipid droplets from dead alveolar macrophages
- Mixed bacterial flora is normally found in patients with chronic pulmonary infections (eg cystic fibrosis, bronchiectasis). Principle organisms are Pseudomonas Aeruginosa (commonest), staphylococcus aureus and Haemophilus influenzae

**Community Acquired Pneumonia**

**Epidemiology**
- 1 per 1,000 admitted annually
- Mortality = 10% (especially old, young, underlying disease)

**Pathogens**

<table>
<thead>
<tr>
<th>Organism</th>
<th>Proportion</th>
<th>Presentation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bacteria</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Strep. Pneumoniae</td>
<td>60 – 70%</td>
<td>Under 5, Over 50</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Abrupt</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Focal chest signs – usually lobar</td>
</tr>
<tr>
<td>Mycoplasma Pneumoniae</td>
<td>5 – 18%</td>
<td>Kids &amp; young adults, 4 yearly epidemic</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Flu like, minimal respiratory signs “walking pneumonia”</td>
</tr>
<tr>
<td>H Influenzae</td>
<td>4 – 5%</td>
<td>Type A: Smokers, COPD, all ages, no distinguishing signs</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Type B in unvaccinated pre-schoolers</td>
</tr>
</tbody>
</table>
Legionella 2 – 5%

Chlamydia (esp. from farm animals), S. Aureus, G- anaerobes < 3%

<table>
<thead>
<tr>
<th>Virus</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Influenza</td>
<td>8%</td>
</tr>
<tr>
<td>Other</td>
<td>2 – 8%</td>
</tr>
</tbody>
</table>

- Unknown organism in 1/3 of cases despite extensive testing. Dual infections occur
- Atypical organisms = mycoplasma, chlamydia, legionella
- GI symptoms in typical and atypical
- Clinical clues:
  - 2 – 3 days: pneumococcus, staph aureus
  - 1 – 3 weeks: mycoplasma/legionella
  - Sputum: foul smelling ⇒ anaerobic (eg aspiration); rust coloured ⇒ pneumococcal
  - Season: summer ⇒ legionella, mycoplasma comes in 4 yearly cycles
  - Chronic lung disease (eg COPD): H Influenzae, Moraxella catarrhalis (have β lactamase)
  - HIV: PCP
  - Neutropenia: G –ive, fungal
  - Alcohol: G –ive, legionella, staph
  - Aspiration (6 – 10%) ⇒ risk of anaerobe ⇒ cavitation. Upper respiratory commensals
  - Cavitation ⇒ S Aureus, G- & Tb
  - Previous viral infection common in bacteria
  - If immunocompromised:
    - Pneumocystis carinii (AIDs)
    - G–ive bacilli: pseudomonas aeruginosa, Klebsiella pneumoniae (neutropenic cancer patients)
    - Fungi: Candida albicans, Cryptococcus neoformans
    - Virus: cytomegalovirus

**Diagnosis**

- Suggested by fever (+ rigors + drenching sweats) + respiratory symptoms (cough, sputum, dyspnoea, pleuritic pain)
- May present with GI symptoms most prominent
- Confused with/DDx: acute bronchitis
- Signs: fever in > 80%, RR > 20, crackles on auscultation, consolidation in 30%
- Post influenza: 70% (?) S. Aureus infection (⇒ microabscesses)
- Can be secondary to abscess, empyema, lung cancer

**Investigation Options**

- CXR: extent, cavitation, effusion, cardiomegaly. False negatives possible if PCP or during first 24 hours
- DDX of consolidation on CXR = atelectasis, PE, ARDS, pulmonary haemorrhage/contusion etc
- **Blood gases**: see VQ mismatch ⇒ hypoxia ⇒ hyperventilation ⇒ ↓PCO2 ⇒ respiratory alkalosis ⇒ ↑A-a gradient
- FBC: WCC if > 15,000 x 10^9 ⇒ bacteria likely cf. virus
- Urea/electrolytes/liver ⇒ severity and underlying disease
- Urine: glycosuria
- Microbiology:
  - Sputum (but 1/3 don’t expectorate and many causative organisms are URT commensals therefore low sensitivity): culture and pneumococcal antigen test (most sensitive test for strep pneumoniae). If can’t get sputum sample, can nebulise with hypo-osmotic saline
  - Blood serum for pneumococcal antigen
  - Blood cultures
  - Culture plural effusion
- Lavage via bronchoscopy may be indicated in immunosuppressed patients and in those suspected of TB who can’t produce adequate sputum
- **Acute and convalescent serum for antibodies** to mycoplasma pneumoniae, legionella, chlamydia pneumoniae (Convalescent = 5 – 6 weeks later, a 4 fold rise in antibody titre or the presence of IgM specific antibody is evidence of recent infection)

**Prognosis/Criteria for Admission**

- Classified as severe if (↑21 times risk of mortality):
  - CURB-65 Score:
    - Age > 65
    - Respiratory rate > 30 bpm (key prognostic indicator)
    - Systolic BP < 100, Diastolic BP < 60 mmHg or low urine output (ie shocked)
    - Confusion
    - Serum urea > 7 mmol/L
  - Comorbid disease: heart failure, AF, diabetes, CORD, cancer, HIV, renal failure, chronic alcohol, etc
- Other markers of severe prognosis:
  - WCC < 4 or > 30
  - PO2 < 60 or inability to get sats above 90% despite O2 therapy
  - CXR shows bilateral/multilobar changes or pleural effusion
  - ↓ albumin
  - Haematocrit < 30%

**Treatment**

- Community treatment:
  - Immediate empirical therapy (must treat as high risk of mortality):
    - Should cover S pneumoniae
    - Erythromycin if atypical eg legionella/mycoplasma suspected
  - Antibiotics: for 5 – 10 days (10 – 14 if Mycoplasma or Chlamydia)
    - Cefuroxime and roxithromycin (according to Humble)
    - Oral amoxycillin 500mg td
    - If allergic to penicillin or atypicals: erythromycin
    - IV benzyl penicillin 1.2 g qd IV if poor absorption (e.g. vomiting)
    - If severe: augmentin OR cefuroxime PLUS erythromycin 1g qd + 3rd generation cephalosporin
- Types of antibiotics:
  - Penicillin: strep pneumoniae. Even if resistant, iv penicillin dose exceeds the MIC, so it’s still effective (doesn’t work though for Meningitis caused by Strep Pneumoniae because CSF penetration is lower)
  - Augmentin, Cefaclor, Tetracycline (not kids), cefuroxime (iv): H Influenzae (5% resistant to amoxycillin), Branhamella Catarrhalis (these two bugs have β-lactamase so augmentin used as has clavulonic acid)
  - Flucloxacinil: Staph aureus
  - Ceftriaxone: penicillin resistant strep pneumoniae, G- bacilli
  - Erythromycin (ie macrolides): mycoplasma, legionella, chlamydia
  - Rifampicin + isoniazid + pyrazinamide: Tb
  - Cotrimoxazole: Pneumocystis carinii
  - Fluconazole or Amphotericin B: Candida, Cryptococcus
  - Ganciclovir: CMV
- Resistant to Augmentin:
  - Mycoplasma pneumoniae
  - Chlamydia pneumoniae
  - Legionella
  - Penicillin resistant strep pneumoniae
- Hospital treatment:
  - Only 0.1% of chest infections get to hospital ⇒ not typical of population as a whole
  - Hospitalise if high pyrexia, cyanosis, tachycardia, tachypnoea, confusion (use CURB-65 score)
  - Oxygen:
    - See Oxygen Therapy, page 82
    - Give sufficient O2 to keep PO2 > 60 mmHg
    - O2 saturation > 90 % preferable
  - Transfer to ICU if:
    - Severe
    - Blood gases bad: PO2 < 60 on FIO2 > 60%, or PCO2 > 48 (should breath faster ⇒ PCO2 should fall – if normal or raised person getting tired ⇒ bad sign)
Respiratory

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Failure to Respond

- Is treatment failing?
  - Some improvement should be seen in 48 – 72 hours, don’t change treatment over this time unless there is a marked deterioration
  - CXR may worsen initially after therapy started: if mild pneumonia this may be normal. If severe, this is a poor prognostic indicator
  - Fever lasts 2 – 4 days, S pneumoniae resolves quickest
  - Crackles will last beyond 7 days in up to 40%. May take more than a month for CXR to clear

- If treatment is failing, consider:
  - Incorrect diagnosis: PE, pulmonary oedema, Wegener’s granulomatosis (ie non-infectious illness)
  - Antibiotic resistant organism
  - Resistant infection: mycoplasma, chlamydia, Staph aureus, TB, PCP (immunodeficient)
  - Complication: empyema, abscess, PE, drug induced fever, atelactasis
  - Underlying disease: lung cause, cancer, cardiac failure, immunodeficiency
  - Drug compliance in outpatients

Hospital Acquired Pneumonia

- Pathogenesis:
  - Aspiration plays a central role (45% healthy subjects aspirate during sleep, proportion increases in poor health)
    - ET tube does not prevent aspiration
  - Progressive colonisation
    - Aerobic gram negative bacteria
    - Within 2-3 days of admission
    - 75% of severely ill patients

- Risk factors:
  - Mechanical ventilation 6-21 fold
  - Age >70 years
  - Chronic lung disease
  - Impaired consciousness
  - Large volume aspiration
  - Chest surgery or trauma
  - H2 blockers or antacids

- Bugs:
  - Pseudomonas Ag 17%
  - Staph aureus 16%
  - Enterobacteriaceae 11%
  - Klebsiella species 7%
  - E Coli 6%
  - H. influenzae 6%
  - Others: Serratia marcescens, Legionella species, Pneumococcus, Anaerobes, Influenza A, Fungal species

- Antibiotic treatment:
  - ICU Patient: IV anti-pseudomonal cephalosporin or penicillin with gentamicin
  - Suspect anaerobic infection: IV anti-pseudomonal cephalosporin with clindamycin or metronidazole
  - Duration: 10-14 days standard; 3 weeks for staph

Respiratory Microbiology

<table>
<thead>
<tr>
<th>Pneumonia</th>
<th>Organisms</th>
<th>Defining features</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bacterial</td>
<td>Lobar</td>
<td>1. Congestion (heavy, congested w blood, fibrinogen in alveolar)</td>
</tr>
<tr>
<td>Broncho-</td>
<td>Typical</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1. S.</td>
<td></td>
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<tr>
<td></td>
<td>GP diplococci</td>
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<tr>
<td></td>
<td>Uncomplicated</td>
<td>2MU IV</td>
</tr>
<tr>
<td></td>
<td>Penicillin</td>
<td></td>
</tr>
<tr>
<td>Condition</td>
<td>Organism</td>
<td>Organism features</td>
</tr>
<tr>
<td>-------------------------</td>
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<td>---------------------------------------------</td>
</tr>
<tr>
<td></td>
<td>GAS (most common cause of bact pharyn.)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Diphtheria (toxin)</td>
<td>Thrush = oral candidiasis</td>
</tr>
<tr>
<td></td>
<td>N. gonorrhoea</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Mixed anaerobes (vincent’s angina)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Fungi</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Candida albicans</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Viruses</td>
<td></td>
</tr>
<tr>
<td></td>
<td>All those below can cause pharyngitis</td>
<td></td>
</tr>
<tr>
<td>Common cold</td>
<td>Rhinovirus</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Coronavirus</td>
<td></td>
</tr>
<tr>
<td>Influenza</td>
<td>Influenza A, B</td>
<td></td>
</tr>
<tr>
<td>Croup</td>
<td>Parainfluenza virus</td>
<td></td>
</tr>
<tr>
<td>(laryngotracheobronchitis)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pharyngoconjunctival fever</td>
<td>Adenovirus</td>
<td></td>
</tr>
<tr>
<td>Infectious mononucleosis</td>
<td>EBV</td>
<td></td>
</tr>
<tr>
<td></td>
<td>A herpes virus</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Can cause hepatitis</td>
<td></td>
</tr>
<tr>
<td>Gingivo-stomatitis</td>
<td>HSV</td>
<td></td>
</tr>
</tbody>
</table>

Respiratory 99
<table>
<thead>
<tr>
<th>Bronchiolitis</th>
<th>RSV</th>
<th>-</th>
<th>SOB, tachypnoea, IC muscle retraction, cough, fever</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>NB. AOM &amp; acute sinusitis caused by same 3 organisms</td>
<td>Strep: Penicillin IV or Amoxicillin oral</td>
<td>H. inf. + m/b catar: Augmentin</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>NB h. inf. not sensitive to erythromycin</td>
</tr>
<tr>
<td>TB</td>
<td>Mycobacterium tuberculosis</td>
<td>Waxy cell wall, can escape macrophage killing</td>
<td>Aerobic bacilli</td>
</tr>
<tr>
<td></td>
<td>Rifampicin</td>
<td>Isoniazid</td>
<td>Pyrazinamide</td>
</tr>
<tr>
<td>Other Mycobacteria</td>
<td>M. avium-intracellulare (cervical lymphadenitis in children, destructive lung d in adults, + GIT + blood + liver/spleen in imm-comp)</td>
<td>M. kansasii (can invade lungs)</td>
<td>M. marinum (contaminated water eg fish tanks – skin + subcutaneous infection)</td>
</tr>
</tbody>
</table>

### Pleural Disease

- **Common problems:**
  - Effusion
  - Empyema
  - Pleural pain
  - Pleural disease
  - Pneumothorax. See Tension Pneumothorax, page 804

### Pneumothorax

- **Classification:**
  - **Primary** spontaneous:
    - Typically occurs in *tall thin men* between the ages of 15 and 30 years
    - Rarely occurs over the age of 40
    - Smoking increases the risk by **20 fold** in a dose-dependent manner
    - Caused by *pulmonary blebs* – small vesicles that can burst
    - **Management:**
      1. Observation is Rx of choice for small asymptomatic Ptx
      2. Simple aspiration is first-line treatment for a symptomatic primary Ptx
      3. Intercostal tube should be inserted if aspiration is unsuccessful (can be small bore). Can be removed 24 hours after bubbling has stopped (ie hole has closed)
      4. Add suction if failure to expand
      5. If still not successful → cardiothoracic opinion re pleurodesis
  - **Secondary** spontaneous:
    - Occurring in the setting of underlying lung disease
    - Have a worse prognosis due to underlying lung disease (COPD, PCP in AIDS, CF, severe asthma)
    - Prolonged air leak is common and surgery often required (if patient is fit enough)
  - Iatrogenic
  - Traumatic
  - **Tension:**
    - Occurs because the opening that allows air to enter the pleural space functions like a valve (ie an oblique entry point), and with *every breath more air enters and cannot escape*
    - Management: insert large bore (14g) needle into 2nd ICS ABOVE rib in MCL
  - **History:**
    - Sudden breathlessness
    - Sometimes pain
• Examination:
  ➢ Hyperresonance
  ➢ ↓BS/↓VR/↓TVF
  ➢ Sometimes tachycardia
  ➢ If tension:
    o Hypotension
    o ↑HR, ↓sats
    o RV strain as it gets squashed (↑JVP, maybe displaced AB, RV heave/lift, palpable P2)
• CXR: no lung markings, mediastinal shift with tracheal deviation away (pushed) from side of damaged lung

Pleural Effusion
• History varies dependent on underlying cause:
  ➢ Exudates:
    o Parapneumonic effusion (exudate)
    o Malignancy (exudate)
    o PE with infarct (exudate)
  ➢ Transudates:
    o Heart failure (transudate)
    o Cirrhosis (transudate)
    o Nephrotic syndrome (transudate)
• Examination:
  ➢ Dullness (stony)
  ➢ ↓BS/↓VR/↓TVF
• Investigations:
  ➢ CXR:
    o PA, lateral and lateral decubitus (does pleural opacity move with gravity)
    o If sufficiently large → displacement (eg trachea) away from side of effusion (as cf collapse which is towards side of collapse)
  ➢ Pleurocentesis (see below)
  ➢ Pleural biopsy
  ➢ US for septa or cysts
  ➢ CT, MRI rarely superior to CT
• Pleural space:
  ➢ Usually 0.4 mls of fluid
  ➢ If ↑ then either ↑ production or ↓ clearance (eg Tb or malignancy blocking lymphatics)
• Pleural fluids:
  ➢ Takes 300 – 500 ml before visible on CXR
    o Can see:
      1. Serous fluid
      2. Blood
      3. Chyle
      4. Pus
    o Other conditions producing pleural effusion: trauma, CT disease, OHSS (ovarian hyperstimulation syndrome)
  ➢ Light’s criteria: the pleural fluid is an exudate if one or more of the following criteria are met:
    o Pleural fluid protein is >50% of serum protein
    o Pleural fluid LDH is > 60% of serum LDH
    o Pleural fluid LDH is more than 2/3 the upper limits of normal serum LDH
    o Ie ↑protein/↑LDH = exudate
  ➢ Transudate:
    o Pleural membrane not diseased
    o Due to change in hydrostatic or osmotic pressure due to distant disease
    o Eg nephrotic syndrome (ie hypoalbuminaemia), cirrhosis or CHF
  ➢ Exudate:
    o Protein-rich (> 30 – 40 g/L)
    o Is an inflammatory process → ↑ protein as leaky capillaries
    o Due to: infection (parapneumonic effusion or empyema), malignancy, Tb, SLE/RA, asbestosis, drug induced
  ➢ Pleural fluid tests:
- pH → is ↓ in empyema
- Cell count → not overly useful
- Gram stain + culture → if ?infection
- Cytology → if ?malignancy
- Total protein
- Albumin: if (effusion albumin)/(serum albumin) > 0.5 then transudate
- LDH: ↑ in exudates
- Amylase: normally none. If present then oesophageal rupture or pancreatitis

- If blood in a pleural tap then:
  - Hit an artery
  - Haemothorax (need to evacuate. NB can bleed 3 litres into one side of the chest → profound shock)
  - Blood in an effusion (eg Tb/cancer). To differentiate from a haemothorax measure the haematocrit

**Empyema**
- = Collection of purulent material (with or without bugs) in any body site: usually refers to pleural space
- Parapneumonic effusions develop in 30-50% of pts with CAP → 15% of these become infected
- Mortality in empyema is 10-20%
- Pathophysiology = parapneumonic exudate → infected parapneumonic fluid (↓pH + glucose) → empyema (frank pus in pleural cavity)
- Pleural infection:
  - The finding of any one of the following indicates pleural infection and requires chest tube insertion:
    - Pus
    - Pleural pH < 7.2
    - Positive gram stain or culture
- Strep pneumoniae and Staph aureus are the main pathogens
- Closely related to lung abscess (necrotising pneumonia)
- Symptoms: fever, sweats, cough, dyspnoea, weight loss, pleurisy
- Signs: stony dullness to percussion, ↓breath sounds, maybe quite localised, fluid in costophrenic angles on X-ray
- Basic management:
  - Inter-costal tube drainage
  - Antibiotics (based on gram stain or culture results; empiric treatment: cefuroxime and metronidazole)
  - Nutrition, DVT prophylaxis etc
  - Aim of treatment is resolution of sepsis (fever, white count, CRP), rather than resolution of CXR changes
  - If drainage fails → need further imaging (CT chest +/- US) to determine drain position/presence of loculations
  - Surgery if failure of sepsis to resolve
  - If unfit for thoracotomy, options include: placement of further drains into locules or streptokinase into locules to break down fibrin
- Usually heals with pleural fibrosis

**Malignant Pleural Effusion**
- Median survival following diagnosis is 3 to 12 months and is dependent on the stage and type of the underlying malignancy
- Most common malignancies:
  - Lung
  - Breast
  - Lymphoma
  - Ovarian
- Investigation:
  - Clinical presentation
  - Pleural fluid cytology (60% are positive)
  - Chest CT scan
  - Invasive diagnostic tests
- Management options:
  - Recurrent aspiration of fluid
  - Chemotherapy for the underlying tumour (small CC + ovarian ca respond well)
  - Pleurodesis (more important requirement for success is complete evacuation of pleural space)
Medical: chest tube → drain pleural fluid → inject sclerosing agent eg talc, tetracycline → clamp tube + allow to drain

Surgical

Venous Thromboembolism

Deep Vein Thrombosis (DVT)

Risk Factors

- Key risk factors:
  - Age
  - Obesity
  - Immobility
  - Co-morbidity

- Others:
  - Post-operative (immobile + hypercoagulable)
  - Pregnancy & immediately post-partum
  - Thrombophilia
  - Smokers on the pill. See Contraceptive, page 551, for risk ratios
  - Obesity, Cancer, Polycythaemia
  - PMHx or FHx of DVT

Presentation

- May be rapidly offset by collateral bypass
- Less than 1/3 present with classic syndrome of calf discomfort, distal oedema, venous distension & pain on forced dorsiflexion of foot
- Homens’s sign: pull big toe up → stretch calf → pain. Of little diagnostic value and could theoretically dislodge a clot
- Exclude Baker’s cyst: herniation from joint space into popliteal space – wouldn’t cause leg swelling
- Approx. 50% are asymptomatic

Investigations

- See Possible Investigations (in PE section), page 106

Treatment

- Aims:
  - Prevent PE
  - Restore venous patency

- Options:
  - Anticoagulant:
    - IV or subcutaneous heparin for 5 days (until warfarin kicks in): aim for APTT 1.5 – 2.5 times normal
    - Oral warfarin for 3 months: 5mg daily then dose adjust to aim for INR 2.0 – 3.0. Can continue longer – haemorrhages, if they occur, are usually early on
  - Surgery: really only if limb at risk. Veins often re-occlude
  - Thrombolytic treatment: better clearance of occlusion, no change to PE risk, ↑risk of bleed or intra-cranial haemorrhage little evidence of net benefit

- Prophylaxis:
  - Cost effective if risk high. Base assessment on clinical risk – lab results not good predictor. If low risk after surgery – early ambulation and stockings may be sufficient
  - 2/3rds ↓ in risk with LMWH (inject daily for duration of risk)
  - Mechanical: intermittent external compression with inflatable cuffs as effective as drugs in moderate risk people – but frequently misused
  - Antiplatelet: aspirin not as effective as anticoagulant but good in the community as LMWH not funded (ie can be prescribed by GP for a temporarily bed-bound elderly or obese person)

Anticoagulant Treatment

- Standard (unfractionated) Heparin:
  - Potentiates antithrombin III at all sites of coagulation activation (cf Low Molecular weight Heparin which only acts at Factor 10)
Dosing:
- 10 fold variability in individual dose response → individual titration required
- T½ = 100 minutes
- Monitor APTT and aim for 1.5 – 2.5. (If goes above 3 then 8 * risk of bleed)
- Monitor after 10 hours (4 – 5 half lives)

Emboli doses:
- IV dose: Loading 5000 IU, maintenance 1400 IU/j (20 IU/kg/hr)
- Subcutaneous: 17,5000 IU 12 hourly, duration of action 9 – 10 hours
- T½ ↓ in large PE ⇒ need infusion not bolus

Standard Heparin Prophylaxis:
- Medical view (surgeons disagree!): 5% DVTs in general surgical operations, 20% in orthopaedics
- Pre-op Prophylaxis:
  - ↓Non-fatal PE by 40% and fatal by 65%
  - ↑Risk of excess bleeding from 3.7% to 6%
- Low dose heparin (never warfarin):
  - 5000 IU standard heparin 12 hourly start 2 hourly pre-op
  - LMW Heparin single dose: more costly and no advantage in most cases
  - Continue for 2 weeks for patients at high risk (biggest mistake is to stop too soon)

Heparin induced bleeding:
- Uncommon for 1st 2 days, then common for days 3 – 10
- Retroperitoneal is a common occult site of bleeding
- Antidote: Protamine sulphate + FPP (clotting factors)

Low Molecular Weight Heparin:
- Is the standard initial anticoagulant therapy in the management of VTE
- LMWH is safer + more effective than IV heparin → means can treat in the community
- Lots of different types, all with different T½ and doses
- Longer T½ (can have once daily dosing), better bioavailability, less platelet inactivation, and potentially less bleeding
- Elimination is not dose dependent (heparin approaches this at high dose)
- Need to adjust for obesity
- Protamine reversal less efficient

Warfarin:
- Competitive inhibition of Vitamin K dependent clotting factors (II, VII, IX, X) and inhibits proteins C and S
- Pharmacokinetics:
  - Very narrow therapeutic index
  - 10 fold variability from dose to plasma concentration, and further 10 fold variability from plasma concentration to effect
  - 99% albumin bound ⇒ Vd = intravascular space
  - T ½ = 25 – 60 hours, biological effect lasts 2 – 5 days
- Contraindications:
  - Teratogenic, but not in breast milk
  - Risks of bleeding, eg peptic ulcer, haemorrhagic stroke
  - On NSAIDs (→ GI bleed; NSAIDs have an antiplatelet effect + ↑ risk of GI bleed due to GI irritation)
- Consider:
  - Can the patient cope with therapy and monitoring (infirm, alcoholic, etc)
  - ↑Warfarin sensitivity if > 65 years due to ↓ liver metabolism
  - Patient education important – lots of different sized/coloured pills
- Dose:
  - Do pre-test INR
  - Start low, monitor on day 3
  - Dose range approx 3 – 9 mg daily (contrary to New Ethicals)
- Target range for INR:
  - Venous thromboembolism: INR of 2 – 3 for 3 months for 1st VTE
  - Non-rheumatic atrial fibrillation:
    - Risk factors: hypertension, previous VTE, recent heart failure
    - Don't anticoagulate patients < 60 years if no risk factors
    - MI: 20% ↓ in mortality and reinfarction but no advantage of warfarin over aspirin except with added fibrillation (in which case aim for INR 2 – 3)
Bleeding:
- Risk factors: age, haemostatic disorder, malignancy, uraemia, GI ulceration, recent surgery, haemorrhagic strokes, low protein states (ie ↓ clotting factors)
- Management:
  1. If INR < 7 withhold doses until INR in normal range (unless severe bleed)
  2. INR > 7 and no prosthetic heart valve: 0.5 mg iv vitamin K (never IM)
  3. If INR > 7 and prosthetic heart valve, don’t use vitamin K unless evidence of an intracranial haemorrhage
  4. If overt bleeding: stop warfarin, give FFP or Prothrombin complex concentrates

Drug interactions:
- Inducers: take 10 days to ↓ warfarin concentration, and warfarin toxicity when stopped. Phenytoin, carbamazepine, phenobarbitone, rifampicin
- Inhibitors: immediate effect → warfarin toxicity. ↓ INR when these are stopped: macrolides, metronidazole, fluoxetine, quinolones (eg ciprofloxacin), chloramphenicol, cimitidine, disulphram
- If massive PE, consider thrombolysis. Echocardiogram to determine RV function useful in assessing risks and benefits

Pulmonary Embolism (PE)
- Very important to do a risk assessment for everyone in hospital or bed-bound at home: are they low, medium or high risk. Prevention is better than cure
- The probability of DVT or PE is determined through the use of a number of methods including clinical assessment, D-dimer, Doppler ultrasound, V/Q scan, CTPA

Presentation
- Frequently undiagnosed (71% of PEs are not diagnosed): always have it as a differential to SOB
- If episodic SOB unresponsive to treatment → ?PE
- Symptoms:
  - Breathlessness
  - May or may not have chest pain
  - Maybe cough
  - Maybe haemoptysis
  - May have fever, but rarely sweating or rigors
- Severity:
  - Mild/moderate:
    - Small: maybe transient chest pain, maybe cough, breathlessness. If pre-existing pulmonary disease may get small infarct with pleuritic chest pain and fever
    - Medium: bronchial arteries are enough to maintain viability of healthy lung tissue. Get chest pain (not always pleuritic), SOB, maybe haemoptysis
  - Submassive:
    - Normal BP, maybe tachycardia
    - Progressive breathlessness as clot keeps breaking off and occluding → RV begins to fail
    - See RV strain:
      1. ↑ JVP
      2. RV heave
      3. Loud P2
      4. ECG changes: ST↓ + TWI in V1-V3 (ie RV); S1Q3T3 (see below). Tachycardia is most reliable sign
      5. ↑ BNP ↑ TnT
  - Massive:
    - Large: classical – 10 days post op, sudden SOB and collapse (often while straining on toilet)
    - If fatal, die within an hour (from circulatory failure, not respiratory failure)
    - May mimic MI (acute SOB, severe chest pain, hypotension, temp, ↑ LDH, syncope)
    - Also cyanosis, gallop rhythm, ↑ JVP, pleural rub, haemoptysis
    - Key feature is hypotension, also see tachycardia
    - Need urgent CTPA before thrombolysis
- Course: frequent PE → pulmonary hypertension → dilated pulmonary artery → enlarged right heart (Cor Pulmonale)

Risk Factors
- Use Pre-test Probability Score (essentially Well’s Score) for suspected PE:
- Clinical signs and symptoms of DVT (at least leg swelling and pain) 3
- Heart rate >100 1.5
- Immobilisation or surgery in previous 4 weeks 1.5
- Previous DVT/PE 1.5
- Haemoptysis 1
- Malignancy (on treatment last 6 months) 1
- An alternative diagnosis more likely than PE -3
- Score <2 = low risk; 2-6 = moderate; >6 = high

- Use Pre-test Probability Score for suspected DVT:
  - Active cancer 1
  - Paralysis, paresis, recent plaster, immobile or surgery in previous 4 weeks 1
  - Localised tenderness along the distribution of deep venous system 1
  - Entire leg swollen 1
  - Asymmetrical calf swelling >3 cm (10 cm below tibial tuberosity) 1
  - Asymmetrical pitting oedema 1
  - Collateral superficial veins (non varicose) 1
  - Alternative diagnosis more likely than DVT -2
  - Score <1 = low risk; 1-2 = moderate; >2 = high

- Others = thrombophilies (eg factor V leiden, protein C or S deficiency, antiphospholipid syndrome, antithrombin III deficiency, prothrombin deficiency)

**Possible Investigations**

- Imaging:
  - CXR: most are normal
  - Doppler US for DVT
  - Ventilation-Perfusion Scan
  - Pulmonary arteriogram: gold standard but not often done
  - CT Pulmonary Angiogram: test of choice for PE

- ECG:
  - Small-medium PE: usually normal except for tachycardia. May be signs of AF or right ventricular strain
  - Massive PE: **S1Q3T3 pattern**: S wave in lead I, Q wave in lead III, inverted T wave in lead III. Tall peaked T waves in lead II.

- Bloods:
  - ABGs: A-a gradient (will be ↑)
  - FBC - check Hb, WBCs, platelets (eg ↑→ hypercoagulable)
  - Clotting times: likely to be normal – these test bleeding disorders, not clotting disorders

- D-dimer test for fibrin degradation products → digested clot (cheap and easy):
  - Almost 100% sensitive therefore excellent NPV but not specific, especially in older adults
  - Higher values are more specific
  - +ve for cancer, trauma, post surgery, sepsis → lots of false positives

- Decision analysis:
  - Aim is to determine level at which probability is sufficiently low to withhold treatment, or sufficiently high to start treatment
  - After a test, if the probability of PE is too high to withhold treatment + too low to treat the patient → a second test must be performed
  - The “test” and “treatment” thresholds depend on a balance between the:
    - Severity of the untreated disease
    - Efficacy of treatment
    - Complications of treatment and tests
    - Properties of the test
  - If low to moderate clinical probability and D-dimer negative: below test threshold
  - If suspect DVT/PE and D-dimer positive, or high clinical probability and D-dimer negative: start treatment (LMWH) and continue testing until diagnosis confirmed or ruled out
  - If > 6% risk of a PE then test
  - If > 48% risk of a PE then treat
  - If risk > 6% but < 48% then further testing
  - Test sequence:
Respiratory

CXR and D-dimer: if D-dimer negative then no DVT/PE. Positive test doesn’t change pre-test odds. If abnormal → CTPA

- If ?DVT → US
- If ?PE → CTPA → if unequivocal then V/Q scan → if still unequivocal → US → if still → pulmonary angio
- V/Q Scan: if positive then treat. If negative, doesn’t change pre-test odds

Pathology:
- Macro large = saddle embolus
- Macro small = wedge-shaped infarcts, sub pleural (b/w pleura + body wall), haemorrhagic
- Micro large = pre-mortem clot, organised, lines of zahn (alternating pale pink bands of platelets with fibrin and red bands of RBCs forming a true thrombus)
- Micro small = necrosis of lung parenchyma, haemorrhage

Treatment
- See Anticoagulant Treatment, page 103
- If massive (hypotension and multiple clots): thrombolysis or surgery
- If submassive (RV strain or lots of clots): consider thrombolysis

Asthma
- Is chronic and obstructive, but not usually categorised with COPD

Asthma in Young Children
See Asthma in Young Children, page 945

History
- Viral infections likely to trigger asthma
- Night time cough and low peak flow can be asthma, ?hay-fever, a cold or bronchitis
- Ask about provoking factors:
  - Living situation
  - Occupation (related to irritants)
  - Allergies, any pets?
  - Seasonal
  - Cold air
  - Irritants (eg fumes)
  - Exercise
  - Night cough
  - History of atopy: eczema
- Classic symptoms (intermittent): SOB, wheeze, cough, tightness (like in angina)
- Think about potential DDx:
  - COPD (chronic bronchitis [but ↑clear sputum ++], emphysema [not intermittent], bronchiectasis [purulent sputum])
  - URTI causing post nasal drip + cough
  - LVF
  - Central airway obstruction/FB
  - Post infective airway hyperresponsiveness

Assessment
- Always do peak flow. Not the same as FEV1, which is more accurate. FEV1 of 50% of predicted = PF of 70% predicted
- If can’t get a wheeze on auscultation, then take a big breath and blow out fast to elicit wheeze (= Forced End Expiratory Wheeze).
- Also listen to heart to ensure it’s not a cardiac cause (can see wheeze with heart failure)
- Examine for signs of allergy/eczema
- Can you demonstrate reversible bronchial constriction? If peak flow (or FEV1 if spirometry available) ↑ by 15% (60 – 70 litre/min; 12% ↑ if spirometry) following bronchodilator. Do best of 3 peak flows, then repeat 15 minutes (= peak response time) after >= 2 doses of a reliever
- There will be significant pathology even if mild:
  - Pseudostratified epithelium gone (desquamation)
  - Thickenened basement membrane

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- There will be significant pathology even if mild:
  - Pseudostratified epithelium gone (desquamation)
  - Thickened basement membrane
• ↑ eosinophils
• Hypertrophy of smooth muscle and glands
• ↑ mucus (mucus gland hyperplasia)

• High-risk asthmatic (markers of ↑ risk of death):
  • Hospital admission in last 12 months
  • Previous life threatening attack
  • Repeated self-administration of high doses of reliever (eg requesting 2 or more reliever prescriptions per month)

• Precipitating factors in a life-threatening attack:
  • In kids (80%) and adults (30%): viral URTI. Most commonly rhinoviruses and coronaviruses ('common cold')
  • Allergen exposure in a sensitised individual
  • Drug sensitivity, eg aspirin
• If severe, then ?other causes: PE, pneumothorax, etc

Classification of Severity/Asthma Plan

• How they feel (ie breathlessness) does NOT correlate to severity (as measured by FEV1). Due to temporal adaptation – if chronically breathless, body turns off perception of breathlessness (cf don’t hear trains if living by a railway line). Unless you MEASURE lung function, you CANNOT assess severity. However, in kids have to rely on symptoms as peak flow unreliable

<table>
<thead>
<tr>
<th>PEF</th>
<th>Symptoms</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Under Control – stable</td>
<td>&gt;80% predicted (best PEF they’ve ever had)</td>
<td>Can exercise easily, symptom-free most days, Not needing reliever on most days.</td>
</tr>
<tr>
<td>Getting Worse - unstable</td>
<td>&lt; 80%</td>
<td>Daily symptoms, waking at night, getting a cold, more short of breath with exercise, needing more reliever</td>
</tr>
<tr>
<td>Severe</td>
<td>&lt;60%</td>
<td>More breathless or wheezy, reliever only lasts 2 – 3 hours. Getting worse despite more preventer</td>
</tr>
<tr>
<td>Emergency</td>
<td>&lt;40%</td>
<td>Hard to speak, feeling faint or frightened, reliever not working.</td>
</tr>
</tbody>
</table>

• Key time to measure peak flow is when asthma is getting worse. No one will do it all the time so don’t ask them to

• Severe asthma:
  • PEF ≤ 50%
  • HR ≥ 120
  • RR ≥ 24
  • Cannot complete full sentence in one breath
  • Only require one of these to be classified as severe

• Life-threatening asthma:
  • PEF ≤ 33%
  • PaO2 ≤ 60/sats ≤ 90% on O2
  • PaCO2 normal or ↑ (should be low as hyperventilating)
  • Silent chest/cyanosis/drowsy (signs of need for intubation)
  • Only require one of these to be classified as life-threatening

Principles of Management

• Asthma plans (see above and here) are recommended as essential in the long-term treatment of adult asthma. Those with formal management plans have half the morbidity of those without them, despite the same treatment

• Also need to establish, avoid and control triggers

• Factors associated with asthma deaths:
  • Long term:
    o Lack of appreciation of chronic asthma severity and risk

Respiratory 108
• Poor compliance
• Discontinuity of medical care
• Under utilisation of inhaled steroids

➢ Fatal attack:
  • Delay in seeking medical help
  • Inability to recognise severity
  • Over-reliance on bronchodilator
  • Insufficient systemic steroid use
  • Lack of written information

• If the management plan is too complicated for the patient, modify (eg just the point at which to see the doctor)
• Compliance is critical ⇒ ownership of treatment by the patient is fundamental – negotiate and educate

Treatment

• Status asthmaticus: severe acute asthma that does not respond to treatment. See Asthma, page 798
• Severe/life-threatening asthma (SOS = salbutamol + O2 + steroids):
  ➢ O2
  ➢ Bronchodilators:
    • Salbutamol (5mg nebs; 100µg x 12 via spacer; as often as required, may need continuous nebs)
    • Ipratropium (antimuscarinic; 0.5mg neb)
  ➢ Steroids: either prednisone per oral (40mg) or hydrocortisone IV (200mg)
  ➢ Theophylline: IV (is a weak bronchodilator – PDE5 inhibitor; has narrow therapeutic index + nasty side-effects)
  ➢ Magnesium: IV (weak bronchodilator; 1.5g over 30min)

• Most important part is use of inhaled corticosteroid. Patient may favour reliever (it obviously does something – reinforce that preventer stops it happening to start with)

• Inhaled corticosteroids:
  ➢ Action: anti-inflammatory and ↓hyper-reactivity
  ➢ Effect: ↑lung function, ↓symptoms, ↓admissions (only drug to do this)
  ➢ If using a β-agonist most days then should be on an inhaled steroid
  ➢ Compliance is very poor – around 50% actually take ICS as prescribed ⇒ use this as an opening line:
    “studies show that only 50% actually take their preventer – are you better or worse than that?”
  ➢ Doses:
    • 200 to 1000 µg/day of Beclomethasone Dipropionate (BDP/Becotide) or Budesonide (BUD/Pulmicort), or
    • 100 to 500 µg/day of Fluticasone Propionate (Flixatide - only difference is potency, not efficacy, ↑side effects)
  ➢ Starting dose: if steroid naïve, better to start low and step up not start high and step down – too hard to wind it back
  ➢ Back titration: in stable patients back titration may be attempted. ½ dose as a one off. If cut too far too fast can rebound within a month. Stopping treatment altogether is likely to cause a relapse
  ➢ Doses by severity:
    • Stable: inhaled steroid bd, β agonist prn. If well controlled can take total steroid dose once a day at night rather than bd ⇒ better compliance
    • Unstable: inhaled steroid qid, β agonist prn. If still not controlled then oral theophylline at night or LABA
    • Severe: systemic steroids, high dose β agonist, O2, medical review. Bronchodilators and inhaled steroids don’t work so well in severe asthma as the major cause of obstruction is mucus plugging and the drugs don’t get through. Steroid dose: start early (takes approx 12 hours to have an effect), 0.4 – 0.6 mg/kg/day = 40 mg for normal adult. In practice: 30 – 40 mg/day until PEF normal, then 20 mg/day for as many days again
  ➢ Side-effects: dose dependent redistribution of fat, electrolyte disturbances, hypertension (ie Cushing’s features), stunted growth in children

• Bronchodilators:
  ➢ Reliever. Short acting inhaled β2 agonist
  ➢ Potent and rapid bronchodilator and a relatively low toxicity. Relaxes airway smooth muscles (plus other effects, e.g. ↓release of mast cell mediators). Adverse effects: muscle tremor and tachycardia common. Use as needed – not regularly – then becomes a guide to severity
- Salbutamol and terbutaline sulphate common. **2 puffs** (as cf with children via spacer) except in severe asthma – use **6 puffs**
- Long acting agonists for more severe asthmatics: **Salmeterol** and Eformoterol (similar effect but ↑ potency). Peak effect 2 – 4 hours, duration 9 – 12 hours
- Use nebulised salbutamol or spacer + MDI in acute asthma attacks
- Theophylline:
  - May have additive effect with β agonist, but ↑ risk of side effects (including ↓ K).
  - Narrow TI.
  - ↑ T½ in heart and liver failure, viral infections, elderly, enzyme inhibitors eg: cimetidine, erythromycin, contraceptives
  - ↓ T½ in smokers, chronic alcohol, phenytoin, carbamazepine, rifampicin, and barbiturates
  - Given IV (very slowly) as aminophylline (too irritant for IM) for severe attack unresponsive to nebuliser
- Others:
  - **Sodium cromoglycate:** non-steroidal preventer – less effective than steroids but fewer side effects. Single dose good for **prevention of exercise induced asthma**
  - Anti-leukotrienes: Leukotrienes → ↑ vascular permeability, ↑ mucus production, ↓ mucus transport, etc.
    - Oral montelukast → 15 % ↑ in FEV1, ↓ use of β agonist. Place in therapy still uncertain
- Follow-up (eg good liaison with GP) following emergency admission is critical to preventing recurrence
- If poor control:
  - Check compliance and technique
  - If still poor → ↑ ICS dose
  - If still poor → add LABA/ICS combo inhaler
  - If still poor → add theophylline (oral)
  - If still poor → oral steroids

**Inhalers**
- Advantages: minimum possible dose, highly targeted, patient controls therapy
- Inhaled steroids → deposition in mouth. If not using spacer, need to rinse, gargle and spit otherwise risk of thrush and hoarse voice. At best, **10% gets to lower airways without spacer**
- Metered dose inhalers (MDI):
  - Autohaler: shake, push lever up, suck. Lower level of suck needed than powder inhalers – but still require good suck to get lower airways deposition. As expensive as powder inhalers. OK from age 8 upwards
  - Standard MDI: (cheap, light and rapid delivery of drug, but co-ordination difficult). From age 12 onwards.
    - Instructions for use:
      - Shake inhaler between each puff
      - Remove cap
      - Hold it upright and pointed backwards
      - Breathe out
      - Fire during 1st 25% of long slow inhalation
      - Hold breath
      - Breathe out after removing inhaler from mouth
- Dry Powder Inhalers: ↑↑ oral deposition. Use from age 5 up (good for use at school when they don’t want to lug a spacer around but their MDI technique is inadequate). Advantages: light, quick delivery, don’t need co-ordination, CFC free. Disadvantages: cost, require high respiratory flow
  - Accuhaler: 60 doses, easy to use, has dose meter
  - Diskhaler: 6 doses
  - Turbohaler: easier to use than disk haler. Red mark inside indicates when its empty

**Spacer Use**
- As effective as a nebuliser. Increases LRT deposition by 4 times
- Eliminate oral deposition of steroids and ↑ lung deposition of both preventers and relievers
- Breath-a-tech with a facemask up to 6. Remove mask as soon as you can (stops nasal filtering – try at age 4 - 5). Need smaller spacer as they have a small tidal volume
- Volumatic without facemask. Need to be able to mouth breath well (ie try from age 2 – 3 onwards)
- Need to inhale within 30 seconds of a puff into the spacer
- One puff at a time
- But plastic spacer → static charge → particles stick. So **wash in detergent once a week and do not rinse bubbles off** (→ microfilm of detergent)
If using a new spacer without washing, need to prime it (10 puffs). Don’t do this in front of patient.

**Chronic Obstructive Pulmonary Disease (COPD)**

- Airflow obstruction that is chronic, as diagnosed by spirometry
- Increased resistance to airflow due to partial or complete obstruction at any level
- Permanent or minimally reversible obstruction of expiratory airflow caused by chronic bronchitis, emphysema or both
- Conditions often overlap and can have classic COPD conditions (eg emphysema, chronic bronchitis, asthma) without a dx of COPD (see right)
- Asthma is only considered COPD when not reversible

**Risk factors:**
- Smoking! (Changes in smoker’s lungs = anthracosis, ca (SCC, Small CC, large cell undifferentiated), chronic bronchitis, centriacinar emphysema, infection)
- Chronic asthma/airway hyper-responsiveness
- A1ATD
- Minor = air pollution; SHS; diet + childhood illness → poor lung development

**Dx:**
- Hx + exam
- Spirometry
- CXR

**PFTs:**
- FEV1/FVC ratio < 70% (indicates airflow obstruction) with a concave expiratory loop
- ↓FEV1 tells how severe airflow obstruction is
- ↑RV secondary to air trapping
- ↑TLC (air trapping)
- ↓DLCO (in emphysema, due to loss of parenchyma, but normal in asthma)

**Severity:**
- Mild: FEV1 > 80% predicted
- Moderate: FEV1 50–80% predicted
- Severe: FEV1 30–50% predicted
- Very severe: FEV1 <30%

**History:**
- Usually smokers (but not always)
- Gradual SOB onset over years
- Sometimes daily cough + sputum production (depending on degree of chronic bronchitis)
- Exacerbations with respiratory infections (worsening cough, sputum, wheeze)

**Physical findings:**
- Tripod position
- Pursed lips
- Barrel chest
- Harrison’s sulcus
- Signs of hyperinflation = ↓chest expansion; resonance/hyperresonance; liver/spleen ptosis; loss of cardiac dullness; ↓BS
- May hear wheeze

**CXR:**
- Hyperinflation: barrel chest, flattened diaphragm, thin heart
- Emphysema: absent peripheral vessels, hypertranslucency (↓lung markings), flattened diaphragm, bullous change
- Bronchitis: thickened bronchial walls (especially end on)

**Abnormalities in gas exchange:**

<table>
<thead>
<tr>
<th>Presentation</th>
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<th>Blue Bloater (Bronchitis)</th>
</tr>
</thead>
<tbody>
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<td>Dyspnoea</td>
<td>Cough, sputum, RHF</td>
</tr>
<tr>
<td>ABG</td>
<td>Hyperinflated</td>
<td>↑markings at bases</td>
</tr>
<tr>
<td>Lung Function Tests</td>
<td>↑TLC, ↓DL CO</td>
<td>Normal TLC and DL CO</td>
</tr>
<tr>
<td>Sleep</td>
<td>Moderate desaturation</td>
<td>Marked desaturation</td>
</tr>
</tbody>
</table>
- Treatment:
  - Only smoking cessation and long term oxygen alters the natural course
  - **Bronchodilators** (both short acting + long acting, + theophylline, + tiotropium) provide symptomatic relief
    - **Tiotropium** is an inhaled long acting anticholinergic, od, → cf ipratropium → more bronchodilation, improved SOB, ↓ exacerbations, ↑ QOL
  - COPD is largely steroid resistant
    - No role for oral steroids in long-term management
    - No evidence that ICS prolong survival or slow the decline in FEV1
    - ICS may ↓ exacerbations in severe COPD (but remember there are side-effects)
  - Long-term O2 therapy indications:
    - Non-smokers on optimal medical management
    - PaO2 ≤ 55 mmHg (at rest during clinical stability)
    - PaO2 of 56 - 60 mmHg in the presence of polycythemia or right heart failure
    - Must be used for at least 16 hours per day (but more is better)
    - Does not make you feel much better but prolongs survival

- Management of an exacerbation:
  - Exclude differentials: PE, LVF, pneumothorax, hyperventilation
  - Is there an infective component: URTI/LRTI
  - Are there complications of COPD:
    - **Cor pulmonale**/pulmonary hypertension (look for signs of RH failure)
    - **Polycythaemia** secondary to chronic hypoxia
    - Low body weight/osteoporosis (from steroids and acidosis)
  - Investigations:
    - FBC (is Hb or WBC ↑), U & E, Glucose
    - ECG
    - If Sats < 92% then ABG
    - CXR
    - Sputum microscopy, culture and sensitivity
    - Peak flow is asthmatic component
    - Spirometry when resolved
    - Echo if cor pulmonale or LVF suspected
  - Treatment:
    - SOS + ABs
    - O2 with goal of saturation ~90% (85-90% according to Perrin; beware CO2 narcosis)
    - Bronchodilation: nebs
    - **Antibiotics**: Usually oral. **Augmentin**, erythromycin, etc. Commonly H Influenzae or M Catarrhalis
    - **Steroids**: 30 – 40 mg/day, stepping down over around 2 weeks
    - Acute NIV (non-invasive ventilation; BiPAP: **less P during exp so can blow off CO2**):
      - Indications = acute exacerbation COPD; moderate/severe dyspnoea (RR>25); pH ≤ 7.35 + hypercapnia
      - Contraindications = absolute (resp arrest, craniofacial trauma, burns etc), relative (CV instability, uncooperative pt etc)
Respiratory

- Benefits = improved resp acidosis, PaCO2, RR, severity of breathlessness; ↓hospital stay, mortality, need for intubation

- Pathology:
  - The sensation of dyspnoea is multifactorial → in emphysema hyperinflation contributes most towards this
  - O2 sats are poorly correlated with dyspnoea

- Hyperinflation → helps to preserve maximum expiratory airflow in COPD by:
  - ↑elastic recoil pressure
  - Enlarging airways to ↓resistance
  - Hyperinflation tends to get worse with exercise → stretched respiratory muscles send signals to the respiratory centre in the brain → muscle work less efficiently

- Natural history:
  - See progressive decline: dyspnoea → activity avoidance → deconditioning + social isolation + withdrawal + depression → more dyspnoea
  - Pulmonary rehabilitation (physio, exercise conditioning) is an opportunity to break the cycle (does not affect disease process/FEV1/PaO2/DLCO however, but ↑QOL and ↓dyspnoea)

- Survival:
  - FEV1 is the best single predictor: 40% FEV1 = 5yr survival 50%; 25% FEV1 = 30%
  - Other predictors of poor prognosis = ↓BMI, frequent exacerbations, smoking, cor pulmonale

Chronic Bronchitis

- Persistent cough with sputum for at least 3 months in 2 consecutive years (useless definition)
- Follows prolonged exposure of the tracheobronchial tree to non-specific irritants → hypersecretion of mucus and structural changes

- Types:
  - Simple chronic bronchitis: no airway obstruction
  - Chronic asthmatic bronchitis: intermittent bronchospasm and wheezing
  - Chronic obstructive bronchitis: heavy smokers with chronic airways obstruction, usually with emphysema. Sputum will be clear/white, only occasionally will be infected (yellow/green)
  - [Cf Chronic infective bronchitis with green sputum ⇒ bronchiectasis]

- Pathogenesis:
  - Chronic irritation (eg inhaled substances such as smoking) and microbiological infections → hypersecretion of mucus obstructing airways. Hypertrophy of submucosal glands in larger bronchi and hyperplasia of goblet cells in small airways
  - Infection maintains the hyper-secretion and causes acute exacerbations
  - Macroscopic appearance: hyperaemia, swelling, mucopurulent secretions in the bronchi
  - Microscopic appearance: increased size of mucus glands. Reid index (ratio of mucous gland layer to thickness of epithelium to cartilage) greater than 0.4. Chronic inflammation → metaplasia to squamous epithelium and dysplasia. Mucous plugging, inflammation and fibrosis. If severe → luminal obliteration

Emphysema

- Enlargement of air-spaces distal to terminal bronchioles and destruction of alveolar walls without fibrosis
- Moderate to severe emphysema is rare in non-smokers
- Aetiology:
  - Cigarettes: usually had a 20-pack year history. Only 15 – 20% of smokers develop obstruction
  - Alpha-1 antitrypsin deficiency
  - Dusts: coal, gold mining, textile, cement and steel making
- FEV1 best single indicator of prognosis
• **Pathogenesis:** disruption in balance of elastin synthesis: \( \uparrow \) in elastolytic activity from neutrophil elastase (smoking \( \rightarrow \uparrow \) neutrophils) and \( \downarrow \) \( \alpha_1 \)-antitrypsin (elastase inhibitor – oxidants in cigarette smoke inhibit \( \alpha_1 \)-antitrypsin). Neutrophils also release free radicals that inhibit \( \alpha_1 \)-antitrypsin

• **Types:**
  - **Centriacinar** (Centrilobular): enlargement of respiratory bronchioles, distal alveoli are spared. (Small particles deposited here – don’t make it right to the end). More severe in upper lobes. Blackened. Bronchi and bronchioles have chronic inflammation. Seen in smokers and coal workers pneumoconiosis
  - **Panacinar** (Panlobular): acinus is uniformly involved from respiratory bronchiole to terminal alveoli. Seen in \( \alpha_1 \)-antitrypsin deficiency (ZZ or MZ alleles on chromosome 14) and as an extension of centrilobular emphysema in smokers. Mean age of onset is 45 – 50 years in non-smokers and 30 – 40 in smokers. Liver disease in 5 – 10 % of adults. Heterozygotes (MZ) predisposed to emphysema if they smoke. Treatment same as for smoking induced
  - **Paraseptal** (distal acinar): proximal acinus is normal, distal part affected. Most prominent sub-pleurally and next to interlobular septi. Often seen in cases of spontaneous pneumothorax in young people
  - **Irregular emphysema:** acinus irregularly involved. Associated with scarring

• **Macroscopic appearance:** voluminous lungs

• **Microscopic appearance:** *large abnormal airspaces, blebs and bullae*. Bronchitis and bronchiolitis

• **Clinical features:**
  - 60 years or older
  - Prolonged history of exertional dyspnoea
  - Minimal non-productive cough
  - Usually have lost weight
  - Use accessory muscles for respiration
  - Prolonged expiration period (lungs collapse due to \( \downarrow \) elastin)
  - **Pink puffers:** \( \uparrow \) respiratory rate maintains O2. Xray: \( \uparrow \) central pulmonary artery size, \( \downarrow \) peripheral vascular markings
  - **Blue bloaters:** \( \uparrow \) PaCO2, \( \downarrow \) PaO2, cyanotic, respiratory centre insensitive to CO2, instead rely on hypoxic drive to breathe. Dangerous to give O2 \( \rightarrow \) \( \downarrow \) ventilatory drive

• **Medical management:**
  - Bronchodilators and inhaled corticosteroids: only if reversible obstruction
  - Smoking cessation (nicotine replacement doubles quit rate)
  - Antibiotics for acute exacerbations
  - O2 with care
  - Encourage exercise/physio
  - Attention to nutrition

**Bronchiectasis**

• Chronic necrotising infection of bronchi and bronchioles (ie *a pneumonia that doesn't clear*) \( \rightarrow \) abnormal airway dilation and destruction of bronchial walls \( \rightarrow \) obstruction due to inflammation, ulceration and distortion

  - = Chronic infective bronchitis

• **Pathogenesis:**
  - **Obstruction** (especially during growth) due to tumour, foreign bodies, mucous impaction (eg in CF and immotile cilia)
  - **Infection** with bronchial wall weakening and atelectesis (eg in necrotising pneumonia). Especially Tb, pertussis, MAC

• **Macroscopic appearance:** affects lower lobes, especially vertical airways and more distal bronchi. Airways may be cylindrical, fusiform or saccular

• **Microscopic appearance:** Acute – inflammatory exudate with desquamation and ulceration of the epithelium. Chronic – peribronchial fibrosis

• **Clinical course:** *foul, bloody sputum, especially in the morning*. (cf clear sputum in chronic bronchitis). Repeated ‘bronchitis’ with wheezing, haemoptysis, and dyspnoea. Coarse crepitations, wheezing, and clubbing.

• **Complications:** obstructive ventilatory insufficiency \( \rightarrow \) dyspnoea and cyanosis. Rarely cor pulmonale, metastatic brain abscesses and amyloidosis

**Obstructive Pathology**

<table>
<thead>
<tr>
<th>Condition</th>
<th>Features</th>
<th>Pathogenesis</th>
<th>Macro</th>
<th>Micro</th>
</tr>
</thead>
</table>

*Respiratory*  114
### Chronic bronchitis
- Persistent cough + sputum for 3/12 in at least 2 consecutive yrs

1. Smoking induced hypertrophy of submucosal glands + hyperplasia of goblet cells → mucus
2. Microbiological infection – role is secondary

### Emphysema
- Abnormal permanent enlargement of terminal airways – destruction of walls without fibrosis
  - Can lead to pulmonary HTN → cor pulmonale
  - Bullae can rupture → pneumothorax
  - Can see shunting and VQ mismatch
  1. Centriacinar – central acini – smoking, distal alveoli spared, upper lobes
  2. Irregular – irregular acini involved
  3. Panacinar – all parts of acini – A1ATD, uniform destruction, distal/terminal alveoli involved, lower lung zones
  4. Paraseptal – distal part of acini

1. Protease-antiprotease mechanism
2. Smoking increases elastase therefore elastic damage
3. A1AT protects against anti-proteases normally

1. Bullae in upper lung
2. Moth eaten appearance of parenchyma
3. Anthracosis

### Bronchial asthma
- Reversible airway obstruction due to:
  1. Chronic inflammation AND
  2. Bronchial smooth muscle hyper-responsiveness - Type 1 hypersensitivity (IgE)
- Rx inflammation with steroids and bronchial smooth muscle hyper-responsiveness with LABAs and SABAs

1. Lungs hyperinflated
2. Atelectasis
3. Thick mucous plugs

1. Bronchial wall thickened BM
2. Increase in size of submucosal glands
3. Hypertrophy of bronchial smooth muscle
4. Mucous – eosinophils + charcot-leyden crystals; can see curschmann’s spirals (coiled basophil plugs)

### Bronchiectasis
- Results from necrotising bacterial infections eg Staph or Klebsiella
- Can be divided into:
  1. Localised (obstruction from tumour/aspiration ) and
  2. Diffuse (infection/CF/immotile cilia) categories

1. Bilat lower lobes → distal airways permanently dilated
2. Purulent material in lumen

1. Neuts + mononuclear (lymphocytes, plasma cells) cells – inflammation
2. Destruction of lining epi – ulceration
3. Fibrosis of underlying wall
Restrictive/Interstitial Lung Disease

### Diffuse Parenchymal Lung Disease

- = Diffuse Parenchymal Lung Disease
- = Reduced expansion of the lung parenchyma
- Pathology affects pulmonary parenchyma (alveoli epithelium, interstitium and capillary endothelium) rather than airways
- Leads to restrictive physiology \( \rightarrow \) ↓expansion of lung parenchyma, ↓total lung capacity, ↓lung compliance:
  - No problem with airflow
  - Lung tissue becomes scarred + stiff
  - Lungs become smaller + harder to move
- Other causes:
  - Secondary to drugs (eg amiodarone)
  - Secondary to radiotherapy
  - In some connective tissue diseases (eg Ankylosing Spondylitis, RA, SLE)

### Acute Interstitial Lung Disease

**Adult Respiratory Distress Syndrome (ARDS)**

- = Diffuse Alveolar Damage (DAD)
- = Shock Lung
- Characterized by a diffuse and usually bilateral pattern of interstitial and alveolar septal injury
- See solid, heavy looking lungs
- Fluffy infiltrates seen on CXR
- Damaged alveolar epithelium + capillary oedema, inflammatory cells, hyaline membranes
- Clinical: rapid onset of life-threatening respiratory insufficiency, cyanosis and hypoxaemia refractory to O2 therapy
- Diagnostic criteria: acute onset, fluid on CXR, capillary wedge pressure < 19 (\( \Rightarrow \) not LH failure), hypoxia
- Aetiology – types of injury:
  - Aspiration: gastric contents or drowning
  - Inhalation of fumes or toxic aerosols, smoke, chlorine, oxygen toxicity
  - Circulating toxins: bacterial endotoxins
  - Other: DIC, high altitude, trauma, radiation therapy, chemotherapy
- Pathogenesis:
  - Results from leakage from capillaries to alveoli spaces: non-cardiogenic pulmonary oedema
  - Leads to a non-compliant lung: smaller tidal volume, poor gas exchange, ↑risk of lung rupture when ventilating
  - Prototypical injury is oxygen toxicity: hyperoxia damage alveolar macrophages (AM) \( \rightarrow \) release O2 radicals \( \rightarrow \) injure lung tissue; AM release cytokines \( \rightarrow \) attract neutrophils, stimulate intravascular adherence, and release further O2 radicals. Vicious circle of damage, especially to septum
  - Other possible initiating mechanisms (alone or in combination): activation of complement cascade, neutrophil aggregation, activation of coagulation \( \rightarrow \) fibrin deposition, etc
- Macroscopic appearance: affects WHOLE lung (if only one lobe affected ?pneumonia). Heavy lungs due to fluid accumulation (interstitial and later alveolar)
- Microscopic appearance:
- Early change: **interstitial oedema**, few cell infiltrates
- Acute exudative stage: microvascular injury → breakdown of basement membrane → leakage of plasma proteins into alveoli. Sloughing of injured type 1 pneumocytes. **Cell debris + exudate form hyaline membrane.** Inflammatory cells in interstitium. **No neutrophils in alveoli** (key differential from pneumonia)
- Proliferative stage: Type II pneumocytes proliferate to cover alveolar surface. Fibroblasts lay down collagen in interstitium and alveolar spaces → interstitial and intra-alveolar fibrosis

**Prognosis:** 50% mortality. Surviving patients may have mild to extensive diffuse interstitial pulmonary fibrosis

**Acute Interstitial Pneumonia (AIP)**
- = Hamman-Rich Disease
- Rapidly progressive interstitial pneumonitis that resembles the organising stage of DAD (?may be a variant)
- Affects young adults, presenting with flu-like syndrome and bilateral infiltrates. Most die of respiratory failure within two months

**Chronic Infiltrative (Restrictive) Lung Disease**
- Common clinical and radiologic features but diverse aetiology and pathology
- Clinical features:
  - Progressive SOB
  - **Cyanosis** due to severe hypoxemia from ventilation-perfusion mismatch
  - **Clubbing** of digits
  - Late in disease: **pulmonary hypertension** due to destruction of alveolar capillary bed
  - Interstitial infiltrate and some exudate in small airspaces
- Diseases leading to chronic infiltrative lung disease:
  - Idiopathic chronic interstitial pneumonias: 13%
  - Environmental lung disease: 25%
  - Sarcoidosis: 20%

**Idiopathic Pulmonary Fibrosis (IPF)**
- AKA cryptogenic fibrosing alveolitis; **UIP**
- Cause unknown
- **Progressive** with a poor prognosis
- Poorly responsive to treatment
- Clinical features:
  - ↑dyspnoea in an over 60 person, over several months or 1-2 years
  - Sometimes a dry cough
  - May have clubbing
  - ↓chest expansion
  - Fine bibasal inspiratory creps
- PFTs:
  - Normal FEV1/FVC ratio
  - ↓FEV1 + FVC
  - ↓TLC + RV
  - ↓DLCO (due to thickened fibrotic tissue in alveolar spaces)
- Radiology:
  - CXR: reticular pattern (fine network of fibrosis)
  - HRCT: peripheral + subpleural, lower zone fibrosis, *honey-comb* appearance
- Diagnosis:
  - Age > 50
  - Gradual onset of otherwise unexplained dyspnoea
  - Bi-basal inspiratory crackles
  - Restriction on PFT’s (including reduced lung volumes and impaired gas exchange)
  - Bibasilar reticular abnormalities on HRCT
  - Exclusion of other causes of ILD (see below)
- Treatment:
  - Responds **poorly** to treatment
  - Monitor regularly (6/12) for complications/need for home O2/potential for transplant
- Types of IPF:
  - Usual Interstitial Pneumonia (UIP, US):
Respiratory

Cryptogenic Fibrosing Alveolitis (UK)

- Most common type of IPF
- Presents with gradual onset of dyspnoea and cough (usually dry)
- Non-uniform slowly progressive disease starting in middle age. Die in several years. No known treatment (don’t respond to steroids). Airflow and blood flow disrupted
- Macroscopic appearance: when advanced lung is small and firm with a honeycomb appearance on cut section
- Microscopic appearance: ranges from normal to fibrotic alveolar walls, with marked variation in the degree of fibrosis from field to field (cf other IPFs which are uniform). Capillary bed slowly destroyed →pulmonary hypertension and cor pulmonale. Inflammatory cells (lymphocytes + macrophages + neutrophils) in interstitium and airspaces
  - Desquamative Interstitial Pneumonia (DIP): more uniform than UIP, with no alternating areas of scarring and normal lung. Filling of alveolar with alveolar macrophages (not desquamated as originally thought). Is it an early stage of UIP? However, may respond to steroids and have a better prognosis. X-ray shows bilateral lower lobe ground glass infiltrates
  - Lymphocytic Interstitial Pneumonia (LIP)
  - Granulomatous Interstitial Pneumonia

Other Causes of Interstitial Lung Disease

- **Drugs:** amiodarone, nitrofurantoin, methotrexate, bleomycin
- Connective tissue diseases: RA, SLE, scleroderma
- Environmental exposure:
  - Inorganic dusts: 
    - Asbestos (asbestosis)
    - Silica (silicosis)
    - Coal dust (coal worker’s lung)
    - Talc
  - **Organic:** proteins from a variety of sources (farmer’s lung, bird fancier’s lung etc etc) → hypersensitivity pneumonia

Hypersensitivity Pneumonitis

- = Extrinsic Allergic Alveolitis
- = Hypersensitivity immune response in the lower airways and alveoli in response to organic agents/proteins
- Sometimes grouped with Pneumoconioses → Occupational Lung Disease
- Immune resistance to protein antigens → acute or chronic attacks on re-exposure
- Lots of causes: farmer’s lung (antigen is thermophilic actinomycoses), pigeon breeder HSP, air-conditioner HSP
- Morphology: chronic inflammatory cells in the alveolar septi, septal fibrosis, obliterative bronchiolitis and non-necrotising granuloma formation (diagnostic on biopsy)
- Presentation variable: acute/subacute/chronic (can → fibrosis) + is related to the frequency + intensity of exposure to organic agent
- Diagnosis:
  - Clinical history of exposure
  - Chest crackles
  - Testing for serum precipitins (antibodies to specific agents)
  - CXR and CT scan varies from normal, to patchy bilateral infiltrates, to fibrosis
  - PFT usually restrictive
- Treatment:
  - Remove the patient or the allergen from the environment
  - Protect the patient from the allergen
  - Prednisone:
    - Most acute forms resolve without need for treatment
    - In some patients with sub-acute or chronic disease steroids are used to hasten recovery

Bronchiolitis Obliterans Organising Pneumonia (BOOP)

- Obliterans ⇒ airways sealed off
- Organising ⇒ fibrosis
- Common response to lung injury from infections, inhaled toxins, drugs, etc
- Major finding: plugs of lose fibrous tissue filling bronchioles and alveoli. Variable chronic inflammatory cell infiltrate is present

Respiratory 118
Respiratory

- Patients improve gradually with steroids (ie different from UIP)

**Pneumoconioses**

- Pulmonary diseases caused by the inhalation of **inorganic** dust (usually **stimulating fibrosis**)

**Asbestos:**
- Occupational exposure to asbestos is linked to:
  - Localised fibrous plaques: dense fibrotic plaques on X-ray – generally asymptomatic
  - Pleural effusions → cough, SOB
  - Asbestosis: Parenchymal interstitial fibrosis. Progressive SOB on exertion. ↓FVC, ↓FEV but ↑FEV/FVC, ↓DL CO, restrictive pattern
  - Bronchogenic carcinoma (5 times risk, 14 times risk if smoker): most common
  - Mesotheliomas (1000 times risk) but still rare. See Pathology, page 124
  - Laryngeal and perhaps extrapulmonary neoplasms
- When asking about occupational exposure, need to go back a long time. Will present in an older man. Ask them what they did when they left school and go from there.
- Pathogenesis: depends on which type of asbestos. Serpentine cryotile form (curly, flexible) is more common, less dangerous, cleared more easily from bronchi and more soluble so don’t persist in the alveoli. Amphibole type (straight, stiff, brittle) rarer, more dangerous, go deeper, penetrate epithelial cells and lodge in the interstitium

**Coal Workers Pneumoconiosis (CWP):**
- Two forms:
  - Simple CWP: accumulation of dust laden macrophages with little pulmonary dysfunction
  - Complicated CWP: progressive fibrosis induced by macrophages
- Macroscopic appearance: Anthracosis, coal nodules progressing to black scars larger than 2 cm in complicated CWP
- Microscopic appearance: Coal laden macrophages, fibrous scarring
- Caplan’s Syndrome: Rheumatoid arthritis with a pneumoconiosis → nodular pulmonary lesions

**Silicosis:**
- Exposure to crystalline silicon dioxide: sand blasting, rock mining, foundry work
- Silica causes activation and release of inflammatory factors by macrophages
- Morphology: discrete pale to black tiny nodules which coalesce into fibrous scars

**Honey Comb Lung**
- End stage of many chronic interstitial lung diseases
- Morphology: small lungs with nodular pleural surface due to interstitial fibrosis retracting the pleura. Large air spaces cause honeycomb effect. Destruction of the capillary bed in the lung → **pulmonary hypertension, RV hypertrophy, cor pulmonale** → death

**Sarcoidosis**
- A systemic disorder of unknown cause characterised by **non-caseating granuloma formation and inflammation**
- Presenting features range from asymptomatic abnormal findings on chest xray to progressive multi-organ failure in rare cases
- Sarcoidosis can be self-limited, chronic or episodic with remissions
- Usually involves a combination of:
  - Hilar adenopathy
  - Interstitial pulmonary opacities
  - Skin, joint, and/or eye lesions
- Rarely involves heart and nervous system
- History:
  - Most patients present with a sub-acute history of respiratory symptoms:
    - SOB on exertion
    - Cough
    - Variable chest pain
  - Systemic symptoms are common:
    - Fatigue, anorexia and weight loss
    - Myalgia
    - Fever
- Examination:
  - General: may have peripheral lymphadenopathy
- Chest signs depend on extent of disease:
  - Usually insp creps
  - Occasionally wheeze (depending on airway involvement)
- Lung function:
  - May be normal
  - A typical **restrictive pattern** is the most common abnormality
    - Spirometry: normal ratio but FEV1 and FVC both reduced
    - Lung volumes reduced
    - DLCO reduced
    - Sometimes airflow obstruction
  - Most useful for following the course of the disease and response to treatment
- Radiology:
  - CXR: bilateral hilar lymphadenopathy, variable pulmonary changes
  - HRCT
- Bloods:
  - Serum **ACE is elevated** (is synthesised by sarcoid granulomas) in about 75% of untreated patients
  - May have hypercalcaemia (see ↑ vit D with granulomas)
- DDx of bilateral hilar lymphadenopathy = **lymphoma + TB**
- Need a **tissue diagnosis** in most cases (from either skin, LN, transbronchial bx or mediastinoscopy)
- Treatment:
  - Many patients never require treatment (can be hard to know when to treat)
  - All organs affected by sarcoidosis respond to **prednisone**
  - Usual initial dose is 40mg for a period of months with gradual reduction to a maintenance dose

**Restrictive Pathology**
- Interstitial lung disease symptoms: same for all: **progressive SOB and dry cough**; most are idiopathic; restrictive pattern w diffusion abnormalities

---

### Fibrosing interstitial lung disease

<table>
<thead>
<tr>
<th>Info</th>
<th>Age</th>
<th>Gender</th>
<th>CT findings/Macro</th>
<th>Prognosis</th>
<th>Steroid response?</th>
<th>Micro</th>
</tr>
</thead>
</table>
| Usual interstitial pneumonia/IPF | Idiopathic | >60 | M>F | Subpleural involvement | 3yrs | No | 1. Heterogenous fibrosis  
2. Honeycomb change |
| Non-specific interstitial pneumonia | Idiopathic | >50 | M=F | Subpleural sparing | 9yrs | Yes | 1. Homogenous fibrosis  
2. Mononuclear cells  
3. No honeycomb |
| Organising pneumonia | Idiopathic  
- A pattern of change in response to lung injury (infection/collagen vasc d) | | | Patchy interstitial infiltrate | | | Polypoid loose fibroblastic plugs filling bronchioles + alveoli (not true interstitial disease) |

**Granulomatous lung disease**

<table>
<thead>
<tr>
<th>Info</th>
<th>Age</th>
<th>Gender</th>
<th>CT findings/Macro</th>
<th>Prognosis</th>
<th>Steroid response?</th>
<th>Micro</th>
</tr>
</thead>
</table>
| Sarcoïdosis | Idiopathic  
SOB/cough/CP | F>M | | Bilateral hilar LAN  
Nodules in lungs | 10% die | | 1. Non-caseating granulomas  
2. May contain asteroid bodies |
### Respiratory System

#### Respiratory System

1. **Interstitial pneumonitis** = chronic inflammatory cells in alveolar walls
2. **Fibrosis**
3. **Granulomas w giant cells**

**NB. TB also causes granulomatous lung d therefore: sarcoidosis, HP, and TB all are granulomatous lung diseases**

### Pneumoconioses – pulmonary diseases caused by inhalation of inorganic dusts

<table>
<thead>
<tr>
<th>Pneumoconiosis</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asbestosis</td>
<td>Crystalline silicate – is fibrogenic + acts as a tumour initiator + promoter</td>
</tr>
<tr>
<td></td>
<td>Related to bronchogenic carcinoma + mesothelioma</td>
</tr>
<tr>
<td></td>
<td>SOB + cough</td>
</tr>
</tbody>
</table>

#### Smoking related disease

<table>
<thead>
<tr>
<th>Disease</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Desquamative interstitial pneumonia</td>
<td>All related to smoking and increased numbers of macrophages seen – the rest is fine print</td>
</tr>
<tr>
<td>Respiratory bronchiolitis interstitial lung disease</td>
<td></td>
</tr>
<tr>
<td>Langerhans cell histiocytosis</td>
<td></td>
</tr>
</tbody>
</table>

#### Honey comb lung

End stage of interstitial lung disease – see fibrous scarring that distorts architecture – enlarged air spaces surrounded by thick fibrous walls

### Neoplasia of the Respiratory Tract

#### Cancer of the Nasal Cavity and Paranasal Sinuses

- **Inflammatory Polyp:**
  - Not a true tumour: overgrowth of stromal tissue – no malignant potential
  - Common in adults, rare in children
  - Associated with cystic fibrosis
- **Sinonasal papilloma:**
  - Benign. Can become malignant. 3% become malignant after removal (poor prognosis). 3% have malignancy in polyp (prognosis better)
  - Usually in adult. Presents with nasal obstruction and painless epistaxis
  - Associated with HPV 6 & 11
- **Sinonasal Carcinoma:**
  - Occupational association: wood turners (adenocarcinoma) and nickel mining
  - Relatively rare (<1% of cancer deaths)
  - 60% 5 year survival, surgical treatment
  - **Squamous cell** most common (look for keratin whors), also adenocarcinoma
  - Stromal overgrowth = desmoplasia ⇒ sign of invasive cancer
- **Nasopharyngeal Carcinoma:**
  - Most common in SE Asia and N Africa, occurs in 15 – 25 and 60 – 69. Presents with epistaxis or obstructed eustachian
Respiratory

Tumours of the Larynx

• Benign non-neoplastic neck lumps:
  ➢ Inflammatory:
    o Lymph nodes: anterior cervical for tonsillitis, jugular digastric for tongue
    o Atypical Tb (especially kids)
    o Deep Neck abscesses: para-pharyngeal or retro-pharyngeal abscesses (can track down into mediastinum)
  ➢ Thyroglossal cysts: cysts in embryological track from tongue to thyroid (usually at level of hyoid)
  ➢ Branchial cysts: ?embryological. Like enlarged anterior node. Contain lots of cholesterol
  ➢ Pharyngeal pouch: Mucosa herniates out through triangle between the cricopharyngeus and thyropharyngeal muscles under pressure from swallowing when upper oesophageal sphincter doesn’t relax properly. Catches food, becomes infected. Treatment: surgery

• Laryngeal Nodule:
  ➢ Due to trauma of vocal cords banging together → oedema (early) → scarring/granulation tissue (late)
  ➢ Only on anterior 1/3 rd of vocal fold
  ➢ Completely benign
  ➢ Gravely voice

• Laryngeal Papilloma:
  ➢ Like sinonasal papillomas
  ➢ Most commonly seen in children
  ➢ Associated with HPV 6, 11
  ➢ Tendency to recur: can become unmanageable → airway obstruction
  ➢ Benign → squamous overgrowth

• Laryngeal Carcinoma:
  ➢ Presentation:
    o Presenting early: if affect vocal cords, invade recurrent pharyngeal nerve, front of mouth
    o Presenting late: supraglottic lesions due to airway obstruction or pain (⇒ deeper), sinus (lots of space)
    o Dysphagia rare
  ➢ 90% are squamous cell carcinoma (like lung)
  ➢ Mostly in males, smoking a major risk factor, also alcohol, radiation, family history, tend to be older (> 50)
  ➢ Classification, prognosis and treatment depends on site (prognosis also depends on stage):
    o Glottic: 60%, on cords, maintained in larynx by cartilage. Treatment: radiotherapy unless spread through cartilage
    o Supraglottic: 30%, above cords, involves false cord. More aggressive, metastasise to cervical lymph nodes
    o Transglottic: < 5%, crosses from one cord to another
    o Infraglottic < 5%, below cords, more aggressive
  ➢ Don’t usually metastasise elsewhere, but lymph node infiltration common
  ➢ Treatment: radiotherapy (⇒ dry mouth) +/- surgery (superficial, hemilaryngectomy, laryngectomy, laryngectomy +/- radical neck resection. Chemo has little effect against SCC (most of them). If laryngectomy then need a tracheostomy (⇒can’t cough, ↑infection, ↓humidification, etc)

Lung Cancer

Smoking

• Latest stats (ie some year close to 2011):

<table>
<thead>
<tr>
<th></th>
<th>Adults</th>
<th>Maori</th>
<th>Pacific</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>23%</td>
<td>46%</td>
<td>36%</td>
</tr>
</tbody>
</table>

• Cigarette smoking and lung cancer:
  ➢ Relative risk is 10 times in regular smoker, 20 times in those smoking > 40 per day
Most important avoidable cause in 20 – 30% of cancers: including respiratory tract, liver, stomach, cervix
Tobacco and alcohol have a multiplicative relationship in oral cavity, throat and oesophagus
Fall in lung cancer mortality begins 5 – 9 years after quitting, back to baseline at 14 years
Abnormal cytology and squamous metaplasia in smokers

Passive smoking:
Passive smoking: relative risk is 3 times normal
Relationship to URTI in children
Possibility of younger children being affected e.g. SUDI
Children of smokers more likely to smoke

Active Smoking:
Demonstrates that knowledge/education is insufficient to ensure behaviour or behaviour change
Health promotion principles of acting at all levels (i.e. individual/community/government) to make healthy behaviour the easy choice

Measurement: Pack-years = (cigarettes per day x years smoked) / 20
Smoking cessation:
Listen first: Why do you smoke? (If it’s stress – what will you do in the future) What’s good about it? What’s bad about it?
What do you know about risks (don’t assume they know about risks – maybe information lack or cognitive dissonance)
Estimate cost for them: what would you do with $2-3,000 per year
Give a positive message: do you want to live longer/better
Need to negotiate with patient: be smart not paternalistic, be realistic, honest
Always put smoking on problem list
Options:
Face-to-face: Information: Quit Book or Can Quit (from cancer society). Quitline 0800 778 778
Nicotine replacement therapy (patches, gum)
Drugs:
  a. Bupropion (antidepressant)
  b. Nortriptyline (anti depressant)
  c. Varenicline (Champex; nicotine partial receptor agonist)

Epidemiology of Lung Cancer
Commonest cancer in the world
In New Zealand:
Leading cause of cancer death in men (23%, bowel 15%, prostate 14%) and third most common in women
Incidence = 4th most common; mortality = highest; males ↓, females ↑
Maori women have the highest death rate from lung cancer of any female population in the world (Maori 2-3 x death rate of non-Maori)
Males predominate, females catching up
60% not resectable at the time of diagnosis
23% of all lung cancers are mixed
Metastases around = primary bronchogenic ca
Smoking:
85% are caused by smoking and are therefore preventable
25% of lung cancer in non-smokers is due to passive smoking
Single most avoidable cause of cancer death
Cause of 60% of cancer death in smokers
Types according to smoking status:

<table>
<thead>
<tr>
<th></th>
<th>% Smokers</th>
<th>% Non-smokers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Squamous Cell</td>
<td>98</td>
<td>2</td>
</tr>
<tr>
<td>Small Cell</td>
<td>99</td>
<td>1</td>
</tr>
<tr>
<td>Large Cell</td>
<td>93</td>
<td>7</td>
</tr>
<tr>
<td>Adenocarcinoma</td>
<td>82</td>
<td>18</td>
</tr>
<tr>
<td>Bronchioalveolar</td>
<td>70</td>
<td>30</td>
</tr>
</tbody>
</table>

Presentation and Survival:

<table>
<thead>
<tr>
<th></th>
<th>Smokers</th>
<th>Non-smokers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Distant disease at presentation</td>
<td>&gt; 50%</td>
<td>10%</td>
</tr>
<tr>
<td>Endocrine disorders</td>
<td>10 – 25%</td>
<td>5%</td>
</tr>
<tr>
<td>5 year survival</td>
<td>5%</td>
<td>17%</td>
</tr>
</tbody>
</table>
Relative incidence changing rapidly:
- ↓Squamous cell
- ↑Adenocarcinoma (now more common than squamous cell in most countries)
- ↑Bronchioalveolar carcinoma
- Large cell constant

**Presentation**
- Fatigue 84%
- Cough 71%
- Dyspnoea 59%
- Anorexia 57%
- Pain 48%
- Haemoptysis 25%
- Others = SVC obstruction, dysphagia, stridor, **weight loss**, bone pain, cord compression, brachial plexus compression (→ Horner’s)

**Diagnosis**
- In smokers, have a very low threshold for doing a CXR eg for chest pain or back pain
- Neck node examination should include nodes medial to SCM attachment to the sternum (exam with flexed neck + head turned toward the side examining). Physical exam more sensitive than imaging
- **Cytology** necessary for management. Use the least invasive route (eg FNA of a neck node if there is one)
  - Sputum cytology
  - Bronchoscopy:
    - Can do washings, brushings, biopsy or lavage (to get more distal stuff)
    - If can’t produce sputum sample, can nebulise with hypo-osmotic saline to induce sputum
    - 1% of transbronchial biopsy → haemorrhage or pneumonia
    - Pleural fluid sample
  - Fine Needle Aspiration (FNA): good for peripheral tumours
- Histology:
  - Bronchoscopy bx
  - Hilar node specimen
  - Resection

**Pathology**
- Mechanisms of mets spread:
  - Direct invasion
  - Trans-coelomic
  - Haematogenous
  - Lymphatogenous
- Metastatic disease patterns:
  - Multiple discrete lesions
  - Pleural involvement
  - **Lymphangitis carcinomatosa** (tumour obstructing lymphatic channels → SOB + pulm HTN; can metastasise via this route)
- Metastatic spread to lung: from breast, RCC, melanoma, any carcinoma or sarcoma
- Bronchogenic ca arises in hilum from bronchial epi; local growth → invasion → metastasis (pleura, LNs, lymph/blood)
- Local effects of ca spread:
  - Bacterial or lipoid pneumonia
  - **Invasion** of pleura, pericardium, large vessels, nerves, oesophagus
- Asbestos + smoking → increased risk of bronchogenic ca but does not further increase risk of mesothelioma
- Cancer mimics on x-ray: infection – TB esp, FBs, fibrosis, sarcoidosis etc

**Types of Lung Cancer**

<table>
<thead>
<tr>
<th>Lung cancer Type</th>
<th>Features</th>
<th>Macro</th>
<th>Micro</th>
<th>Prognosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-small cell SCC</td>
<td>Metaplasia to squamous epi (smoking → metaplasia → dysplasia → carcinoma)</td>
<td>1. Central large bronchi</td>
<td>1. Eosinophilic (pink)</td>
<td>Syr 10%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2. Cream grey mass</td>
<td>2. Intercellular junctions</td>
<td></td>
</tr>
</tbody>
</table>

*Respiratory* 124
<table>
<thead>
<tr>
<th>Respiratory</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Squamous Cell Carcinoma:</td>
<td></td>
</tr>
<tr>
<td>- Most common form</td>
<td></td>
</tr>
<tr>
<td>- Males &gt; females, ↑ with age</td>
<td></td>
</tr>
<tr>
<td>- Central tumour: presents late with invasion of lymph nodes</td>
<td></td>
</tr>
<tr>
<td>- Can block airway → distal pneumonia</td>
<td></td>
</tr>
<tr>
<td>- Pathogenesis: BPDE in smoke binds p53 mutational hot spots → mutation. Sequence of changes from squamous metaplasia to dysplasia to carcinoma in situ to invasive carcinoma</td>
<td></td>
</tr>
<tr>
<td>- Macroscopic: Arises in major bronchus, grey-white hard granular neoplasm, central cavitation in large cancers, uninvolved lung shows smoking related pathology (eg emphysema)</td>
<td></td>
</tr>
<tr>
<td>- Microscopic appearance: pink when stained (due to cytoplasma), keratin whirls and intracellular bridges (diagnostic), band in central cytoplasma, large irregular nucleus, nuclear pleomorphism, hyperchromatism (ie darker), coarse chromatin clumping, mitosis, large nucleoli, usually arranged in sheets</td>
<td></td>
</tr>
<tr>
<td>- Complications: metastatic disease to lymph nodes, brain, liver and adrenals</td>
<td></td>
</tr>
<tr>
<td>- Overall five year survival 10%</td>
<td></td>
</tr>
<tr>
<td>- Surgical treatment preferred: but may patients may have insufficient pulmonary reserve</td>
<td></td>
</tr>
<tr>
<td>Small Cell Carcinoma:</td>
<td></td>
</tr>
<tr>
<td>- = 'Oat cell' carcinoma</td>
<td></td>
</tr>
<tr>
<td>- Central ⇒ poor prognosis</td>
<td></td>
</tr>
<tr>
<td>- Very aggressive</td>
<td></td>
</tr>
<tr>
<td>- Treatment: chemotherapy +/- radiotherapy – not surgery as will have metastasised</td>
<td></td>
</tr>
<tr>
<td>- Neuroendocrine origin</td>
<td></td>
</tr>
<tr>
<td>- Pathogenesis: BPDE in smoke binds p53 mutational hot spots → mutation</td>
<td></td>
</tr>
<tr>
<td>- Macroscopic description: perihilar and surround large bronchi. Grey-white or haemorrhagic. May be more extensive microscopically</td>
<td></td>
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<table>
<thead>
<tr>
<th>Adenocarcinoma</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>- Males &gt; females</td>
<td></td>
</tr>
<tr>
<td>- Smoking related</td>
<td></td>
</tr>
<tr>
<td>- Central</td>
<td></td>
</tr>
<tr>
<td>3. Anthracosis</td>
<td></td>
</tr>
<tr>
<td>4. Cavitation + necrosis</td>
<td></td>
</tr>
<tr>
<td>3. Keratin aggregates</td>
<td></td>
</tr>
<tr>
<td>4. Cytologic features of malignancy</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Large cell undifferentiated</th>
<th></th>
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<tbody>
<tr>
<td>1. Very poorly differentiated – no longer recognised as SCC or adenocarcinoma</td>
<td></td>
</tr>
<tr>
<td>2. Smoking related</td>
<td></td>
</tr>
<tr>
<td>1. Anaplastic cells (large, pleiomorphic)</td>
<td></td>
</tr>
<tr>
<td>2. Giant cells, spindled morphology</td>
<td></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Small cell</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Central hilar location</td>
<td></td>
</tr>
<tr>
<td>2. Large, white fleshy lesions</td>
<td></td>
</tr>
<tr>
<td>3. Anthracosis</td>
<td></td>
</tr>
<tr>
<td>4. Smoking related changes in other lung</td>
<td></td>
</tr>
<tr>
<td>1. Small blue cells</td>
<td></td>
</tr>
<tr>
<td>2. Little cytoplasm</td>
<td></td>
</tr>
<tr>
<td>3. Crush artefact (squashed)</td>
<td></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>NE</th>
<th></th>
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</thead>
<tbody>
<tr>
<td>1. Nests of tumour cells</td>
<td></td>
</tr>
<tr>
<td>2. Fibrous stroma</td>
<td></td>
</tr>
<tr>
<td>3. Eosinophilic cytoplasm</td>
<td></td>
</tr>
<tr>
<td>4. Immunohistochem +ve for chromogranin + synaptophysin</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Mesothelioma</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Diffuse pleural lesion</td>
<td></td>
</tr>
<tr>
<td>2. Encases lung invades chest wall, lung, mediastinum, vasculature</td>
<td></td>
</tr>
<tr>
<td>1. Gland-like structures</td>
<td></td>
</tr>
<tr>
<td>2. Spindled</td>
<td></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Plural</th>
<th></th>
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</thead>
<tbody>
<tr>
<td>1. Well diff – glands</td>
<td></td>
</tr>
<tr>
<td>2. Poorly diff – intracytoplasmic mucin only</td>
<td></td>
</tr>
<tr>
<td>3. Keratin aggregates</td>
<td></td>
</tr>
<tr>
<td>4. Cytologic features of malignancy</td>
<td></td>
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</table>

<table>
<thead>
<tr>
<th>Adenocarcinoma</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>- Glandular epi origin</td>
<td></td>
</tr>
<tr>
<td>- Non-smokers (and smokers)</td>
<td></td>
</tr>
<tr>
<td>- Peripheral</td>
<td></td>
</tr>
<tr>
<td>1. Peripheral</td>
<td></td>
</tr>
<tr>
<td>2. Cream grey mass</td>
<td></td>
</tr>
<tr>
<td>3. Anthracosis</td>
<td></td>
</tr>
<tr>
<td>4. Cavitation + necrosis</td>
<td></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Small cell</th>
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</thead>
<tbody>
<tr>
<td>• Cigarette smoking</td>
<td></td>
</tr>
<tr>
<td>• Very aggressive</td>
<td></td>
</tr>
<tr>
<td>• Central around hilum</td>
<td></td>
</tr>
<tr>
<td>• Ectopic hormone production (ACTH, ADH)</td>
<td></td>
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</tbody>
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<tr>
<th>NE</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>• Associated with asbestos exposure</td>
<td></td>
</tr>
<tr>
<td>• Cells of origin = mesothelium of visc + parietal pleura</td>
<td></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Plural</th>
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</tr>
<tr>
<td>• Cells of origin = mesothelium of visc + parietal pleura</td>
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<table>
<thead>
<tr>
<th>Small CC</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>• Neuroendocrine tumour of bronchial epi</td>
<td></td>
</tr>
<tr>
<td>• Benign course</td>
<td></td>
</tr>
<tr>
<td>• Non-smokers</td>
<td></td>
</tr>
<tr>
<td>• Secretes 5HT3</td>
<td></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Carcinoid</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>• Neuroendocrine tumour of bronchial epi</td>
<td></td>
</tr>
<tr>
<td>• Benign course</td>
<td></td>
</tr>
<tr>
<td>• Non-smokers</td>
<td></td>
</tr>
<tr>
<td>• Secretes 5HT3</td>
<td></td>
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</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>NE</th>
<th></th>
</tr>
</thead>
</table>
- Microscopic appearance: small cells, scant cytoplasm (blue when stained – predominantly nuclei), ovoid, dense, hyperchromatic so nucleoli not usually seen, mitotically active, pleomorphic nuclei. Fragile → crushed causing blue streaks
- Complications: metastatic disease to lymph nodes, brain, liver and adrenals
- Two year survival 25%
- Treatment: chemotherapy. Surgery useless unless palliative

- Large cell carcinoma:
  - Undifferentiated (the ‘waste basket’ category)
  - Central
  - White ⇒ desmoplastic
  - Microscopic appearance: Can’t tell cell of origin, contains giant cells, moderate amount of cytoplasm
  - Quite aggressive

- Adenocarcinoma:
  - Less common, Male = female
  - Occurs peripherally not centrally ⇒ more easily resectable (unless into pleura – poor prognosis)
  - Less association with smoking
  - Association with previous scarring (eg Tb)
  - Microscopic appearance: looks like it’s trying to form glands, ascini, desmoplastic stroma

- Bronchoalveolar carcinoma:
  - Distinctive variant of adenocarcinoma
  - Slowly crawls along bronchioles
  - Good 5 year survival but poor prognosis: drown in mucin
  - Type of adenocarcinoma

- Carcinoid tumour:
  - Low grade tumour derived from neuroendocrine cells
  - Occurs younger (mean is 45) than the more frequent bronchogeneic carcinomas
  - Occur in lung, bowel, other sites
  - 90% Central types: 70% survive 5 years
  - 10% Peripheral types: rarely metastasise
  - Look like oat cell, but behave very differently. Grows by expansion rather than infiltration

- Mesothelioma:
  - Primary pleural tumours, including benign and malignant (also tumours of the peritoneum, tunica vaginalis and pericardium)
  - Benign mesothelioma does not produce pleural effusion and has no relationship to asbestos
  - Malignant mesotheliomas arise in either visceral or parietal pleura, produce pleural effusion (can be unilateral) and are related to asbestos. Drain effusion and re-xray (looking for lumpy pleura). Do cytology on fluid. Invades lung and often other thoracic structures. Presents in 5th to 7th decade, with lag after exposure of > 20 years. Diagnosis by imaging and biopsy. Poor prognosis. See Pneumoconioses, page 119.

- Adenosquamous carcinoma: rarer tumour with squamous and glandular features. Aggressive, bulky, peripheral tumour
- Pancoast tumour/syndrome: lung cancer (usually squamous) in the apex extending to supraclavicular nodes and involving 8th cervical and 1st and 2nd thoracic nerves → shoulder pain radiating in ulnar distribution. May also involve cervical sympathetic nerves and cause Horner’s Syndrome (ipsilateral enophthalmos – sunken eye, ptosis, miosis and dry skin)

**Systemic Effects of Lung Carcinoma**

- **Paraneoplastic syndromes** = symptoms that cannot be explained by local or distant spread or hormones usually produced by tissue of origin:
  - Endocrinopathies cushing’s (ACTH – small CC); SIADH (ADH – small CC); hyperca (PTH – SCC); carcinoid syndrome
  - Nerve + muscle = myasthenia – immunologic – bronchogenic ca
  - Derm disorders = acanthosis nigricans (hyperpig in skin folds) – immunologic – bronchogenic ca
  - Vascular = venous thrombosis – tumour products activating clotting – bronchogenic ca
  - Osseous = clubbing – bronchogenic ca

- Often the presenting problem:

<table>
<thead>
<tr>
<th>Type</th>
<th>Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Squamous Cell Carcinoma</td>
<td>Hyperparathyroidism (PTHrP) (↑Ca which may → arrhythmias)</td>
</tr>
<tr>
<td>Small Cell Carcinoma</td>
<td>Cushing’s Syndrome (ACTH)</td>
</tr>
</tbody>
</table>
Hyponatraemia (ADH)
Neuropathy and Psychosis (may be due to ↑neurotransmitter)

All Types  Gynaecomastia (HCG) in many poorly differentiated cancers

- Common metastases sites = cervical nodes, liver, brain, bone, adrenals, kidneys, lung, pleura, pericardium, spinal cord

**Prognosis**

- Slight improvement
- 5 year survival for all cases 13%
- Prognostic factors:
  - Stage: most important factor
  - Age < 40 worse (diagnosed late)
  - Gender: female worse (diagnosed late)
  - Site
  - Size > 6 cm worse

**Staging:**

- Critical to prognosis and treatment decisions
- Staging systems are regularly refined
- TNM system (not usually used for Small Cell as these have usually metastasised by diagnosis):
  - T: tumour size and invasion
  - N: which mediastinal nodes are involved
  - M: no metastases or metastases present
- TNMs are grouped to give stage groups ranging from IA to IV

**Treatment**

- Factors to consider:
  - Location of primary tumour
  - Extent of disease
  - Associated clinical complications
  - Non-malignant comorbidities
- Significant difference between Non-small cell and Small cell:
  - Non-small Cell:
    - Surgery: resection is the gold standard, but only 20% have resectable disease at diagnosis. Surgical studies are highly selected and not representative of the general population. Need to be early stage, medically fit, adequate respiratory reserve
    - Radiotherapy: majority will require RT:
      - Usually palliative (eg for haemoptysis, pain or dyspnoea)
      - Radical → confined to small volume disease
      - Neo-adjuvant → before surgery
      - Adjuvant → after surgery, limited role eg chest wall surgery
      - Can cause lung fibrosis
    - Chemotherapy:
      - Myriad of dosing regimes, combinations, etc.
      - Neo-adjuvant → pre-op with a view to downstaging inoperable disease; improves median survival by 6/52 (some survive longer)
      - Radical → only applicable to small cell ca
      - Adjuvant → recent studies demonstrate benefit
      - Palliative
      - Cisplatin and gancitabine are used in Wellington
  - Small Cell:
    - 70 – 80% have metastasised at diagnosis (to brain – 60%; BM, liver, adrenals, bone)
    - Survival at 5yr is 10% with chemo + RT (much better than it used to be)
    - Very rapid doubling time (can be 3 days)
    - No place for surgery
    - Often see SVC obstruction
    - Mainly managed with chemo +/- radiotherapy (makes a dismal outlook a bit better)
    - RT used to consolidate chemo response or for palliation
    - Prophylactic brain irradiation as chemo doesn't cross BBB
    - Very chemo-responsive but resistant cancer cells eventually will kill
• Risks of chemo/RT = toxic, treatment related death, cost
• Benefit = tumour response, ↓ symptoms etc

Sleep Apnoea

• See also:
  ➢ Drug Treatment of Insomnia, page 859 for Treatment of Insomnia
  ➢ See also Tiredness, page 13

Sleep

• It is active, complex, highly regulated
• Involves different neuronal groups, at least 5 separate neurotransmitters eg **orexins**
• Exact purpose is not understood
• Governed by homeostatic and circadian processes
• Composed of two fundamentally different states: REM sleep & NREM sleep
• Three states of being:
  ➢ Awake
  ➢ REM sleep
  ➢ Non-REM sleep (light sleep = stage 1 and 2; deep sleep = stage 3 + 4)
  ➢ Deep sleep tends to occur earlier in the sleep with REM occupying more time towards the end of the sleep period
• Sleep circadian rhythm:
  ➢ Sleep/wake cycling (amount, time spent in different stages as above)
  ➢ Related to body temperature
  ➢ **Hormone secretion involved** - ACTH, LH, FSH, TSH, **melatonin** (important: when eyes open, light striking eye causes melatonin production to be switched off – needs to be bright light eg sun)
  ➢ Cardiopulmonary variables change with sleep - blood pressure, myocardial infarction (more common first thing in the morning), pulmonary function
  ➢ Drug metabolism and gastric acid secretion changes during sleep
• Varies according to circadian cycle: two sleep gates each day, 2 – 3 pm and 10 – 11 pm (correlates with ↑ melatonin)

Sleep deprivation (insufficient sleep):

• Is common
• Affects mood, memory, reaction times and performance
• Concept of 5 hours core sleep has been challenged
• Performance may be affected if sleeping < 7 hours/night
• Obstructive sleep apnoea is the most common cause of excessive sleepiness → MVA (driving drowsy is the same as driving drunk)
• Causes of ↑ day time sleepiness:
  ➢ **Insufficient sleep** (eg sleep restriction)
  ➢ Obstructive sleep apnoea (see below)
  ➢ Central sleep apnoea:
    o No respiratory effort + no nasal/oral airflow due to absent or diminished ventilatory drive
    o Variety of causes including neuromuscular and chest wall deformities
    o Also seen in severe heart failure (Cheyne-Stokes is a form of CSA, see below)
    o Treatment: depends on cause; O2, PAP, medication for HF etc
  ➢ **Cheyne-Stokes Respiration** (see right): usually with **advanced heart failure**.
  Destabilisation of respiratory control centres
  ➢ Upper airway resistance syndrome (no actual apnoea)
  ➢ Periodic limb movements in sleep (PLMS):
    o Associated with restless leg syndrome
    o Leads to fragmented sleep
    o Also hot legs at night, cramps
    o Occurs in renal failure and anaemia
    o Treatment: codeine or anti-Parkinson drugs
  ➢ **Narcolepsy**:
    o Caused by deficiency in the hypothalamic neuropeptide system: orexins/hypocretins
    o Normal sleep at night and frequently going to sleep during the day whilst active
Can see sleep paralysis, waking from sleep but unable to move
- Goes into REM sleep early
- Vivid dreams (hypnagogic hallucinations)
- HLA linkage, affects young, twice as common as MS
- Cataplexy (sudden loss of muscle tone in response to emotional stimuli eg laughing).
- Dx: sleep study looks at daytime napping more than night-time + sleep latency test to measure how long it akes to get to sleep and whether REM sleep is seen in naps
- Treatment: stimulants during the day (eg Ritalin)

REM behaviour disorder:
- Normally during REM sleep, muscle tone is absent → prevents acting out of dreams
- Here, muscle tone is active and dreams can be acted out

**Idiopathic** hypersomnolence

**Drugs:** alcohol, sedatives
**Psychiatric** eg depression
**Hypothyroid**
**Anaemia**

**Insomnia:**
- 1/3 of population will suffer insomnia at some point, more common in women
- = Difficulty initiating or maintaining sleep with daytime consequences
- Identify predisposing, precipitating, perpetuating factors
- Sleep diary is useful
- CBT can be useful

**Normal breathing:**
- Inspiration: uses Genioglossus and other muscles to dilate trachea, and intercostals and diaphragm to create negative pleural pressure
-Expiration: much more passive

**Normal changes during sleep:**
- Carotid bodies much less sensitive to ↑CO2 and ↓O2
- ↓Intercostal & accessory muscle tone
- →↓tidal volume →↓ventilation →↑PCO2 by 5 mmHg →↑HR, flushed, warm periphery

### Assessment of Sleep Disturbance

- Keeping a **sleep diary** can be very useful (ie when went to bed, how long took to get to sleep, how long slept for, refreshed in mane etc)
- Ask questions around causes of excessive daytime sleepiness (as above)
- Take a good sleep history:
  - What are **normal sleep habits**? (when to bed, when to sleep, awakenings, when up, how many hours)
  - **Position** slept in
  - Wake up feeling **refreshed**?
  - **Daytime somnolence** (work, driving, talking to someone, reading, TV etc)
  - Caffeine/ETOH in evening?
  - **Medications/PMHx/occupation**
  - Anyone tell you you **snore**? Heard through a wall?
  - Anyone tell you you **stop breathing**? How long?
  - **Parasomnias** (sleep walking, night terrors etc)
  - Run through Epworth Sleepiness Scale (chance of dozing when reading/TV/sitting inactive/passenger in car/lying down to rest/talking/after lunch/stopped at traffic; mean = 6; >10 is a problem)
- Can do **Sleepiness test** as a more objective measure than the Epworth Sleepiness Scale: see if pt falls asleep in 20min with no stim
- Can do **Awake test** as more objective measure than ESS: see if pt can stay awake for 40min with no stim

### Treatment of Sleep Disturbance

- First check for: anxiety, depression, comfort, incontinence (eg diuretics), dementia, and treat these
- Normal ageing increases wakefulness during last 4 hours of sleep (reassure patient insomnia is ‘normal’)
- Education
- Good sleep habits:
  - Reduce light, noise and extremes of temperature in the bedroom.
  - Avoid caffeine, nicotine and alcohol before bedtime.
  - Avoid a **heavy meal** within two hours of bedtime, however a light snack may help if you are hungry.
- **Regular exercise** late in the afternoon or in the early evening may deepen sleep but do not exercise vigorously within three hours of bedtime
- In order to achieve relaxation at bedtime, allow about **one hour of quiet activity** prior to bedtime, such as reading, watching television or listening to music
- Develop a **bedtime ritual** such as reading or listening to relaxing music, clean your teeth etc. so that your body knows that you are getting ready to go to sleep
- *Don’t go to bed too early.* That is, *don’t go to bed unless you are feeling sleepy.* If you try to go to sleep too early before feeling sleepy you will have difficulty getting to sleep. This may make you feel irritated and frustrated about not feeling sleepy, not falling asleep and anxious about how you will cope the next day
- **Do not stay in bed if you are awake.** If you go to bed when you are feeling tired and sleep but do not fall asleep within **about 15-20 minutes** (estimated time only, do not use a clock), get out of bed, go to another room and do something mundane until you feel sleepy again. Repeat this procedure until you fall asleep quickly
- **Get up at the same time in the morning** as this will help train your body clock. Do not sleep in on weekends or after a late night
- **Try not to nap during the day** as this tends to reduce your sleepiness at night and results in poorer quality sleep during the night
- **Do not worry if you can’t get to sleep at night because worry and anxiety will delay sleep even more.** The harder you try the worse it will be. If you get very little sleep one night you will still function the next day although you may be a little more irritable and tired than usual

- Maximise exposure to morning daylight/ bright light
  - Light intensity > 2000 lux (normal room light 4-500 lux)
  - **Open curtains,** breakfast en
  - **Environment, walk**
- In holidays: progressively advance wake up time by 15-30 mins each day over one week
- Other treatments:
  - Bright light treatment
  - Melatonin 3-5 mg at night
  - **Avoid drowsy driving:**
    - If you feel tired or drowsy don’t drive
    - Follow your doctor’s advice re/sleep disorder e.g. if you have OSA and use CPAP
    - Get a **good night’s sleep before driving.** (Do not cut your sleep short – get to bed early and do not stay up late packing)
    - **Avoid alcohol the night prior** and during your trip (will disrupt sleep + ↑ tiredness; sleepiness + alcohol have an additive effect)
    - Avoid any sedative medications
    - Travel during non-sleeping hours
    - Don’t drive if you feel sleepy *(if sleepy, stop and rest. Have a brief nap in your car – Have a 10-15 minute break after every 2 hours, drink coffee)*
    - Drive with a companion and *share the driving*

**Obstructive Sleep Apnoea Syndrome**

- Most common sleep breathing disorder
- NB. Apnoea = **no resp for >10s**; hypopnoea = partial obstruction >10s
- **Pathogenesis:** ↓ muscle tone + anatomical factors (eg obese) + neural factors (eg stroke) → upper airway narrows → apnoea due to collapse → arousal → impairment over time of sensitivity to daytime ↑PCO2
- **Findings:** see continued respiratory effort (ie chest/abdo movement) but no air movement in and out, with desaturations and arousals. Preceding this, might see loud snoring
- Epidemiology:
  - Prevalence = 2-4% of adult population
  - More common in:
    - Men and post-menopausal women
    - Middle age
    - In kids with craniofacial syndromes
    - Short jaw
Alcohol users
- Overweight

Symptoms: Loud snoring, apnoea, daytime tiredness, early morning headache, poor short-term memory, dry throat/mouth, ↓ libido

History questions:
- When do you go to bed and when do you get up (sleep restriction)?
- How long does it take you to get to sleep?
- Do you snore, in any posture (the norm with OSA). Need witness accounts
- Has anyone ever told you you stop breathing during sleep? For how long?
- Do you feel refreshed on waking?
- Where do you fall asleep (eg TV, reading etc, ever at work/driving?)
- Other medical conditions: depression, anaemia, hypothyroidism, etc
- Medications and when do you take them: can keep awake at night or make you sleepy during the day

Examination features suggesting OSA = obesity, ↑ neck circumference, small oropharynx, recessed mandible

Severity index:
- Number of apnoea (>10s)/hr of sleep: 0-5 is normal
- 5-20 is mild, 20-40 is moderate, >40 is severe

Consequences:
- ↓ concentration, ↓ memory, ↑ accident risk, ↓ libido, premature mortality, precipitate respiratory failure in mild COPD
- CV effects:
  - Hypertension
  - MI
  - CVA
- In kids: less apnoea (if there is apnoea then ?SIDS/epilepsy), more noisy breathing/restlessness, wake a lot at night, hyperactive during the day, growth delay (↓ GH secretion due to ↓ slow wave sleep)

Diagnosis:
- Requires sleep study → polysomnography
- Measures muscle movements, airflows, O2 and CO2, EEG waves, eye movements, ECG etc during sleep
- Allows severity assessment
- Can do overnight oximetry but only detects 2/3 of cases

Treatment:
- Conservative:
  - Weight loss (did it start with weight gain?), smoke reduction, sleep posture modification
  - CPAP for moderate/severe: air splint prevents airway collapse through whole breath cycle. Need to titrate pressure → is very effective. Mask fitting etc can make CPAP difficult
  - Treat allergic rhinitis
  - Medication: Sleeping pills make it worse – stop them
  - Dental devices
- Surgical:
  - Kids – tonsils and adenoids
  - Adults:
    1. Mandibular advancement
    2. Gastric bypass → ↓ weight
    3. Tracheostomy
    4. Uvulopalatopharyngoplasty (UPPP) – but doesn’t deal with all sites of occlusion and stops CPAP working

Miscellaneous Lung Diseases
- Goodpastures Syndrome (= Antibasement Membrane Antibody Disease – ABMA):
  - Simultaneous rapidly progressive glomerulonephritis and haemorrhagic pneumonitis
  - Present with renal failure and haemoptysis
  - Due to anti-basement membrane antibodies deposited along alveolar walls and in glomeruli (type II immune reaction)
  - Usually occurs in young men, treated with steroids and cytotoxic drugs
  - See also RPGN
- **Alveolar Proteinosis**: Peripheral alveoli filled with pink, granular, acellular material. No treatment, variable course, clears in a few years. Prone to infection so steroids worsen the condition by depressing the immune system. Bronchial lavage effective in acute episodes.
- A number of vasculitis affect the lung. Eg Wegener’s granulomatosis, allergic angiitis and granulomatosis. Also collagen diseases such as SLE and Rheumatoid arthritis.
- **Pulmonary Hamartoma**: benign localised proliferation of normal tissue components (hyaline cartilage with respiratory epithelium, maybe fibrous tissue, fat, blood vessels). Usually found as incidental findings on X-ray.
- **Langerhans cell**: diagnostic cell seen in eosinophilic granuloma. = histiocytosis X and pulmonary eosinophilic granuloma. A large histiocyte with one bland folded nucleus, abundant eosinophilic cytoplasm with indistinct cell borders. Proliferative disorder of histiocytes. X-rays show multiple nodules scattered through both lungs.
- **Langhans giant cell**: (not the same as Langerhans cell) multinucleated giant cell in granulomas, with nuclei arranged around the periphery of the cell in a horseshoe pattern.
- Sequestration:
  - Extralobular: Congenital. Mass of lung tissue not connected to bronchial tree and outside the visceral pleura.
  - Intralobar sequestration: usually acquired. Within the visceral pleura but not connected to the bronchial tree.
- Differential of Solitary lung nodule:
  - Tumour: benign (bronchial adenoma or pulmonary hamartoma) or malignant.
  - Tb.
  - Sarcoidosis.
  - Other granuloma: eg fungal.
  - Haematoma (ie blood clot, eg in cavity following lung contusion)

**Pulmonary Hypertension**
- **Primary** = idiopathic, rare, usually in young women.
- **Secondary** = more common – chronic lung disease, heart disease, recurrent PEs, autoimmune disorders.
- Right heart works harder to eject blood into lungs → **cor pulmonale**: RVH caused by resp problem ie PHTN → SOBOE, weakness, peripheral oedema.
- **Macro** = increased vascular markings near hilum on CXR; atheroma in large pulmonary arteries.
- **Micro** = hypertrophy of media of small arteries and arterioles.
Endocrine Basics

- Endocrine: secretes directly into blood eg pituitary, thyroid, pancreas, adrenals
- Exocrine: secretes into a duct system eg breast, liver (bile), pancreas (digestive enzymes)
- Calcitonin’s effects:
  - Bone: suppresses resorption of bone by inhibiting the activity of osteoclasts, releasing calcium and phosphorus into blood
  - Kidney: calcium and phosphorus are prevented from being lost in urine by reabsorption in the kidney tubules

History

- Symptoms widespread and often insidious
- Enquire about previous endocrine gland problems, surgery, etc
- Major symptoms:
  - Changes in appetite and weight:
    | ↑Appetite | ↓Appetite |
    |---------|---------|
    | ↑Weight | Cushing’s Syndrome, hypoglycaemia, hypotalamic disease | Hypothyroidism |
    | ↓Weight | Thyrotoxicosis, uncontrolled DM | Adrenal insufficiency (also GI causes and malignancy) |
  - Bowel:
    - Diarrhoea ⇒ hyperthyroidism or adrenal insufficiency
    - Constipation ⇒ hypothyroidism or hypercalcemia
  - Heat/cold intolerance
  - Sweating: hyperthyroidism, phaeochromocytoma, hypoglycaemia, acromegaly (also anxiety and menopause)
  - Skin thinning: either ↓androgens (old men and post-menopausal women) or ↑Cortisol
  - Amenorrhoea: ↑PRL (by only a little), ↑Cortisol (takes bigger increase), ↑↑hyperthyroidism
  - Nocturia: ↓ADH, or Diabetes from ↓insulin, ↑cortisol or ↑GH

Diabetes Mellitus

Diagnosis of Diabetes

<table>
<thead>
<tr>
<th></th>
<th>Fasting blood glucose</th>
<th>2 hours post glucose tolerance test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetes (one or the other)</td>
<td>&gt; 7.0 (was 7.8) mmol/l</td>
<td>&gt; 11.1 mmol/l</td>
</tr>
<tr>
<td>Impaired Glucose Tolerance: IGT</td>
<td>&lt; 7.0</td>
<td>7.8 – 11.1</td>
</tr>
<tr>
<td>Impaired Fasting Glucose: IFG</td>
<td>6.1 – 6.9</td>
<td>&lt; 7.8</td>
</tr>
</tbody>
</table>

- For Gestational Diabetes:
  - Screening: at 28 weeks, non-fasting glucose load of 50g. If ≥ 7.8 should have gestational glucose tolerance test
  - Gestational Glucose tolerance test: 75 g load when fasting. Fasting level ≥ 5.5 OR 1 hour post glucose load of ≥ 11 OR 2 hour post glucose load of ≥ 8.5 (some say 9.0) ⇒ gestational diabetes.
  - 1 – 3 % of pregnancies have gestational diabetes
- Suggested regime for screening for type 2 diabetes (Screening for type 2 diabetes, NZMJ 26 April 2002)
  - Test if > 5% of diabetes ⇒ Europeans over 50 and non-Europeans > 40 years of age
  - Yearly screening for anyone found to have IGT or IFG
  - Best to test with morning fasting glucose – although use random test with caution if conditions approach fasting or post-glucose load conditions
  - Finger prick testing not accurate enough
  - HbA1c not recommended for screening: different methods for testing and different normal ranges
Type 1 Diabetes (Juvenile Onset Diabetes)

- A chronic, progressive autoimmune process in genetically susceptible people, triggered by environmental factors
- Eventually cannot survive without insulin treatment. Ketoacidosis will develop unless insulin given (if any endogenous insulin then no ketones; ketogenesis pathway very sensitive to insulin)
- Incidence up to 20 yrs: 10 – 15/100,000; incidence is ↑
- Prevalence: 0.25 – 3 % (10 – 15% of all diabetics)
- Peak age of incidence is 12 – but can present at any age (even after 40). Surges in presentation at 3- 4, starting school. ?Viral exposure
- 85 – 90% have no family history, but family history confers ↑ risk
- Overt diabetes is not apparent until β-cells destruction reaches ~ 10% of original
- Honeymoon period: exogenous insulin given → temporary ↑ functioning of remaining β-cells and ↓ requirement for exogenous insulin (for a period)
- Antibodies:
  - Islet Cell Antibodies: risk of IDDM ↑ with ↑ level of ICA. Frequency in newly diagnosed IDDM is 65 – 85%.
  - GAD (glutamic acid decarboxylase) antibodies: mildly specific antigenic enzyme released from islet cells when destroyed. Can test for these in prodromal stage
  - Insulin autoantibodies
- Acute presentation:
  - Hyperglycaemia (polyuria when glucose > 10 mmol/l, polydipsia), tiredness, weight loss, polyphagia
  - Also cramps, blurred vision, superficial infections
  - Ketoacidosis (now reasonably rare) also has nausea, vomiting, and drowsiness
- Currently being investigated for prevention in high risk individuals (ie have antibodies but not frank disease):
  - Early oral insulin therapy → autoimmune modulation – this seems to prolong the onset of symptoms by up to 4 years
  - Nicotinamide (vitamin B) supplementation (does not work)
- Treatment goals:
  - Stable blood sugar
  - Prevent/monitor complications
  - Promote normal growth and development
  - Maintenance of normal weight

Type 2 Diabetes

- Characterized by the combination of:
  - Peripheral insulin resistance
  - Inadequate insulin secretion by pancreatic beta cells
- ↑FFA → insulin resistance → leads to ↓ glucose transport into muscle cells, ↑ hepatic glucose production, and ↑ breakdown of fat
- For T2DM to occur, both defects must exist. For example, all overweight individuals have insulin resistance, but diabetes develops only in those who cannot increase insulin secretion sufficiently to compensate for their insulin resistance. Their insulin concentrations may be high, yet inappropriately low for the level of glycermia
- Presumably, type 2 diabetes mellitus develops when a diabetogenic lifestyle (ie, excessive caloric intake, inadequate caloric expenditure, obesity) is superimposed upon a susceptible genotype
- About 90% of patients who develop type 2 diabetes mellitus are obese

Investigations

- Glucose testing
- HbA1c. Any reduction worthwhile. Target is <= 7.0. Not all willing or able to achieve this
- Ketonuria
- 24 hour urine and measure C-peptide: by-product of insulin production (have they any endogenous insulin – as long as replacement insulin hasn’t → islet cell atrophy)
- Fundoscopy

Endocrine and Electrolytes

134
Lipids

BP: want diastolic < 85 and systolic < 135 (especially for young or existing microalbuminuria)

Microalbuminuria:
- Nephropathy has two phases:
  1. Normal blood pressure, creatinine, and urine but microalbuminuria
  2. Overt nephropathy: proteinuria, hypertension, ↑creatinine and ↓GFR
- Normal level < 20 mg/24 hours. Microalbuminuria = 30 – 300 mg/24 hours. Dipstick detects > 150 g/l (ie insensitive)
- Microalbuminuria hard to test (needs 24 hr urine). So use albumin:creatinine ratio. Normal < 2.8 in men, < 4.5 in females in random test
- If abnormal result then patients qualify for statins with cholesterol > 6 (normal threshold > 9)
- See Diabetic Nephropathy, page 311

NB. If parents request testing of siblings if they’re worried, can test HbA1c and islet cell auto-antibodies
- Can also see minor hyperglycaemia during intercurrent illness, can also test HbA1c + ICA if concerned

Complications

Pathology:
- 1. Advanced glycosylation end products:
  - Elevated intracellular levels of glucose cause non-enzymatic covalent bonding with proteins, which alters their structure and inhibits their function
  - Glycosylated proteins are implicated in the pathology of diabetic neuropathy + other long term complications
- 2. Sorbitol/aldose reductase pathway:
  - Implicated in complications that result in microvascular damage to nervous tissue, and also to the retina and kidney
  - In a hyperglycemic state, the affinity of aldose reductase for glucose rises, meaning much higher levels of sorbitol
  - Sorbitol cannot cross cell membranes and when it accumulates, it produces osmotic stresses on cells by drawing water into the cell
- 3. Protein kinase C:
  - Hyperglycaemia → ↑ PKC activation/activity
  - May cause ↑ in vascular permeability, angiogenesis, cell growth and apoptosis, vessel dilation, cytokine activation, basement membrane thickening and extracellular matrix expansion

Microvascular disease:
- Due to thickened walls and laying down of advanced glycosylation end-products
  - 1. Retinopathy. After 30 years 80% have background retinopathy and 7 – 8% are blind (see Focal Ischaemic Retinal Disease, page 218). Also ↑ Sorbitol → cataracts
  - 2. Nephropathy
  - 3. Neuropathy: peripheral and autonomic

Macrovascular disease:
- Coronary heart disease. Male diabetics have 2 times risk, females 4 times risk. Very high risk if other risks present (eg ↑BP, lipids, smoking etc)
- Accelerated atherosclerosis (but lesions look the same)
- CVA
- PVD

Nephropathy:
- See also Diabetic Nephropathy, page 311
- Onset of diabetes leads to:
  - Functional changes: ↑GFR, Reversible albuminuria
  - Structural changes: GBM thickening, mesangial expansion
- After 30 years, 30 – 40% have nephropathy. Unlikely if hasn’t developed after 30 years (?some protective factors)
- Glomerular damage:
  - Nodular glomerulosclerosis. Acellular hyaline material (Kimmelstiel-Wilson Lesion): BM proliferates (ie collagen expansion of mesangial matrix) → sclerosed and fibrotic due to fibroblast infiltration → chronic renal failure. Earliest sign is microalbuminuria, due to pores getting bigger. Eventually leads to diffuse GS
  - Diffuse glomerulosclerosis: glomerular loop obstruction → necrosis (seen in hypertension or any end-stage renal disease)
Mesangial proliferation + fibrosis
BM thickening
Arteriolar hyaline sclerosis (as cf hypertensive changes where afferent, not the efferent arteriole is affected)
- Papillary necrosis: least blood supply → susceptible to ischaemia
- Also pyelonephritis and reflux lead to kidney damage
- Immune deficiency: white cells affected when glucose > 14 mmol/l
- Neuropathy:
  - Glycosylation of nerve
  - Demyelination of nerve due to sorbitol accumulation in Schwann cells → slowed conduction
  - Autonomic sensory AND motor neuropathy (eg foot deformity, fallen arches)
- Autonomic neuropathy leads to bladder problems, impotence, gastroenteropathy
- All lead to → Diabetic foot
- Special management in surgery, pregnancy and in intercurrent illness

Management of New Onset Diabetes Without Ketoacidosis
- Education of child and family in diabetes management – generally as an outpatient
- Establish on insulin
  - Dose will change over first few days/weeks
  - Honeymoon phase often seen (as above)

Management of Diabetic Ketoacidosis
- Pathophysiology (from starship guidelines):
  - ↑ hepatic + renal glucose production + impaired peripheral glucose utilisation → hyperglycaemia + hyperosmolality
  - ↑ lipolysis and unrestrained production of ketoacids (beta hydroxybutyrate and acetoacetate), resulting in ketonaemia and metabolic acidosis
  - Osmotic diuresis (due to hyperglycaemia), loss of electrolytes and dehydration, which can exacerbate the metabolic acidosis
  - NB. K+ from cells swaps with H+ to ↓ acidosis + is lost in diuresis; when acidosis corrected, K+ + H+ swap back and total body K+ is depleted, therefore needs replenishing
  - Signs: nausea, vomiting, thirst, abdominal pain, delirium, coma, acetone fetor, hypotension, tachycardia, metabolic acidosis (Kussmaul breathing: deep, rapid sighing breathing), hyperosmolality
  - Treatment:
    - ABC, oxygen
    - IV crystalloid (NS): may need 4 – 6 L. Give 10ml/kg if shocked or severely dehydrated. Be cautious with rehydration as there is a risk of cerebral oedema (see below) – give replacement fluids over 48hrs
    - Potassium 20 mmol in first 6 hours then 10 mmol/hr according to plasma levels. If plasma K high then delay adding K until this has normalised
    - Insulin infusion: 0.05-0.1 U/kg/hr. Do not bolus insulin. Resistance to insulin may suggest sepsis, insulin antibodies
    - Monitoring:
      - One-to-one close nursing
      - Blood glucose
      - Electrolytes
      - Acidosis. May need HCO3
  - Cerebral oedema:
    - Usually seen in first 24 hours after starting rehydration
    - Can be seen if vigorous rehydration + insulin, causing glucose to be taken-up into cells and therefore ↓ osmolality so fluid shifts into ICF
    - Warning signs:
      - Major: age inappropriate incontinence, altered mentation, sustained deceleration in HR
      - Minor: vomiting, HA, lethargy, age <5, DBP >90mmHg
    - Treat immediately with mannitol

Hypoglycaemia
- Mostly related to insulin therapy
- Consequences are more severe in children
- Severe hypoglycaemia is uncommon during the first year after presentation
• α-cells also get wiped out eventually and therefore glucagon is ↓
• Hypoglycaemic unawareness can occur with glucose < 3mmol/L
• Associated autoimmune diseases can contribute (coeliac, addison’s, hypothyroid)
• S & S: cold, clammy or sweaty skin; pallor; ↓ concentration; shakiness; irritability; fatigue; nervousness; excess hunger; HA; blurred vision; fainting + LOC
• Prevention:
  ➢ Give appropriate insulin analogue regimes
  ➢ Training in recognition of symptoms
  ➢ Nocturnal monitoring with continuous glucose monitoring (SC glucose sensor – measures and can alarm when low)
  ➢ Working towards HbA1c targets

**Ongoing Management of Diabetes**

• Acute symptoms are main reason for seeking treatment. But good control is more than just keeping out of trouble. Involves significant education
• For impaired glucose tolerance and impaired fasting glucose: *lifestyle change and monitoring*
• Four key areas to address:
  ➢ Diet:
    o Aim is to achieve optimal growth, maintain glycaemic control, ideal body-weight, prevent complications
    o Essentially a healthy diet:
      ➢ CHO > 50% (especially complex)
      ➢ Fat 30-35% (<10% saturated, >10% monounsat, <10% polyunsat)
      ➢ Protein 10-15%
    o Regularity of intake is key
    o Not about cutting out sugar – fat is more important
    o **Glycaemic index**: how quickly blood glucose rises when food eaten; lower GI better
    o **Carbohydrate counting**: measuring CH content in g per meal and adjusting insulin accordingly – useful for some pts
  ➢ Sick days:
    o Warn about *effects on blood sugars of another illness* (eg ‘flu) →↑ blood sugars
    o Requires *more regular monitoring of both BG and ketones*
    o Don’t just stop taking insulin if not eating
  ➢ **Insulin**:
    o Use fast acting for glucose peaks following meals, + long acting for basal rate (→ suppress gluconeogenesis overnight)
    o Conventional regime: twice daily with both fast and long acting
    o Intensive regime: fast acting before each meal and long acting at night (= 4 jabs a day)
  ➢ Exercise:
    o ↑ sensitivity to insulin
    o Adjust insulin regimen to the individual’s exercise plan
    o Encourage as much exercise as possible
• Should also include assessment of (or screening for):
  ➢ Complications:
    o Microvascular (retinopathy, nephropathy, neuropathy)
    o Macrovascular (MI, CVA, PVD):
      ➢ Address other CV risk factors (eg stop smoking, address dyslipidemia)
      ➢ Aim for BP of 130/80 if normal kidney function
      ➢ Aim for BP of 120/75 if microalbuminuria
    o Also: cataracts
  ➢ Glycaemic control: aim for an HbA1c of 7% (lower than this is associated with ↑ risk of death)
• **Biguanides**:
  ➢ Metformin
  ➢ ↑ Insulin sensitivity, ↓ gluconeogenesis, won’t → hypoglycaemia
  ➢ SE: nausea, vomiting, B12 malabsorption
  ➢ Not in hepatic and renal disease or pregnancy. Not in hypoxic lung disease or cardiac disease
• **Sulphonylureas**:
  ➢ Glipizide/gliclazide
- ↑insulin release from β-islet cells (=> must have some left for it to work + cells must not be insulin resistant), ↓gluconeogenesis and glycogenolysis

- Can → hypoglycaemia

- SE: nausea, vomiting

- Not in hepatic and renal disease or pregnancy

- Monitoring: HbA1C (normal < 6.5), daily blood sugars (before breakfast)

- Diabetes Complications Control Trial (DCCT, 1993) examined 1441 volunteers (ie motivated) in two groups: conventional treatment (insulin once or twice daily) and intensive (3 or 4 times daily). Intensive therapy reduced risk of complications, but ↑hypoglycaemia – aim is to find the perfect balance between complication risk and hypoglycaemia risk

**Examples**

<table>
<thead>
<tr>
<th>Case</th>
<th>Age</th>
<th>BMI</th>
<th>Fasting Gl</th>
<th>Post-prandial Gl</th>
<th>Ketones</th>
<th>Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>50</td>
<td>35</td>
<td>6.5</td>
<td>12</td>
<td>-</td>
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<td>2</td>
<td>50</td>
<td>35</td>
<td>12</td>
<td>14</td>
<td>-</td>
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</tr>
<tr>
<td>3</td>
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<td>25</td>
<td>12</td>
<td>14</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>4</td>
<td>50</td>
<td>18</td>
<td>12</td>
<td>14</td>
<td>+</td>
<td>Weight loss</td>
</tr>
</tbody>
</table>

- Case 1: has more insulin than case 2 (insulin resistance is proportional to BMI, but her glucose is lower => earlier presentation than case 2. Treatment: diet + metformin (can → diarrhoea secondary to malabsorption). If very overweight, check LFT

- Case 2: pancreas starting to fail

- Case 3: weight loss may not do much. Are they CHO deficient (↑CHO → ↑insulin release)? May start with sulphonylureas. May need insulin sooner

- Case 4: Type 1. Will be catabolic – need protein. Quick test with sulphonylureas but will need insulin at earlier stage

**Other Pancreas Problems**

- Exocrine:
  - Neoplastic = pancreatic ductal carcinoma/cystic tumours
  - Non-neoplastic = pancreatitis

- Endocrine:
  - Neoplastic = endocrine tumours eg gastrinoma, insulinoma, glucagonoma
  - Non-neoplastic = DM

- Pancreatic investigations:
  - EUS (endoscopic US) with FNA => cytopathology assessment

**Thyroid**

**Assessment**

- Clinical
- Anatomic pathology (cytology + histology)
- Biochemical
- Radiological (both diagnosis + FNA/bx guidance)
- The gland itself: enlarged, smooth, nodules, tender, etc
- Specific features: eg autoimmune (exophthalmos) or pituitary disease
**Physiology**

- TRH (hypothalamus) → TSH (anterior pituitary) → T3 and T4 (thyroxine → peripherally converted to T3)
- T3 & T4 stored in thyroid follicles as thyroglobulin
- T3 exerts greater negative feedback on the pituitary. Only takes a 10% rise in fT4 to suppress TSH
- T3 is considerably more metabolically active (ie potent) than T4
- **Liver converts T4 → T3**, as does kidney and muscle
- T4 goes down first in hypothyroid. Only measure T3 in hyperthyroid (as it drives symptoms)
- Bound in plasma to thyroid binding globulin
- Intercurrent illness: FT4 rises (liver stops converting T4 to T3 straight away – want to be catabolic) then T4 falls to subnormal levels as thyroid production slows. FT3 falls from onset. TSH slowly falls to subnormal levels with severe illness. (ie similar pattern to hypopituitarism)

**Thyroid Pathology**

- See Thyroid Nodules
- Neoplastic lesions:
  - Benign eg adenoma
  - Malignant:
    - Papillary carcinoma
    - Follicular carcinoma
    - Medullary carcinoma
    - Poorly differentiated
    - Anaplastic
- Non-neoplastic lesions:
  - Multinodular goitre:
    - Endemic iodine deficiency or dyshormonogenesis
    - See ↑TSH which is trophic to thyroid → development of multiple nodules
    - Some nodules are hyperplastic (proliferating small follicles)
    - Some nodule show involution with secondary changes of haemorrhage, cystic degeneration, scarring
  - Graves disease
  - Hashimoto’s thyroiditis
  - De Quervain’s thyroiditis
  - Reidel’s thyroiditis

**Goitre**

- Normal gland weighs about 30 g
- Nodular or diffuse
- Can be hyper, eu, or hypo-thyroid
- Check size, shape, consistency, mobility
- Check for dysphagia, stridor, laryngeal nerve palsy (especially multinodular)
Thyroid Tests

- Plasma **TSH**: Newer sensitive test means low levels can be measured. Can be used as a reliable screening test as a stand-alone
- Free T4 and T3
- Plasma T4 (= bound T4 + free T4). False high in pregnancy, oestrogens (↑TBG). False lows with NSAID, phenytoin, steroids, TBG deficiency
- Thyroid isotope scanning: to look for hot spots or cold spots
- Thyroid antibodies: raised in Hashimoto's and so Graves
- TRH test: Inject to test thyroid. If minimal increase in TSH then: Hyperthyroidism, multinodular goitre, thyroxine replacement, euthyroid Graves disease, autonomous thyroid nodule

Thyroid Imaging

- Can use nuclear medicine, ultrasound (little routine use – can guide FNA), CT (not for intra-thyroid lesions but demonstrates extension and mass effects) or MRI. Only when suspicion of significant pathology
- Before scanning thyroid (with 99MTC pertechnetate), stop iodine supplements (eg kelp), thyroxine, and angiography (contrast contains iodine). Gland must be ‘hungry’
- Normal uptake is 1 - 3%. If it takes up too much then hyperthyroid
- If diffuse uptake then Grave’s. If multinodular then:
  - Cold nodules: 80% are cysts or regressive nodules. 20% are malignant → FNA
  - Hot nodules: maybe with decompensation in rest of gland (↓uptake due to ↓TSH)

Thyroid Eye Disease

- Retro-orbital inflammation and lymphocyte infiltration. May → optic nerve compression (→ colour desaturation and ↓acuity). Does not parallel degree of toxicosis
- At presentation, patient may be euthyroid, hypothyroid or hyperthyroid
- Management: Early referral. Check for keratitis with Rose Bengal eye-drops. Lubricant eye drops. Systemic steroids. Surgical and other treatments
Hyperthyroidism

- **Symptoms**: ↓weight, appetite↑, frequent stools, tremor, irritability, hot intolerance, sweating, oligomenorrhoea, infertility
- **Signs**: tachycardia, AF, warm peripheries, thyroid enlargement or nodules
- Additional signs in Grave’s disease:
  - Exophthalmos (bulging eyes)
  - Lid lag (lid lags eye when following your finger descending slowly)
  - Vitiligo (growing patches of skin depigmentation due to ↓melanocytes)
  - Pretibial Myxoedema (due to amyloid)

**Tests**

- Progression:
  - TSH suppressed first, while fT3 and fT4 normal ⇒ *TSH is the most sensitive test*. Suppresses with minor changes in fT4
  - fT3 rises next ⇒ mild symptoms
  - fT4 rises last ⇒ severe symptoms
- Screening: **fT4 and TSH** (TSH is most sensitive test)
- Severity: **fT4 and fT3** (fT3 ↑ first)
- Antibodies: *thyroid microsomal and thyroglobulin antibodies* (only present in 80% of Graves at presentation)
  - If goitre, ultrasound, thyroid scan
  - Test visual fields, acuity and eye movements. Referral if positive. Steroids to reduce swelling

**Causes**

  - Most common when < 50 (↑ multinodular goitre as you get older)
  - Probably results from *autoantibodies against TSH receptors*. Check for hTSAABs [human Thyroid stimulating auto-antibodies = TSI [thyroid stimulating immunoglobulin]]
  - Measure thyroid microsomal and thyroglobulin antibodies
  - May cause normochromic, normocytic anaemia, ↑ESR, ↑calcium, abnormal LFTs
  - Histology: large hyperchromatic nuclei, retracted thyroglobulin. Follicles same as in follicular carcinoma but carcinoma shows invasion of blood vessels
- Toxic adenoma:
  - = *Plummer’s Disease*, autonomous nodule. Often hyperthyroidism arising in a multinodular goitre
  - A nodule producing T3 or T4 → *hot* spot on scan
- Subacute thyroiditis/Destructive inflammation:
  - = *De Quervain’s Disease*. Usually resolves in 3 – 6 months. If rapidly destructive then acute thyroiditis
  - = Inflammation of the thyroid secondary to:
    - Pregnancy: autoimmune. Gland may not be tender
    - Infection: coxsackievirus (echovirus) and mumps. Tender gland
  - Pathophysiology: URTI → acute follicular inflammation → protein + T4/T3 released into interstitium → granulomatous inflammation → resolution
  - Has a hyperthyroid + hypothyroid phase
  - Goitre (often painful). Usually self-limiting
  - If severe, then 3 phases:
    - 1. Prodromal: may be 4 – 6 weeks longs
    - 2. Hyperthyroid: Release of preformed T3 and T4. TSH low. If very bad, fT4 will be 100 (normal = 10 – 24). ↑ESR in parallel with ↑T4
    - 3. Hypothyroid/regenerating: For 2 weeks – 2 months. In proportion to severity of hyperthyroid phase. T3 and T4 will go very low (?gland exhausted), TSH will remain depressed for a while longer (ie resembles secondary failure)
  - Doesn’t respond to carbimazole as it’s releasing preformed hormone. Carbimazole stops formation of hormone. If mild then wait. If severe, then antagonise peripheral effects (eg propranolol). Steroids work but prolong illness
  - Histology:
    - Neutrophils attack cuboidal epithelium (acute inflammation)
    - Thyroglobulin leaks out → granuloma formation
Endocrine and Electrolytes

Multinodular goitre:
- See haemorrhage, cyst formation, fibrosis. Is an ongoing destructive process
- Pathogenesis:
  - Follicle hyperplasia → capillary hyperplasia → local anoxia → acellular 'cold' regions → minor haemorrhage → fibrosis → calcification
  - Follicle hyperplasia → somatic mutation → varying levels of appearance and function of follicles → local autonomy from TSH and local poor I concentration → hot and cold nodules
- Post-partum thyroiditis: hyper or hypo thyroid. Hypothyroid may persist
- Other:
  - Self medication (↑T4 but ↓T3)
  - hCG excess (stimulates thyroid)
  - TSH dependent pituitary tumours (very very rare)

**99Tc Scan**
- Measures trapping of tracer/iodine by the gland
- See:
  - Graves' disease = diffuse uptake
  - De Quervain's (hyperthyroid phase) = blocked uptake (salivary gland uptake is comparable to that seen in thyroid)
  - Autonomous hot nodule = hot spot
  - Multinodular goitre = multiple hot spots

**Treatment**
- Drugs:
  - Thioureylenes: Carbimazole
  - ↓ formation of TH by inhibiting peroxidase and ↓ the oxidation of I
  - 40 mg/day PO for 4 weeks, then reducing every 1 – 2 months, withdraw after 18 months, 50% relapse
  - Or try block and replace strategy (ongoing carbimazole and replacement T4), propylthiouracil
  - Risk of agranulocytosis with Carbimazole and propylthiouracil
  - Toxic multi-nodular goitre and toxic adenoma unlikely to remit following drugs
  - Partial thyroidectomy: risk to recurrent laryngeal and parathyroids. May be hypo or hyper post surgery
  - Radioactive iodine (I¹³¹): will ultimately become hypothyroid

**Hypothyroidism**
- = Myxoedema if severe
- Signs and symptoms:
  - Symptoms:
    - Unhappy, no spark
    - ↑ weight, constipation
    - Cold intolerance
    - Menorrhagia (excessive menstruation, ↓T3 → ↓oestrogen breakdown)
    - Lethargy, depression, dementia, ↑sleep
    - Symptoms insidious and subtle (T3 receptors in nuclei of nearly all cells – govern metabolism, modulation of other hormones, O₂ consumption, regulation of protein synthesis, etc, etc)
  - Signs:
    - Bradycardia
    - Dry skin and hair
    - Goitre
  - Signs of myxoedema (↑hydration of subcutaneous tissue):
    - Non-pitting oedema (eyelids, hands, feet)
    - Yellowing of skin (myxoedema absorbs carotene. Sclera unaffected)
    - Thickened tissues, voice change (oedema in vocal cords), carpal tunnel syndrome
    - Hirsutism
  - If severe: slow, slurred speech (swollen tongue, slow thought), intention tremor (cerebellar effects), muscle weakness and pain, deafness (reverses with treatment), paranoid ideation, agitation, coarser hair, hair stops growing but no diffuse hair loss, slowly relaxing reflexes (contraction normal, relaxation slow – not specific to hypothyroidism), plethora (deep red cheeks), hypotension, ↑ADH release →
hyponatraemia, normocytic normochromic anaemia, but no neuropathy (except secondary to, say, carpel tunnel)

- Myxoedema coma: presents in coma with history of above symptoms. Exclude: alcoholism, epilepsy, diabetes mellitus, use of sedative medication, or clear suggestion of a fall predisposing to a subdural haematoma. With myxoedema may find pleural effusion, ascites, myocardial oedema (→ arrhythmias), no focal neuropathies (unless concurrent CVA), possibly hypoglycaemia

- Progression of primary hypothyroidism:
  - Normal TSH is 0.35 – 5.3
  - Prodromal hypothyroidism:
    - TSH 4.0 – 10.
    - fT4 usually still normal. fT3 up marginally (failing gland ↑ proportion of T3)
  - Partial hypothyroidism:
    - Early symptoms
    - TSH > 10 – 15
    - fT3 and fT4 falling, but may still be normal. fT3 falls later than fT4
  - Severe:
    - With time develop myxoedema
    - TSH > 60. fT4 < 6.0

**Diagnosis**

- Screening and severity: fT4 and TSH (TSH RR = 0.4-3.8)
- Primary: TSH rises (is most sensitive test) with minor changes in fT4 (before clinical features)
- Secondary (rare): Test fT4. TSH remains in normal range but is inappropriately low for the fT4 level
- Thyroid antibodies: almost all have positive antibodies at diagnosis (MS + TG)
- Thyroid scan not indicated
- If pituitary disease, screen for other hormone failure/tumours
- Normochromic macrocytic (or normocytic) anaemia

**Causes**

- Spontaneous (autoimmune):
  - Hashimoto’s Thyroiditis: autoimmune disease, lymphocyte and plasma cell infiltration. Goitre. Usually older women. Often euthyroid + goitre. Invasion of polyclonal lymphocytes. Have oncocytes (cells with ↑ mitochondria)
  - Spontaneous primary atrophic hypothyroidism. Autoimmune = Hashimoto’s without the goitre, associated with IDDM, Addison’s and Pernicious anaemia. F:M = 6: 1
  - Woody Thyroiditis (Riedel’s Thyroiditis): fibrous replacement of the thyroid (end stage)
- Iatrogenic:
  - Following thyroidectomy and radio-iodine treatment
  - Drug induced: eg amiodarone (→ hypo or hyper), lithium, iodine or kelp in expectorants
  - Not deep x-ray treatment to face and neck (does lead to nodular goitre)
- Juvenile:
  - Dyshormonogenesis: eg partial deficiency of peroxidase → gland hyperplasia → restore deficiency.
  - Expect: mild ↑ TSH, goitre and mildly hypothyroid
  - Agenesis/sublingual thyroid
  - Di George Syndrome. Absent thymus, hypoplasia of parathyroid glands, lymphopenia
- Secondary:
  - TSH deficiency: isolated, panhypopituitarism, hypothalamic disease
  - 1% of Grave’s go onto hypothyroidism
  - Iodine deficiency
  - High doses of iodine (eg ask about kelp)

**Treatment**

- If TSH between 6.0-8.0 or if symptomatic → therapeutic trial with thyroxine
- Thyroxine: takes 4 – 5 days to have any impact (ie not useful acutely). Review after 12 weeks. Adjust dose to keep TSH < 5 mu/L. T½ = 7 days so adjusting dose takes long time
- Note: hypothyroid → slow drug metabolism
- If pre-existing heart disease, introduce very slowly. Consider propranolol
Intercurrent Illness

- Intercurrent illness = anything = flu, pneumonia, MI

Diagnosis

- fT4:
  - ↑ by up to 20%, maybe out of the RR during the first day or so of intercurrent illness
  - Subsequently falls potentially to subnormal levels which are roughly proportional to the severity of disease
- fT3:
  - Falls rapidly from onset of illness to low levels, roughly proportional to disease severity
  - fT4 converted to rT3 in liver instead of fT3
- TSH:
  - Remains normal initially
  - Falls to mildly subnormal levels with severe illness

Thyroid Nodules

- Are common (occur in 10 – 60% depending on definition) but clinical malignancy is rare (2 – 10/100,000/year)
- Malignancy is unusual
- Almost always has a good prognosis
- Cytology is key

Evaluation:
- Presents with lump in lower neck
- Age: young with nodules more likely to be cancer
- Gender: females have more nodules, male’s nodule more likely to be cancer
- Risk factors: radiation, radioiodine, family history, large solitary nodule bigger risk than many small ones

Clinical

- Can be single or multinodular
- Symptoms:
  - Systemic: ↓ weight and appetite, night sweats
  - Local: pain, stridor
- Signs:
  - Mobile lesions that move vertically with swallowing
  - Can see Pemberton’s sign = hands above head, compresses thyroid against veins and + trachea → face becomes red and can see stridor
  - Clinical signs of malignancy are uncommon: invasion → hoarseness, fixation, LAN; anaplastic → rapid growth, persistent pain
- Check for lymphadenopathy
- Tests:
  - fT4, TSH: usually normal thyroid function
  - Tumour markers: thyroglobulin, calcitonin
  - Imaging: not specific: cold spots – can be cancer but also normal. Hot spots unlikely to be cancer
  - 99Tc scan: defines autonomous hot nodules; functioning nodules are rarely malignant
  - Thyroid US
  - FNA for cytology
    - 95% true positives for papillary + follicular tumours
    - Bethesda system for thyroid FNA reporting = unsatisfactory/benign/follicular lesion of undetermined significance/suspicious for follicular neoplasm/malignant
  - Histology post-operatively for tissue diagnosis
- Management:
  - Refer
  - Lobectomy or subtotal thyroidectomy
  - Remnant ablation with RA I
  - T4 replacement therapy

Benign Types

- Haemorrhage into a thyroid cyst: painful and instantly palpable
- Adenoma:
  - Benign, circumscribed nodule composed of proliferating thyroid follicles;
difficult to distinguish from hyperplastic nodule
- Represents a true benign monoclonal neoplasm
- **Always follicular, encapsulated** (no invasion), universally benign
- Usually cold on scan, may be hot ie **can be autonomous or non-functioning** (T3 secretion may predominate)

**Malignant Types**

- **Papillary thyroid carcinoma:**
  - 80% of thyroid cancers
  - May be thyroglobulin positive on immunohistochemistry
  - F > M; peak age 30-40yrs; is the radiation induced tumour
  - Composed of invasive thyroid follicles
  - Have **papillary** (finger like) architecture (see below) with fibrovascular core
  - Metastasises to **lymph nodes** (50% at diagnosis)
  - May also see calcification ⇒ **Psammoma Bodies** (also found in meningiomas, serous cystadenoma of the ovary)
  - Use FNA to dx
  - **Features:** nuclei overlap, papillary structures with fibrovascular core, psammoma
  - **Prognosis:** If extra-thyroid lesions then 62% survival @ 15 years

- **Follicular carcinoma:**
  - Rarely multifocal, **capsular invasion, metastasises via blood vessels**. If gross invasion then 50% survival at 6 years. Hard to differentiate from adenoma on FNA
  - Cannot diagnose with cytology ⇒ need to see capsule to dx invasion therefore bx (as hard to differentiate from adenoma)
  - **More aggressive** than papillary
  - For gross pictures, see webpath here; for micro, see here

- **Anaplastic** (undifferentiated carcinoma): **highly malignant**, old age, poor prognosis

- **Medullary/C Cell carcinoma:**
  - From parafollicular cells (↑serum calcitonin)
  - Usually part of Multiple Endocrine Neoplasia Syndrome (MEN) 2
  - See amyloidosis
  - Also lymphoma and mets
  - **Treatment:** near total thyroidectomy. If staging indicates high risk then radioiodine for remnant ablation

**Other**

- **Multinodular goitre:**
  - With time, all thyroids have:
    - Anatomical heterogeneity: cold/fibrosed regions, hyperplasia, calcification, etc
    - Functional heterogeneity: various degrees of autonomy
  - If pronounced, then multinodular goitre:
    - Can be substantially enlarged with cystic/nodular appearance
    - Growth may ⇒ haemorrhage ⇒ tender
    - Treatment: Cut it out or thyroxine (slows it down)

- In addition to a tumour, a single nodule may be:
  - A hyperplastic nodule (ie physiological)
  - Multinodular goitre with a prominent nodule
  - Thyroglossal duct cysts (see Neck Lumps, page 987)

**Parathyroid**

- See Calcium section
- Calcium metabolism:

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Hyperparathyroidism:
- **Primary**: ↑PTH → ↑Ca2+
  - Ca ↑ but generally < 3.0, PO low normal or low, PTH ↑ or high normal
  - Usually detected as incidental finding. If symptoms: pain/fracture, renal stones, constipation, abdominal pain, depression. Also maybe dehydration, ↑BP, thirst, nocturia, stuff joints, myopathy
  - Associations: endocrine neoplasia (e.g., pancreas, pituitary, phaeochromocytoma, and thyroid)
  - Causes: single (90%) or multiple adenoma, carcinoma, hyperplasia
  - Tests: ↑Ca, ↓PO4 (unless renal failure), ↑ALP, PTH raised or normal. XR for ‘pepper pot skull’ and pelvis
  - Treatment: surgery
- **Secondary** Hyperparathyroidism: ↓Ca → ↑PTH. Causes: ↓Vitamin D and chronic renal failure (see 315 – complications of chronic renal failure)
- **Tertiary** Hyperparathyroidism: continued secretion of PTH after prolonged secondary hyperPTH
- **PTH related protein (PTHrP)**: produced by some tumours – causes some of the hypercalcaemia seen in malignancy

Hypoparathyroidism:
- **Primary** HypoPTH. E.g. after neck surgery. ↓Ca and ↑PO4, normal ALP.
  - Associations with pernicious anaemia, Addison’s, hypothyroidism, hypogonadism
- **PseudohypoPTH**: Failure of target cell response to PTH. Round face, short metacarpals and metatarsals

Adrenal Cortex

Adrenal Physiology

Endocrine and Electrolytes
- Produces:
  - Mineralocorticoids: e.g., aldosterone (from zona glomerulosa)
  - Glucocorticoids: e.g., Cortisol - affects CHO, protein and lipid metabolism (from zona fasciculata)
  - Androgens and oestrogens (from zona reticularis)
  - Catecholamines (from medulla)

- Cortisol:
  - Corticotrophin releasing factor (CRF from the hypothalamus) → ACTH (from pituitary) → Cortisol
  - Postulated that Cortisol inhibits a general or uncontrolled inflammatory response to tissue damage following insult. Raised in trauma, infection, severe psychiatric disease
  - ACTH production is inhibited potently by Betamethasone and Dexamethasone, Prednisone has intermediate potency and hydrocortisone (i.e., cortisol) has the lowest potency of these agents
  - Cortisol is excreted as urinary free cortisol
  - Morning level (2 am – 8 am) is twice evening. Severe stress can override diurnal pattern

- Summary of best tests:

<table>
<thead>
<tr>
<th>↑Cortisol</th>
<th>↓Cortisol</th>
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<tbody>
<tr>
<td>24 hour urine</td>
<td>↓Renin</td>
</tr>
<tr>
<td>Low dose dexamethasone</td>
<td>Short Synacthen test</td>
</tr>
</tbody>
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Adrenal Pathology
- Neoplasms = metastatic tumour/adenoma/phaechromocytoma/neuroblastoma
- Non-neoplastic lesions = TB
- Investigations = CT guided FNA → referred to cytopathology

Cushing’s Syndrome
- Chronic glucocorticoid excess, either exogenous or endogenous (adrenal or pituitary neoplasm, or ectopic ACTH secretion)

- Signs:
  - Tissue wasting, myopathy, thin skin, purple abdominal striae, easy bruising
  - Osteoporosis
  - Water retention
  - Supraclavicular fat-pad ("buffalo hump")
  - Predisposition to infection, bad wound healing
  - Hirsutism, amenorrhoea, hyperglycaemia (30%)

Assessment of Glucocorticoid Excess
- Need to diagnose presence of GC excess first then tests to define the cause
- Screening tests:
  - 24h urinary free cortisol (normal < 280 nmol/24 hr). If positive then high dose dexamethasone suppression test.
  - Alternative is overnight low dose dexamethasone suppression test: give 1 mg po at midnight, check cortisol at 8 am (normal 450 – 700 nmol/L). False positives with depression, obesity and drugs affecting metabolism of dexamethasone (e.g., phenytoin, phenobarbitone)
  - Midnight cortisol nearly as good: but must do as an inpatient (need to wake to do it and be unstressed) – midnight is low point of diurnal cycle, if high then diurnal cycle depressed

Assessment of Cause of CS
- Adrenal disease:
  - ACTH suppressed (low/low normal)
  - CT scan: adrenal tumour seen
- ACTH dependent:
  - ACTH is high normal or ↑
- Pituitary tumour:
  - MRI scan: as sensitive as petrosal sinus sampling (CT is frequently negative)
  - Bilateral petrosal catheterisation: ACTH + cortisol sampling after CRF injection; distinguishes responsive pituitary ACTH, giving CD, pituitary ACTH or suppressed pituitary function, from ectopic ACTH, and can lateralise the tumour in the pituitary
  - Dexamethasone suppression: demonstrates cortisol FB control of tumour with mild suppression on 2 mg + clear suppression on 8 mg
- Ectopic ACTH source:
- CT relevant areas (lung, pancreas, mediastinum, thyroid)
- Bilateral petrosal catheterisation
- Venous catheterisation for ACTH of suggestive areas on CT
- Dexamethasone suppression (does not suppress)
- Miscellaneous other tests: electrolytes, GTT (for DM), bone density

**Treatment**
- Exogenous corticosteroid administration: reduce as much as possible. In asthma, use inhaled steroids
- Cushing’s Disease: (adrenal hyperplasia secondary to pituitary tumour, F > M, peak age 30 – 50). **Some, but not normal, suppression** of cortisol with high dose dexamethasone. Treatment: surgical removal of pituitary adenoma
- Adrenal gland adenoma or carcinoma: **no suppression** of cortisol with high dose. **Undetectable ACTH.** Treatment: surgical removal
- Ectopic ACTH production: especially small cell carcinoma of the lung and carcinoid. **No suppression of cortisol** with high dose dexamethasone. **Plasma ACTH generally >250 ng/L. Hypokalaemic alkalosis is common**
- Can block adrenal cortisol production with ketoconazole

**Hypoadrenalism**

**Primary: Addison’s Disease**
- **Primary adrenal failure:** Failure of glucocorticoids – both have similar hypotensive and electrolyte effects (different mechanisms but additive)
- **Pure glucocorticoid (eg cortisol) deficiency gives:**
  - Hypotension (postural and resting BP) due to:
    - Depletion of plasma renin substrate (angiotensinogen): cortisol is permissive to PRS production and lowers angiotensin levels and hence vascular tone
    - Reduced cardiac contractility and stroke volume due to sodium shift from ECF to ICF (with tendency to hyperkalaemia reciprocal to the Na cell influx)
    - These lead to secondary effects including ↓renal plasma flow, reduced GFR and mild elevation in urea
  - Hyponatraemia results from:
    - Mineralocorticoid effects of cortisol
    - Shift of Na+ from ECF into cells – K shifts out
    - Very high ADH (vasopressin) levels
    - Reduced renal free water clearance (in part from ADH excess and from the reduced GFR)
- **Pure mineralocorticoid (ie aldosterone) deficiency gives:**
  - Reduced Na uptake exchanging for K+ and H+ in renal distal tubule and in other epithelial surfaces (gut, sweat) → hyponatraemia +/- hyperkalemia
  - Secondary effects: hypotension, reduced GFR, clearly raised urea, raised K+
- **Acute presentation:**
  - ↑K, ↓Na, ↑Cr
  - Think of adrenal insufficiency in all cases of hyperkalemia or hyponatremia, uncommon however
  - Cr is raised from pre-renal failure
- With suspected Addison’s, need to check for features of:
  - Mineralocorticoid deficit (few, but relate to salt depletion)
  - ACTH excess (MSH: hyperpigmentation;NFB leads to ↑ACTH which is split from POMC, a precursor for both ACTH + MSH)
  - A pituitary lesion (space occupying effects)
  - Hypopituitarism (gonadal, thyroid, prolactin or GH deficiency, PRL excess, ADH/vasopressin)
  - History of glucocorticoid medication
- **Symptoms:** very non-specific, weakness, abdominal pain, depression, ‘viral illness’, anorexia, D&V, nausea, *pigmentation in palmar creases and buccal mucosa* (takes ↑↑ACTH/MSH), arthralgia, myalgia, weight loss, nocturia, confusion, irritability, constipation, dehydration, dizziness (eg due to Na depletion → *postural hypotension*), hypoglycaemia (reduced gluconeogenesis; lack of cortisol will obscure adrenergic effects of hypoglycaemia), ↓libido, vitiligo (autoimmune mediated depigmentation of patches of skin). Not constipation or dehydration in pure cortisol deficiency
- **Addisonian Crisis:** tachycardia, fever, shock, coma
- **Diagnostic tests:**
  - Plasma renin (most sensitive indicator of mineralocorticoid insufficiency)
Short ACTH stimulation test (Synacthen)
- Better than 24 hr urine Cortisol (midnight cortisol test is equivalent to 24 hour urine).
- Usually test at 0 and 30 minutes
- Use long Synacthen test (0, 4, 6 hours) only when in doubt
- If Cortisol doesn’t rise then do prolonged ACTH stimulation test over 3 days (eg to differentiate between Addison’s and prednisone suppression).
- Basal (8 – 9 am) plasma ACTH will determine gland or origin (if high then primary, if low then secondary)
- Basal (8 – 9 am) plasma Cortisol little help due to wide normal range
- Test for adrenal antibodies and check for signs of Tb (eg calcification on Xray)
- Also test electrolytes, hypoglycaemia, uraemia, mild acidosis, hypercalcemia (?)from pre-renal failure), normocytic anaemia, abnormal LFTs, ↑eosinophilia, ↓neutropenia
- Causes:
  - 80% idiopathic (autoimmune). Associated with Graves, Hashimoto’s, T1DM, pernicious anaemia
  - Tb, metastases (insufficiency only after 90% of both adrenals destroyed)

Secondary Hypoadrenalism: Pituitary Failure
- Recent onset: no diagnostic test for adrenal insufficiency; can use IV insulin tolerance test for ACTH + cortisol response to hypoglycaemia (check cortisol prior to doing test)
- Tests for longstanding (ie > 6 – 8 years)
  - Short Synacthen test: measures adrenal atrophy
  - Insulin tolerance test: check for ACTH and cortisol release. Little data to judge normal range → not often used clinically

Adrenal Atrophy
- From glucocorticoid therapy
- Occasionally short Synacthen test shows a delayed response
- Long Synacthen less convenient but more reliable

Steroid Medication
- Replacement doses for Cortisol:
  - Hydrocortisone = 15 mg per day, have to take 3 times a day due to short T½, and to avoid plasma peaks (→ side effects, eg osteoporosis)
  - Prednisone: 7 mg per day. Longer T½
  - Adjust by measuring cortisol (ie 24 hour urine cortisol). Replacement therapy does not usually suppress elevated ACTH
  - No abrupt changes in dose, increase in intercurrent illness. If vomiting then iv dose
  - Use Fludrocortisone for aldosterone replacement
- Withdrawal:
  - Withdrawal of long term prednisone needs to be done slowly (ie monthly reductions) due to atrophy
  - Signs of GC deficiency imply withdrawal is too fast

Assessment for Replacement Hydrocortisone Dose
- Hydrocortisone is the usual replacement therapy
- Clinical assessment should involve photos to follow appearance changes (of Cushing’s)
- Bone density needs to be checked especially if amenorrhoea or post-menopausal
- Can use plasma “day curve” to check the replacement dose (cortisol levels at 2 and 4hrs post a dose)
- Can measure urine free cortisol, also screen blood sugar, BP occasionally

Congenital Adrenal Hyperplasia
- Autosomal recessive
- Gene defect coding for enzymes involved in synthesis of cortisol +/-aldosterone
- 21 hydroxylase commonly
- Leads to ↓cortisol/aldosterone → ↑CRH + ACTH → ↑androgen production
- Presentation in females:
  - Ambiguous genitalia at birth due to excess adrenal androgen production in utero
  - Mild forms of 21-hydroxylase deficiency are identified later in childhood because of precocious pubic hair, clitoromegaly, or both, often accompanied by accelerated growth and skeletal maturation due to excess postnatal exposure to adrenal androgens
Milder deficiencies of 21-hydroxylase (or other enzymes) activity may present in adolescence or adulthood with oligomenorrhea, hirsutism, and/or infertility.

Presentation in males:
- Generally not identified in the neonatal period because the genitalia are normal
- If defect is severe and results in salt wasting, neonates present at age 1-4 weeks with failure to thrive, recurrent vomiting, dehydration, hypotension, hyponatremia, hyperkalemia, and shock (classic salt-wasting adrenal hyperplasia)
- Less severe deficiencies of 21-hydroxylase present later in childhood because of the early development of pubic hair, phallic enlargement, or both, accompanied by accelerated linear growth and advancement of skeletal maturation

**Hyperaldosteronism**
- Excess of aldosterone independent of renin-angiotensin system
- Signs: hypertension, hypokalaemia, alkalosis, Na is normal or slightly raised
- Causes: >50% due to unilateral adrenocortical adenoma (Conn’s Syndrome). Other causes include hyperplasia, carcinoma, genetic defect
- Tests: test K 3 times on salt replete diet (no diuretics, etc for 4 weeks). If < 3.7 mmol, test for aldosterone or renin. Exclude renal artery stenosis (↑BP and ↓K+), high renin (eg secondary to hepatic failure)
- Treatment: surgery and/or spironolactone

**Phaeochromocytoma**
- = Benign (usually) unilateral tumour in adrenal medulla producing catecholamines
- Signs: episodic hypertension, restlessness, anxiety, sweating, weight loss, tremor, cold feet, palpitations
- Test: HMMA (breakdown products) in urine
- Treatment: surgery – careful management of BP before and after surgery

**Pituitary Gland**

- **Anterior pituitary** releases: ACTH, GH, FSH, LH, TSH, PRL
- **Posterior pituitary** releases: ADH, Oxytocin (made in the hypothalamus)
- Under dominant tonic control (stalk failure → hormone failure): LH, FSH, GH, TSH, ACTH
- Under dominant inhibitory control (via DA; stalk failure → ↑ levels): PRL
- Vasopressin (ADH): produced in hypothalamus, released in pituitary. Stalk failure → polyuria for a few weeks until ↑release in median eminence

**Imaging the Pituitary**
- Pituitary fossa is in the superior sphenoid bone, covered superiorly by the diaphragm sellae, with a central aperture for the infundibulum. The suprasellar cistern includes the infundibulum and the optic chiasm
- Pituitary is usually 6 mm in kids, 8 mm in men and postmenopausal women, 10 mm in women of child bearing age, 12 mm in pregnancy and postpartum. Gradual involution beyond 50 years old
- ‘Pituitary bright spot’: posterior pituitary is normally hyperdense. Lost in diabetes insipidus
Normal pituitary fossa has a flat top, or concave (dips down)
Microadenomas: < 10 mm, don’t normally take up contrast. Are usually hormone secreting (that’s why they’re found)
Macroadenomas: > 10 mm, most are not hormone secreting, found because of space occupying effect
Sellae and suprasellar lesions:
- An empty sellae is due to herniation of the suprasellar cistern into the sellae → flattening of gland (with or without disturbance). Also secondary to hypophysectomy, post-radiation or infarction
- Cranioopharyngiomas:
  - Relationship with EBV
  - Suprasellar tumours that may extend into the sellae
  - Calcification often present on x-ray
  - Kids and young adults
  - Cause pituitary insufficiency, visual impairment, hydrocephalus, hypothalamic disturbance
- Meningiomas: MRI shows close meningeal attachment and enhancement post-contrast
- Optic nerve gliomas: in kids. Extend along optic nerve

**Hypopituitarism**
- Causes: hypophysectomy, pituitary irradiation, adenoma (either functional or non-functional), other intracranial tumours, Sheehan’s Syndrome (pituitary necrosis after post-partum haemorrhage), TB
- Check symptoms of:
  - Gonadal and GH (→ bone strength): early to fail
  - Thyroid: intermediate to fail
  - Adrenal: last to go
  - Also look for PRL (need a little for LH peak to happen), vasopressin, space occupying lesions (test visual fields and for Oculomotor palsy)
  - ADH/Oxytocin only fail completely if hypothalamic tumour or major suprasellar extension
- Symptoms: insidious onset, afternoon tiredness, pallor, anorexia, ↓libido (can be due to many illnesses to and ↑PRL), impotence, amenorrhoea, no menarche by 16, headache, depression, hypothyroidism, reduced body hair in males (due to hypogonadism – is also normal in older age – but not front baldness – that’s due to androgens), intolerance of intercurrent illness and postural hypotension (hypocortisolism), mild fluid retention (myxoedema and ↓cortisol → water retention), mild anaemia, pallor (yellow of myxoedema, and anaemia), also marked behavioural changes
- Signs: breast atrophy, small testes, ↓muscle to fat ratio, ↓hair, thin flaky wrinkled skin, postural hypotension, visual field defect
- Differentials: depression, dementia, subdural bleed (although more acute), slowly progressive tumour
- The age of presentation makes a difference:
  - Prepubertal failure slows growth, delays puberty
  - Post-pubertal failure reduces gonadal activity
  - Post-menopausal women: high FSH and LH would be normal. If FSH within normal range then → very sensitive test of early pituitary failure (menopausal should normally be high)
  - Cranioopharyngiomas are the commonest cause of pituitary failure in children, but can be found at any age
- Types of lesion:
  - Mostly hypopituitarism comes from non-functioning pituitary adenomas (adenomata)
  - But also cranioopharyngioma, GH or prolactin secreting tumours
  - Most other causes are rare: pituitary apoplexy (a pituitary haemorrhage, mostly into a pre-existing tumour) and pituitary infarction (occasionally during delivery)
- Sites of tumour extension from the fossa:
  - Suprasellar affects optic nerve
  - Parasellar affects III, IV and VI nerves
  - Infraellar shows xray changes

**Tests**
- Assessing anatomical complications:
  - CT/MRI
  - Visual fields
  - CN III, IV, VI + V sensation
- Assessment for cause:
  - Radiology for tumour
  - Assessment for hypothalamic cause (visual field – inferior field defect, assess for diabetes insipidus)
• ? hypothermia: basal hypothermia will only come with hypothalamic damage

- **Hormone tests:**
  - Basal T4, TSH and PRL, U&E (hyponatraemia), FBC (normochromic normocytic anaemia)
  - Triple stimulation test (unless heart disease or epilepsy): As inpatient with iv access, inject **insulin, TRH and GnRH**. Look for ↑GH, ↑Cortisol (due to ↑ACTH), ↑TSH, ↑PRL (due to ↑TRH)
  - LH and FSH insufficient on their own without checking testosterone as well (may be ↓due to ↑testosterone). Also LH & FSH tests are not sensitive enough to distinguish low from low-normal
  - Cortisol too variable to be a useful check of pituitary
  - Very high PRL indicates a prolactinoma, which can cause pan-hypopituitarism
  - An overnight Metyrapone test - give Metyrapone orally at midnight and measure plasma cortisol and its biosynthetic precursor at 8.30am. *Metyrapone blocks the synthesis of cortisol* leading to a build-up of 11-deoxycortisol and reduced negative cortisol feedback → a raised ACTH. Cortisol, ACTH and 11-deoxycortisol all remain low in hypopituitarism or long-standing suppression of the HP adrenal axis by drugs

- **Assessing severity:**
  - **Gonadal:**
    - Males – testosterone, LH and FSH
    - Females: menstrual history, LH and FSH
  - **Thyroid:** fT4 and TSH
  - **Adrenal:** Short Synacthen test (false negatives possible) or urine free cortisol (not sensitive)
  - **Growth Hormone:**
    - Simple sample (after 10 am) or IGF1
    - GH stimulation tests: insulin
  - **Vasopressin:** overnight urine concentration (osmolality)

**Treatment**
- Hydrocortisone and thyroxine
- Maybe GH
- Testosterone in men
- *Oestrogen* for pre-menopausal women

**Pituitary Tumours**
- Symptoms caused by local pressure, hormone secretion or hypopituitarism
- *Almost always* benign adenomas

- **Classification:**
  - **Macroadenoma:** >1cm; visual symptoms (bitemporal hemianopia), can be non-functioning + present only with visual symptoms
  - **Microadenoma:** <1cm; **endocrine symptoms** (eg PRL → amenorrhoea/galactorrhoea; GH → acromegaly; ACTH → Cushing’s etc)

- **Histological classification:**
  - Chromophobe (70%): half produce PRL, some non-secretory, a few produce ACTH or GH
  - Acidophil (15%): Secrete GH or PRL
  - Basophil (15%): secrete ACTH

- Effects of pressure: **headache** (felt anywhere over head, local or general), **bitemporal hemianopia** (initially of superior quadrants), III, IV or VI **palsy**, CSF rhinorrhoea (erosion through floor of sellae)
- Tests: as for hypopituitarism → CT/MRI. Water deprivation test if diabetes insipidus is suspected. Important to get anatomical pathology post-operative tissue diagnosis
- Treatment: surgery (trans-sphenoidal or transfrontal). Hormone replacement. Bromocriptine (DA-agonist) for PRL secreting tumours. Radiotherapy (but side-effects common)

**Prolactinoma**
- 30% of functioning adenoma
- Can lead to amenorrhoea, galactorrhoea, infertility
- May undergo dystrophic calcification → “pituitary stone”
- DA normally inhibits PRL + therefore dopaminergic drugs (*Bromocriptine*) can be used to treat

- **Immunoperoxidase** stain showing prolactinoma
Growth Hormone Secreting Adenoma

- ↑ GH stimulates the liver to produce IGF1 which causes many of the clinical manifestations
- Acromegaly:
  - ↑ size of facial bones, prognathism (protruding jaw)
  - ↑ size of hands + feet
  - Insulin resistance
- Somatostatin (from hypothalamus) normally inhibits GH + therefore can treat with somatostatin analogue or GH receptor antagonist
- Will show characteristic GH immunoperoxidase pattern + monotonous cell proliferation on H & E stain

ACTH Secreting Adenoma

- → Cushing’s disease
- ACTH stimulates the adrenals → hypercortisolism (Cushing’s syndrome):
  - Central obesity
  - Thin skin
  - Insulin resistance etc
- ACTH precursor molecule (POMC) stimulate MSH → melanocytes → skin pigmentation
- Removal of the adrenals in Cushing’s disease can cause a large destructive pituitary adenoma (Nelson syndrome)

Prolactinaemia

- Physiology:
  - PRL has both a pulsatile and diurnal pattern: rises dramatically during sleep
  - Dopamine inhibits prolactin
  - PRL is raised by:
    - Oestrogen → slightly ↑PRL (ie women higher than men)
    - TRH → slightly ↑PRL (used in pituitary stimulation test)
    - T5 dermatome stimulation → ↑PRL (but breastfeeding won’t increase the size of a prolactinoma)
    - PRL rises through pregnancy
    - Drugs: most major tranquillisers (ie antipsychotics), Metoclopramide (Maxolon) therapy for nausea blocks dopamine → ↑PRL. Aldomet (alpha-methylDOPA) is the only hypotensive agent which increases prolactin (via dopamine depletion)
    - Can rise due to emotional or physical stress (including stressful venipuncture → artefact)
    - High in chronic renal failure
    - Hypothyroidism → ↑TRH →↑PRL
    - Sarcoidosis
    - Post-pill amenorrhoea (if due to other causes usually resolves < 1 year)
  - PRL level is not effected by progesterone or nausea
- Most common pituitary presentation. Presents early in women (amenorrhoea), late in men
- Symptoms:
  - Women: ↓libido, weight gain, apathy, vaginal dryness (due to hypooestrogen), amenorrhoea (very sensitive to ↑PRL, infertility due to ↑PRL →↓LH peak, ↑PRL suppresses progesterone), galactorrhoea (will need to differentiate from breast inflammatory exudate – clear or green). If infertility, always check the man (cause of 1/3 of problems of infertility)
  - Men: impotence, ↓libido, reduced facial hair, local pressure effects, galactorrhoea (30%), mildly ↓testosterone (but asymptomatic). Not gynaecomastia (usually only in ↓testosterone or ↑oestrogen)
- Investigations:
  - Basal prolactin between 10.00 – 12.00 h (repeat 2 – 3 times); lab will screen for macroprolactinaemia
  - CT, MRI for anatomic complications
  - Assess pituitary function
- Management:
  - If tumour < 10 mm (unlikely to be seen on Xray): bromocriptine to restore fertility avoids complications of ↓oestrogen due to ↑PRL (could take pill instead). May → postural hypotension. Commence slowly otherwise nausea. Good prognosis. No known teratogenic effects of bromocriptine – but still withdrawn on becoming pregnant if possible
  - Treat macroadenoma with surgery if bromocriptine fails to reduce size of PRL. But if pressure effects or pregnancy is contemplated then surgery. Monitor PRL
  - Prolactin deficiency causes failure of lactation but has no other know ill effects. Deficiency is very rare
Acromegaly

- Usually presents between 30 – 50 years. Rare (3/million/year)
- Symptoms: insidious onset (look at old photos), coarse oily skin, large tongue, bossing of supraorbital ridge, ↑shoe size and teeth spacing, spade-like hands, carpel tunnel syndrome, progressive heart failure, goitre
- Symptoms due to: periosteal growth (gigantism if the condition starts before closure of the bony epiphyses), fibrous tissue growth (→ skin thickening), organomegaly (eg cardiomegaly, hepatomegaly, splenomegaly, testicular enlargement), cartilaginous growth (↑ears, nose, costochondral junctions), neurological overgrowth (→ peripheral neuropathy, exacerbated by soft tissue swelling)
- Complications:
  - DM
  - HTN
  - Cardiomyopathy
  - ↑lipids
  - Hypopituitarism
- Tests:
  - ↑IGF-1 (insulin like growth factor) indicates GH secretion over the previous 24 hrs
  - GH day curve (highly variable – normally undetectable, spikes 10 times a day, mainly during deep sleep)
  - Oral glucose tolerance test. If GH doesn’t fall then acromegaly, anorexia nervosa, poorly controlled DM, or Cushing’s
  - Assess prolactin secretion (10-20% of acromegalic tumours co-secrete PRL)
  - Tests as for pituitary tumour
- Treatment: trans-sphenoidal surgery if young. External irradiation for elderly. Somatostatin (Octreotide) if patient is not fit for surgery
- GH deficiency in children → growth retardation. One high GH level excludes deficiency. Take after sleep or exercise

Other Endocrine Problems

- Hirsutism: male pattern of hair in a female. Common (10%). If normal menstruation then no increased testosterone production ⇒ benign. If abnormal menstruation then polycystic ovary syndrome with androgen hypersecretion or late onset congenital adrenal hyperplasia with deficiency of 21-hydroxylase enzyme
- Virilism: male secondary sex characteristics in a woman. Rare. Amenorrhea, deep voice, temporal hair recession, hirsutism. Refer for androgen secreting adrenal and ovarian tumours
- Galactorrhoea: may come with thyroid failure (primary or secondary), with a raised prolactin (prolactinoma, pituitary stalk section and especially drugs) and occasionally with acromegaly
- Gynaecomastia: abnormal amount of breast tissue in males. May occur in normal puberty. Due to an ↑in the oestrogen : androgen ratio. May result from liver disease (↓metabolism of oestrogen) or testicular tumours (↑oestrogens) or with hyperthyroidism. Commonest causes are drugs: eg spironolactone, cimitidine, digoxin
- Hypogonadism: due to hypopituitarism, post-orchitis (eg from mumps), chemotherapy, irradiation, cirhosis, alcohol (toxic to Leydig cells), various syndromes
- Impotence: common in old age. Psychological causes are common (eg if clear stressor, or if morning erections still occur). Major causes: diabetes, drugs (diuretics, β-blockers, major tranquillisers, alcohol, antidepressants, cimetidine), hyperthyroidism, hypogonadism, ↑PRL, cirhosis, cancer

Multiple Endocrine Neoplasia Type 1

- Mutation in chromosome 11
- 1/40,000
- Variable expression (not everyone will have same tumours or all the tumours)
- See (HEP C):
  - Hyperparathyroidism
  - Enteropancreatic endocrine tumours (often multicentric + include gastrinoma + insulinoma)
  - Pituitary adenomas (often prolactinomas)
  - Others eg Carcinoid, benign skin tumours, adrenal adenomas

Multiple Endocrine Neoplasia Type 2

- 1/50,000
- Mutation in RET proto-oncogene

Endocrine and Electrolytes
- See (PM PM):
  - Parathyroid hyperplasia → hypercalcaemia
  - Medullary thyroid cancer
  - Adrenal Phaeochromocytoma (often bilateral)
  - Marfanoid features + mucosal neuroma (type 2B; see right: tongue neuromas)

Electrolytes

- See also ECG Abnormalities Due to Electrolyte Disturbances, page 38
- Arrest due to electrolyte abnormalities is uncommon except for hyperkalaemia
- See Emergency use of Electrolytes

### Osmolality

<table>
<thead>
<tr>
<th>Conditions that increase osmolality</th>
<th>Conditions that decrease osmolality</th>
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<tbody>
<tr>
<td><strong>Serum</strong></td>
<td><strong>Urine</strong></td>
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<tr>
<td>Dehydration/sepsis/fever/sweating/burns</td>
<td>Dehydration</td>
</tr>
<tr>
<td>Diabetes mellitus (hyperglycemia)</td>
<td>Syndrome Inappropriate ADH secretion (SIADH)</td>
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<tr>
<td>Diabetes insipidus</td>
<td>Adrenal insufficiency</td>
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<tr>
<td>Uremia</td>
<td>Glycosuria</td>
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<tr>
<td>Hypernatremia</td>
<td>Hypernatremia</td>
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<tr>
<td>Ethanol, methanol, or ethylene glycol ingestion</td>
<td>High protein diet</td>
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<tr>
<td>Mannitol therapy</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Serum</strong></th>
<th><strong>Urine</strong></th>
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<tbody>
<tr>
<td>Excess hydration</td>
<td>Diabetes insipidus</td>
</tr>
<tr>
<td>Hyponatremia</td>
<td>Excess fluid intake</td>
</tr>
<tr>
<td>Syndrome Inappropriate ADH secretion (SIADH)</td>
<td>Acute renal insufficiency</td>
</tr>
<tr>
<td></td>
<td>Glomerulonephritis</td>
</tr>
</tbody>
</table>
Disorders of Osmolality

- Serum osmolality approximates \(2 \times \text{Na} + \text{glucose} + \text{urea}\) (USE THIS CALCULATION IN Na PROBLEMS)
- Thus high sodium always represents high osmolality
- Low Na usually represents low osmolality except for pseudohyponatremia, hyperglycaemia, high urea or in the presence of an exogenous osmotically active substance eg alcohol
- While hypo or hypernatraemia can be caused by alterations in sodium balance, in the clinical setting they are almost always due to water balance and the adjustments secondary to these. The use of diuretics causing Na loss is an important exception

Sodium and Water Physiology

- 60% of body weight is water; 2/3 intracellular, 1/3 extracellular
- Osmolality = in both compartments
- Na is restricted to the ECF, maintaining the ECF volume + determining ICF volume
- Water excess or deficit → plasma osmolality changes and ANP and ADH control
- Na excess or deficit → volume changes and RAAS control
- Hypernatremia = hyperosmolality + signals ICF volume contraction
- Hyponatremia = hypoosmolality + signals ICF volume expansion
- Obligatory water loss ~ 800ml/d
- Water intake ensured by CNS thirst centre
- ADH limits water excretion – released by post pit in response to ↑ tonicity or ↓ circulating volume

Sodium Summary

- Low sodium:
  - Dilution: appropriate or inappropriate (SIADH)
  - Loss: sweat, GI, renal
- High sodium:
  - Retention: central or renal
  - Water loss

Hyponatraemia

Key Points

- Normal value of Na: 135 – 145 mmol/L
- Hyponatraemia is not a diagnosis – it is found in diverse conditions. Body Na may be low, normal or high. Relative water retention is a common factor
- Condition and treatment can be hazardous. If correct too fast then → pontine demyelination
- Treatment must be slow and monitored closely
- Treatment can range from water restriction or diuresis to sodium restriction or normal saline. Need to know underlying cause
- Don’t use hypotonic fluids post-op unless Na is high. Eg dextrose saline – glucose absorbed very quickly post surgery → hypotonic
- Appropriate renal response to Na loss is excretion of urine low in Na + Cl (ie reabsorb more)
- Appropriate renal response to H2O excess is excretion of dilute urine (~20-80osm/L) – if urine is less dilute, then indicates presence of active ADH

Symptoms

- The big baddy is underlying cerebral oedema (water from ECF → ICF). Bigger problem if abrupt onset. Rapid correction can cause central pontine melanosis
- Symptoms don’t correlate well with [Na]
- Early: anorexia, headache, nausea, vomiting, muscle cramps, weakness
- Advanced: mutism, dysarthria, impaired response to verbal or painful stimuli, bizarre behaviour, hallucinations, asterixis, incontinence, respiratory insufficiency, spas tic quadriaparesis in 90%
- Late: (too late to do much) decorticate or decerebrate posturing, bradycardia, hypo or hypertension, dilated pupils, seizures, respiratory arrest, coma, polyuria (central diabetes insipidus)
- Should always be a differential in post-operative coma
Aetiology

- Either **Na depletion or water gain** (usually water gain)
- Body Na may be high, low or normal
- Inappropriate water retention: eg **drugs** (most common – eg antiepileptics), ↑**ADH**, kidney or thyroid problems
- May be borderline hyponatraemic before (eg long term use of diuretics)
- Normally, ADH will ↑ if ↑osmolality or ↓blood volume
- **Operative stress or serious illness → syndrome of inappropriate ADH** (in most people) → water retention (especially in women, smaller starting fluid volume). NB it’s not really inappropriate – the body is making a justifiable physiological response: I’m stressed so conserve water rather than throwing it out.
- Ageing impairs fluid homeostasis → wider swings happen easily
- **Common causes: diuretics, IV infusion of the effectively hypotonic dextrose saline**, oedematous conditions, hypovolaemia, RF, severe hyperglycaemia + SIADH

Assessment

- **History: fluid losses, diuretics**, other medications
- Clinical findings: pulse, blood pressure, volume assessment, oedema, thirst, skin, input/output
- Laboratory:
  - Creatinine, urea, glucose, HCO₃, K, plasma osmolarity, urine Na and osmolarity
  - Severe hyponatraemia is < 125 mmol/l: nausea, malaise, headache
  - < 115 mmol/l: convulsions
- Look for:
  - Low Na and ↓serum osmolality
  - Urine osmolality higher than expected (>200 and usually > serum osmolality)
  - Urinary sodium higher than expected (> 30)
  - Normal pituitary, adrenal, cardiac, and renal function
- Clinically useful grouping (⇒ volume assessment critical):
  - **Hyponatraemia with oedema**: heart failure + diuretic, cirrhosis, nephrosis (impairment of water loss via increased ADH +/- Na loss)
  - Hyponatraemia with dehydration:
    - Urine [Na] > 20 mmol/l: Diuretics, Addison’s Disease, Salt losing nephritis
    - Urine [Na] < 20 mmol/l: Vomiting, Diarrhoea, Skin loss
    - Usually rehydrate slowly with normal saline
  - Hyponatraemia with euvolaemia and reduced plasma osmolality:
    - Urine [Na] > 20 mmol/l: **Chronic water overload** (eg primary polydypsia, chronic SIADH – central or malignancy, etc)
    - Urine [Na] < 20 mmol/l: **Acute water overload** (eg acute SIADH, oxytocin for induced labour, etc)
    - Treat with fluid restriction < 1000 ml/day, and treat underlying cause
- Complicating factors:
  - If plasma osmolarity is high then measure glucose. *Hyperglycaemia → shift of water out of muscle cells (ICF → ECF)*: Na ↓1 mmol/L for every 4 mmol/L ↑ in glucose
  - If osmolarity is normal then pseudo-hyponatraemia (eg hyperlipidaemia, hyperproteinaemia). An artefact: Na has been incorrectly measured in plasma volume rather than plasma water

**Urine Osmolality and Sodium**
- Range = ~ 50mosm/kg – 900mosm/kg
- Na is not normally the main contributor to urinary osmolality (UOs) + is virtually absent when urine is very concentrated
- DDx of hyponatraemia with UOs over 100 = fluid losses with hypovolemia, ↓ effective circulating volume, SIADH, renal insufficiency, diuretic therapy and rarely adrenal insufficiency or hypothyroidism
- **Urinary Na falls to < 20mmol/L even in early hypovolemia** and often will be < 10. This is because of secondary hyperaldosteronism related to fluid loss in eg vomiting or ↓ effective circulating volume in CHF
- Urinary Na is higher in chronic water overload, >20mmol/L and often over 40. UOs will often be moderately high, as in SIADH
- In acute water overload, both urinary Na and UOs will be low

**Approach to Diagnosis**
- Is plasma osmolality low?
- Is ECF volume low?
- Is effective arterial volume low?
- **Normal osmolality = pseudohyponatraemia:**
  - Hyperlipidaemia, hyperproteinaemia
  - Na incorrectly measured in plasma volume rather than plasma water
  - Artefactual + no treatment
- High osmolality:
  - **Hyperglycaemia** causes a shift of water out of muscle cells resulting in hyponatraemia
  - Na falls 1mmol/L for every 4mmol/L rise in glucose
  - Other osmotically active solutes such as mannitol + sorbitol act similarly
  - Urea + ethanol freely enter the ICF and therefore do not lead to a water shift
Endocrine and Electrolytes

Low osmolality:
- Leads to expanded ICF and brain swelling
- If ECF volume is contracted, then look for Na loss
- If ECF volume is high/normal then look for low effective arterial volume or ADH release

Contracted ECF volume:
- Loss of Na leads to volume contraction, leading to ADH release + thirst
- Common causes = renal (diuretics, renal salt wasting, osmotic diuresis – diabetes), non-renal (GIT or skin)

Normal or high ECF volume:
- Low arterial volume (oedema states)
  - Hypoalbuminaemia, capillary leakage
  - Cardiac failure
  - Leads to ADH release + thirst

Normal arterial volume (SIADH):
- If ECF/circulating volume normal + urine not optimally dilute, then ADH release is inappropriate
- Expect normokalaemia, normal a-b balance + low plasma urea

Abnormal stimulation of pituitary:
- Pulmonary or CNS disease
- Hypothyroidism, hypoadrenalism
- Pain, nausea, vomiting anxiety
- Release of ADH-like substance:
  - Solid neoplasms esp small cell lung
  - Oxytocin for labour induction
- Drugs:
  - Potentiate action of ADH eg oral hypoglycaemics, PG inhibitors, caffeine
  - Stimulate release eg nicotine, morphine, tricyclics, cytotoxics

Syndrome of Inappropriate ADH secretion
- = SIADH
- See Diabetes Insipidus, page 164

Normally ADH will ↑ if either serum osmolality ↑ or BV ↓ → retained water → ↓ SOs and ↑ BV
- In some clinical states, secretion of ADH continues in the absence of these normal stimuli → water is retained and dilutes all blood components
- The ↑ volume causes ↑ loss of Na in the urine and this together with the ↓ excretion of water leads to an ↑ UOs

Diagnosis is by exclusion, must meet these criteria:
- Low serum Na and low SOs
- UOs higher than expected (>200 + usually > SOs)
- Urinary Na > expected (> 30mmol/L)
- No evidence of hypovolemia
- Normal cardiac, adrenal, pituitary and renal function
- Not on diuretics
- Responds to water restriction with ↑ in serum Na + Os

Aetiology:
- Ectopic ADH Production (relatively rare): malignancies of lung (small cell), bronchus, brain, kidney, duodenum, pancreas
- Central production:
  - Cerebral infections, trauma, tumours, haemorrhage
  - Lung disease, eg pneumonia
  - Severe pain
- Drugs: eg morphine, carbamazepine (anti-epileptic)
- Can be seen in AIDS patients (?combination of above factors)

Treatment:
- Water restriction and ID and treatment of underlying cause
- NS is incorrect rx for SIADH:
  - NS contains 154mmol/L of Na; if used to treat hyponatremia due to SIADH, SOs will ↑ transiently because the osm of the saline is higher than that of the pt
  - The Na is then all excreted because of the volume expansion but about half the water is retained because of the ↑ ADH
  - The net effect is to further lower Na by about 2mmol/L for each L given
Remember that stress and ↓ CV both ↑ADH. This is appropriate but does render post surgical pts susceptible to water overload, especially if solutions with free water are used such as dextrose or dextrose/saline

ADH is ↑ in HF with ↓ CV and this contributes to fluid overload

**Diuretics and Hyponatremia**

- Common but usually mild
- Maximum hyponatremia occurs within 2 weeks with further change only if there is vomiting, diarrhoea, change in water/Na intake or ↑ dose
- Most serious cases are caused by thiazides (NaCl in DT). Hyponatremia is a result of this plus the ADH response to mild volume depletion ie more Na is lost than water
- Loop diuretics are more potent in terms of loss of both Na and water, ADH is ↑ by volume depletion but its ability to ↑ water absorption is limited as the medullary osmolar gradient is ↓ by loop diuretics

**Common Scenarios**

- Prolonged vomiting and rehydration with Gastrolyte – only contains 60 mmol/L Na
- If dehydrated (eg vomiting) and on diuretic, ADH still conserves water, but ↓Na retention so ↓[Na]. We preserve volume at the expense of osmolarity
- Serious post-operative problem. Especially women after elective surgery (eg gynaecology wards). Hypothesis: surgery → ↑ADH (eg due to pain), dextrose also given in belief that it slows catabolism and promotes healing – but together they lead to ↓[Na]
- Sample cases:

<table>
<thead>
<tr>
<th>Case</th>
<th>1</th>
<th>2</th>
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<table>
<thead>
<tr>
<th>Heart Failure + diuretic: too dried out</th>
<th>Nephrotic syndrome</th>
<th>Water overload</th>
<th>SIADH</th>
<th>Pseudo hyponatraemia or something osmotically active (eg ↑glucose)</th>
<th>Renal failure</th>
<th>Severe vomiting</th>
<th>Ketoacidosis</th>
<th>Diuretic</th>
</tr>
</thead>
</table>

- Case 9 (see above): 72 y/o woman found unconscious also had hemiparesis. BP 140/90, hydration adequate. On diuretic for hypertension.

**Treatment**

- Principles:
  - Raise the sodium at a safe rate (no more than 12mmol/L in 24 hours)
  - Treat the cause
- Basic regimes:
  - If volume depleted (Renal/GI losses, diuretics, adrenal insufficiency): saline isotonic to the patient or normal saline. Extra Na will have a small effect but ↑volume → ↓ADH → excess water excreted
  - Normovolaemic or oedematous (SIADH, renal failure, polydypsia, oedema): water restriction + continue to replace Na losses; if necessary, use diuretics + replace Na + K losses
  - If contracted ECF volume: expand the ECF by giving solution isotonic to the pt; ADH levels will fall leading to profound water diuresis; rapid correction is associated with central pontine myelinosis
    - Aim to increase Na by 0.5-1mmol/L/hr if only mildly symptomatic + no more than 12mmol/L in first 24hrs
    - Raise Na by 3-6mmol/L acutely if pt convulsing
  - If severe symptoms or if sodium < 110 then ?hypertonic saline:
    - ↑Na by no more than 12 mmol per 24 hours: keep rate smooth. Key judgement is speed of infusion. No front loading. If no symptoms – maybe go slower
If serious HF in whom both RAA and ADH are ↑ and who are thirsty due to ECV depletion: therapy is aimed at removal of water because giving Na will ↑ oedema. Allow mild asymptomatic hyponatremia to persist while using a loop diuretic + and ACEi

Monitor 2 hourly. Manage in high dependency unit. Detect and treat hypoxia

Adverse neurological consequences of rapid correction: myelin breakdown in the pons, patchy symmetrical lesions elsewhere in the brain. But risk of not treating acute cerebral oedema far exceeds the small risk of osmotic demyelination

Maybe frusemide to ↑free water excretion

Calculation of Na required to Raise Serum Concentration to a Desired Level

The amount required is estimate from:
- Na deficit = volume of distribution x Na deficit/L
- Volume of distribution is in TBW ie about 60 and 50% of LBW in men and women

Thus to raise Na from 108 to 120 in a 60kg woman:
- Na deficit is 0.5 x 60 (LBW) x (120-108) = 360mmol
- 3% saline contains 513mmol/L so 700ml is required
- Na is retained in volume depletion, thus ↑ serum levels but volume deficits are not corrected
- In SIADH water is lost

Dehydration vs Volume Depletion

Dehydration:
- Often used loosely to describe a volume depleted patient
- Correctly it refers to ↓intracellular water, following fluid shifts from ICF to ECF
- Water is lost (either as pure water or as hypotonic fluid) → ↑osmolality and thirst
- Treatment is water replacement (dextrose)

Volume depletion:
- Losses from the ECF (isotonic sodium) → ↓circulating volume
- ↓BP, ↑tachycardia, ↓tissue turgor
- Treatment is replacement of NaCl

Dehydration and volume depletion can co-exist

Hypernatraemia

- Indicates ICF volume contraction
- Can lead to cerebral haemorrhage
- Usually due to water loss + associated thirst disorder
- Minimum urine volume is usually ~ 400ml/d + max osmolality ~ 1200mosm/L
- Usually not due to ↑ total body sodium – total sodium is low, normal or high. Kidney is good at excreting excess Na (except if swamped – eg near drowning)
- Always means the patient is hyperosmolar
- Thirst and ↑ADH protect against hyperosmolality ⇒ don’t see hypernatraemia where the thirst mechanism is normal and there is access to water
- Cellular dehydration → neurologic symptoms: lethargy, weakness, irritability, seizures, etc. Cerebral oedema if it is rapidly corrected

Symptoms

- ↑SOs creates an osmotic gradient that leads to movement of water from cells to the CSF; dehydration of brain cells → neuro sx
- Signs and symptoms may be few unless hypernatremia develops quickly
- Early: thirst, lethargy, weakness, restlessness, confusion
- Later: twitching, seizures, coma (Na >160)
- Brain shrinkage can cause vascular rupture with cerebral or SA bleeds

Osmotic Adaptation to Hypernatremia

- The cerebral dehydration caused by hypernatremia is transient. Within hours the brain adapts to ↑ plasma osm by ↑ its own osm. Water movement then returns cell volume towards normal
- Cerebral contraction lowers hydraulic pressure in cerebral interstitial fluid, causing a gradient that favours movement of water from CSF into the interstitial fluid
- Brain cells take up Na, K, Cl and organic solutes. Organic solutes are known as osmolytes or idiogenic osmoles and are probably mainly glutamine, glutamate and inositol
Generation of Hypernatremia

- Can result from Na retention or water loss but mostly always the latter
- Water loss in excess of Na loss occurs with losses through the skin and respiratory tract or in dilute urine or incorrect IVF replacement
- Water loss, usually marked by polyuria, requires either ↓ secretion of ADH (central DI) or renal resistance to the effect of ADH (nephrogenic DI)
- ↑ ADH and thirst are protective mechanisms, driven by ↑ osm. Thus serious hypernatremia is virtually never seen in subjects with a normal thirst mechanism and access to water
- This happens even if secretion or action of ADH is impaired: thirst provides the ultimate protection
- In adults, hypernatremia is most commonly seen in the elderly as increasing age is a/w ↓ osmotic regulation of thirst but release of ADH is retained
- Even maximum secretion of ADH is not sufficient to retain enough water to offset insensible losses
- Effects of GI losses:
  - Can predispose to hypo or hypernatremia
  - Diarrhoea is roughly isotonic to plasma but the ionic composition is variable:
    - In secretory diarrhoea Na and K is similar to plasma so loss produces volume depletion without a direct effect on plasma Na
    - Volume depletion ↑ ADH and thirst and if hypotonic replacement is given water retention with hypernatremia can occur
    - Osmotic diarrhoea tends to cause water loss in excess of Na so predisposes to hypernatremia
- Vomiting leads to:
  - Loss of both electrolytes and water but are usually hypotonic to ECF so would tend towards hypernatremia however there is significant volume depletion as well as dehydration and such pts are often very thirsty
  - Replacement of losses with water corrects the water deficiency but not the Na depletion therefore dilutional hyponatremia is common

Classification

- 1. With water and sodium deficiency where water loss > sodium loss (ie lost hypotonic fluid):
  - Eg vomit, diarrhoea, sweat, osmotic diuresis (urine osmolarity not low), burns
  - Will be at least some volume depletion
- 2. With normal total body sodium (pure water depletion):
  - Unable to drink (old, babies, sick, etc)
  - Central diabetes insipidus (urine volume ↓ + osm ↑ if give ADH) – seen in trauma esp basal skull fracture, neurosurgery, SOL, infection, hypoxia, drugs
  - Nephrogenic diabetes insipidus (see page 164) – no response to ADH; ↓ ADH effect in lithium, congenital, hypokalaemia, hypercalcaemia or loss of medullary hypertonicity (renal interstitial disease, generalised kidney disease, idiopathic) or osmotic diuresis (urine osmolality not low; consider glucose, urea, mannitol)
- 3. With increased total body sodium:
  - Excess iv hypertonic saline, ingestion of sea water, mineralocorticoid excess (low sodium output) (⇒ expanded ECF)
  - Essentially either:
    - 1. Water > salt loss → low ECFV
      - Renal losses = osmotic diuresis (eg ↑BG), loop diuretics, post-obstruction, post ATN → UNa > 20; UOs variable
      - Extrarenal losses = osmotic diarrhoea, insensible losses (sweat) → UNa < 20; UOs ↑↑
    - 2. Pure water loss → “normal” ECFV
      - Renal losses = DI → UNa variable; UOs ↓↓
      - Extrarenal losses = unreplaced insensible losses (altered mentation, no access to water or hypodipsia) → UNa < 20; UOs ↑↑
    - 3. Salt > water excess → high ECFV
      - Hypertonic Na containing solutions (eg IV NaHCO3), primary hyperaldosteronism → UNa > 20; UOs variable but >1
Urine Osmolality

- The normal response to hypernatremia is to thirst and ↑ ADH → renal water retention
- UOs can ↑ to 900-1200 under maximal effect of ADH and this is reached at SOs of 295-300
- If serum Na is over 150 there must be at least a partial defect in release or action ADH if UOS is < 800 and exogenous ADH will ↑ UOs only if there is CDI
- Urinary concentrating ability should be normal in those with Na overload, insensible losses and primary hypodipsia without CDI. UOs will be > 800 (ADH effect) and urinary Na will be < 20 with water loss. Urinary Na would be much ↑ with Na overload (hypervolemia) and UOs is variable
- Either severe CDI or NDI is present if urine is hypotonic to plasma in hypernatremia. Giving ADH will differentiate between as there will be at least a 50% ↑ in UOs and a fall in volume in CDI

Approach to the Diagnosis of Hypernatraemia

- CALCULATE OSMOLALITY! $2[Na] + \text{urea} + \text{BG}$
- Is the ECF volume expanded?
  - Due to the Na gain eg hypertonic saline, ingestion of salt water, replacement of hypotonic Na loss with isotonic saline (treatment of hyperglycaemia)
  - Treat with diuretics + give free water
- Has the body weight changed?
- Is the thirst response normal?
  - Absence of thirst suggests generalised or localised CNS lesion
- Is the renal response normal?
  - Abnormal renal response – abnormally dilute or large colume urine suggests an ADH or renal problem

Treatment

- Chronic: may be asymptomatic even at 170 – 180 mmol/l due to adaptation by brain ⇒ gradual correction
- Assess volume status: most will have a water deficit for which IV dextrose is appropriate
- If also an obvious ECF deficit (hypovolemia) and hx suggests loss of Na containing fluid then saline is appropriate as initial therapy
- Less marked Na and volume deficits may sometimes be treated with ½ NS but 1/5 NS and dextrose is more common
- Oral replacement with water should be started asap
If water deficit then:
- Stop the water loss: give ADH, prevent osmotic diuresis, etc
- Estimate fluid deficit assuming that only free water was lost:
  - For a woman: deficit = 0.4 x body weight x (plasma Na/140 – 1)
  - Use 0.5 for a man
- SLOWLY (over 36-48 hrs) give oral water or iv dextrose (Watch for hyperglycaemia, rate ~ 300 ml/hr. Add sodium if history suggests loss of sodium containing fluid and patient is not polyuric)
- Aim for Na reduction of 1 mmol/L/hr and no more than 12 mmol/24 hours

Cases
1. 78 y/o man admitted after a 3/52 hx of feeling unwell and ↓ mental state over last 3/7. Noted to be hypovolemic. Serum Na 159, Cr 170, urea 18, SOs 400, UOs 420 → hx would reveal thirst and polyuria. Large amount of osmotically active substance in the serum → BG was 70mmol/L
2. 80 y/o woman from nursing home with 4/7 hx of viral illness with fever and confusion. Na 165, Cr 126, urea 12, SOs 340, UOs 900 → Severe hypernatremia with few signs of hypovolemia suggests mainly water loss. The loss is shared between the ICF and ECF therefore preserving ECFV. Concentrated urine suggests water loss must be due to insensible losses from skin and respiration with inadequate water replacement (ie old, young, sick)
3. 56 y/o man in ICU post MVA. Na 142 on admission but at day 2 was 165 with UOs 80 → very dilute urine indicates renal water loss; CDI caused by HI
4. 45 y/o woman with sarcoidosis c/o having to drink 8-10L of water/d. Na 134, SOs 274 and UOs 80 → polyuria and polydipsia with a low UOs are due either to primary polydipsia or to CDI or NDI; sarcoidosis can cause all 3; water restriction followed by vasopressin would confirm if the situation was not so clear cut eg partial CDI vs polydipsia

Diabetes Insipidus
- Characterised by complete or partial failure of either ADH secretion or the renal response to ADH
- There is a diuresis of dilute urine, 2 – 30L/day
- Most retain near normal Na as their thirst mechanism is intact, they have polyuria and polydipsia
- If CDI also affecting hypothalamic thirst centre → severe ↑ Na
- Symptoms: polyuria, dilute urine despite dehydration, polydipsia
- Central DI:
  - ↓Water resorption in kidney due to ↓ADH secretion from posterior pituitary → low urine osmolality (eg 150 mosmol/kg) despite dehydration. > 5/l per day urine requires hypothalamic damage as well as posterior lobe
  - Causes of central DI: head injury, tumour, metastasis, sarcoidosis, vascular lesion, inherited, drugs (eg phenytoin), idiopathic (50%)
- Nephrogenic DI:
  - Reduced response by kidney to ADH
  - Causes of nephrogenic DI: ↓K, ↑Ca, drugs (lithium), pyelonephritis, congenital, loss of medullary hypertonicity (eg renal interstitial disease)
- Tests:
  - U&E, Ca, plasma and urine osmolality
  - Water deprivation test. Stop drinking then measure urine for 8 hours. If osmolality > 800 mosmol/kg then DI excluded. If diuresis continues, give nasal desmopressin and continue measuring to distinguish between central vs nephrogenic

Potassium
- Normal value of K: 3.5 – 5 mmol/L
- Standard western diet contains ~ 70 mmol/day = renal excretion
- IC concentration ~ 140mmol/L; the ratio of ICF/ECF K is the main determinant of the resting membrane potential across cell membranes; changes in the ratio can cause fatal arrhythmias
- Normal distribution is maintained by NaKATPase pumps
- Insulin + catecholamines cause uptake of K into cells by activating the pumps
- Urine is the major normal route for elimination of K + also conserves it when necessary
- K+ is secreted into urine by tubular cells; the main determinants of this are the serum concentration and aldosterone
• Excreted in the distal tubule (K and H swapped for Na) under the influence of aldosterone. High HCO3 excretion also → ↑ K loss (eg alkalosis)
• Small ↑ in serum K stimulate secretion of aldosterone thus promoting excretion of K + the converse is true
• Shifts from ICF to ECF in response to:
  ➢ Insulin deficiency
  ➢ β-blockers
  ➢ Acidosis (swaps with H+)
  ➢ Cell necrosis
• Investigations:
  ➢ pH (H+)
  ➢ HCO3: usually ↑ when K ↓ and vice-versa except when there is acidosis (eg renal tubular necrosis, diarrhoea)
  ➢ Creatinine
  ➢ Urinary K: > 20 mmol/L ⇒ renal K loss
  ➢ Na: ↓ in hyperkalaemia, consider renal tubule disorder, ↓ mineralocorticoid
  ➢ Glucose
  ➢ ECG (if widened QRS complexes give Ca). See ECG Abnormalities Due to Electrolyte Disturbances, page 38
• Key differentials: diabetic ketoacidosis, renal failure

Summary
• Low:
  ➢ Redistribution: alkalosis, β-agonists (salbutamol)
  ➢ Loss: GI, renal, thiazide or loop diuretics
  ➢ ↓ Intake (starvation, surgery)
• High:
  ➢ Redistribution: acidosis
  ➢ Massive cell lysis
  ➢ ↓ Excretion: DRUGS (eg ACE inhibitors), renal failure, hypoaldosteronism

Hyperkalaemia
• Causes:
  ➢ 1. ↑ intake: rare for oral intake by itself to cause ↑ K; inappropriate rate of IV infusion
  ➢ 2. ↓ excretion:
    ➢ Renal failure
    ➢ Diuretics, ACEi (ACEi blocks aldosterone)
    ➢ Mineralocorticoid deficiency (eg Addison’s, hyporeninaemic hypoaldosteronism)
      o HH probably accounts for most cases of hyperkalaemia without other obvious cause
      o It occurs in older folks with mild renal impairment that would not usually ↑ K; half have T2DM
      o Hyperkalemia is mild with symptoms in 25%
      o Cause is unclear but is characterised by low renin + aldosterone – but sufficient aldosterone to prevent Na loss
      o Aetiology unclear
  ➢ 3. Shift into ECF from ICF :
    o Acidosis, insulin deficiency
    o Pseudohyperkalaemia, in vitro haemolysis (K leaches out of cells due to using a syringe rather than a vacutainer, or left too long or refrigerated etc; if haemolysed, lab will report this)
      o Massive tissue damage → cell lysis
  ➢ 4. Serum sample or thrombocytosis
• Symptoms: Muscle weakness but not until very high levels (~ 8mmol/L)
• Signs:
  ➢ Myocardial depression, peaked T wave, flat P wave, wide QRS, VF
  ➢ Diarrhoea, abdominal pain, muscle excitability
• Approach to the diagnosis of hyperkalaemia:
  ➢ 1. Is the hyperkalemia real? (eg haemolysis of RBCs, EDTA contamination, serum sample, thrombocytosis)
  ➢ 2. Is there a shift of K from ICF to ECF? (eg metabolic acidosis, β-blockers, insulin deficiency, rhabdomyolysis, cell lysis)
  ➢ 3. Is the renal excretion low? (look at urinary K excretion)
    o If not, then unusually high K intake

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If so, consider: low aldosterone (ACEi, hyporeninemia in renal disease or with NSAIDs or DM; adrenal gland problem eg addison’s disease) or renal unresponsiveness to aldosterone (interstitial nephritis or K sparing diuretics)

- **Treatment:**
  - If severe (> 6.5 mmol/L with symptoms or > 8 regardless of symptoms) consider:
    - ECG (should start at 6.5mmol/L)
    - IV calcium gluconate – stabilises myocytes but doesn’t change K
    - Glucose 50 g + soluble insulin 10 U over 15 mins
    - β2 agonist (salbutamol)
    - Dialysis if extreme
    - Promote renal losses - diuretics
  - If moderate (5.5 – 6.5 mmol/L): Calcium resonium 15 g po (calcium binding resins), ↑renal loss through diuretics, mineralocorticoids

- **Cases:**
  - 1. 16 y/o with coma after hx of severe weight loss, thirst + polyuria over 4/52. Glucose 35, pH 6.8, Na 130, K 6.7, ketones → DKA *
    - NB. K+ is high due to INSULIN DEFICIENCY predominantly, in addition to exchange with H+ due to acidosis
  - 2. 84 y/o man on frusemide for HF. Seen to be hypokalemic (2.3), therefore frusemide stopped, K+ infusion started + ACEi (HF) on top of renal impairment led to hyperkalemia 3 days later
  - 4. 82 year old woman admitted with very high platelets and serum K of 7.2.
    - Pseudohyperkalemia seen in high platelets and serum samples (plasma AFTER clotting)
    - Clotted blood has ↑ K as cf non-clotted blood as damaged cells leak K
    - ↑ K seen in thrombocythemia is due to the > number of platelets involved in the clotting process
    - Need to ask for plasma K sample

**Hypokalaemia**

- **Causes:**
  - 1. GI losses (ECF volume contraction):
    - Vomiting, NG suction → ALKALOSIS → ↑HCO3 in urine and ↑ aldosterone → renal loss of K
    - Diarrhoea: → K loss and metabolic ACIDOSIS (lose HCO3)
  - 2. Renal losses:
    - Diuretics: thiazides or loop
    - Renal tubular acidosis, toxic drugs etc
    - ECF normal or high: high aldosterone or hypermineralocorticoid (eg Cushing’s)
  - 3. K shift into cells: metabolic alkalosis, insulin, β-adrenergics (salbutamol)
  - 4. ↓ Intake (starvation, surgery): rare as a cause in itself

- **Urinary K may be useful to suggest renal or extra-renal:**
  - Levels < 20mmol/L suggest extra-renal losses (eg GIT)+
  - Levels > 20mmol/L suggest renal loss but do not exclude extra-renal loss also (if high can do urinary pH as well)

- **Symptoms:**
  - Muscle weakness, cramps: rhabdomyolysis if severe
  - GI: constipation, ileus
  - Polyuria, nocturia
  - Urine – if ↑ volume then diuretics or osmotic diuresis, if not consider aldosterone action

- **Signs:**
  - Arrhythmias, PR prolonged, wide QRS, inverted/depressed T waves, U waves, VF
  - GI ileus, muscle weakness, hypotonicity, digoxin toxicity, alkalosis
  - Renal dysfunction: ↓ ability to concentrate + acidify urine; ↑ HCO3 reabsorption

- **Treatment:**
  - Generally oral is sufficient, IV necessary sometimes
  - May have large total body deficit (eg DKA). Replacement KCl up to 40 mmol/hour

- **Cases:**
  - 1. 19 y/o pregnant woman. Serial values with falling K+ + HCO3, everything else normal → salbutamol tocolysis → K+ shift

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Endocrine and Electrolytes
- 2. 4 y/o child. K+ 2.1 (3.2–4.8), high Cl, low HCO3. Urine Na + K <10 (therefore not renal losses) → diarrhoea with K+ + HCO3 loss

- 3. 76 y/o asymptomatic woman follow up with GP. K+ = 3.0. Most likely cause → newly started thiazide

- 4. 18 y/o woman with weakness, hypokalaemia + metabolic acidosis. Had a hypochloremic hypokalemic metabolic acidosis → bulimia (vomiting + laxatives + thiazides). DDx: Bartter’s syndrome → K+ reabsorption defect

- 5. 32 y/o woman admitted on several occasions with weakness, hypokalemia + metabolic alkalosis. Urinary Na, K + Cl were all high → diuretic abuse

**Calcium**

- See also Parathyroid, page 145

**Summary**

- If low Mg, then no ↑ in PTH in response to ↓Ca (lack of Mg inhibits the release of PTH)
- Normal value of Ca: 2.12 – 2.65 mmol/L
- PO4 RR = 0.8–1.4 mmol/L
- 40% of calcium is bound to albumin. Adjust Ca for changes in albumin (0.025 per 1g of Albumin). Take sample uncuffed

**Low:**
- Hypothyroidism: abscess/gland destruction, ↓Mg, resistance to PTH (pseudo)
- ↓Vit D: renal failure, malnutrition
- Secondary hyperparathyroidism

**High:**
- ↑PTH: primary or tertiary
- Paraneoplastic: PTHrH, bone metastasis
- ↑Vitamin D: nutritional, ↑conversion (sarcoid)

**Hypercalcaemia**

- Generally a serum Ca under 3mmol/L reflects primary HPT; above 3 reflects a malignancy or decompensation of primary HPT due to dehydration + salt depletion
- Signs: “Bones, stones, groans and psychic moans”. Also abdominal pain, vomiting, constipation, polyuria (Ca potentiates ADH effect), depression, anorexia, weakness, ↑BP, renal stones, cardiac arrest
- Most commonly see primary hyperPTH in the community and malignancy in hospital

- Causes:
  - Transient/arterfacts
  - Primary hyperPTH: see parathyroid section
  - Malignancy:
    - Mechanisms of hypercalcemia in malignancy are complex: erosion of bone by osteolytic mets, PTHrP (has a homologous amino terminal sequence to PTH), osteoclast stimulating factors etc etc
    - ↑Ca, often above 3.0, PO high normal or ↑ if PTH suppressed, ALP may be ↑ (mets), urinary Ca is high
    - Multiple myeloma will see Bence Jones protein or abnormal plasma protein electrophoresis
  - Familial hypocalciuric hypercalcaemia:
    - See ↑Ca, PO low normal or normal, PTH high normal, urine Ca clearance ratio low
    - Inherited abnormality of Ca sensing receptor measuring the Ca at the wrong level
    - Is benign
    - Screen for it with 24 hour urine comparing CrCl to Ca clearance: ratio is low
  - Vitamin D excess:
    - ↑Ca, normal or high normal PO, ↓PTH, hypercalciuria, ↑1,25diOH cholecalciferol
    - Seen in granulomatous disease, any disease with lymphoid hyperplasia: sarcoidosis, lymphoma, TB
  - Tertiary HPT
  - Medications (lithium, thiazides etc)
  - Other: assay error, dehydration

- NB: acidosis → H displaces Ca on albumin → ↑free Ca
- Tests: need to do albumin, PO4, ALP, PTH, vit D, PTHrP + urinary calcium excretion
- If albumin raised:
  - Urea raised → dehydration
  - Urea normal → cuffed specimen
- Albumin normal or low:
Phosphate low or normal (and urea normal): primary or tertiary hyperparathyroidism

Phosphate ↑ or normal:
  - ↑ ALP: Bone metastases (most common primaries are breast, kidney, lung, thyroid, prostate, ovary, colon), sarcoidosis (↑ Vitamin D conversion in the lungs), thyrotoxicosis
  - Normal ALP: myeloma, vitamin D excess, Ca supplements

- **Treatment:** If Ca > 3.5 mmol/l or severe symptoms:
  - Rehydrate and correct any hypokalaemia and hypomagnesaemia
  - Diuretics once rehydrated (frusemide, avoid thiazides)
  - Bisphosphonates (pamidronate): lower Ca over 2-3 days by inhibiting osteoclasts

- **Cases:**
  1. 36 y/o woman with polyuria + nocturia. Na normal. Ca = 3.4 + PO4 elevated. Cr slightly elevated. As Ca so high, malignancy needs be disproven. → was vitamin D overdose (need to take massive OD to get to this level)
  2. 60 y/o man with renal colic. Ca was 2.85 + PO4 just above LLN. Ca 2.6 4 years previously → primary hyperPTsm → renal stones. Time course is not supportive of malignancy. PTH was at the upper end of the RR (should be completely suppressed)
  3. 23 y/o woman went to GP + asked to have her Ca checked. Was elevated at 2.68, PO4 normal. No symptoms. → familial hypocalciuric hypercalcaemia. PTH would be mid-range, urinary Ca excretion is low
  4. 46 y/o man feeling unwell, depressed + lethargic. Ca 2.9 + PO4 lower end of RR. How would you Ix? → PTH (was very low). Was a heavy smoker → CXR → adenoca of lung with hypercalcemia of malignancy

### Hypocalcaemia

- **Symptoms:** tetany, depression, carpo-pedal spasm (wrist flexion and fingers drawn together), neuromuscular excitability (eg tapping over parotid causes facial muscles to twitch – Chvostek’s sign)

- **Causes of hypocalcaemia:**
  - Spurious: HYPOalbuminemia
  - Primary hypoPT: see parathyroid section (↓ corrected Ca, high normal or ↑ PO, ↓ PTH)
  - ↓ Mg → ↓ PTH → hypocalcaemia
  - Thyroid or parathyroid surgery
  - Vitamin D deficiency:
    - Mild deficiency gives suboptimal 25OH cholecalciferol, ↓ 24hr urinary Ca + a trend to ↑ PTH, normal Ca
      - Bone changes = ↑ bone turnover due to secondary hyperparathyroidism (osteoid proportionate to osteoblast + osteoclast numbers ie high turnover osteoporosis)
      - Common in early vit D def in the elderly
    - Moderate def gives severe changes with ↓ PO, ↑ ALP
      - With ↑ vit D deficiency, the ↑ secondary hyperPT now gives a ↓ PO
      - This ↓ osteoid mineralisation (patchy osteomalacia)
      - Still a normal Ca
    - Severe def gives ↓ Ca as well
      - All skeletal surfaces are covered with osteoid, therefore the secondary hyperPT cannot mobilise Ca from bone
      - Now frank ↓ Ca, may be tetany
  - Secondary hyperPT: If ↑ PO4 then chronic renal failure (failure of Vitamin D conversion), hypoPTH or Pseudohypothyroidism
    - If PO4 normal or ↓ then osteomalacia (↑ ALP), over hydration or pancreatitis
    - Drug therapy eg frusemide

- **Cases:**
  1. 75 y/o woman with pins and needles + facial twitching. Ca 1.6 + PO4 low at 0.5. Albumin 30g/L + ALP ↑. Corrected Ca was 1.8. → vitamin D deficiency with osteomalacia
  2. 65 y/o male with CRF. Ca 2, albumin 30, ALP 200, PO4 ↑ at 2.5. → CRF, PTH would be ↑
  3. 40 y/o male with collapse post ETOH binge. K 1.0 (↑↑), Mg 0.3 (↓↑). Ca 1.6 PO4 1.2. → Mg depletion from crap diet + ETOH. Low Ca due to ↓ Mg (→ ↓ PTH)

### Vitamin D Deficiency

- **Seen with:**
  - ↓ sunlight exposure
  - ↓ synthesis from a given UV exposure (eg dark skin)
  - ↓ consumption of foods w high vit D content
- Malabsorption
- Chronic liver disease
- Elderly especially at risk of insufficiency – oldies skin has less capacity to synthesise vitamin D following UV exposure
- Consequences in the elderly are osteoporosis + osteomalacia
- Elderly require supplementation (800-1000 units/d)
- Recommended level of at least 50nmol/L (although 75nmol/L perhaps a better aim)
- No danger of toxicity therefore just supplement without testing for deficiency

**Cases**
- Always ask for corrected Ca
- Exam question: “Comment on observed abnormalities and explain them”

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</table>

- Case 1: RF with renal osteodystrophy
- Case 2: multiple myeloma (high TP and ↓ albumin, ↑ Cr) therefore do electrophoresis to determine poly or monoclonal
- Case 3: primary hypoPTism

**Magnesium**
- Stored 65% in bone, 35% in cells
- Concentration generally follows Ca and K
- Excess:
  - Usually in renal failure ⇒ treat renal failure not magnesium
  - Symptoms: neuromuscular depression → ↓ BP → CNS depression
- Deficiency:
  - Causes: severe diarrhoea, ketoacidosis, alcohol, TPN, with ↓ Ca or ↓ K (especially diuretics)
  - Symptoms: tetany (same as ↓ Ca, ↓ K gives weakness), fits, arrhythmia
- Treatment: Mg salts either po or iv

**Chloride**
- Is Cl a useful test?
  - Cl usually moves in parallel with Na + it is more helpful to consider the causes of high or low Na
  - Exceptions are some a-b disturbances in which Cl may shift independently of Na, related to disturbance in HCO3:
    - High Cl with low HCO3 in normal AG MA
    - Low Cl with high HCO3 in some cases of MAL (eg in severe vomiting HCl is lost + hypochloraemic MAL develops, the pt is volume depleted + MAL is perpetuated by generation of more HCO3 as Na is avidly retained by the kidney in the presence of Cl depletion. K depletion contributes to the alkalosis which cannot be corrected until deficits of volume/Cl/K are corrected
- Cl normally tracks Na except in metabolic acidosis. Eg severe vomiting: ↓ HCl (⇒ hypochloraemic metabolic alkalosis) and volume depletion (⇒ kidney retains Na ⇒ generation of HCO3 and K depletion). Correction of alkalosis requires correction of volume, chloride and K

**Acid-Base balance**

<table>
<thead>
<tr>
<th>Acid-base disorders</th>
<th>Biochemical parameters</th>
<th>Pathophysiology</th>
<th>Compensation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metabolic acidosis</td>
<td>pH ↓ HCO3↓</td>
<td>↓ HCO3- either from GI tract or kidney ↑ H+ from lactic or ketoacidosis or RF</td>
<td>is respiratory via ↑ ventilation + ↓ PCO2, PCO2 will ↓ by 1.2 for each 1.0 ↓ in HCO3</td>
</tr>
<tr>
<td>Metabolic alkalosis</td>
<td>pH ↑ HCO3↑</td>
<td>↑ HCO3 via complex mechanisms</td>
<td>is respiratory via ↓ ventilation + ↑ PCO2, PCO2 will ↑ by 0.6 for each 1.0 ↑ in HCO3</td>
</tr>
</tbody>
</table>
(renal/GI loss of H+, Cl−, K+; shifts of K+ from ECF to cells, volume depletion, hyperaldosteronism, gain of HCO3) → This mechanism is limited by hypoxia

**Respiratory acidosis**
- pH ↓ PCO2 ↑
- ↑ PCO2 as resp excretion of CO2 lags behind production → always due to impaired alveolar vent
- is metabolic via ↑ HCO3 and is biphasic:
  - **acute:** HCO3 ↑ immediately by 1.0 for every 10 ↑ in PCO2 (as PCO2 ↑, CO2 + H2O → H2C03 → H+ + HCO3)
  - **chronic:** HCO3 ↑ by a further 2.5 for each 10 ↑ in PCO2 (via renal retention of HCO3)
- NB. Full compensation is 3.5

**Respiratory alkalosis**
- pH ↑ PCO2 ↓
- ↓ PCO2 due to ↑ alveolar ventilation driven by central (e.g. trauma, infection, drugs, anxiety) or pulmonary (pneumonia, asthma, PE, ventilation) mechanisms
- is metabolic via ↓ HCO3 and is biphasic:
  - **acute:** HCO3 ↓ immediately by 2.0 for every 10 ↓ in PCO2
  - **chronic:** HCO3 ↓ by a further 3.0 for each 10 ↓ in PCO2 (via renal loss of HCO3)
- NB. Full compensation is 5.0

**Approach**
- Is pH acidaemic, alkalaemic or normal?
- If normal, are HCO3- and PCO2 normal?
- If acidaemic or alkalaemic, is the primary disturbance respiratory or metabolic?
- Is compensation appropriate?
- If not, or if normal pH with abnormal HCO3- and PCO2 = a mixed a-b disorder
- NB. Compensation has nothing to do with pH – more to do with whether HCO3- and PCO2 has adjusted appropriately

**Chemistry**
- pH = measure of concentration of H ions; a tightly controlled physiologic system
- Acid = substance that releases a H ion
- Base = substance that accepts a H ion
- Strength depends on degree of dissociation
- H+ present in the body in equilibrium with H2CO3:
  - H2O + CO2 ↔ H2CO3 ↔ H+ + HCO3
  - Henderson Hasselbach Equation:
    \[
    \text{pH} = 6.1(pK_a) + \log \frac{[\text{HCO}_3^-]}{0.03[\text{PCO}_2]}, \text{or} \\
    \text{pH} = 6.1(pK_a) + \log \frac{\text{Kidney Production of HCO}_3^-}{\text{Respiratory Regulation of CO}_2}, \text{or} 
    \]
- pH can be estimated from serum HCO3 (in range 8-44mmol/L):
  - pH = 7 + ([HCO3 + 15]/100) eg if HCO3 = 11, pH = 7.26
  - Normal range for pH is 7.35 – 7.45 (=45 – 35 nmol/L of H+ ion)
  - Range of pH compatible with life is about 6.8 – 7.8 = H+ concentration of 160 – 16 nmol/l
  - Intracellular + extracellular buffering systems = HCO3, proteins, phosphates → net result is ↓ HCO3
  - Lots of other buffering systems
- Compensation:
  - Never complete
  - Respiratory:

**Endocine and Electrolytes**
o pH (H+) measured in the medulla (chemoreceptors)
o Compensates rapidly
o If pH low then pCO2 reduced to compensate; if high, then pCO2 increased

Renal:
o Altered bicarbonate reabsorption
o Titratable acid excretion: organic buffers in tubules acidifies urine. Excretes 30 – 50% of acid produced each day
o NH4 excretion: formed in tubules, ↑ takes days. Excretes 50 – 70% of acid

**Bicarbonate and Carbon Dioxide Ratio**

- The ratio is crucial – i.e. the pH remains normal so long as the ratio remains normal
- This is the basis of physiological compensation by the kidneys/lungs for a-b disorders
- Mixed a-b disorders are common + can be detected by clinical suspicion and compensation rules; clues to a mixed a-b disorder:
  - Compensation not as predicted for a single disorder
  - pH is normal with both HCO3- and PCO2 abnormal

- **NB.** Compensation for a single disorder will not restore pH completely to normal + complete compensation takes time
- **NB.** Baselines are 24 for HCO3 + 40 for PCO2

**When to Use ABGs**

- Patients who do not require BGs:
  - Those with uncomplicated asthma/MI
  - Those with normal systemic perfusion + no dyspnoea or hyperventilation
- Patients who do require BGs:
  - Cyanosis, perfusion failure or hypotension, vasoconstriction/sweaty, ?septic shock, cardiorespiratory arrest
  - ?DKA
  - Pneumonia, ?PE or pulmonary oedema, exacerbation of COPD, asthma with fatigue or speech difficulty, smoke inhalation (+ COHb)
  - Poisoning
  - Liver failure

**Respiratory Alkalosis**

- **Causes:**
  - Hypoxia
  - Lung disease: PE, asthma
  - Anxiety
  - Fever, sepsis
  - *Salicylate overdose*: stimulates respiration, will subsequently develop metabolic acidosis
- ↓PaCO2, ↑pH, initial alterations in [HCO3] are minimal, if it persists then kidneys compensate

- **Compensation:**
  - Acute: HCO3 ↓ by 2 for each 10 ↓PCO2
  - Chronic: HCO3 ↓ by a further 3 (ie total of 5) for each 10 ↓PCO2 [renal loss of HCO3]

**Respiratory Acidosis**

- **Causes:**
  - PCO2 excretion lags production – eg severe asthma (initially asthmatics hyperventilate)
  - Pulmonary disease, muscular diseases, etc
  - CNS depression: primary or drugs/toxins
  - Asphyxia, smoke inhalation
- As PCO2↑ then CO2 + H2O →H+ + HCO3-
- ↑PaCO2 →↓pH, initial alterations in [HCO3] are minimal, if it persists then kidneys compensate (↑HCO3 reabsorption, ↑NH3 formation and excretion):
  - Acute: HCO3↑ by 1 for each 10 ↑PCO2
  - Chronic: HCO3↑ by a further 2.5 (ie 3.5 of total) for each 10 ↑PCO2
- For example:
### Metabolic Acidosis
- Net gain of acid
- Causes:
  - Accumulation of acid (anion gap > 18 mmol/L): $\uparrow$H+ (ketoacidosis, lactic acidosis, ingestion of salicylates, methanol), renal failure (failure to excrete H+)
  - $\downarrow$HCO3 (anion gap < 18 mmol): GI tract loss (eg diarrhoea), renal loss (eg $\downarrow$carbonic anhydrase), hypoaaldosteronism
- Compensation:
  - Rapid: PCO2 $\downarrow$ by 1.2 for each $\downarrow$1 in HCO3 (baseline = 24) - rapid
  - Slow: $\uparrow$HCO3 reabsorption and $\uparrow$NH4 excretion by the kidneys

### Metabolic Alkalosis
- Net loss of acid
- Causes:
  - Loss of H+:
    - Vomiting (suspect surreptitious if low Cl)
    - NG suction
    - Renal loss (hyperaldosteronism)
  - Increase in HCO3 reabsorption:
    - K depletion (Conn’s, Cushing’s, drugs, diuretics).
    - Volume depletion, eg $\uparrow$Aldosteronism $\rightarrow$ $\uparrow$Na/H exchange
  - Gain in alkali: eg NaHCO3 administration
- Compensation:
  - PCO2 $\uparrow$ by 0.6 for each $\downarrow$ in HCO3. Limited by hypoxia
  - Final compensation is by renal excretion of HCO3 – requires correction of Cl, K and volume

### Summary of Compensation Rules

<table>
<thead>
<tr>
<th></th>
<th>Acute</th>
<th>Chronic</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>CO2</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acidosis $\uparrow$</td>
<td>$\uparrow$1</td>
<td>$\uparrow$ further 2.5 (total 3.5)</td>
</tr>
<tr>
<td>Alkalosis $\downarrow$</td>
<td>$\downarrow$2</td>
<td>$\downarrow$ further 3 (total 5)</td>
</tr>
</tbody>
</table>

|                      |                          |
|----------------------|                          |
| **HCO3**             |                          |
| Alkalosis $\uparrow$  | $\uparrow$0.6            |
| Acidosis $\downarrow$| $\downarrow$1.2          |

### Mixed Acid/Base disorders
- Suspect if:
  - Clinical grounds
  - Compensation rules not obeyed
  - Normal pH but abnormal PCO2 and HCO3
- Examples:
  - Respiratory + Metabolic Acidosis: Pulmonary oedema + cardiac arrest
  - Respiratory + Metabolic Alkalosis: Over-ventilation + Nasogastric suction
  - Respiratory Alkalosis + Metabolic Acidosis: Septic shock or Salicylate OD
  - Respiratory Acidosis + Metabolic Alkalosis: COPD + Diuretic
  - Metabolic Acidosis + Metabolic Alkalosis: Renal failure + vomiting

### Interpreting Blood Gas Results
- Arterial blood taken in 2 ml syringe containing heparin (to stop clotting) and transported on ice
- Look at pH: 7.36 to 7.44 is normal
- Look at PCO2. If < 36 then hyperventilation. If > 44 then hypoventilation.
- Look at HCO3. If < 22 then metabolic acidosis. If > 26 then metabolic alkalosis. But HCO3 depends on PCO2. So (to work out if it’s just compensation, or there is a metabolic problem as well as a respiratory one):

---

<table>
<thead>
<tr>
<th></th>
<th>PCO2</th>
<th>HCO3</th>
<th>pH</th>
</tr>
</thead>
<tbody>
<tr>
<td>Uncompensated</td>
<td>80</td>
<td>24</td>
<td>7.10</td>
</tr>
<tr>
<td>Acute</td>
<td>80</td>
<td>28</td>
<td>7.17</td>
</tr>
<tr>
<td>Chronic</td>
<td>80</td>
<td>38</td>
<td>7.30</td>
</tr>
</tbody>
</table>
For acute changes (hours): a fall in PaCO₂ → a normal HCO₃⁻ less for every 10 mmHg ↓ in PaCO₂. A rise in PaCO₂ → normal HCO₃⁻ 1 greater for every 10 mmHg ↑ in PaCO₂.

For chronic changes (days): a rise in PaCO₂ results in a normal HCO₃⁻ 4 greater for every 10 change in PaCO₂.

**Anion Gap**

- AG = Na + K – [Cl + HCO₃⁻]
- Usually 8 – 16 milliequivalent/l (measure of charge)
- The concept relates to the fact that in body fluids the sum of positive charges must = the sum of negative charges
- Na + K = 95% of positive; Cl + HCO₃⁻ = 85% of negative
- Na + K + UC = Cl + HCO₃⁻ + UA, therefore UA – UC = AG (u = unmeasured, a = anions, cations)
- The AG is affected by change in UA or UC, but in practice only ↑ UA matters eg ketones, lactate, alcohol metabolites, organic acids
  - These produce acid, the H⁺ is buffered → ↓ HCO₃⁻
  - Cl is unchanged, UA ↑ and AG ↑ - there is a high AG MA
  - In the type of MA caused by loss of HCO₃ there is no ↑ in UA but Cl ↑ because of renal retention in place of HCO₃, thus there is a normal AG MA
- **High anion gap**: = extra acids eg *ketoacidosis, lactic acidosis, renal failure, poisoning* (salicylate, methanol, ethanol, ethylene glycol)
- **Low anion gap**: = loss eg *GI loss of HCO₃*, therapy for diabetic ketoacidosis, ingestion of HCl or NH₄Cl
- **Practical use limited** – cause of metabolic acidosis obvious from history and observation
- Most labs have deleted it from electrolyte profile

**Base Excess**

- Given on all arterial blood gas results
- **BASE** = Concentration of titratable base when titrating blood or plasma with a strong acid or base to a plasma pH of 7.40 at PCO₂ of 40 mmHg at 37°C
- Intent is to remove the impact of the respiratory component leaving just the metabolic component:
  - If +ive: metabolic alkalosis → deficit of non-carbonic acid
  - If –ive: metabolic acidosis → excess of non-carbonic acid
- BUT recognises normal compensation as an extra disturbance. May be useful for anaesthetist (eg simple and acute disturbances)
- **BE does not give a good estimate of the severity of any metabolic component coexisting with a respiratory component except in the very acute phase; BE recognises normal compensation as an extra a-b disorder; BE adds no information and may be confusing**

**Examples**

<table>
<thead>
<tr>
<th>Disturbance</th>
<th>Scenario</th>
<th>Uncompensated</th>
<th>Compensated</th>
<th>Note</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Metabolic acidosis</strong></td>
<td>DKA causing ↓ HCO₃ by 12</td>
<td>pH = 6.1 + log 12/0.03 x 40 = 7.1</td>
<td>- 24 – 12 = 12</td>
<td>Final compensation</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>12 x 1.2 = 15</td>
<td>i.e. correction of a-b d relies on renal</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>40 – 15 = 25</td>
<td>excretion of acid w regeneration of HCO₃</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>pH = 6.1 + log 12/0.03 x 25 = 7.3</td>
<td></td>
</tr>
<tr>
<td><strong>Metabolic alkalosis</strong></td>
<td>HCO₃ has increased to 40 due to vomiting</td>
<td>pH = 6.1 + log 40/0.03 x 40 = 7.62</td>
<td>- 40 – 24 = 16</td>
<td>Limited by hypoxia –</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>16 x 0.6 = 9.6</td>
<td>as PaCO₂ approaches 60; PO₂ approaches 65</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>40 + 9.6 = ~ 50</td>
<td>(room air)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>pH = 6.1 + log 40/0.03 x 50 = 7.52</td>
<td></td>
</tr>
<tr>
<td><strong>Respiratory acidosis</strong></td>
<td>Chronic respiratory disease has ↑ PCO₂ to 80</td>
<td>pH = 7.1, PCO₂ = 80 + HCO₃ = 24</td>
<td>acute: pH = 7.17, PCO₂ = 80 + HCO₃ = 28 (i.e. HCO₃ + [40/10 = 4 x 1.0 = 4])</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>chronic: pH = 7.3, PCO₂ = 80 + HCO₃ = 38 (i.e. HCO₃ + 4 + [40/10 = 4 x 2.5 = 10])</td>
<td></td>
</tr>
<tr>
<td><strong>Respiratory alkalosis</strong></td>
<td>Chronic hyperventilation has ↓ PCO₂ by 20</td>
<td>pH = 7.7, PCO₂ = 20 + HCO₃ = 24</td>
<td>acute: pH = 7.63, PCO₂ = 20 + HCO₃ = 20 (i.e. HCO₃ - [20/10 = 2x 2.0 = 4])</td>
<td></td>
</tr>
</tbody>
</table>
### Scenario | Blood gases | Interpretation | Compensation
--- | --- | --- | ---
1 | Pt admitted to ED semicomatose + hyperventilating (NB. hypervent = either resp alk or comp for met acid) | **pH = 7.00**  
**HCO₃ = 3mmol/L**  
**PCO₂ = 14mmHg** | → Metabolic acidosis  
→ 1.2 x [24-3] = 25.2 (actual ↓ is 26) | → PCO₂ low due to resp compensation  
→ there is full compensation
2 | Pt admitted to ED semicomatose + hyperventilating | **pH = 7.40**  
**HCO₃ = 12mmol/L**  
**PCO₂ = 20mmHg** | → Mixed a-b disorder  
→ pH normal w v abnormal HCO₃ + PCO₂, suggesting mixed disorder | → If this is MA, max ↓ in PCO₂ would be to 26, as the level is 20, suggests there is also resp alk  
→ Starting with PCO₂ indicates that HCO₃ is too low for comp for RAL
3 | 64 yo man w severe COPD has complications after AAA repair, requiring ventilation + NGT suction | **pH = 7.81**  
**HCO₃ = 50mmol/L**  
**PCO₂ = 30mmHg** | → Severe alkalaeia  
→ Both high HCO₃ + low PCO₂ cause this  
→ MAL from ↑ HCO₃ should lead to ↑ PCO₂ (to around 55mmHg)  
→ There is thus a very large resp alkalosis, much worse than the apparently modest ↓ PCO₂  
→ If this was RAL, HCO₃ should drop to 22 as comp  
→ The level of 50 indicates a large MAL with the RAL  
→ This occurred as PCO₂ was actually high preop + HCO₃ was ↑ in compensation for the chronic RA – the HCO₃ was further ↑ by the loss of acid in the gastric fluid; at the same time, the high PCO₂ was ↓ by ventilation
4 | 60 y/o man collapsed post sudden onset SOB. Exam + CXR = pulmonary oedema. | **pH = 7.02**  
**HCO₃ = 15**  
**PCO₂ = 60**  
**PO₂ = 40** | Exam question:  
Interpret this ab data, indicating the type of ab disturbance + give brief reasons for your conclusions  
→ Mixed ab disorder:  
  ➢ pH indicates acidaemia  
  ➢ ↑PCO₂ indicates hypoventilation = RA  
  ➢ ↓HCO₃ indicates MA
5 | 60 yo woman w severe COPD has developed HF. Rx w diuretics has caused significant hypokalaemia | **pH = 7.40**  
**HCO₃ = 38**  
**PCO₂ = 65** | Exam question:  
Interpret this ab data, indicating the type of ab disturbance + give brief reasons for your conclusions  
→ Mixed ab disorder:  
  ➢ Normal pH  
  ➢ ↑PCO₂ indicates RA ?secondary to CO₂ retention  
  ➢ ↑HCO₃ indicates MAL ?chronic compensation for RA  
  ➢ Co-existing RA + MAL  
→ If RA with metabolic compensation:  
  ➢ 65-40 = 25; HCO₃ should ↑ by 3.5 (full comp) for every 10 ↑ in CO₂ therefore:  
  ➢ 2.5 x 3.5 = 8.75  
  ➢ 24 (HCO₃ baseline) + 8.75 = 32.75 therefore 38 is too high for metabolic compensation alone  
→ If MAL with resp compensation:  
  ➢ 38-24 = 14  
  ➢ 14 x 0.6 = 8.4  
  ➢ 8.4 + 40 = 48.4  
  ➢ As PCO₂ is 65, this is too high for resp compensation
Neurology

History

• Want to know the answer to three questions:
  ➢ 1. Is there a focal lesion or a general insult?
  ➢ 2. Where is the lesion (based on history and exam): Eg Weakness:
    o Upper motor neuron:
      ➢ Motor cortex
      ➢ Internal capsule
      ➢ Brain stem
      ➢ Spinal cord
    o Lower motor neuron:
      ➢ Anterior horn cell
      ➢ Nerve root
      ➢ Brachial/lumbosacral plexus
      ➢ Peripheral nerve
      o Neuromuscular junction
    o Muscle
  ➢ 3. What is the lesion (based on history – mode of onset and progression)?
    o Is it infarct, haemorrhage, inflammatory, tumour or degenerative
    o Use VITAMIN C & D (vascular, infection/inflammation, trauma, autoimmune, metabolic,
      idiopathic/iatrogenic, neoplastic, congenital, degenerative/drugs)
  ➢ Describe findings as either:
    o Mono or polyneuropathies
    o Proximal or distal
    o Symmetric or asymmetric

• Differentials:
  ➢ Inability to walk: Parkinson’s, spinal cord (demyelination, compression, disease due to ↓B12 or syphilis),
    cervical spondylosis, polymyositis, myasthenia gravis, Guillain Barre, hereditary motor and sensory
    neuropathy, MS, diabetic neuropathy, motor neuron disease, alcoholic neuropathy
  ➢ Brief loss of consciousness: Stokes Adams attacks, VT, postural hypotension, hysterical unconsciousness,
    vasovagal syncope (fainting), epilepsy, CVA
  ➢ Coma and Stupor: hypoglycaemia, Wernicke’s encephalopathy, sedative or narcotic drug overdose, post
    anoxic coma, CVA, status epilepticus, meningitis, encephalitis, delirium, coning. See Coma and Stupor,
    page 196
  ➢ Space occupying lesion: bleed, tumour, cyst, abscess, TB granuloma, AVMs, hydrocephalus

Physical Exam

• Hard to incorporate with rest of physical exam ➞ do it on its own
• Tailor the exam to the clinical problem (full exam can take an hour)
• Avoid suggestion: rather than ‘Is this sharp’ or ‘do you smell the perfume’ say ‘what do you feel/smell’
• Quick list:
  ➢ Observe: including wasting and fasciculations
  ➢ Cranial nerves
  ➢ Tone
  ➢ Power
  ➢ Reflexes
  ➢ Coordination
  ➢ Sensation: position, vibration, pin prick, light touch

Mental State Exam

• Wanting to test:
Distributed cognitive function:
  - Attention/concentration
  - Memory
  - Word finding

Localised cognitive functions
  - Speech
  - Visuo-spatial

If suspicious from history need assessment of the following:
  - State of consciousness: alert, drowsy, stuporous, comatose (assess with GCS)
  - Other observations from mental state exam (See Mental State Examination, page 688)
  - Orientation: date, their name, age, who are their relatives
  - Remote or long-term memory: phone number, Prime Minister, recent events in the news
  - Registration and Immediate recall: Memorise 3 objects, recall after 3 minutes. Repeat 4 or 5 digits in reverse
  - Others: abstract thinking, serial 7’s

Can use Mini-mental status test: but not sensitive to subtle impairments

Language
  - If difficulty following instructions, appears confused, etc
  - Requires assessment of spoken and written response to both spoken and written questions
  - Observations: fluency, word finding, grammatical errors, understanding questions
  - Naming objects: ask about whole object then parts – wristwatch and strap
  - Repetition: No Ifs ands or buts
  - Auditory comprehension: ↑ly complex commands, eg Close your eyes, touch your left ear with your right thumb and stick out your tongue
  - Writing: write a simple sentence, their name and address
  - Reading: read aloud

Cranial Nerve Exam
  - 1: Olfactory: Smell. Not if doing general screen. Close eyes. Check each nostril patent then test (eg scented soap on ward). Poor smell common (smoking, allergies, ageing). Also in Alzheimer’s, Parkinson’s, MS, chemotherapy. Most serious association: frontal lobe tumour, presents with personality change, self-neglect, dementia
  - 2: Ophthalmic nerve: lesions common and serious. Check if they normally wear glasses. Test:
    - Acuity: (use pinhole if they’ve forgotten their glasses). Test each eye separately
    - Visual fields: confrontational testing: first just hold hands in each visual field and ask what they see. Then wiggle one finger, then the other, then both, in all visual fields (or count fingers)
    - Hemianopia:
      - Pituitary lesion →bitemporal hemianopia (nasal retina affected). Bring red pin from affected field into normal – gain of red colour is convincing. Upper temporal field in one eye is typically affected first
      - Parietal lesion →visual inattention
  - 3, 4, 6: Seeing double. Complicated to sort out
    - Look for ptosis
    - Smooth tracking: Fix on finger, draw H in the air, ask for report of diplopia, watch for one eye lagging or nystagmus (a few beats in extreme gaze is normal)
    - Examine pupils at rest, light reflexes and near reflex
    - Voluntary eye movement:
      - Look up, down, left, right. Often elderly have trouble looking up anyway
      - Cover test: look at target, cover one eye, does other eye move? Reverse. Shows which is fixing eye
      - If diplopia found, find field where it’s maximal. Weak eye moves less; good eye overshoots. Use stick man drawn on tongue depressor
    - Problems locating target (overshoot and come back) →?cerebellar
  - 5: Trigeminal Nerve
    - Sensory 5th: Test light touch and pinprick in all 3 divisions on both sides (separate pathways in the brain stem). Test corneal reflex (early sign of lesion) – patient looks up, use cotton wool on cornea (more sensitive than sclera)

7: Facial Nerve. Wrinkle forehead and ‘show your teeth’ (not smile). Look for lower face weakness. Upper face (eg screw up eyes) better preserved in UMN, both similarly affected in LMN (eg Bell’s palsy – can be due to HSV, onset in days, recovery in weeks/months, rarely parotid tumour). Note symmetry, fasciculation, and abnormal movements. Don’t normally test taste.

8: whispered voice at arms length, with patient’s eyes close. Mask opposite ear by rubbing your finger and thumb together beside it.

9 (glossopharyngeal and vagus nerves): back of mouth, say ahh, uvula up in midline. Check swallowing. Gag normally not tested – if you do, test both sides. Unilateral absence abnormal, bilateral absence may be normal.

11 (accessory): shake and shrug shoulders. Observe sternomastoid and trapezius at rest for wasting, fasciculation, or dystonia. Look sideways, try to return head against resistance. Compare strength of shoulder shrug on each side. Rarely useful, unless confirming site or suspected lesion. Always test neck extension if diffuse muscle weakness – if abnormal indicates lesion above C1/C2.

12: Hypoglossal nerve. Tongue. Examine at rest then protrude. If fasciculation → motor neuron disease. Deviates towards the weak side. Push tongue into check against your finger. Try rapidly alternating movements of protruded tongue or rapid la-la-la.

Motor Examination

- **Observation** for congenital maldevelopment, wasting, fasciculation and abnormal movements (tremor, chorea, myoclonus, dystonia).
- **Assessment of tone**: resistance to passive movement (must be relaxed). ↑Tone due to:
  - Rigidity (Basal ganglia): uniform resistance to slow passive movement, may be jerky (cogwheel rigidity). Affects flexors and extensors equally.
  - Spasticity (upper motor neuron). Rapid passive movement → maximal tone to start with, decreases suddenly as muscle is lengthened. Most marked in flexors of arms and extensors in legs. Due to reflex contraction to muscle stretch.
  - Clonus: maintaining stretch (eg of ankle plantar flexors) → further repetitive beating.
- **Power**: compare between sides
  - Test in position where patient has mechanical advantage: you shouldn’t be able to win then if it’s normal.
  - Grade as follows:
    - 0: no contraction
    - 1: a flicker/trace of contraction
    - 2: active movement with gravity eliminated
    - 3: active movement against gravity but not against resistance.
4: active movement **against gravity and resistance, but reduced power** (ie *can be overcome*; covers wide range – can classify as mild, moderate or severe weakness)

5: normal power

**Motor exam of the arms:**

- Observe arms at rest, then outstretched with eyes closed (check for drift – non-specific test). Look for wasting of 1st dorsal interosseus and abductor pollicis brevis
- Assess tone at elbow (flexion/extension and supination) and wrist (flexion/extension) with slow and rapid movements
- Arms (start at top and work down)
  - Shoulder abduction (deltoid, C5, axillary nerve). Arms out like chicken wings – push it down
  - Elbow flexion (biceps, brachialis, C5-6, musculocutaneous nerve) – pull me in
  - Elbow extension (triceps, C7, radial). Arm bent up in front - push me out
  - Wrist extension. (Extensor carpi ulnaris and radialis, C6-7, radial nerve). Extended ‘cocked’ wrist – push it down
  - Finger extension (extensor digitorum, C7). Fingers straight out – push them down just distal to MP joint
  - Finger flexion (flexor digitorum, C8). Try to uncurl curled up fingers
  - Abduction of index finger (ulnar nerve, T1, dorsal interosseus)
  - Abduction of thumb (median nerve, T1, abductor pollicis). Try and push raised thumb down into palm. Look for atrophy of thenar eminence

**Motor Exam of the legs:**

- Observation of legs: while standing, walking, lying down. **ALWAYS** observe posture and gait: movement of arms, stride length, broadness, smoothness. Stand with eye’s closed and feet together (Romberg test).
- Look for wasting of tibialis anterior and small muscles of feet
- Check for tone
- Check for clonus. Flex hip and knee to 45 degrees, externally rotate hip, rapidly dorsiflex foot and hold. Two or three beats of clonus may be normal if symmetrical
- **Power in Legs** (patient lying down):
  - Hip flexion (ilio-psoas, L1-2, lumbar plexus). Push down on raised straight leg
  - Hip extension (gluteus maximus, sciatic nerve, L5-S1). Lift ankle of straight leg
  - Knee Extension (quadriiceps, femoral n, L3-4). Bend knee, try to push ankle in
  - Knee Flexion (hamstrings, sciatic nerve, L5 – S1)
  - Ankle dorsiflexion (tibialis ant peroneal n, L4 – 5): push on top of foot while toes raised
  - Ankle plantarflexion (gastrocnemius, sciatic nerve, S1 – 2): push on bottom of foot
  - Ankle inversion (tibialis ant & Post, peroneal and tibial n, L4 – 5). Patient bends foot in and try and pull it back
  - Ankle eversion (peronei, peroneal nerve, L5 – S1): Patient bends foot out and try and pull it back
- **Rapid leg tests:**
  - If they can walk on their heels, then no foot drop (L5 or common peroneal)
  - If they can walk on their tiptoes, then no S1 lesion (plantar-flexion)
  - To test proximal leg function, crouch and stand up

**Differentiating Upper and Lower Motor Neuron lesions**

<table>
<thead>
<tr>
<th></th>
<th>Upper</th>
<th>Lower</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weakness</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Tone</td>
<td>↑ (unless acute), Spasticity or Rigidity (mainly Parkinson’s)</td>
<td>↓</td>
</tr>
<tr>
<td>Wasting</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Reflexes</td>
<td>↑ (unless acute)</td>
<td>↓</td>
</tr>
<tr>
<td>Fasciculations</td>
<td>No</td>
<td>Yes</td>
</tr>
</tbody>
</table>

**Reflexes**

- **Key is for them to be relaxed**
- **Arm (Clench teeth if no response):**
  - Biceps (C5/C6)
  - Triceps (C7)
  - Supinator (C5/C6)
  - Can also do finger reflex if suspect C8 lesion: tap your fingers while placed over outstretched fingers of face up hand. Often normally absent
- **Leg (if no response, interlock fingers of both hands and pull just before tap)**
  - Patella (hold knees up) (L3/L4)
Ankle (passively dorsiflex ankle) (S1). 3 ways: hand on dorsum of foot and tap hand, directly on Achilles tendon, or kneel on chair with foot hanging off, tap Achilles tendon (most sensitive)

- Grading reflexes:
  - 0: absent
  - +: just present
  - ++: brisk normal
  - +++: very brisk

- Plantar responses: put patient at ease! Normal response is plantar flexion (down). If upper motor neuron lesion, big toe up and other toes fan out (Babinski). Not positive if withdrawal response (hip and knee flexion) due to over response

- Superficial Abdominal reflexes: Not tested routinely. Stroke lightly with sharp object in each quadrant towards midline. Normal reflex is contraction. Tires quickly

Co-ordination

- Rapid alternating movements of hand: supinate and pronate hand rapidly (dysdiadochokinesia)
- Finger-nose-finger test. Make sure pt’s arm is fully outstretched when testing. Not too fast (may mask intention tremor)
- Heel-knee-shin test
- Heel-toe walking: tests midline cerebellar vermis
- Romberg: tests dorsal column sensory loss (ie proprioception). Rare in clinical practice
- Important syndromes including ataxia (incoordination of movement):
  - **Cerebellar haematoma**: Sudden onset of progressive headache, vomiting, and inability to stand or walk. Later progressive drowsiness, lateral gaze palsy from pontine compression. Decompressive surgery can be lifesaving
  - **Wernicke's Encephalopathy**: confusion, ataxia, nystagmus. 6th nerve palsy. On recovery: impaired short-term memory, confabulation. Common with prolonged vomiting, poor nutrition, not confined to alcohol

Sensory test

- Issue is where and why to test. What do you expect to find? Do this last so you have some idea what to look for. Very easy to suggest to patient
- Common scenarios:
  - Hemisensory loss: stroke, peripheral root and nerve lesion
  - Glove or stocking: spinal cord lesion or peripheral neuropathy
- Get patient to close eyes. Stimulate at irregular intervals so patient can’t anticipate them. Test from abnormal to normal. Don’t try to completely map – just test key boundaries
- Key Dermatomes:
  - Stand on S1
  - Sit on S3
  - Groin: L1
  - Umbilicus: T10
  - Nipple: T5
  - T2 meets C4 on line connecting axilla: should be clear difference across this line in any lesion between T2 and C4
  - Middle Finger: C7
- Position sense: hold big toe by the sides, explain which way is up and down, then test. Has low yield in practice. Try functional test: can they stand up with eyes closed?
- Vibration: 128 Hz fork. On bony prominences (what do you feel?). Move up until its positive. Bunion → medial malleolus → tibial tuberosity → anterior iliac spine. Test fingers for completeness. First sensation to go in progressive deterioration
- Pinprick: Use large safety pin and discard after use. Toes, fingers, face (no more unless suspicious, eg ↓ reflexes). Is it sharp or blunt? Can alternate sharp and blunt end to see if they can tell the difference. More reliable than light touch if both damaged
- Temperature: Not usually done if pin prick done
- Light touch (cotton wool)
- Others (not routine):
  - Two point discrimination
  - Stereognosis: recognising objects by their feel (coin, key, etc). Normal hand first
  - Graphaesthesia: write numbers on the hand
- Sensory inattention: touch sides separately and together – which is being touched?

10 Minute Neuro Exam – RP
- Wash your hands.
- Introduce yourself to the patient, and ask permission to examine them.

**Mental State**

| AMT | 1. Time to nearest hour  
|     | 2. Year  
|     | 3. Age  
|     | 4. Date of birth  
|     | 5. An address - for example 42 West Street - to be repeated by the patient at the end of the test  
|     | 6. Name of hospital, residential institution or home address, depending on where the patient is situated  
|     | 7. Recognition of two persons - for example, doctor, nurse, home help etc – “do you know what I do?”  
|     | 8. Year first world war started  
|     | 9. Name of prime minister  
|     | 10. Count backwards from 20 to 1  
| Score of < 6 = dementia |

**Cranial Nerves**

<table>
<thead>
<tr>
<th>I</th>
<th>Not routinely tested</th>
</tr>
</thead>
</table>
| II | 1. Test for visual neglect w simultaneous movements in corresponding areas of R + L hemifields  
|     | 2. VA + with pinhole (snellen → counting fingers → hand movements → light; 6(distance)/3(can read at 6 what people at this d can normally read; smaller fraction = worse)  
|     | 3. Visual fields  
|     | 4. Pupillary reaction to light + accommodation (PERLA)  
|     | 5. Examine fundi  
|     | 6. Colour vision |

| III |  
|     | ● Observe eye position + ptosis + nystagmus  
|     | ● Test eye movements + diplopia  
|     | ● Test saccades + gaze holding/nystagmus = test ability to make + sustain voluntary eye movements: R, L, up, down, using finger + nose as targets (eg look at my finger [which is out to the R, L, up, down alternately], look at my nose)  
|     | ● Pursuit eye movements = test ability to pursue smoothly a target – eg your finger, horizontally from side to side |

| IV | As for III |

| V | Sensory: light touch + pinprick in V1, V2, V3; corneal reflex if relevant (?BS or 5th CN lesion);  
|   | Motor: jaw opening - lateral deviation. Masseter + temporalis strength |

| VI | As for III |

| VII | Eyebrow raising, forcible lid closure, showing teeth, filling cheeks with air with lips closed |

| VIII | Whispered voice in each ear while masking other ear; if deafness check Weber’s + Rinne’s |

| IX | “Ahhhh” – symmetrical SP + uvula movement; cough – demonstrates adduction of both vocal cords |

| X | As above |

| XI | Shrug shoulders (traps); rotate head against force (SCM) |

| XII | Inspect tongue resting (wasting, fasciculations) + on protrusion (deviation) |

**Tone**

| Inspect | Wasting, fasciculations, involuntary movements |
| Arms + legs | For spasticity, hypotonia + for rigidity |
| Clonus | Relaxed movements of ankle then sudden dorsiflexion |

**Power**

Isolate joints and get pt to move against gravity first; also, allow movements from position of strength eg elbow flexion from already partially flexed position |

| Shoulder | Abduction |
| Elbows + wrists | F + e |
| Fingers | Extension at MCPJ + flexion at DIPJ (grip fingers) + finger abduction (w fingers adducted + examiners hand against index finger – ask to push index finger out against examiners fingers) |
| Thumb | Abduction (in plane through index finger perp to palm [push down to the ground] – detects median nerve or C8/T1 weakness) |
| Hip + knee | F + e |
| Ankle | Inversion + eversion, dorsiflexion + plantarflexion (preferably by rising on tip toes) |
**Coordination**

<table>
<thead>
<tr>
<th>Test</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Finger-nose test</td>
<td>Walk on heels then on toes – tests balance + strength</td>
</tr>
<tr>
<td>Heel-shin test</td>
<td></td>
</tr>
<tr>
<td>Heel-toe (tandem) walking</td>
<td></td>
</tr>
<tr>
<td>Eyes</td>
<td>Evaluate symmetrical eye movements (as above) + presence of nystagmus</td>
</tr>
<tr>
<td>Alternating hand movements</td>
<td>For dysdiadachokinesis</td>
</tr>
</tbody>
</table>

**Reflexes**

<table>
<thead>
<tr>
<th>Test</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Deep tendon</td>
<td>Ankle jerk (S1, S2), knee jerk (L3, L4), supinator + biceps (C5, C6), triceps (C7, C8)</td>
</tr>
</tbody>
</table>

**Sensation**

<table>
<thead>
<tr>
<th>Test</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ask</td>
<td>The pt to outline (ie draw with finger) any areas of sensory loss</td>
</tr>
<tr>
<td>Vibration</td>
<td>Toe + thumb</td>
</tr>
<tr>
<td>Proprioception</td>
<td></td>
</tr>
<tr>
<td>Light touch</td>
<td>Over face, distal dermatomes of hands + feet, testing distal dorsum of fingers + toes just prox to nail bed</td>
</tr>
<tr>
<td>Pinprick</td>
<td>Don’t get pt to try and discriminate between the two (too confusing)</td>
</tr>
</tbody>
</table>

**Gait**

<table>
<thead>
<tr>
<th>Test</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inspect</td>
<td></td>
</tr>
<tr>
<td>Other tests</td>
<td>Romberg, heel-toe walking etc</td>
</tr>
<tr>
<td>Antalgic gait</td>
<td>Weakness of hip abductors – pelvis falls towards unsupported side + swinging limb too low to clear the ground. Pt compensates by leaning away from unsupported side. Due to neuromuscular weakness post THJR, CDH etc</td>
</tr>
<tr>
<td>Trendelenberg gait</td>
<td>Hips adducted + internal rotated so that thighs rub. Ankle plantarflexed – tip toe walking. Caused by SC d</td>
</tr>
<tr>
<td>Anserine gait</td>
<td>Bund-like waddle – seen in pts w muscular dystrophies. Bilat abductor weakness, take short steps tilting body side to side</td>
</tr>
<tr>
<td>Foot drop</td>
<td>High stepping gait – inability to dorsiflex ankle. Footslap seen. Causes = LMN disease, peripheral neuropathy</td>
</tr>
<tr>
<td>Spinal stenotic gait</td>
<td>Stiff legged w circumduction + reduced toe clearance. Progresses to wide-based, unsteady, shuffling + spastic gait as lumbar impingement leads to reduced proprioception</td>
</tr>
<tr>
<td>Spastic paraplegic gait</td>
<td>Hips adducted + internal rotated so that thighs rub. Ankle plantarflexed – tip toe walking. Caused by SC d</td>
</tr>
<tr>
<td>Sensory ataxia</td>
<td>High stepping gait, wide based, foot slap. Loss of proprioception. Caused by neuropathy (syph in times past)</td>
</tr>
<tr>
<td>Cerebellar gait</td>
<td>Unsteady, staggering, cautious. Sway side to side. Wide based. Caused by cerebellar d or ETOH intoxication</td>
</tr>
<tr>
<td>Hemiplegic gait</td>
<td>Stiff, foot dragging gait. UL shows adduction + flexion, LL extended + foot internally rotated – affected leg swung (circumduction) + upper body tilts to unaffected side to allow this to happen. Cause = hemispheric CVA</td>
</tr>
<tr>
<td>Apraxic gait</td>
<td>Hesitation in starting + short shuffling steps. Frontal lobe lesion</td>
</tr>
<tr>
<td>Parkinsonian gait</td>
<td>Frozen gait. Axial rigidity, shuffling, freezing episodes, turning en bloc (shuffling slowly around), forward leaning.</td>
</tr>
<tr>
<td>Malingered gait</td>
<td>No objective signs of neuro dysfunction, no pattern</td>
</tr>
</tbody>
</table>

**Cognitive Functions**

**Localised Cognitive Functions**

- Dominant hemisphere:
  - Speech, reading and writing
  - Calculation
  - Praxis (higher motor control of learned movement)
- Non-dominant hemisphere:
  - Neglect: visual, auditory, tactile
  - Dressing or constructional apraxia (impaired planning/sequencing of movements not due to weakness, incoordination, or sensory loss; due to dissociation of parts of the cerebrum, often parietal lobe)
  - Visuo-perceptual: object recognition (fragmented drawings) and faces (Prosopagnosia)
  - Prosody: expressive aspects of speech

**Attention/Concentration**

- Depends on the reticular activating system, thalamus, frontal and medial temporal lobes
- Test: orientation in time and place, serial subtractions, spelling WORLD backwards etc
Memory

- **Implicit**: learned responses, reflexes and motor skills
- **Explicit**:
  - Episodic:
    - Left hippocampus: verbal, right visuo-spatial, faces, etc
    - Temporally specific personal experiences
    - Lost in diffuse brain disease (dementia) and bilateral limbic disease (amnesic syndrome)
  - Semantic:
    - *Facts, concepts, words, meanings* (eg object naming, what do you cut bread with, etc)
    - In the **temporal** neocortex (left)
    - Lost in dementia
  - Working memory:
    - *Very short term recall*: words, numbers, melodies
    - Under *frontal lobe executive control*: important for dual task performance
    - Patients can have damage to just one of working or long term memory (eg Korsakoff)
    - Psychosis patients have normal working memory, but cannot make:
      - New memories (anteriograde): Word list learning
      - Retrieve long-term memories: recall public events, autobiographical details

Higher Cognitive Function/Executive Function

- Situated in the **pre-frontal area** (non-motor frontal lobes)
- Functioning best established from informants and observation
- Clinical features of frontal lobe lesions:
  - **Poor planning**: can’t initiate and carry out a sequence of actions to complete a goal, can’t do two things at once
  - **Can’t control impulses**: irritable, irascible
  - Deterioration of personal relationships, social habits and hygiene
  - Dulling of curiosity and vitality, jocular, puerile
  - Lack energy

Cerebellar Disease

- **DANISH**:
  - Dysdiadachokinesia
  - Ataxia (unsteadiness or incoordination of limbs, posture, and gait; a disorder of the control of force and timing of movements leading to abnormalities of speed, range, rhythm, starting, and stopping)
  - Nystagmus
  - Intention tremor/overshoot
  - Slurred speech
  - Heel-toe walking/hypotonia

Common Peripheral Nerve Lesions

- Patterns of presentations:
  - Unilateral defined areas of weakness/sensory loss in hand or foot
  - Peripheral neuropathy
  - **Paraparesis**: weakness of both legs. Rare but critical. Usually spinal cord lesion
  - Muscle disease (rare): initial proximal pattern of weakness – neck flexion, shoulder abduction, hip flexion
  - **Hemiparesis** due to stroke: 1/day in Wellington (this one is not peripheral)
- Hand:
  - Common Lesions:
    - **Ulnar** neuropathy: Elbow compression → weakness of finger but not thumb abduction. Thumb adduction weak (paper test). Weakness of long flexors of 4th and 5th fingers. Wasting of interossei. Sensory loss on little finger
    - **Median** nerve compression in Carpal Tunnel Syndrome: weakness and wasting of abductor pollicis brevis, with numbness of palmar surface of fingers 1, 2, 3 and lateral 4. Tingling/pain which wakes at night
    - **C7 Radiculopathy**: pain from neck, shoulder, arm and forearm. Weakness of *elbow, wrist and finger extension*
    - **C6 Radiculopathy**: *Weakens elbow flexion and wrist extension*. Sensory loss of dorsolateral forearm, thumb and index finger
- **Radial nerve** (Saturday night Palsy): Unable to dorsiflex the wrist or extend fingers or thumb.

  - **Less Common Lesions:**
    - Peripheral neuropathy: weakens small muscles of the hand, glove sensory loss
    - T1 root lesion: Weakness of small hand muscles, sensory loss on medial arm and often Horner’s syndrome

- **Leg:**
  - **S1 Radiculopathy:** Pain in back, buttocok, thigh, leg, and foot, numbness of the lateral border of the foot. Mild **weakness of eversion and plantarflexion**, depressed ankle jerk
  - **L5 Radiculopathy:** Pain in back, buttocok, thigh, leg, and foot, numbness of medial border of the foot and big toe, **weakness of inversion and dorsiflexion**. No reflex change
  - **Common peroneal nerve lesion from compression at the fibula head:** Painless, severe weakness of dorsiflexion and eversion, with normal inversion, and numbness on the lateral foot and dorsum of the foot. Maybe sudden onset with severe **footdrop**. Ankle jerk normal. 80% of nerve palsies causing foot drop recover over 3 – 4 months. Differentiating foot drop:

    | Common Peroneal Lesion | L5 Lesion |
    |------------------------|----------|
    | Ankle jerk             | OK       |
    |                        | May be depressed (normally S1) |
    | Inversion              | OK       |
    |                        | Weak     |
    | Eversion               | Weak     |

**Brain Anatomy**

- **Grey matter anatomy:** neurons + glia (astrocytes – support neurons + gliosis, oligodendrocytes, microglia)
- **White matter anatomy:** glia (astrocytes, oligodendrocytes, microglia, myelin sheaths)
- **Ventricular system anatomy:** ependymal cells line ventricles, choroid plexus produces CSF
- Revise it!
- **Cerebro-spinal Fluid – CSF:**
  - Made in choroid plexus on floor of lateral ventricles and roof of 3rd ventricle
  - Flow: Lateral ventricles →foramen of Munro (intraventricular foramen) →3rd ventricle →Aqueduct of Sylvia →4th Ventricle →via 3 foramen to cisternal spaces of subarachnoid space →arachnoid granulations →venous sinuses
The Spinal Tracts

Ascending tracts
- Fasciculus gracilis
- Fasciculus cuneatus
- Anterior spinocerebellar tract
- Lateral spinocerebellar tract
- Anterior spinohlamic tract

Descending tracts
- Lateral corticospinal tract
- Rubrospinal tract
- Anterior reticulospinal tract
- Olivospinal tract
- Vestibulospinal tract
- Tectospinal tract

- Often called the posterior white columns
- Carry discriminative touch and conscious proprioception

- Lead to the thalamus, the pathway for crude touch, pain, temperature, pressure

- From the spinal cord to the cerebellum
- Carry subconscious proprioceptive stimuli
- Proprioception is "body sense" and "muscle sense", the perception of body position and muscle position necessary for coordinating movements

- These tracts come from a variety of locations in the brain, as a group are termed the "extra-pyramidal tracts", and are generally associated with balance and muscle tone

- The corticospinal tracts carry voluntary motor stimuli from the cerebral cortex to motor neurons in the spinal cord. They are also called the "pyramidal tracts" because some of them cross in the pyramids of the medulla
Intracranial Haemorrhage

- Usually due to:
  - Trauma: typically extra/epi-dural or subdural
  - Spontaneous (usually due to cerebrovascular disease): brain parenchyma and subarachnoid

### Intracranial Haemorrhage

<table>
<thead>
<tr>
<th>Location/Type</th>
<th>Cause</th>
<th>Features</th>
</tr>
</thead>
<tbody>
<tr>
<td>Epidural haemorrhage</td>
<td>MMA damage 2 to skull trauma (often #)</td>
<td>Blood accumulates in potential space b/w periosteum + bone under art P. Effects seen within hours</td>
</tr>
</tbody>
</table>
| Subdural haemorrhage | Tearing of bridging veins (as brain is floating but bridging veins are fixed) | 1. Blood accumulates in potential space b/w dura + arachnoid under venous P. 
   2. More common in old (atrophy) + young 
   3. Effects seen after ~48hrs |
| Intracerebral haemorrhage | Hypertension – rupture of charcot-bouchard microaneurysms Can also be seen after fat embolism following long bone # | 1. >60yrs 
2. Most central (lacunar infarct – small infarcts in deeper parts of brain: BG, thalamus etc) 
3. Sudden death from mass effect or rupture into ventricles |
| Subarachnoid haemorrhage | 1. Berry aneurysm rupture 
2. Extension of haematoma into SA space 
3. Rupture of hypertensive haemorrhage into ventricles | Diffuse blood over the surface of the brain. NB. CSF collected in series of 3 tubes one after the other – if RBC count drops in tube 3 = traumatic tap. Xanthochromia (yellow - bilirubin) indicates previous haemorrhage |

Adapted from Hayman et al. and Maix and Thomke.
4. AVM  
5. Bleeding disorders

**Extradural Haemorrhage**
- Due to head trauma, especially with skull fracture (although not necessary in children)
- Lentiform shaped arterial bleed (⇒ high pressure ⇒ rapid progression)
- Skull fracture leads to one of:
  - Blood from middle meningeal artery forces its way between dura and inner table of skull (normally intimately related) – rapid, displacing cerebral tissue → herniation
  - Laceration of dural venous sinus → slow, delayed findings, less dense, less common
- Dura fixed at sutures so doesn't go past these (eg will be bounded by coronal and lambdoid sutures)
- Dura has two layers: the outer forming the internal periosteum of the calvarium, the inner forming the septae which compartmentalise the calvarium

**Subdural Haemorrhage**
- Following trauma: 50% also have a brain injury (swelling, contusion, laceration, etc)
- Bleed from bridging vein into the space between the arachnoid and dura mater (low pressure ⇒ slower progression)
- ↑Risk in old people due to relative cerebral atrophy
- Traverses right round the inside the calvarium: cresenteric shaped bleed, very flat (may need to look carefully to distinguish from the skull)
- Most common location is over the lateral aspects of the cerebral hemispheres
- Poor prognosis due to large size and associated brain injury
- Classification:
  - Acute < 3 days
  - Subacute 4 – 21 days
  - Chronic > 21 days (eg minor injury in elderly, hypodense (blood broken down), lots of midline shift
- If not detected, the haematoma undergoes organisation → granulation tissue. This can rebleed

**Subarachnoid Haemorrhage**
- Into the space between the arachnoid mater and pia mater – where CSF is
- Bleed may be focal, or diffusely spread through subarachnoid space (will flow into sulci and be bilaterally symmetrical)
- Incidence: 15 per 100,000
- Signs/symptoms: sudden severe headache, loss of consciousness, meningism (neck stiffness, vomiting, photophobia, fever), maybe focal neurological signs, fundi
- Spontaneous: ruptured aneurysm (70%), Arteriovenous Malformation (AVM, 10%), hypertensive bleed, bleed into a tumour, hypocoeagulable state
- Traumatic: injury to leptomeningeal vessels, rupture of intracerebral vessels, contusion, laceration
- Aneurysm:
  - 2% post mortem pts; rupture most common in 5th decade
  - Aetiology unknown – HTN + smoking RF or IEL abnormalities
  - Mostly situated in branch points of COW
  - Associated with connective tissue disorders (eg Marfan’s) and PCKD
  - Mostly saccular rather than fusiform
  - Saccular: due to ↓elastic laminar (?)congenital = Berry Aneurysm. No muscle layer and thickened hyalinised intima
  - Fusiform: due to atheromatous degeneration
  - Mycotic: due to septic emboli – usually more peripheral in brain
  - Dissecting: may extend either from aortic dissection or from internal carotid artery (complication of angiography)
  - 85% in the anterior circle of Willis. Posterior communicating artery → unilateral 3rd nerve palsy (dilated pupil, ptosis, etc)
- Arterio-venous malformations:
  - Localised developmental failure → shunt from an artery to a vein → gradually dilates → distension of veins under arterial pressure
  - Most in the territory of the middle cerebral artery
  - Can present with haemorrhage or epilepsy
Investigations: CT, CSF if CT not helpful and no risk of ↑ICP (make sure blood is not from a bloody tap)

Treatment:
- Analgesia, rest (maintain normotensive)
- Rebleeding: 30% die from 1st bleed, 60% from rebleed (25% within 2 wks)
- Clip or endovascular coiling
- Vasospasm: 5 – 15% have stroke due to vasospasm (peak 3 – 10 days post bleed) despite all treatment. Cause: ?oedema around vessels → compression. Prevention with fluids, drugs (CCBs – nimodipine) and monitoring electrolytes

Complications:
- Acute: if intraventricular extension → ependymitis → obstruction of aqueduct → acute obstructive hydrocephalus. Also cerebral oedema and vasospasm of the affected artery (→ infarct). Rebleed
- Delayed: fibroblast proliferation in arachnoid space and at granulations → communicating hydrocephalus

Hypertensive Intracerebral Haemorrhage
- Mainly due to rupture of small penetrating vessels secondary to hypertension – which causes:
  - Hyaline arteriolar sclerosis in small arteries and arterioles → weakening of vessel
  - Minute aneurysms (Charcot-Bouchard microaneurysms)
- Main sites are in the BG + BS + cerebellum: putamen, thalamus, pons, cerebellum (lacunar infarcts)
- → Haemoma → compression → brownish discolouration of surrounding tissue

How Old is Blood on a Film
- On CT:
  - < 24 hours: homogenous high density lesion, well defined margins, prognosis related to size of clot
  - Then oedema develops, ↑ the mass effect, less homogenous
  - First week is hyperdense cf brain tissue (clotting → contracting)
  - 2 – 3 weeks isodense
  - 3 – 4 weeks is hypodense cf brain tissue. Breakdown of haemoglobin → ↑osmotically active particles → water diffuses in
- On MRI:
  - T1: fluid is black: hypointense
  - T2: fluid is white: hyperintense
  - If contrast enhancement → ring enhancement, then either an abscess or metastatic deposit

Stroke
- = The acute onset of focal or global neurologic deficit presumably of vascular origin lasting > 24 hours (WHO)
- Includes ischaemic stroke, intracerebral haemorrhage and subarachnoid haemorrhage
- Aetiology:
  - Risk in NZ in 65 – 74 is 1:100, in 85+ is 1:30
  - 80% due to atheroma, thrombosis and embolism, especially following heart (recent MI, AF, RF disease) or vessel pathology
  - Nearly half the people having a new stroke are already in institutional care or needing help with daily activities
  - 25% of strokes are in people who have had a previous stroke
- Differential to stroke: TIA, Migraine, Trauma, space occupying lesion (sub-dural haematoma, tumour, abscess), infections, hypoglycaemia, delirium, MS and spinal cord pathology/injury
- Isolated signs seldom due to a TIA or stroke: dizziness, unconsciousness

Site of Lesion
- Site of lesion:
  - 75% hemisphere
  - 25% posterior circulation
  - 20% lacunar
- Pathophysiology: Brain has high and constant need for blood supply
- Signs of cerebral involvement:
  - Dominant hemisphere: language disorder (dysphasia; middle cerebral artery)
  - Non-dominant hemisphere: disorders of knowing (agnosia) and doing (apraxia), visual or sensory neglect
  - Loss of integrated cerebral function (eg cognitive impairment, memory, abstract thought)
  - Failure of inhibition of lower centres (eg spasticity and urinary incontinence)
  - Seizure activity: abnormal electrical activity in brain tissue around areas of ischaemia

Neuro-Sensory
Hemianopia

Classes:

1. Total anterior circulation infarction (TACI: Anterior = Carotid artery ⇒ anterior and middle cerebral arteries):
   - Language or visuospatial disorder (depending on side)
   - Homonymous hemianopia
   - Motor deficit in two or more of face, arm or leg
2. Partial anterior circulation infarction (PACI): 2 of 3 of TACI criteria
3. Posterior circulation infarction (POCI: Posterior = Basilar artery ⇒ posterior cerebral artery): variety of presentations, including ipsilateral cranial nerve palsy with contralateral motor and/or sensory deficit, isolated cerebellar dysfunction, isolated homonymous visual field defect

Common lacunar syndromes (small deep white matter infarcts):

- Pure motor hemiparesis
- Pure sensory abnormality
- Ataxic hemiparesis
- Sensori-motor stroke
- Dysarthria and clumsy hand

Signs of brainstem involvement:

- Diplopia, bilateral weakness or numbness, vertigo, ataxia

### Brainstem Syndromes

<table>
<thead>
<tr>
<th>Syndrome</th>
<th>Structures Affected</th>
<th>Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medial Medullary</td>
<td>Hypoglossal nerve (12)</td>
<td>Atrophy and paresis of tongue, deviates to ipsilateral side</td>
</tr>
<tr>
<td>(due to Ant. Spinal or Vertebral artery)</td>
<td>Medial lemniscus</td>
<td>Contralateral loss of discriminative touch and proprioception</td>
</tr>
<tr>
<td></td>
<td>Pyramid</td>
<td>Contralateral hemiparesis</td>
</tr>
<tr>
<td>Lateral Medullary</td>
<td>Spinal trigeminal n. &amp; tract</td>
<td>Ipsilateral loss of pain/temperature on face</td>
</tr>
<tr>
<td>(due to Vertebral, PICA, maybe AICA)</td>
<td>Spinothalamic tract</td>
<td>Contralateral loss of pain/temperature on body</td>
</tr>
<tr>
<td></td>
<td>N. ambiguous</td>
<td>Loss of gag reflex, dysphagia, dysarthria, swallowing problems</td>
</tr>
<tr>
<td></td>
<td>Inferior cerebellar peduncle</td>
<td>Ipsilateral ataxia</td>
</tr>
<tr>
<td></td>
<td>Vestibular n.</td>
<td>Nystagmus, vertigo</td>
</tr>
<tr>
<td></td>
<td>Dorsal motor n.</td>
<td>Vomiting</td>
</tr>
<tr>
<td></td>
<td>Descending sympathetic fibres</td>
<td>Ipsilateral Horner’s syndrome</td>
</tr>
<tr>
<td>Basal Pontine Syndrome</td>
<td>Abducens</td>
<td>Ipsilateral medial deviation of the eye</td>
</tr>
<tr>
<td>(due to Basilar and pontine arteries)</td>
<td>Facial</td>
<td>Ipsilateral paralysis of face</td>
</tr>
<tr>
<td></td>
<td>Medial lemniscus</td>
<td>Contralateral loss of discriminative touch and position sense</td>
</tr>
<tr>
<td></td>
<td>Corticospinal tract</td>
<td>Contralateral hemiparesis</td>
</tr>
<tr>
<td>Mediobasal mesencephalic syndrome</td>
<td>Oculomotor</td>
<td>Ipsilateral outward deviation of eye</td>
</tr>
<tr>
<td>(due to aneurysm of posterior Circle of Willis or Basilar)</td>
<td>Edinger-Westphal</td>
<td>Ipsilateral dilated pupil, no light reflex</td>
</tr>
<tr>
<td></td>
<td>Corticospinal tract</td>
<td>Contralateral hemiparesis</td>
</tr>
<tr>
<td></td>
<td>Red nucleus</td>
<td>Contralateral cerebellar ataxia</td>
</tr>
</tbody>
</table>

Transient Ischaemic Attacks (TIAs)

- 30% of untreated TIAs eventually have a stroke, aspirin reduces this by a quarter
- Presence of carotid bruit not sensitive for stenosis (ie can have stenosis without it, may not have significant stenosis with it)
- Surgery for carotid stenosis giving TIAs: beneficial if stenosis > 70%, ↓risk of ipsilateral stroke. Other studies less variable (NNT if asymptomatic = 17, if symptomatic then 6 – 7)
Angiogram morbidity = 1.5%, surgical morbidity 1.5 – 6.3% (if not vascular trained)

Management

- Investigations:
  - FBC: exclude polycythaemia and anaemia. Do electrolytes and renal function
  - ESR: exclude vasculitis
  - Glucose
  - ECG/CXR for heart disease, AF
  - CT – 5% don’t have a stroke, also exclude haemorrhage before antithrombotic treatment, and to assess for carotid surgery (>70% stenosis)

- Treatment:
  - Aspirin → small improvement in outcome if not haemorrhagic
  - Warfarin if mitral stenosis or AF
  - tPA if within 4 hours and there is visible evidence of infarct covering < 1/3 of MCA territory on CT
  - Immediate anti-hypertensive therapy only if hypertensive encephalopathy is suspected (will have papilloedema)
  - Assessment of swallowing by a speech-language therapist: 40% of hospitalised stroke patients have swallowing problems, can → aspiration. Gag reflex is not sufficient to indicate normal swallowing. Nil by mouth until assessed (ie for 12 – 24 hours) unless clearly dehydrated
  - Watch for cerebral oedema over next 24 hours if large stroke. Restrict fluids, iv mannitol
  - Early rehabilitation: turning to prevent bed sores, limiting bed rest
  - Assessment for depression (common following stroke) and urinary incontinence

Prognosis

- After 6 months, 1/3 are dead, 1/3 have moderate disability, 1/3 have good recovery
- Poor prognosis if haven’t started to make a good recovery after 2 weeks (acute assessment not reliable)
- Risk factors for poor prognosis: prior stroke, persistent incontinence, cognitive/perceptual deficits, poor previous functional status or social supports, poor sitting balance

Pathology Overview

- Ischaemic stroke:
  - Most common (85%)
  - Caused by:
    - 1. Thrombosis (atherothrombotic)
    - 2. Embolism
    - 3. Systemic hypoperfusion
  - RF: HTN, AF, atherosclerosis risk factors, vasculitis etc

- Haemorrhagic stroke:
  - Due to ruptured blood vessels (eg ruptured charcot-bouchard microaneurysms)
  - Intracranial/intracerebral bleed
  - Extracranial bleed (eg subdural, SA, epidural)
  - Caused by HTN
  - Reperfusion injury

- Brain undergoes liquefactive necrosis:
  - Loss of normal tissue architecture – resembles liquid – collapse of normal tissue structure
  - Areas of normal + areas of dead tissue
  - Gliosis (astrocyte proliferation (bright pink cytoplasm + large nucleus), foot processes extended, neovascularisation)
  - Cavitation ensues

Vascular Pathology

- Primary intra-cerebral haemorrhage:
  - Eg Sub-arachnoid haemorrhage or Intra-cerebral haemorrhage related to trauma
  - Due to high blood pressure or lobar haemorrhage (?due to amyloid deposition in vascular walls)

- Ischaemic stroke:
  - Thrombotic: occlusion – depending on collateral flow
- Embolic stroke
- Other: vasculitis, cerebral venous thrombosis, carotid artery dissection, etc

- Extent of infarction depends on:
  - Adequacy of collateral flow (via circle of Willis). *Little/no collateral flow for the deep penetrating vessels*
  - supplying the thalamus, basal ganglia, and deep white matter
  - Presence of previous occlusive lesions
  - Location and rapidity of the occlusive process

- Infarcts are of two types:
  - Haemorrhagic (red) infarcts
  - Non-haemorrhagic infarcts: pale, bland, anaemic

<table>
<thead>
<tr>
<th>Cerebral infarction</th>
<th>Macro</th>
<th>Micro</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute ischaemia</td>
<td>Collapse of normal structure – soft appearance; <em>blurring of grey-white matter interface</em></td>
<td>Red neurons – most prone to hypoxia</td>
</tr>
<tr>
<td>Early infarction</td>
<td>Area of pallor surrounding florid oedema</td>
<td></td>
</tr>
<tr>
<td>Liquefactive necrosis</td>
<td>Gliosis = gemistocytic astrocytes (↑in number, change in morphology – foot processes); macrophages eating dead crap</td>
<td></td>
</tr>
<tr>
<td>Old</td>
<td>Cavitation</td>
<td>Cavitation</td>
</tr>
</tbody>
</table>

**Thrombotic Infarction**

- = ischaemic stroke
- Arterial occlusion usually due to in-situ thrombosis from a plaque rupture, or emboli
- Most common sites for atherosclerotic involvement are:
  - Carotid bifurcation
  - Origin of the middle cerebral artery
  - Either end of the basilar artery

<table>
<thead>
<tr>
<th>Pathology</th>
<th>Imaging</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 24 hours</td>
<td>Cytotoxic intracellular oedema</td>
</tr>
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<td></td>
<td></td>
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<td></td>
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<tr>
<td>1 – 7 days</td>
<td>Tissue necrosis, maximal intracellular oedema, blurring of grey-white interface, tiny haemorrhagic infarcts</td>
</tr>
<tr>
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<td></td>
</tr>
<tr>
<td>7 – 21 days (Subacute)</td>
<td>Resolving oedema. Marginal capillary ingrowth. Progressive liquifications</td>
</tr>
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</tbody>
</table>

- Healing in the brain: don’t want scarring as the remaining tissue doesn’t need protection (it’s still within the skull) and scar contraction would damage surrounding tracts. So instead of scarring, you get gliosis and cavity formation

**Embolic Infarction**

- Mural thrombosis → emboli. Most common sources are plaques within the carotid arteries and cardiac mural thrombi
- Most commonly affects middle cerebral artery
- Embolus responsible for ischaemia lyses within 1 – 5 days → reperfusion into ischaemic brain (lost the ability to autoregulate)
- This leads to ↑ perfusion, especially of grey matter and basal ganglia (lots of capillaries). ↑Oedema (would be ↓if thrombotic) → ↑ mass effect. Cortical petechial haemorrhages. If these are extensive and merge → haemorrhagic infarct
- CT: previously hypodense become iso/hyperdense
Haemorrhagic Infarcts

- Usually secondary to embolic infarct
- Result from high reperfusion pressure, or following anticoagulation in thrombotic infarcts (e.g., heparin)
- May develop within 21 days following an embolic infarct
- Difference between haemorrhagic infarct and Intracerebral haemorrhage:

<table>
<thead>
<tr>
<th>Haemorrhagic infarct</th>
<th>Intracerebral Haemorrhage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inhomogeneous</td>
<td>Homogeneous</td>
</tr>
<tr>
<td>Wedge-shaped or rectangular</td>
<td>Round/Oval</td>
</tr>
<tr>
<td>Indistinct border</td>
<td>Sharp margins</td>
</tr>
<tr>
<td>Predominantly cortical</td>
<td>Predominantly white matter</td>
</tr>
</tbody>
</table>

Haemodynamic Infarcts

- **Global** ischaemia (as of focal cerebral ischaemia i.e., thrombotic or embolic infarct) = cardiac arrest, shock, hypotension → leads to **watershed/border zone infarcts** (seen in between vascular territories – least perfused areas)
- Border zone infarcts/watershed
- Vaso-occlusive disease + disturbed autoregulation → temporary uncompensated **decrease in perfusion pressure**
- Affects watersheds between vascular territories (may → haemorrhagic infarct), especially between the middle and anterior cerebral arteries
- Can lead to transient ischaemic attacks and infarction

Lacunar Infarcts

- **Hypertension** → arteriolar sclerosis of the **deep penetrating arteries** of the:
  - Middle cerebral artery → basal ganglia and internal capsule
  - Posterior cerebral and basilar communicating arteries → mid-brain and thalamus
- Arteriolar sclerosis → hyaline → disrupted lumen → small infarct → small round lacunae (hole)

Cerebral Venous Occlusion

- Confined to certain patients: pregnancy, post-partum, diabetes mellitus

Head Trauma

Types of Injury

- Effects of head trauma:
  - Direct trauma (e.g., under skull fracture)
  - Cerebral contusion (coup or contracoup)
  - Shearing: diffuse axonal injury → petechial haemorrhage in midbrain, corpus callosum and cerebrum
  - Cerebral swelling
  - Intracranial haemorrhage: epidural, subdural, subarachnoid, intracerebral
  - Concussion: no absolute definition but period of loss of consciousness and anterograde or retrograde amnesia
- Types of skull fracture:
  - Simple: linear of vault
  - Depressed
  - Compound: open to skin or sinuses
  - Skull base → rhinorrhoea or otorrhoea
- Principal injuries from acceleration/deceleration injury:
  - 1. Contusion: coup and contracoup
  - 2. Subdural haematoma from ruptured bridging veins
  - 3. Diffuse axonal injury (shearing injury). Ranges from concussion (very mild, temporary, physiological disturbance) to severe

Assessment

- **ABC**
- Gross assessment:
  - Localise injury by looking for lumps, depressed fractures, etc
  - **CSF** from nose or ears → basal skull fracture
  - Neuro assessment:
Use level of consciousness: **GCS** – best *response to verbal, motor and eye response*. See Glasgow Coma Scale (GCS)

- Also *pupillary size* and exam, limbs

- In diffuse injury the main enemy is ischaemia, which leads to oedema
- In localised injury, oedema is the main enemy – acts like a mass lesion
- Presume **cervical spine injury** until cleared:
  - Need 3 x-ray views: anterior, lateral and peg (open mouth to view facet joints of C1 and C2, and odontoid peg)
  - Clearance requires clear x-rays AND normal exam. If x-rays clear but tender C spine then CT
- Assess other systems
- Investigations:
  - Cervical spine x-ray, even if minor, for occult dens or cervical fracture
  - CT brain if GCS < 15, neuro signs in limbs, cranial nerve palsy or CSF leak
- Criteria for admission, etc:
  - **Discharge if GCS 15**, low velocity, no seizures or fractures, adequate supervision at home and readmission checklist given to patient
  - Admit if: loss of consciousness/marked post traumatic amnesia or under 5 or over 50
  - CT indicated if GCS < 15 at 4 hours or < 9 at any time, seizures or focal neurological signs
  - Neurosurgical referral if compound head injury or GCS < 15

**Raised Intracranial Hypertension (ICP)**

- Other causes of ↑intracranial pressure:
  - Bleeding
  - Neoplasm
- Brain oedema results from:
  - Inflammatory lesions
  - Infarction
  - Head injury
  - Neoplasms
- Types of brain oedema:
  - Vasogenic cerebral oedema: ↑permeability of cerebral vessels
  - Cytotoxic cerebral oedema: rare. Toxic effect → intracellular oedema
  - If severe acts as a space occupying lesions
- ↑ICP leads to displacement of CSF and compression of veins, then herniation of the:
  - 1. Cingulate herniation: cingulate gyrus under the falx
  - 2. **Uncal herniation** (transventorial herniation):
    - Uncus of the temporal lobe is forced into the *gap between the midbrain and the edge of the tentorium* → compression of *ipsilateral* oculomotor nerve → *fixed and dilated pupil*, and *collapses* the ipsilateral *posterior cerebral artery*, causing an infarct in its distribution
    - As the herniating uncus displaces the midbrain laterally, the *contralateral cerebral peduncle is compressed against the edge of the tentorium*, causing *ipsilateral paralysis*, another false localizing sign
    - Duret haemorrhage: caudal displacement of the brainstem and stretching of its vessels causes a variety of haemorrhagic lesions in the midbrain and pons (secondary brainstem haemorrhages - Duret) that can devastate the reticular activating substance and other brainstem centers, resulting in focal neurological deficits and coma
  - 3. **Tonsillar herniation**: cerebellar tonsils (tonsillar herniation) into the foramen magnum (fatal); duret haemorrhages
- Features of coning:
  - Transtentorial: progressive drowsiness followed by pupil changes
    - If unilateral cerebral swelling then stretching of ipsilateral 3rd nerve → ↓PS innervation (PS more sensitive)
    - If diffuse bilateral swelling involving brain stem then impairment of both sympathetic and parasympathetic → mid position, irregular pupils
  - Posterior fossa coning: headache, stiff neck, ↑BP, ↓pulse
- Treatment of intracranial hypertension:
  - Aim: Keep ICP low. Principle danger is ↑ICP → ischaemia, transtentorial herniation and coning
  - ABC:

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**Neuro-Sensory** 195
Maintain airway. If breathing OK then lateral position. 100% O2
Intubate if GCS < 9
Aim to keep CPP (Coronary Perfusion Pressure) > 70. CPP = MAP less the greater of ICP or JVP. Coronary blood flow = CPP / CVR (cerebral vascular resistance)
In general, keep BP normal:
- If hypotension then ↓perfusion pressure (bad)
- Use colloids to maintain BP at 120 – 160 systolic (don’t over-hydrate, especially infants)
- Diuretic: frusemide 40 mg iv
- Tilt head up → ↑venous return → ↓venous pressure → ↑perfusion pressure
- ↓O2 requirements by sedation (Propofol or barbiturates eg thiopentone) and cooling
- Hyperventilate → reduce CO2 to 30 – 35 mmHg → ↓cerebral blood flow → ↓cerebral blood volume → ↓brain volume → ↓ICP (but only for short term otherwise ischaemia)
- Cushing’s Reflex (bradycardia, ↑↑hypertension) kicks in when O2 falls below 20 mls/100g/min (Cushing’s triad = ↓HR ↑BP, irregular respiration)
- Mannitol 0.5 – 1g/kg over 20 mins iv if life threatening – draws fluid from brain, but also a diuretic, so watch for hypotension
- Intraventricular drain: drain fluid from ventricle if severe
- Evacuation of intra-cerebral bleeds
- Seizures: Clonazepam 0.25 mg/min up to 1 mg plus loading dose of phenytoin
- Nutrition, urine and bowel management
- Steroids not effective after head injury

Coma and Stupor
- Checking eyes:
  - Doll’s Eye: do eyes remain fixed on target when head is turned. Tests inputs from the neck muscles.
    Requires linking via medial longitudinal fasciculus of nerves 3, 4, and 6 on both sides
  - Vestibulo-Ocular reflexes: caloric response. 1 ml of ice water evokes nystagmus beating to the opposite side in a normal person. If unconscious, see only deviation without corrective nystagmus
  - In deepening diffuse coma without structural damage, the Doll’s eye disappears, then the Caloric response. If pupils still reactive then no coning

Due to Structural Damage
- Only if affecting brain areas required to maintain consciousness: usually infarct, bleed or inflammation
- Reticular Activating System: periventricular grey matter from mid pons up, including the hypothalamus and deep grey matter of both hemispheres
- Most supra-tentorial lesions produce coma due to oedema → compression of deep hemispheric structures (paramedian diencephalon)

Due to Diffuse Depression of Brain Function
- Usually metabolic encephalopathy
- Key differential from structural damage: pupillary reflexes retained
- Features: clouded consciousness, difficulty concentrating, altered sleep wake patterns
- Two basic types:
  - Delirium or acute toxic psychosis: agitated, hallucinatory, severely disorientated
  - Acute confusional state: quieter than delirium
- Immediate evaluation: Glucose, thiamine, Na, Ca, Creatinine, pH, PO2, PCO2, lumbar puncture, sepsis (septicaemia, lung, urinary tract, meningitis)
- Later: LFT, Sedatives, Blood and CSF culture, Electrolytes and Mg, Coagulation, EEG (absence status)
- Outcome:
  - Sedative drug poisoning: equivalent to GA and will recover with treatment
  - Other medical causes: depends on cause, severity and extent. Only 15% make a good recovery if in coma for more than a few hours
  - Traumatic: better outlook, related to age, 50% die (many instantly), if ophthalmologic signs of brain stem dysfunction then 90% die or remain vegetative

Vasovagal Syncope (Fainting)
- = Temporary loss of consciousness due to the sudden decline of blood flow to the brain
- Vasovagal syncope usually has an easily identified triggering event such as emotional stress, trauma, pain, the sight of blood, or prolonged standing
Due to reflex bradycardia and peripheral vasodilatation
- ↓cerebral blood flow:
  - Postural hypotension
  - ↓Cardiac output: arrhythmia, VT, periods of asystole (Stokes-Adam disease)
- NOT due to: TIA, hypoglycaemia, alcohol. These take longer to recover
- Onset is preceded by nausea, vomiting, pallor and closing in of the visual field
- Duration is less than 2 minutes
- Rare = incontinence, involuntary tonic-clonic movements and confusion after an episode
- Often groggy and unwell afterwards but not confused
- Myoclonus common (seizure like movements, vocalisations): only 10% motionless

Stokes-Adams Attacks
- Classical description of a Stokes-Adams attack is of collapse without warning associated with a loss of consciousness lasting a few seconds not minutes
- Stokes-Adams attacks are typically associated with complete heart block - however this condition also been described in other diseases such as tachy-brady syndrome

Abnormal Speech
- Types:
  - Dysphonia/dysarthria: problems with the mechanics, not ideas, of speech production (eg nerves involved in motor control, connective tissue disease, etc). Say ‘baby hippopotamus’
  - Broca’s (expressive) dysphasia: non-fluent speech with malformed words. Reading and writing are impaired but comprehension intact. Patients understand questions. Infero-lateral frontal lesion
  - Wernicke’s (receptive) dysphasia: empty fluent speech. Maybe mistaken for psychotic speech. Reading, writing and comprehension are impaired. Posterior superior temporal lobe lesion
  - Cerebellar disease: ataxia (incoordination) of the muscles of speech → slurred and irregular speech
  - Pseudo-bulbar palsy: UMN. Exaggerated jaw jerk, difficultly swallowing, maybe emotional liability. Due to upper motor neuron lesion above the mid pons due to bilateral CV disease, severe MS or motor neuron disease
  - Bulbar palsy: LMN eg facial nerve, Guillain Barre, etc

Assessment:
- If speech fluent, grammatical and meaningful or patient can repeat a sentence ⇒ dysphasia unlikely
- If the patient can comprehend simple instructions with several steps ⇒ Wernicke’s unlikely

Parkinson’s Disease
- Bradykinesia, tremor (70% of cases) and rigidity (unilateral onset) but no early difficulty with gait
- Also lack of arm swing (usually only one side at outset), lack of facial expression, paucity of movement, depression. 30% become demented (either due to Alzheimer’s or widespread Lewy bodies). Also postural hypotension
- Gradual progression and prolonged course
- Pathology:
  - Gross: Pallor of substantia nigra
  - Micro: ↓in melanin-containing dopaminergic neurones with secondary reactive gliosis. Lewy Bodies may be present in remaining neurones (eosinophilic intracytoplasmic inclusions)
- Treatment:
  - L-Dopa → dyskinesias, and on-off effects after 3 – 5 years. The mainstay of treatment. Give minimum dose to control symptoms, not necessarily signs
  - Carbidopa: prevents peripheral breakdown of L-Dopa
  - For younger patients, begin with a dopamine agonist (bromocriptine, pergolide)
  - Selegiline, a MAO-B inhibitor delays the time needed for the subsequent introduction of L-Dopa
  - Anticholinergics: stop ACh induced hyper-reactivity: but dry mouth, urinary retention, blurred vision
- Other causes of Parkinsonism. Parkinson Disease is a disease of exclusion:
  - Drug induced parkinsonism eg phenothiazines including antiemetics (eg Maxalon)
  - Multisystem atrophy: also have cerebellar ataxia, eye movement disorder, autonomic dysfunction and pyramidal signs
  - Huntington’s Disease: early presentation may mimic Parkinson’s, rather than a movement disorder with chorea, myoclonus and dystonia
  - Wilson’s Disease: consider in younger patients. Behaviour disturbance, dystonia, flapping tremor. Rare but treatable
Diffuse Lewy Body Dementia: Males 2:1. All demented eventually. Most have rigidity, bradykinesia but tremor uncommon. Usually begins with cognitive impairment. See Dementia, page 731

**Dystonias**
- A movement disorder characterised by inappropriate and involuntary muscle movements
- Sustained muscle contractions cause twisting and repetitive movements or abnormal postures
- There is impairment of muscle tone resulting in an abnormal posture with excessive contraction of antagonist muscles. A limb is usually held in an extreme of flexion or extension. Facial muscles and the tongue may be involved
- Most dystonias are caused by basal ganglia disturbance
- Blepharospasm:
  - Causes eyes to close all the time, especially in light, wind, etc
  - Tx: inject botulinum toxin
- Hemifacial spasm
- Cervical dystonia: neck turning, head back, etc

**Demyelinating Disease**
- Selective, primary destruction of myelin
- Diseases of CNS and PNS myelin do not affect the other
- CNS Demyelinating disease:
  - Multiple Sclerosis
  - Acute Disseminated Encephalomyelitis
  - Progressive Multifocal Leucoencephalopathy (PML)
  - Toxins
  - Leucodystrophies
- PNS Demyelinating Diseases:
  - Guillain-Barre Syndrome:
    - GBS is a heterogeneous grouping of immune-mediated processes generally characterized by motor, sensory, and autonomic dysfunction
    - In its classic form, GBS is an acute inflammatory demyelinating polyneuropathy characterized by progressive symmetric ascending muscle weakness, paralysis, and hyporeflexia with or without sensory or autonomic symptoms
  - Diphtheria
  - Diabetes Mellitus
  - IgM Paraproteinaemia
  - Leucodystrophies
  - Hypertrophic neuropathies (eg Charcot-Marie Tooth Disease)
- Secondary Demyelination:
  - Infarction
  - Abscess
  - Contusion/Compresssion

**Multiple Sclerosis**
- Chronic autoimmune demyelination of CNS (not PNS) neurons
- Epidemiology:
  - Female to male = 2: 1
  - 1/800
  - Peak age of onset 20 to 40 years
  - Marked racial difference in susceptibility. Caucasian most common. Africans/Asians rare
  - Genetic risk modified by environmental risks up to age 15 (from studies of immigrants)
  - Risk 15 times higher if first degree relative with MS. Associated with HLA-DR2 haplotype
- Can be sensory or motor
- **Diagnosis: two lesions** in different places at different times. Lesions normally visible on MRI
  - “Neurologic defects separated in time due to white matter lesions (at least 2) separated in space”
- One spinal cord lesion may account for diffuse symptoms. As it grows through a spinal cord column a single lesion may progressively affect other areas
- Highly variable course. Relapsing and remitting
- Worse after exercise
- Clinical features:
- Optic neuritis
- Neurogenic bladder dysfunction (urgency is common)
- Impotence
- Sensory deficits (tingling in a restricted distribution e.g. spreading up a leg and resolving over a few weeks)
- UMN defects (most commonly spastic weakness of legs)
- Cerebellar involvement (ataxia, dysarthria, nystagmus)
- Vertigo

- Pathology:
  - **Autoimmune destruction of oligodendrocytes + myelin sheath**, triggered by a viral infection in a genetically susceptible host
  - Multiple plaques distributed throughout the cerebral hemispheres (especially periventricular white matter), optic fibres, brain stem, cerebellum and spinal cord
  - Active plaques: are soft yellow or pink and granular. Myelin breakdown → foamy macrophages, T-suppressor cytotoxic cells, T-helper cells, and plasma cell infiltrate. Also reactive astrocytes
  - Chronic plaques: well defined, sclerotic and grey. Sharply defined areas of demyelination with compacted astrocytes processes (⇒ gliosis)
  - **Macro**: white matter lesions
  - **Micro**: luxsol fast blue stains myelin – will see pink around outside of plaque but pale on inside; macrophages + lymphocytes, ↓ oligodendrocytes
  - Poor correlation between number of plaques and symptoms

- Treatment:
  - β-interferons
  - Steroids
  - Plasmapheresis

**Progressive Multifocal Leukoencephalopathy (PML)**
- Like MS: multiple discrete foci of myelin destruction with relative preservation of axons
- Caused by JC virus (DNA papovavirus common in the community) in immunodeficient patients
- Relentlessly progressive
- Pathology: multiple lipid laden macrophages, oligodendrocytes with ground-glass nuclei (viral inclusions)

**Motor Neuron Disease**

**Amyotrophic Lateral Sclerosis (ALS)**
- Most common form of progressive Motor Neuron Disease
- Affects upper motor neurons (i.e. layer five of the motor cortex) and lower motor neurons (anterior horn cells)
- 1 – 3 per 100,000 per year
- 5 – 10% autosomal dominant, rest sporadic
- Cause unknown
- Clinical presentation:
  - **Lower motor neurons**: fasciculations, progressive wasting of muscles, bulbar involvement → difficulty chewing etc, weakness of respiratory muscles
  - **Upper motor neurons**: spasticity, muscle stiffness, hyperreflexia
  - Sensory, bowel, bladder, ocular movements and cognitive functions relatively preserved
  - Median survival 3 years

- Pathology:
  - Neurons shrink and accumulate lipofuscin (lipofuscin is a brownish pigment left over from the breakdown and absorption of damaged blood cells)
  - No macrophage or inflammatory response
  - Disappearance of axons in corticospinal and corticobulbar tracts → astrogliosis → lateral sclerosis
### Other CNS Degenerative Diseases

<table>
<thead>
<tr>
<th>Degenerative disease/Dementia</th>
<th>Features</th>
<th>Pathology</th>
</tr>
</thead>
</table>
| **Alzheimer’s disease**      | ~ 10% familial – earlier presentation, multiple genetic defects | Gross = cerebral atrophy (widened sulci due to ↓gyri mass)  
1. Neuritic plaques (neurofilaments w amyloid core)  
2. Neurofibrillary tangles (neurofilament protein in cell bodies)  
3. Amyloid angiopathy (amyloid deposits in small vessels - congophilic) |
| **Lewy Body disease**        | ~ 20% of dementia cases 3 overlapping disorders:  
1. Parkinson’s  
2. ANS failure  
3. Dementia | Lewy bodies: abnormal protein aggregates + ubiquitin with cytoplasmic inclusions (round + pink bodies seen) |
| **Parkinson’s disease**      | ↓ SN melanin-containing DA-producing cells | Lewy bodies |
| **MID**                      | Stepwise deterioration in cognitive function  
RF are as for atherosclerosis, HTN particularly, AF | Multiple lacunar infarcts manifest as small cavities |
| **Pick’s disease**           | Uncommon, clinically similar to AzD | 1. Frontal atrophy ++  
2. Abnormal tau gene – microtubular abnormalities |
| **Huntington’s disease**     | 1. Autosomal dominant CAG triplet repeat of h. gene on Ch 4  
2. Age 20-50 (next gen will see earlier onset of d)  
3. Chorea (involuntary motor s + s) + dementia | 1. Decreased basal ganglia + loss of brain tissue  
2. Ventricles appear dilated |
| **Spongiform encephalopathy**| • CJD, Kuru, Scrapie, BSE  
• PrP – normal protein in neurons – undergoes conformational change to β-pleated sheets → induces more change | 1. Increased vacuoles (spongiform)  
2. Gliosis  
3. Decreased neurons |

### Epilepsy
- See Seizures, page 958 for Epilepsy in Childhood, Benign Febrile Convulsions and Anoxic Seizures
- 1:200
- Onset after age 20 ⇒ 10% chance of tumour
- Very long list of differentials to epileptic seizure: See Other Spells, page 204
- Hard to differentiate (i.e. between epileptiform + non-epileptiform): going blue, frothing at mouth and incontinence can happen in pseudo-seizure. Epiletics may not have post-ictal phase
- **Gold standard is EEG**: but can’t do this in A&E. Fall back is checking whether the person is in any way aware (then it can’t be generalised) – eg localising to pain (sternal rub, squeeze thumb nail), drop their hand onto their face

### Approach/Framework
- ALWAYS use this pattern!
• Is it a seizure (epileptiform)/What are the symptoms?
  ➢ When do the seizures occur? What happened before the seizure?
  ➢ Does patient know they’re going to have a seizure? Are there any visual, olfactory, other sensations at the beginning?
  ➢ What can the patient recall (before/during/after)?
  ➢ During: Detailed description from observers:
    o Are they aware – will they respond?
    o Are there automatisms?
    o Is there dystonic posturing?
    o How long did it last?
  ➢ After the seizure:
    o Are they confused?
    o Can they speak?
    o Any post-ictal Todd’s (weakness on one side/limb)?
    o Bitten tongue/lips?
    o Incontinence?
  ➢ Check history: evidence of brain injury, infection, on anticonvulsant meds
  ➢ Any other types of seizures:
    o Any absence (ever stop in middle of what they’re doing, go blank)?
    o Any myoclonic jerks (like jerk when going to sleep, only during the day)?
    o Any GTCS

• Seizure location:
  ➢ Frontal: focal tonic or clonic motor activity, posturing, prominent motor automatisms but no orofacial or experiential automatisms
  ➢ Central: focal clonic seizures with preservation of awareness
  ➢ Temporal: experiential, gustatory or olfactory hallucination. Motion arrest, automatisms
  ➢ Parietal: exclusively somatosensory manifestations
  ➢ Posterior: polymodal sensory, visual, auditory or somatosensory hallucinations

• If the seizure was epileptiform, what is the cause?
  ➢ 1. Epilepsy
    o Recurrent unprovoked seizures
    o Common – 0.5-1% incidence; 5% have isolated seizures
    o Multiple number of disorders under the title, “epilepsy”
    o The majority of people who have 1 seizure will never have another; majority who have 2 seizures will have more
    o Genetic:
      ➢ Known genetic or presumed genetic (e.g. channelopathies)
      ➢ Seizure core symptom
    o Structural/metabolic:
      ➢ Distinct other condition that is associated
      ➢ Acquired (stroke, trauma, infection)
      ➢ Genetic (TS, MCD – separate disorder between epilepsy and genetic defect)
    o NB. Syndrome = age + seizure type + clinical features + examination + EEG findings
  ➢ 2. Benign febrile convolution (age 6/12 – 72/12)
  ➢ 3. Single seizure
  ➢ 4. Acute symptomatic seizure:
    o An “epileptic” seizure that occurs in a normal brain with normal cells
    o There is an insult to the cells which results in a seizure
    o Examples: infection (meningitis/encephalitis), trauma (acute HI), metabolic (hypoglycaemia, hypocalcaemia), hypoxic, drug OD/withdrawal, vascular (CVA)
  ➢ Any of the above could be either generalised or focal (see below)

• What electroclinical/epilepsy syndrome does this pt have?
  ➢ Clinical entities which are reliably identified by a cluster of electroclinical characteristics:
    o Age
    o Seizure type
    o Clinical features (including FHx, PMHx eg meningitis, development)
    o Symptoms
    o EEG findings
    o Prognosis
If patient does not fit one of the well-recognized syndromes then epilepsy can be described by aetiology and seizure types but this is not a syndrome

Non-epileptic events:

- Physiological
  - Syncope (vasovagal + cardiac)
  - Migraine
  - Sleep-related (night terrors, sleep myoclonus, head banging, narcolepsy)
  - Movement disorder (tics, paroxysmal dyskinesias, ataxias)
  - Other (vertigo, rigors, GOR, apparent life-threatening event, delirium)

- Psychological
  - Behavioural events i.e. Pseudo-seizures
    a. Pseudo-seizure (or Non-Epileptic Seizure): either factitious disorder (are deliberately faking) or conversion disorder (they think it’s real) (See Somatoform Disorders, page 731)
    b. Pseudo-seizure more common in women (10:1) and those with a medical connection (eg doctor/nurse in family, someone with epilepsy)
  - Panic attacks
  - Mannerisms
  - Stereotypies
  - Self-stimulation
  - Day dreaming

Epileptic seizures happen more if:

- Tired
- Ill, fever
- Stressed
- Not taking medication (but these are not classified as ‘provoked’ as they wouldn’t provoke a seizure in a normal person)

Seizure Types

- Generalised: bilaterally symmetrical without local onset
  - Awareness is lost
  - Originate at some point within and rapidly engage bilaterally distributed networks (can be asymmetrical)
  - Generalised Tonic Clonic (Grand Mal) Seizures:
    o Seconds-minutes (<5min)
    o Tonic phase: 10 – 20 secs – extension phase then tremor begins – repetitive relaxation of tonic contraction. May be expiratory noise (e.g. scream)
    o Clonic phase: usually 30 seconds, random movements (starts fast, low amp, then slow and large amp), tongue often bitten
    o Often sigh at the end and become floppy
    o Post-ictal confusion or sleepiness
    o May be incontinent or bite tongue
    o May be clonic-tonic-clonic

- Absence (Petit Mal) Seizures:
  o Characteristic type of absence attack
  o Sudden onset
  o Childhood or adolescent onset, associated with 2.5-4/sec spike and wave on the EEG
  o Loss of awareness: blank stare and unresponsive for 5 – 15 seconds
  o No post-ictal confusion or sleepiness
  o May also have automatisms (lip smacking, chewing, blinking) and mild clonic motion (usually eyelid movement at 3 Hz).
  o May be induced by hyperventilation
  o 80% have no further seizures after 20 years old. Can also have atypical absence seizures
  o Treat with ethosuximide or sodium valproate

- Atonic:
  o Complete, sudden loss of tone lasting seconds
  o Completely collapse, may injure themselves
  o Often not much post-ictal confusion or sleepiness
  o Loss of awareness
  o May be subtle (i.e. just head)

- Tonic: Sustained contraction, maybe with fine tremor
- Myoclonic: Sudden, very brief (<1s) jerk but still generalised
- Clonic: Rhythmic jerking
- Infantile spasms:
  - Sudden bilateral symmetrical jerk, extensor or flexor. Can be subtle, come in clusters
  - Usually around 3 – 6 months, boys > girls
  - May grow out of the spasms
  - Bad prognosis: cerebral palsy, retardation, etc
  - Medical emergency: try to urgently get them under control
- Unclassified seizures:
  - Spasms: clusters of brief sustained contractions which occur during drowsiness
  - NB. Spasms = rapidly ↑ amplitude of muscle activity followed by rapidly ↓ amplitude

- Focal: Begin locally
  - Previous terminology = simple + complex partial seizures + secondarily generalised tonic clonic seizure
    - Simple partial seizures = consciousness is preserved
    - Complex partial seizures = focal seizures in which consciousness is altered (eg blank unresponsiveness followed by automatisms, eg lip smacking, other semipurposeful activity) – usually temporal lobe but may be frontal. Can go on for minutes. Aware it is coming (cf absence which is sudden)
    - Partial seizure secondarily generalised: they have an awareness first
- New terminology = focal:
  - Without impairment of consciousness or awareness
    - With observable motor or
    - Autonomic components or
    - Involving subjective sensory or psychic phenomena only
  - With impairment of consciousness or awareness (dyscognitive) – altered awareness during seizure = “with impairment” i.e. doesn’t need to be completely unaware
    - Evolving to a bilateral convulsive seizure
- Localising it:
  - The beginning is what is important for localisation
  - Preceding aura: olfactory, visceral, auditory, visual, déjà vu
  - Lateralising features:
    - Unilateral clonic, tonic or dystonic (contraction of agonist and antagonist muscles – might happen in one arm/hand, giving clue to location) posturing
    - Post-ictal Todd's Syndrome/Paresis: if they have one area of weakness after a seizure (ie one hand weaker than the other) then it started locally
  - Non-lateralising features → automatisms:
    - Automatisms can be either reactive (altered response to something happening eg dystonia) or innate (seizure spreads to part of brain triggering a movement/action – will always be the same)
    - Generally indicate a lack of awareness
    - Automatic behaviour is usually seen in complex partial seizures: but can be in absence (petit mal) seizures. Eg Oral or manual automatisms

**Treatment**

- Diagnosis is clinical. EEG helps with severity, classification, to localise a surgically remediable abnormality (eg hippocampal sclerosis), and to differentiate pseudo-seizures
- Don’t treat until you’re sure it’s epilepsy
- Anticonvulsants suppress seizure activity in 80%
- Principles of drug treatment:
  - When to treat: often wait for second seizure – although treatment after the first → ↓ occurrence, but no long term change in outcome
  - Use only one drug
  - Tailor drug to seizure type
  - Introduce slowly. Takes about 5 days to stabilise a change in dose
  - Monitor drug level: for other than phenytoin, this is to check compliance. Beware – plasma level at which seizure control is obtained is variable
  - Consider withdrawal of drugs after 2 years without seizure, slowly over 6 months
- Mode of action unknown – but may ↓ GABA breakdown, as well as modifying flux of Na, K and Ca ions
- Usual drugs:
  - Idiot’s guide: carbamazepine for partial seizures and Valproate for generalised
### Seizure type

<table>
<thead>
<tr>
<th>Partial Seizures</th>
<th>Examples of conventional drugs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Simple partial,</td>
<td>Carbamazepine (<em>Tegretol</em>),</td>
</tr>
<tr>
<td>Complex partial</td>
<td>Phenytoin, Sodium Valproate</td>
</tr>
<tr>
<td>Partial secondarily generalised</td>
<td>(Epilim), Penobarbitone, Primidone</td>
</tr>
</tbody>
</table>

### Generalised seizures

| Absence          | Clonazepam (a BZD), Ethosuximide, Valproate |
| Myoclonic        | Valproate |
| Tonic-clonic     | Carbamazepine, Phenytoin, Valproate, Penobarbitone, Primidone |

- Conventional drugs have hepatic clearance
- Side Effects:
  - General lethargy, ↓concentration, unsteadiness, dizziness
  - ↑LFTs: but serious hepatotoxicity rare. Especially Valproate
  - Rarely bone marrow suppression
  - Pregnancy:
    - Epilepsy often worsens during pregnancy
    - Plasma concentration of drugs falls due to pharmokinetic changes and ↓compliance
    - Teratogenic: 3% risk of malformation on 1 drug (also, epilepsy itself can be teratogenic - hypoxia during seizure)
    - % in breast milk varies by drug
  - Specific drugs:
    - Carbamazepine: enzyme inducer
    - Phenytoin: Dose-dependent kinetics → small ↑ in dose may → ↑↑ in plasma concentration, SE: ataxia, peripheral neuropathy, gingivitis
- Must be seizure free (with or without treatment) for **12 months** before you can drive. **Obliged to tell LTSA on diagnosis if the patient won’t and continues to drive**

### Status Epilepticus

- Repeated seizures without regaining consciousness
- No one knows how long is too long: but **after 10 minutes ↑risk of damage**
- If not sure whether it’s epileptiform then must still treat for status
- Treatment:
  - Protect and maintain airway, insert oral airway
  - Prevent injury
  - 100% oxygen
  - Diazepam 10 – 20 mgs iv, not exceeding 2 – 5 mgs per minute. If no iv access give rectally with 10 – 20 ml normal saline. Duration is brief and another anticonvulsant is required. Avoid repeating diazepam → cardiorespiratory collapse. If no response give clonazepam 1 – 4 mg iv
  - Phenytoin 50 mg/min iv (25 mg/min in cardiovascular disease), usual adult dose 1250 mg in 100 mls saline over no more than 20 minutes. Monitor BP and heart rate
  - If established, give phenobarbitone
  - If refractory, then anaesthesia with propofol or thiopentone. Taper after 12 – 24 hours

### Other Spells

- Commonly misdiagnosed as seizures – see non-epileptic events
- Paroxysmal non-epileptic events **without** altered consciousness: Jitteriness, *migraine with focal aura*, hyperventilation, *acute paroxysmal vertigo*, shuddering attacks, *anxiety states* (eg panic attack), psychosis, drug induced dystonias, masturbation, tics, etc
- Paroxysmal non-epileptic events **with** altered consciousness: Day dreaming, *breath holding spells*, reflex syncope, TIAs, psychosis, pseudo-seizures, delirium, metabolic disorders, other brain insult (infection, haemorrhage), ritualistic movements, migraine, arrhythmias, drugs substance abuse
- Paroxysmal non-epileptic events related to sleep: benign sleep myoclonus of infancy, head banging, night terrors, hypnogogic jerks, sleep walking, sleep apnoea

### Brain Tumours

- CNS tumours:
  - **Bimodal age distribution** (more common in young + old)
  - 70% of childhood tumours in post fossa; 70% of adult tumours in cerebral hemispheres

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*Neuro-Senosry* 204
Childhood tumours are generally tumours of immature cell origin (e.g., medulloblastoma or low grade astrocytoma).

### Brain Tumours

<table>
<thead>
<tr>
<th>Type</th>
<th>Features</th>
<th>Macro</th>
<th>Micro</th>
</tr>
</thead>
<tbody>
<tr>
<td>Astrocytoma</td>
<td>- Can see in brain or SC</td>
<td>Well diff, often child</td>
<td>I: PXA (pleomorphic xanthoastrocytoma): → Rosenthal fibres (pink/red)</td>
</tr>
<tr>
<td></td>
<td>- 80% of primary adult brain tumours, 4th-6th decade</td>
<td></td>
<td>II: Diffuse fibrillary: increased cellularity but still mostly well</td>
</tr>
<tr>
<td></td>
<td>- Seizures, HA, focal neuro signs</td>
<td></td>
<td>differentiated</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>III: Anaplastic: increased cells, pleomorphic, mitosis, gemistocytic</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>astrocytes</td>
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<td></td>
<td></td>
<td></td>
<td>IV: GBM:</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>1. As above + increased vascularity +</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>2. Palisaded necrosis (cells palisade around necrotic area) +</td>
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<td></td>
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<td></td>
<td>3. Glomeruloid bodies (vascular endothelial proliferation - looks</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>like kidneys)</td>
</tr>
<tr>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Oligodendroglioma</td>
<td>- 15% of primary brain tumours</td>
<td>Well circumscribed</td>
<td>1. Increased # + size of oligo</td>
</tr>
<tr>
<td></td>
<td>- 1p, 19q deletions, can use FISH to dx</td>
<td></td>
<td>2. Fried egg appearance of oligo</td>
</tr>
<tr>
<td></td>
<td>- 4th-5th decade</td>
<td></td>
<td>3. Fine vasculature (chicken-wire)</td>
</tr>
<tr>
<td></td>
<td>- Symptoms as above</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>- Slower growing than astro</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ependymoma</td>
<td>- Arise near ventricles (4th + SC)</td>
<td></td>
<td>[Rosettes (red cells 'rosette' around BVs)]</td>
</tr>
<tr>
<td></td>
<td>- Generally low grade</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Medulloblastoma</td>
<td></td>
<td></td>
<td>1. Small blue cells</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>2. Cyto features of malig</td>
</tr>
<tr>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Meningioma</td>
<td></td>
<td></td>
<td>1. Whorling of cells</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>2. Psammoma bodies (calcium)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>3. Hypercellular with similar size +</td>
</tr>
</tbody>
</table>
Most attached to dura
- Grade II: atypical, >4 mitotic fig per HPF, recur
- Grade III: anaplastic (malig), >20MF/HPF, recur

3. Homogenous shape nuclei

Mets
- From lung, breast, melanoma, kidney, GIT

Seen in vessel territory, often multiple and at grey-white matter junction

**Epidemiology**
- 2% of all cancer deaths
- 20% of paediatric neoplasms (21 per 100,000 at 2 years)
- Incidence 8 – 10 per 100,000 per year
- Incidence lowest in teens rises to 16 per 100,000 in 70’s

**Histology**
- Cell types in the brain:
  - Neurons
  - Microglia (lymphocytic derived, phagocytic function)
  - Oligodendrocyte (myelination)
  - Choroid cells (make CSF)
  - Astrocytes (structural support, star shaped, multiply in sites of injury)
  - Ependymal cells (line ventricles)
  - Meningothelial cells
  - Pituitary, lipophages (histiocytes which phagocytose lipid rich myelin – non-specific marker of white matter destruction)
- Neuropli = intercellular matrix in the CNS – tangled processes of neurons, astrocytes, oligodendrocytes
- Tumour → vasogenic oedema
- Incidence of neoplasms:
  - Neuroepithelial (ie intrinsic brain cells) → Gliomas: 52%  
    - Astrocytoma: 44%. When severe = Glioblastoma Multiforme (GBM)  
    - Ependymoma 3%  
    - Oligodendroglioma: 2%  
    - Medulloblastoma: 3%
  - Metastatic 15% (eg breast, lung)
  - Meningioma: 15%
  - Pituitary: 8%
  - Vestibular Schwannoma: 8%
  - Also retinoblastoma
- Different incidence in children:
  - Normally posterior fossa (as opposed to anterior fossa in adults) and different frequencies of different types
  - Most common tumours are pilocytic astrocytoma and medulloblastoma

**Astrocytoma**
- Locally invasive
- Presentation:
  - ↑ICP from obstructive hydrocephalus and from space occupying lesion
  - Focal neurological deficit
  - *Epilepsy*: % of high grade astrocytoma present with seizure
  - Endocrine
- By age:
  - Cerebral hemispheres in middle and old age
  - Spinal cord in young adults
  - Cerebellum and pons in childhood
- Pathology:
  - Benign = won’t recur if removed. However, also need to be accessible to have a good prognosis
  - Heterogeneous – range from well-differentiated to anaplastic
  - Graded from 1 (low grade, and hard to differentiate from reactive gliosis although these rarely produce a distinct mass) to 3 (anaplastic) to 4 (glioblastoma multiforme – GBM, mitoses common compared with
low grade, pallisading necrosis differentiates it from grade 3). Low grade have a tendency to become high
grade and are also hard to cure due to their infiltrative nature

- Grossly: Infiltrative. Either firm or soft/gelatinous. GBM is heterogeneous with focal haemorrhage and
  necrosis
- Pilocytic variant of astrocytoma: most common astrocytoma of childhood. Excellent prognosis. Cystic.
  Usually in cerebellum
- Astrocytomas (grade 3 or 4) are the most common gliomas to arise subsequent to radiotherapy (usually 5
  – 25 years later)

* Investigations: CT and MRI
* Management:
  - Dexamethasone: ↓vasogenic oedema → ↓ICP
  - Anticonvulsents → ↓seizures
  - MR spectroscopy → biopsy by framed stereotactic or image guidance
  - Surgery: debulking or macroscopic excision (only if not deep or eloquent areas otherwise too much
damage from surgery – use radiotherapy for these)
  - Arguments for macroscopic excision. High-grade gliomas weigh 100g at diagnosis = 10E11 cells. After
macroscopic excision will still have 10E10 cells. Effective radiotherapy →10E8 cells. Chemo/radio therapy
only kills cells in division

**Prognosis**
- For GBM: Median survival:
  - Without surgery, 17 wks
  - With surgery, radio and chemo, 51 wks
- For low grade glioma: 50% 5 year survival if total macro

**Other Neuroepithelial Tumours**
- Subendymal giant cell astrocytoma: associated with tuberous sclerosis
- Neuronal tumours: not common. Include:
  - Gangliocytomas
  - Gangligliomas: better prognosis
  - Cerebral neuroblastoma: Rare, in children. Resemble peripheral neuroblastomas – ‘small round blue-cell
tumours’
- Oligodendroglioma:
  - 5 – 15% of gliomas
  - Radiographically, well demarcated and often show calcification (key differential)
  - Grossly: gelatinous masses +/- cysts and/or haemorrhage
- Ependymoma: usually in fourth ventricle → outflow obstruction. Also in intramedullary portions of the spinal
  cord. Slow growing and not malignant but poor prognosis. CSF spread is common. Significant histological
  features: ‘true’ rosette and perivascular pseudo-rosette. Numerous subtypes
  lumen
- Pineal Neoplasma: Intrinsic tumours are Pineocytoma and Pineoblastoma. Germ cell tumours are the most
  common, including choriocarcinoma, teratoma, etc. Present with mass effects in men aged 20 – 40.
  Differential: lymphoma or metastatic cancer
- Hemangioblastoma: Highly vascularised, cystic tumours, mainly in the cerebellar hemispheres
- Craniopharyngioma: Arise from the epithelium of Rathke’s pouch – part of the embryonic nasopharynx the
  forms the anterior lobe of the pituitary. Present due to mass effects in children and adolescents. Histology:
  see keratin pearls.
- Primitive Neuroectodermal Tumours (PNETs):
  - Rare tumours in children arising from primitive glial or neuronal precursor cells. Aggressive and poor
    prognosis. Usually “small round blue-cell tumour” (differential includes lymphoma)
  - Medulloblastoma: a distinctive PNET. Occurs exclusively in the cerebellum, mainly in children, mainly as a
    midline mass. Cause CSF obstruction and spread via CSF
- Schwannoma: In the cranial vault, nearly all schwannomas are attached to the 8th cranial nerve in the
cerebellar pontine angle ⇒ acoustic neuroma
- Lymphoma: Either originated in the CNS or from systemic invasion (usually affect the meninges). Usually B-
cell lymphomas
Pituitary
- Pituitary Adenoma: benign neoplasm in anterior lobe of the pituitary
  - Present with either mass effects (including on the rest of the pituitary) and/or excess hormone secretion
  - At any age or sex, but most common in men aged 20 – 50
  - Classified on the basis of hormones they secrete by immunocytochemistry. Poor correlation between acidophils, basophils and chromophobes and the hormones secreted
- Carcinomas are rare. Diagnosis requires gross brain invasion or discontinuous spread

Metastatic Brain Tumours
- 20% have intracranial mets at autopsy
- In 15% primary organ not found
- Surgery for solitary met if primary site controlled or for symptomatic control or for diagnosis
- Most mets are carcinomas. 80% are due to (in ↓frequency): lung, breast, skin (melanoma), kidney and GI
- Prognosis:
  - Melanoma & lung solitary: < 30% 1 year survival
  - Breast solitary: 50%
  - Undetermined solitary: 50%

Meningioma
- 20% of primary intracranial neoplasms
- Incidence peaks in females aged 40 - 50
- Benign in 90 – 95%
- Occur anywhere round brain
- Well circumscribed → mass effects
- Histology: meningotheelial whorls and psammoma bodies
- Tx: surgical excision

Spinal Cord Syndromes
- Prognosis depends on time to treatment: speed is important
- Trauma:
  - Transfer to specialist unit within 24 hours unless medically unstable
  - Catheterise: bladder won’t work → urinary retention
  - Check underneath them before transferring. An unfelt pen or other object will cause a full thickness pressure sore during 2 hour transfer → 3 months to heal
  - 200 per year in NZ (same as severe HI). Mainly young men → long term disability, lots of ongoing psychological problems
- Brown-Sequard syndrome:
  - Due to hemisection of the cord
  - Is characterised by loss of ipsilateral motor function and TVP and contralateral loss of pain and temperature sensation
- Extrudal spinal cord compression (EDSCC):
  - Usually cancer. Also haemorrhage (epidural haematoma) or epidural abscess
  - Key questions: where is the lesion, what is the lesion (eg weight loss, past cancer history ⇒ cancer)
  - If there is a clear level below which there is sensory abnormality ⇒ spinal cord
  - If both legs then spinal cord (usually). Can be parasagittal meningioma (very rare)
  - Are arms normal? if so T2 highest possible level
  - If there are signs of an upper motor neuron lesion in the legs then it MUST be above the cell bodies of L3 – S5 in the conus of the spinal cord, which is at T12 vertebral level ⇒ if UMN lesion then it is in thoracic spine or above
  - 95% have pain at the site of compression → very good indicator. Tap gently down spinal cord with tendon hammer
  - Imaging: MRI
  - If can’t be completely sure it’s cancer MUST biopsy (eg chronic infection)
  - Cancers:
    - Lymphoma
    - Female: breast
    - Male: lung, sometimes prostate
• **Transverse Myelitis:**
  - Inflammation of spinal cord itself
  - Same symptoms as EDSCC, but no compressing signs on MRI (usually normal – NO mass lesion)
  - *Usually due to a demyelinating type inflammation – can be due to MS (= 2 demyelinating lesions in the CNS at different times and different places)*
  - Could also be sarcoidosis → granulomas and inflammation (very rare to only occur in spinal cord)

• **Corda Equina Syndrome (CES):**
  - Triad:
    - Leg weakness
    - Sensory loss
    - Sphincter problems (usually overflow not urgency – ie LMN)
  - Classic description: ‘saddle anaesthesia’ – anaesthesia in sacral dermatomes – eg feels like cotton wool when sitting on the toilet seat. May be only symptom. Usually bilateral
  - If due to central disc prolapse can be fixed if treated urgently **medical emergency**
  - 95% of disc prolapses are at L4/L5 or L5/S1: but most are laterally into nerve root, not central into cauda equina

• **Acute Inflammatory Demyelinating Polyradiculopathy (AIDP):**
  - = Guillian-Barre
  - = Demyelination of multiple peripheral nerves
  - Symptoms: ascending paralysis. Affects arms, legs and respiratory. Only a portion will get to ventilatory arrest, but can deteriorate very quickly ⇒ *test FEV1 4 hourly while normal (normal > 4 l), to ICU if < 2 l. (O2 saturation and PO2 won’t tell you till too late)*
  - Predominantly motor problem: unlikely to be AIDP if lots of sensory symptoms
  - Signs: **LMN and arreflexia** (arreflexia is a classic sign)
  - Tests:
    - Lumbar puncture: ↑protein but no ↑WBC
    - Nerve conduction studies: motor conduction < 30 m/sec (normal > 40 – 50 m/sec)
  - Treatment: **IV γ globulin and plasmapheresis** (plasma exchange). Heparin to prevent PE
  - Not related to Chronic Inflammatory Demyelinating Polyradiculopathy

**Headaches**

• See also Headaches, page 957 for Headaches in Children
• Recent onset of severe headache: the most common cause is idiopathic
• Ask about associations/antecedents
• Red flags:
  - Fever
  - Change in mental status/personality
  - Fits, focal neurological signs, sudden and severe
  - Affected by postural change, normally headache free, waking at night or in the morning with a headache
• Treatment: Ongoing unchanged tension or migraine headache: TCAs
• Differential of morning headache:
  - ↑ICP
  - ↑CO2 (eg sleep apnoea)
  - Diabetic going hypoglycaemic overnight

**Tension Headaches**

• **Most common** type of primary headache disorder
• Tension headache describes *a pain which has at least two of the following* characteristics:
  - Mild to moderate in severity
  - Bilateral
  - Often felt as a pressure or constriction
  - Not accompanied by significant systemic upset or neurological deficits
  - Not aggravated by routine physical activity such as walking or climbing stairs
• Episodes of headaches usually last from **30 minutes to 7 days**
• Nausea or vomiting does **not** occur but there might be either **photophobia or phonophobia** associated with the disease
• Cause of the headache cannot be attributed to another disease e.g. - post trauma, brain tumors etc
• The spectrum of severity includes:
Patients with mild and infrequent attacks who do not consider that they have a disease
Patients with daily, almost continuous, pain
- Tension type headaches may be seen together with migraine in some patients with frequent headaches
- **Triggered by stress** (as cf migraine triggers)
- Often a chronic daily headache, gradual onset (chronic)
- Sleep not disturbed, treat by ↓stress (massage, relaxation) ?Depression
- Types: post-coital, ergotamine misuse

**Cluster Headache**
- Clusters of extreme, recurrent non-throbbing deep pain in and around one eye, spreading onto the face
- Eye typically becomes swollen and watery and nasal congestion seen
- Attacks usually occur one or more times daily for 6-8 weeks, and then subside for months or years
- Attacks are more common at night
- They may be triggered by alcohol

**Migraine**
- Migraine is a syndrome characterised by:
  - Periodic headaches with complete resolution between attacks
  - An attack may be composed of the following stages:
    o 1. Prodrome
    o 2. Aura
    o 3. Headache
    o 4. Resolution
- The frequency of attacks is variable:
  - As high as several per week
  - As low as several per lifetime
- A prodrome is a vague change in mood or appetite
- An **aura** is a clear neurological symptom:
  - Visual disturbance
  - Motor or sensory disturbance
- In children, migraine is a diagnosis of exclusion
- Generally: visual symptoms, unilateral, throbbing, nausea
- Trigger factors: altered sleep, overexertion, menstruation, changes in stress, changes in weather, chemical trigger, chocolate
- Treat: ergotamine

**Other**
- **Facial structure**: eg TMJ dysfunction, sinusitis, NOT teeth
- **Neuralgia**: eg idiopathic, trigeminal neuralgia
- **‘True vascular headache’**: associated with TIA/stroke, artery dissection, giant cell arteritis
- **Associated with ↑ICP**: focal lesions, venous thrombosis, meningitis, severe hypertension
- **Acute**: ?meningitis, sinusitis, head injury, SAH
- Associated with post Lumbar puncture

**Myasthenia Gravis**
- **Antibodies to Ach receptors** → weakness, fatigue with repetition
- Affects **eye** movement in 15%
- Treatment:
  - Neostigmine/pyridostigmine: ACh-Esterase inhibitors
  - Immunosuppressives: Prednisone, azathioprine, cyclosporin
  - Take out thymus – many have hyperplasia or thymoma
- **Myasthenia Gravis Crisis**:
  - Triggers: Respiratory infection, change in medication
  - Respiratory failure due to weakness, can be insidious
  - Consider ICU admission and ventilation
- **Lambert-Eaton myasthenic syndrome**:
  - Autoimmune against pre-synaptic membrane Ca^{2+} channels: motor (proximal muscles 1^{st} eyes later) + ANS involvement (dry mouth,
constipation, impotence), Hyporeflexia which **improves after exercise**

- A/w small cell lung cancer
- **Rx:** IVIg.

**Other Neurological Emergencies**

- Meningococcal meningitis
- Temporal arteritis/Giant Cell Arteritis: See Giant Cell Arteritis/Temporal Arteritis, page 445

**Other**

- **Trigeminal neuralgia:**
  - Momentary **severe** shooting pain in one division of 5th nerve due to touching, chewing or speaking
  - Most are idiopathic but can be related to vascular compression of the trigeminal nerve
  - Responds to Tegretol (carbamazepine)
- **Locked-in syndrome:** **pontine infarction** → quadriplegia and variable loss of all reflex and horizontal eye movements. Vertical eye movement or eyelid movement may be the only means of communication
- **Cerebellar infarction/haemorrhage:** vertigo, headache, and abnormalities of eye movements (eg saccadic deficits). May lead to life threatening compression/coning of the brainstem

**Benign Intracranial Hypertension**

- Suspect in those with ↑ICP (?SOL) but no mass found on Ix.
- ** Px:** Obese women with chronic morning headache headache, blurred vision (with enlarged blind spot – papillodema).
- **Rx:** Weight loss, Acetazolamide, Loop diuretics, Prednisolone.
- Consider therapeutic LP - drain pressure.
- Chronic → ventricular-peritoneal shunt.

**Eyes**

**Anatomy**

- **Fovea:** dip in middle of retina. Only photoreceptors, neural connections heaped up around it
- **Macula:** ill defined area around fovea
- **Uvea = iris, ciliary body and choroid.** Iritis = anterior uveitis
- **Reflex pathway:** retina → optic nerve → optic chiasm → optic tract → lateral geniculate nuclei → optic radiation and brain stem → Edinger Westphal nucleus → 3rd nerve
History

- Common presenting complaints:
  - Loss of vision: blurred, double, distorted, field loss, glare, colour defect
  - Disturbance of sensation: pain, itching, photophobia. If sharp pain → surface, if throbbing pain → deeper lesion
  - Changes in appearance: red and/or discharge
- Associated symptoms
- Past ocular history: trauma, surgery, spectacles
- General medical history: diabetes, allergy, medications
- Family History: squint, glaucoma, refractive error
- Social History: Assess impact on function (eg work, hobbies, support, dependents). Also smoking → ↑incidence of cataract

Physical Examination

- Trying to work out where is the problem: refractive, obstruction of light through the transparent tissues of the eye, or neural problem
- Check for visual neglect (non-dominant hemisphere problem)

Visual Acuity

- One at a time. Wear glasses
- Snellen’s Chart: Distance of chart (normally 6 metres)/Distance they could read. Smaller fraction is worse
- If can’t see chart at all, then Count Fingers (CF) at X metres
- If can’t count fingers then Perceive Light (PL): flash torch on and off in eyes – can they see it
- Check with pinhole, if clearer ⇒ refractive error or corneal scarring, refer to optometrist. If worse ⇒ retinal pathology
- Also check colour, stereo vision
- Presbyopia – lose short vision not long

Visual Fields

- Test using red pin sitting close to pt, covering eyes in direct line

Eye Movement

- Look at neutral position, look at position of reflection of light from pupil
- Follow the finger
- Diplopia

Eyelid, Conjunctiva, Sclera, Cornea

- Be systematic: look for changes in shape, size, position, colour, transparency, is it focal or diffuse
- Using torch, fluorescein if indicated + magnifying glass
- Evert eyelids
- Ectropion/entropion

Pupils

- Pupil reflexes: To light and accommodation. Should be simultaneous and equal. Swinging light test: Alternate light from one eye to the other, swapping it quickly. Both pupils should stay the same. Sensitive and complete test of neural pathways. If this shows a problem, test for an efferent pupillary defect with the near reflex test
- Pupillary response to light and accommodation – relative difference between the 2 pupils
- Shape
- Horner’s syndrome

Ophthalmoscopy

- View video here
- Get patient to look at target a long way away: relaxes accommodation. Dim the light → dilation
- Dilate pupil with tropicamide (not atropine, T½ too long)
• Check for:
  ➢ **Red reflex** defects: eg cataract, intra-ocular blood
  ➢ Reduced transparency (compare two eyes)

• Cup and disk:
  ➢ Disk is 15 degrees nasal to fixation. To examine macula, get patient to look **directly** at the light
  ➢ Check disk for distinct margins and symmetry
  ➢ Physiology cup is blood vessels in the centre of the nerve – not nerves
  ➢ Normal cup to disc ratio < 1/3 (but lots of variation). Check it’s the same in both eyes
  ➢ Large and/or deep cup sign of glaucoma (vessels ‘diving into’ the cup) – especially if eyes different. **Large ratio**
  ➢ Papilloedema: non-inflammatory nerve oedema due optic nerve axon flow obstruction or ↑ICP → **red disk swelling towards you, blurred margins of disk** but no early visual loss. Venous obstruction may → haemorrhage. If bilateral then ↑ICP
  ➢ Papillitis: optic nerve head inflammation → swollen disk with visual loss. If unilateral then optic neuritis (↓colour vision, orbital pain), sarcoidosis, Tb, Syphilis, etc
  ➢ Pseudopapilloedema: occurs in hypermetropia, disc is smaller than normal and crowded

• Fundus pathology: maculopathy, optic neuropathy, retinal detachment
• Refractive errors: hard to focus on retina
• Arteries: narrow, bright red, windy. Veins: thicker, straight
• Amount of melanin in choroid layer → variation in pigmentation of retina. Deep green patch = coronial nevus (benign)
• Clinical usefulness depends on good instrument, good technique, knowledge of normal anatomy and normal variations

### Loss of Vision
- Is it bilateral or unilateral?
- Sudden:
  ➢ Ie woke up with it
  ➢ => **Vascular: central retinal artery or vein occlusion**, ischaemic optic neuropathy, vitreous haemorrhage, CVA, preretinal haemorrhage
- Suddenish:
  ➢ Over hours: Closed angle glaucoma
  ➢ Gradual over a few days: infection, inflammation, retinal detachment, optic neuritis, **temporal arteritis**
- Gradual:
  ➢ Months to Years
  ➢ Refractive, cataract, primary open angle glaucoma, age related macular degeneration, retinopathy (eg diabetes, hypertension)
- **Chronic visual loss:**

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<tr>
<th></th>
<th>Unocular</th>
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<td>Dilate for Fundoscopy</td>
<td>Malignant melanoma, optic atrophy</td>
<td>Maculopathies, optic atrophy, papilloedema</td>
</tr>
</tbody>
</table>
Refractive Errors

- Myopia: light focused in front of retina; can see objects nearer to them
- Hypermetropia: light focused behind retina; can see objects further away

Acute Visual Disturbance

- REFER ALL!
- Floaters/flashers = vitreous detachment, vitreous haemorrhage or early retinal detachment
- Horizontal field loss = retinal vascular problem
- Vertical field loss = abnormality posterior to optic chiasm
- Central field loss = macular abnormality
- Lack of light perception = central retinal artery occlusion
- Wavy lines + distorted objects progressing to central vision loss = disciform macular degeneration
- Remember VA only disturbed if macula involved

Gradual Visual Loss

- Refractive errors
- Corneal disease
- Cataracts
- Primary open angle glaucoma
- Age related macular degeneration – loss of pigmented cells of macula
- Diabetic maculopathy – proliferative + non-proliferative
- Hereditary degeneration eg retinitis pigmentosa
- Management of GVL = ensure good lighting, low vision aids (mag glass), psychosocial support

Age Related Macular Degeneration

- = Loss of visual acuity with peripheral vision intact
- Observe stippling and depigmentation of macular
- Can be uni or bilateral
• Age-related types:
  - **Dry** (atrophic) macular degeneration: *thinning of macula, gradual*. No cure. *Atrophy of photoreceptors, loss of outer nuclear layer*
  - **Wet** (exudative) macular degeneration: May be due to Choroidal Neovascular Membranes, *unilateral with onset over several weeks*. Straight lines appear wavy → refer as laser treatment slows progression

**Symptoms:** blurred central vision, distortion of straight lines

**Eye Trauma**

- **Mechanical:** blunt/sharp, superficial/penetrating
- **Chemical:** alkali the worst. *Local anaesthetic then irrigate for 30 minutes* (less time already irrigated before presentation). If not toxic nor significantly inflamed, if VA OK and no fluorescein staining then chloramphenicol eyedrops qid for 5 days
- **Radiation:** UV, thermal, arch flash. Comes on hours after exposure, is very painful. Eye is very red, multiple fine specks of fluorescein staining. Usually resolves in 24 hours. Treat as an abrasion (pad both eyes)
- **Hyphema:** blood in anterior chamber. Refer for opinion but don’t normally treat. Check for corneal abrasion, traumatic mydriasis, eye movements, blowout fracture of orbital floor, intraocular bleed
- **Penetrating Eye Injuries** can be missed by subconjunctival bleed. Always refer if at risk. If metal vs. metal, always do an xray otherwise blind from Fe toxicity. Also rose thorns. *Teardrop shaped cornea is a PEI until proven otherwise*. Refer immediately. Lie down, im antiemetic to prevent vomiting. Keep NBM
- **Distorted pupil:** penetrating injury until proven otherwise ⇒ nil by mouth, shield eye, antibiotics, antiemetic, refer
- **Foreign bodies:** remove with 25-gauge needle and topical anaesthetic drops. Steady fixation of eye is key. Always evert upper eyelid to look for further foreign bodies
- **Corneal abrasions:** *Very painful and photophobic*. Stain with fluorescein. Most heal within 24 hours. Refer if abrasion large or central, if cornea hazy, VA reduced or eye is very inflamed. Double pad eye well. Apply *chloramphenical* ointment stat and bd for 5 days. Never give anaesthetic drops to take home – can cause ulceration and blindness
- **Lid laceration:** sew up anything not penetrating, or not involving lid margin or tear drainage (refer these)

**Retinal Detachment**

- Higher risk in near-sighted (myopic)
- Can be caused by blunt trauma
- Due to *vitreous shrinkage*, tears/holes in retina (eg with age), or underlying pathology
- Symptoms: *sudden changes in vision* – watery or shadowy patch, *sudden ↑ in number of floaters* (spots in vision), *loss of visual field* (like a descending curtain)
- Need rapid treatment: seal tear with *laser*
- Causes:
  - Exudative detachment: accumulation of fluid under the retina due to leaky vessels, eg tumour, vascular abnormality
  - Traction detachment: vitreous becomes organised following trauma or neovascularisation and pulls on the retina

**Cataracts**

- **Lens opacity**
- Normal part of ageing, seen in DM, some congenital conditions, uveitis + post injury
- Symptoms depend on unilat vs bilat
- Symptoms = difficulty reading, recognising faces + TV watching, vision worsens in bright light, *halos*
- Signs = decreased VA, decreased red reflex, change in appearance of lens

**The Red Eye**

- Pain + loss of vision = corneal ulceration, iritis, acute glaucoma
- Purulent discharge = bacterial conjunctivitis – Rx *chloramphenicol* drops
- Clear discharge = viral or allergic conjunctivitis
- Two morphological types of red eye:
  - **Ciliary injection/flush** (deep vessels therefore bad; corneal/ant ch/iris) – REFER!!!!!
Appears as a red ring around the limbus of the cornea (the ciliary flush), and the individual vessels, which form a parallel arrangement, are not clearly visible.

Ciliary injection may indicate a more serious deep-seated inflammatory condition such as anterior uveitis or a deep corneal infection.

**Diffuse injection** *(superficial eg conjunctivitis)*

- **Different types of red eye**: conjunctivitis, scleritis + episcleritis (localised area of inflammation), corneal ulceration, iritis, anterior uveitis, acute angle closure glaucoma, subconjunctival haemorrhage

- **Glaucoma**: acute angle closure:
  - See hazy cornea
  - Irregular oval pupil
  - Diffuse injection – pain + n & v – REFER!!!

- **Corneal ulceration**: bact, fungal, viral often 2 to abrasion – REFER!!!

- **Never use steroids** in an undiagnosed red eye (can worsen ulcers, etc)

- **Diagnostic Tree**:
  - Uniocular:
    - No pain, vision normal: subconjunctival haemorrhage, episcleritis, pterygium, conjunctivitis
    - Pain and normal vision: if no corneal staining: Anterior uveitis, scleritis, HZO. If corneal scarring: HSV, marginal ulcer
    - Pain and vision reduced: If no corneal staining: severe uveitis, angle closure glaucoma, secondary glaucoma. If corneal staining: HSV, Bacterial keratitis, HZO
  - Binocular:
    - No pain, good vision: bacterial, viral or allergic conjunctivitis
    - Pain, vision good or poor: viral or chlamydial keratoconjunctivitis

- **Subconjunctival bleed**: self limiting unless severely hypertensive or coagulopathy

- **Conjunctivitis**:
  - Initially unilateral, may → bilateral due to cross infection
  - Feeling of surface grittiness
  - Causes:
    - Infective: See Eye Infections, page 218
    - Allergic: eg eczema, allergy to protein deposits on poorly cleaned soft contacts
    - Chemical/mechanical
  - Baby: 1 month with pus discharge → urgent referral (?blocked and infected lacrimal duct)
  - **Never pad** a discharging eye

- **Blepharitis**:
  - = Lid inflammation
  - Eyelash ‘dandruff’
  - **Meibomian gland dysfunction**: usually staph infection. 30ish glands under they eyelid normally secrete lipid to cover tear film
  - Clean with saline or bicarbonate solution

- **Chalazion**:
  - Red nodule in the lid
  - Due to obstruction and infection of a Meibomian gland
  - Microscopically *granulomatous inflammation* (basically a burst sebaceous gland)

- **Corneal Ulcer**: See HSV infections below.

- **Keratitis**:
  - Corneal inflammatory disease
  - Symptoms: deeper, aching pain
  - Aetiology: infective, contact lens, staph hypersensitivity, exposure keratopathy (eg 7th nerve palsy)
  - Signs: speckled light reflex ⇒ corneal oedema

- **Shingles affecting face**: refer within 7 – 10 days to check for intra-ocular complications. Pain is due to trigeminal neuralgia

- **Iritis**:
  - *Frontal headache, photophobia*, not watering. Usually unilateral
  - White cells and fibrous exudate in anterior aqueous. May be white cells at bottom of cornea
  - Usually autoimmune: Ankylosing Spondylitis, Crohn’s. Treat with steroids, and dilating drops to keep iris mobile
  - Rarely infective (eg Tb)

- **Episcleritis**

*Neuro-Senosry*
= Localised inflammation of sclera. Treatment: topical NSAIDs
Acute onset, mild pain, young adults, usually sectorial, no corneal signs
Cf Scleritis: pain, VA decreased, tender, sectorial or diffuse, corneal signs

- Pterygium:
  - Conjunctival overgrowth growing over cornea. Age related changes due to sun exposure
  - Refer if enlarging and vascularised. Differential: squamous cell carcinoma.
  - Pinguecula: White epibulbar nodule similar to pterygium

- Acute Glaucoma: See Primary Closed-Angle Glaucoma, page 217

Glaucoma
- Usually due to outflow obstruction: damage to the trabecular meshwork overlying the canal of schlemm → ↑resistance to flow → ↑steady state intraocular pressure → ↓vascular perfusion of the neural tissue → blindness
- Classification:
  - Primary:
    - Open angle (chronic)
    - Closed angle (acute)
  - Secondary: eg iritis, trauma, blood in the eye, etc

Primary Open-Angle Glaucoma
- Primary open angle glaucoma = chronic open angle glaucoma – no symptoms until severe visual damage has taken place as rise in P takes ages + eye compensates. Most common glaucoma – resistance to outflow not well understood
- Epidemiology:
  - Leading cause of preventable blindness
  - Risk factors: age, near-sightedness, African/Asian ancestry, family history, past eye injury, a history of severe anaemia or shock, steroid medication
  - Most common sort, gradual impairment of aqueous drainage, insidious loss of sight
  - 2% of over 50 years
  - 1 in 7 risk if primary relative has it
- Presentation:
  - Central field defect – arcuate shape with macular sparing
  - Cupping of the disk due to ischaemic atrophy of the nerve fibre layer
  - Bullous keratopathy – oedema of the cornea
- Screen with tonometry (measuring intra-ocular pressure), test visual fields
- Is diagnosed by cupping of the optic disk: not by ↑intra-ocular pressure. 17% of people with glaucoma have 'normal' IOP
- Pathology:
  - ↑resistance to outflow (pathogenesis not clearly understood) → ↑aqueous humour → ↑intra-ocular pressure (normal is < 22 mmHg)
  - Leads to damage to ganglion nerve cell axon (final output) at the optic nerve head. Due to vascular insufficiency as nerves exit the eye
  - Affects peripheral bundles preferentially: spares papillo-macular bundle
- Treatment: Medication, laser treatment to enlarge the drain (trabeculoplasty)

Primary Closed-Angle Glaucoma
- Acute angle closure glaucoma – rapid IOP rise
- Iris is pushed forward and acutely occludes the trabecular meshwork → ↓drainage
- Rare but vision threatening
- Symptoms = unilateral, haloes around lights, pain, field loss, nausea and vomiting
- Signs = hazy cornea, diffuse injection, irreg pupil, dilated non-reactive pupil
- Give pilocarpine (cholinergic agonist → ciliary muscle contraction & relaxation of trabecular network) and REFER!!!!
- Precipitating factors: long-sighted (narrow anterior chamber, narrow iridocorneal angle), and when pupil dilated for a long time (dim light)
- Can be congenital
- Once resolved, put hole through iris (iridotomy): no further obstruction possible
Secondary Glaucoma

- Secondary open angle glaucoma: Outflow system is obstructed mechanically by debris (ie gunge up trabecular meshwork). Rare. Eg Haemolytic glaucoma, lens protein glaucoma
- Secondary closed angle glaucoma: Can be due to neovascularisation ‘zipping up’ the angle, secondary to ischaemic eyes (eg diabetes, central retinal vein occlusion)

Eye Infections

- **Viral Infections:**
  - Adenovirus types 8 (epidemic) and 3 and 7 (sporadic). Conjunctivitis with pre-auricular lymph node hyperplasia. Over about a week get *small white spots* (WBC accumulations) just below the surface of the cornea
  - HSV:
    - Gives Herpes Simplex Keratitis
    - *Dendritic ulceration* with neovascularisation. Chronic inflammation and scarring. May lead to small white vesicles around the eye.
    - Viewed with *fluorescein* drops under cobalt light (stains where there is no epithelium)
    - Branching pattern \(\Rightarrow\) Herpes Simplex Virus. *Never give steroids*: → worse infection → permanent damage
- **Bacterial:** Usually pus. Always *bilateral*:
  - Standard bacterial conjunctivitis: treatment *chloramphenicol* eye drops
  - Trachoma: Due to Chlamydia. *Commonest cause of blindness in the tropics*. Less common than other causes in NZ. Chronic. Suspect if no response to topical antibiotics. Initially the conjunctival epithelium is infected \(\Rightarrow\) scarring of the eye lid \(\Rightarrow\) abrasion of cornea \(\Rightarrow\) over years get pannus (fibrovascular layer) over the cornea
  - Gonorrhoea: ↑pre-auricular nodes

Optic Nerve Lesions

- **Optic atrophy:** *pallor of the optic disk*, and damage to the retinal nerve layer, optic nerve or tract leading to ↓visual acuity or field loss. Due to neuritis, compression, ischaemia, glaucoma
- **Optic Neuritis:** Age 18 – 40, more common in women. *Pain on movement of eye, with central fog patch, colour desaturation*. Worsens over hours to days, may lose sight completely, gradually improves over 4 – 6 weeks. *70% chance of developing MS* over 10 years
- **Anterior Ischaemic Optic Neuropathy:** Sudden painless unilateral visual loss in an older person. Seldom improves. Due to occlusion of the arterioles to the optic nerve head
- **Compressive Optic neuropathy:** insidious loss of central vision in one eye, especially colour. Usually meningoima of optic nerve

Nerve Lesions Affecting Eye movement

- Ptosis and miosis (constricted pupil) (Horners syndrome) – due to lesions in the brain stem, in the apex of the lung, in the neck or on the carotid artery (eg carotid dissection)
- Ptosis & dilated pupil (mydriasis) non reactive to light: 3<sup>rd</sup> nerve palsy – eye turned *down and out* due to weakness of MR, SR, IO, and IR
- Differential for Ptosis: idiopathic (esp elderly), myasthenia, muscular dystrophies, myotonic dystrophy
- Nystagmus: if present in all directions will be central (commonest cause is antiepileptics)

Retinal Vascular Disease

- Damage to large vessels in the eye
- Occlusion of the central retinal artery:
  - Due to *atheroma*, thrombus, embolus, arteritis
  - Retina is *white* and totally infarcted
- Occlusion of the central retinal vein:
  - Haemorrhagic infarction
  - Collateral supply means some vision is recoverable
  - Retina is a mass of red, veins big and tortuous, cotton wool spots

Focal Ischaemic Retinal Disease

- Affects small vessels
- Features:
Cotton wool spots:
- Fluffy and off-white/yellow
- Due to micro-infarction → superficial area of necrosis and oedema
- Axons are disrupted and become distended (cytoid bodies)
- Resolve in 6 weeks

Hard exudates:
- Discrete, brighter white, often around macula
- Plasma leaks from damaged capillaries (secondary to thickened basement membrane) in the outer plexiform layer (deeper in the retina) and forms proteinaceous lakes
- Resolves over several months

Haemorrhage:
- Usually arises from microemboli/thrombi damaging vessels
- Flame: a small arteriole bursts into nerve fibre layer and spreads along nerve fibres
- Dot: capillary bursts into outer plexiform layer
- Blot: into the subretinal space
- Roth’s spots: central white infarct surrounded by haemorrhage (seen in IE)

Microaneurysms:
- Round or oval dilations of capillaries – look like lots of very little red dots
- Central in diabetes, peripheral in central retinal vein occlusion
- Due to reduced numbers of pericytes surrounding capillaries

Neovascularisation:
- Response of the eye to vascular insufficiency, secondary to angiogenesis factors from ischaemia: proliferate around the margin of non-perfusion. Detect with fluorescein angiogram
- Appears as fine lace work of new vessels. They leak and bleed
- Sites:
  - Iris surface → neovascular glaucoma, ectropion uvea
  - Pupillary membrane → Posterior Synichiae
  - Vitreal Surface → haemorrhage, pre-retinal fibrovacular membranes →scarring →retinal detachment
  - Easy to see if over optic disk (normally should only be large vessels)

Differentiating between Hypertensive and diabetic retinopathy:

<table>
<thead>
<tr>
<th>Vessel</th>
<th>Arterioles</th>
<th>Capillaries/veins</th>
</tr>
</thead>
<tbody>
<tr>
<td>Site</td>
<td>Superficial nerve fibre layer</td>
<td>Deep (non-proliferative) Superficial (proliferative)</td>
</tr>
<tr>
<td>Pathology</td>
<td>Medial hypertrophy</td>
<td>Pericyte loss</td>
</tr>
</tbody>
</table>

Diabetic Retinopathy
- Non-proliferative (background) retinopathy = microaneurysms, cotton wool spots, hard exudates, dot haemorrhages
- Only affect VA when macula involved
- Proliferative retinopathy = new vessels on retina or in vitreous, haemorrhage
- Treat with laser + maintaining low BG
- REFER = those with proliferative changes + macular involvement or VA changes. Monitor others
- See also Diabetes Mellitus, page 133
- 1/3 diabetes with > 30 years disease will lose some sight. Diabetics 25 times more likely to go blind
- Risk related to duration ⇒ Type 1 more likely to cause damage
- Retinal exam essential:
  - At diagnosis for maturity onset (may have had diabetes for 5 – 10 years)
  - After 5 years for juvenile onset and annually thereafter
  - Fluorescein angiography (injected in arm then photograph retina) to test for neovascularisation
- Causes: Thickened basement membrane of retinal microcirculation → leakage, oedema, nonperfusion and micro-aneurysms
- Macular retinopathy: boggy, leaky macula → blurred vision
- Non-proliferative retinopathy (= Background Retinopathy):
Progression: oedema (→ blurred vision) → microaneurysms → hard exudates → cotton wool spots → small haemorrhages → venous bleeding

- Proliferative retinopathy:
  - Neovascularisation
  - Retinal detachment due to contraction of subsequent scars
  - Vitreous haemorrhage (can also be due to vitreous collapse tearing at retina or retinal venous occlusion – usually due to ↑BP → expanded artery → compresses adjacent vein)

- Treatment:
  - Regular checks
  - Blood sugar control
  - Treatment of vascular disease (eg ↓BP)
  - Laser treatment (photocoagulation): 2 – 3,000 burns (but NEVER on macula). ↓O2 demand → ↓neovascularisation Complications: ↓peripheral and night vision, macula oedema
  - Vitrectomy: if non-resolving vitreous haemorrhage or fibrovascular contraction of vitreous (which has risk of → retraction of retina → tear)
  - Retinal repair: reattach retina
- Diabetes can also cause: neovascular glaucoma (blocking flow past lens), more susceptible to damage from ↑IOP, cataract, extraocular muscle palsy

Hypertensive Retinopathy
- Rarely causes visual loss. Requires diastolic BP > 120 for many years
- Stages:
  - Stage 0: no changes
  - Stage 1: ‘copper-wiring’ of arterioles due to thickening of the walls due to medial thickening (very subjective)
  - Stage 2: arteriovenous nipping – thickened arterioles compressing underlying veins
  - Stage 3: soft-exudates and/or flame haemorrhages (spread longitudinally along fibres)
  - Stage 4: papilloedema plus the above
- Bilateral and symmetric. More cotton wool spots (nerve fibre hypoxia)
- Retinopathy regresses if hypertension controlled (cf diabetes which doesn’t)
- See also Hypertension, page 47

Tumours
- Can occur on the iris, ciliary body, choroid

Malignant Melanoma of the Choroid
- Presentation: elderly, usually white, visual loss from retinal detachment or incidental
- Retinal appearance: light to darkly pigmented ovoid, elevated mass. Many variants
- 2nd most common site of melanoma after the skin
- Prognosis depends on cell type (Spindle A, Spindle B, Epithelioid or Mixed) and Stage. Overall 50% at 15 years

Retinoblastoma
- Life threatening
- 1:20,000 live births. First few years of life
- Types:
  - 60% sporadic
  - 40% familial (90% bilateral and/or multifocal)
- Presentation: strabismus (squint), ‘white’ patches on pupillary/red reflex (leukocoria), red eye
- Pathogenesis:
  - Due to variety of mutations in the tumour suppressor gene RB1 at 13q14 – inactivates a protein which downregulates cell growth
  - Need both alleles to be mutated to cause cancer. Hereditary neuroblastoma = inherit one defective gene from parent, with other allele in one cell undergoing spontaneous mutation. If non-hereditary, need to acquire mutations to both alleles in one cell
- Gross appearance: flat, elevated, diffuse, multicentric pale tumour nodules of plaques
- Microscopic appearance: small round cells with hyperchromatic nuclei, rosettes are characteristic, areas of necrosis and calcification
Treatment: remove eye
Complications:
- Metastasis eg in CNS. From occurrence in eye to spreading down the optic tract is ~ 6 months
- Survivors have a 20% chance of developing malignant tumours at 10 years: osteosarcoma or rhabdomyosarcoma
- Prognosis: 90% 5-year survival (less if optic nerve invasion).

Paediatric Ophthalmology

Assessment
- **Vision**: fixation (test independently and together), pictures, symbol matching, E
- **Alignment**: inspection, alternating cover test
- **Squint** inspection:
  - **Corneal reflection** when looking at bright light source. Should be in the centre of the pupil on both sides. Cover good eye and see if corneal reflection shifts over the pupil of the bad eye
  - Check for equal sclera on either side of iris. Wide bridge of nose may give pseudo squint
  - Can have squint without amblyopia as long as brain alternates which eye it looks through. If preference for one eye, then amblyopia

Amblyopia
- = “Lazy eye”
- Affects 2 to 3 per 100 children. Can only occur in childhood while visual pathway still developing
- **Usually unilateral**: maybe bilateral if bad astigmatism or hypermetropia. If unilateral no effect on reading/writing. Treat as insurance against problems in good eye
- Affects central vision: peripheral vision OK
- Three major causes:
  - **Squint**: Most common cause: misaligned or crossed eyes. The crossed eye is ‘turned off’ to avoid double vision
  - **Unequal focus (refractive error)**. One eye is more near/far sighted or astigmatic
  - Visual obstruction: eg cataract
  - Also caused by ocular motor defects
- Treatment: **force the use of the weak eye by covering the good one** (for weeks or months), plus correcting refractive errors with glasses

Refractive Errors
- Myopia
- Hypermetropia: if equal and severe then squint due to accommodation
- Stigmatism
- **Anisometropia**: difference between two eyes (especially if one normal and other long sighted) – accommodation just makes normal eye go out of focus

Other
- Congenital cataract:
  - Can be autosomal dominant
  - Check for red reflex within 6 weeks
  - May be uni or bilateral, part of a syndrome or isolated
- Congenital epiphora:
  - Watery eye. Common – lacrimal system not fully developed
  - Spontaneous resolution the norm. Conservative treatment until 12 months. Massage +/- antibiotics (stagnation of tear drainage)
- Perinatal eye infections
- Retinoblastoma: See Retinoblastoma, page 220
- Retinopathy of prematurity:
  - Very premature babies (low risk if over 30 weeks or 1200 g)
  - Due to hypoxia and oxygen toxicity
  - Spectrum from severe to norm
  - Problem with vascularisation → retinal detachment over time
- Congenital Glaucoma: rare. One cause of red watery eye
Vestibular

Examination of Eye Movements

- **Nystagmus:**
  - Peripheral cause: fine, unidirectional, horizontal or rotatory
  - Beats to the side opposite the lesion, worse when looking to that side
  - Named for the direction of the fast phase
  - Is inhibited by fixation (i.e., will be quicker if you close one eye and try fundoscopy on the other)
  - Bi-directional or vertical nystagmus is always **central** in origin

- **Control of eye movement:**
  - **Saccades:** voluntary quick refixation eye movement. If hypometric then undershot → number of small saccades to catch up → overshoot → reverse saccade
  - Parietal lobe controls ipsilateral smooth pursuit and contralateral saccades. Impairment over 70 may be normal
  - Impaired pursuit also due to cerebellar and brainstem lesions

- **Vestibulo-ocular reflexes:**
  - = Eye movements to compensate for head movement: maintain stable picture on retina
  - **Doll’s eye:** eyes stay focused on target when head moves

**Benign Paroxysmal Positional Vertigo (BPPV)**

- Usually **posterior semicircular canal**. Due to **debris in canal** (CaCO3 crystals). Usually cause unknown or ageing, but may follow trauma or infection. Fluid movement → distorted stimulations to nerve due to particles → different input from 2 vestibular end organs
- Posterior canals are in the snow-plough position, and are the lowest. Collect debris from the anterior and horizontal canal
- Leads to ↑ discharge to ipsilateral superior oblique and contralateral inferior rectus → **torsional nystagmus**
- Can also be due to horizontal semicircular canal

- **Symptoms:**
  - Brief attacks of vertigo precipitated by certain head movements (e.g., getting into or out of bed, rolling over). Less severe when repeated
  - May spontaneously remit and relapse

- **Hallpike manoeuvre:**
  - Rotatory or torsional nystagmus beating toward affected ear when tipped down, after a brief latent period (5 – 10 secs). If immediate then ?central cause. Last about 20 secs and reoccurs again when sitting up. Effect fatigues with retesting (material disperses in process of testing)
  - Performed with the patient sitting upright with the legs extended
  - The patient’s head is then rotated by approximately 45 degrees
  - The clinician helps the patient to lie down backwards quickly with the head held in approximately 20 degrees of extension. This extension may either be achieved by having the clinician supporting the head as it hangs off the table or by placing a pillow under their upper back
  - The patient’s **eyes are then observed for about 45 seconds as there is a characteristic 5-10 second period of latency prior to the onset** of nystagmus
  - If rotational nystagmus occurs then the test is considered positive for benign positional vertigo
  - During a positive test, the **fast phase of the rotatory nystagmus is toward the affected ear**, which is the ear closest to the ground
  - The direction of the fast phase is defined by the rotation of the top of the eye, either clockwise or counter-clockwise

- Usually resolves over weeks or months
- No cochlear symptoms

- **Treatment:**
  - Drug therapy not helpful
  - **Canalith Repositioning:** induce symptoms → shifts particles into a chamber not sensitive to movement
  - For right ear: sit on edge of bed, turn head 45 degrees to the left, lean all the way down to the right then quickly through 180 degrees to the left, then back to upright. May be easier with eyes closed. Repeat after 2 – 3 minutes. Do every three hours
Acute Peripheral Vestibulopathy

- **Acute labyrinthitis** = **vestibular neuronitis**, can be post-viral infection
- **Symptoms**: acute and continuous vertigo, worse with any movement, lasting several days with nausea and vomiting, but **no auditory or neurological symptoms**
- **Signs**:
  - Unsteady walking (eg heel-toe)
  - Fine horizontal/rotatory nystagmus beating away from the lesion
  - Vestibulo-ocular reflex is absent/impaired on passive head rotation toward the lesion, requiring voluntary eye movement to regain fixation (catch-up saccade)
- Most likely to be horizontal canal affected

**Other**

- Vertigo may follow head injury. Eg temporal bone fracture tearing 8^th^ nerve
- Infarct with occlusion of the internal auditory artery → affects hearing and balance
- Chronic bilateral vestibulopathy → imbalance and oscillopsia (sensation of the world moving on head movement) due to inadequate vestibulo-ocular reflex. Usually due to gentamycin toxicity
- **Migraine** may have vestibular symptoms
- **MS**: vertigo is a classic feature
Ear

External Ear
- Congenital Abnormalities: usually unilateral. Common ones:
  - Preauricular tag: only cosmetic
  - Preauricular sinus: get infected
- Otitis Externa:
  - Localised: furuncle (boil) or furunculosis
    - Very painful, may abscess and discharge
    - Usually staph aureus
    - Tx: Oral antibiotics, may need drainage
  - Diffuse (more common)
    - Skin infection: viral or bacterial, or underlying dermatitis (more chronic, less pain and swelling but itchy). If longstanding and treatment resistant, ?fungal (eg aspergillus) – less painful, but blocked and debris, look for hyphae
    - Treatment: swab, clean out canal, topical antibiotics (drops with steroids →↓swelling)
- Canal trauma from itching, ear cleaning. Resolves spontaneously (unless infected)
- Wax: produced by ceruminous glands (only in the ear) over cartilaginous part. Slightly acid ⇒ antibacterial. Carries debris out
- Insect in ear. Drown it and take out at leisure
- Exostosis: common benign finding. Overgrowth of bone in internal 1/3 of canal, following exposure to cold water (surfers, divers). May ⇒ obstruction
- Neoplasms: on pinna: BCC or SCC – require excision

Middle Ear
- Middle ear cleft = ear drum + tympanum + eustachian tube
- Ear drum:
  - Should see malleous, top towards the back
  - May see incus through the drum. If internal jugular very high, may see it at bottom
  - Main part called pars tensa, pars flaccida at top

Otitis Media
- See Acute Otitis Media, page 938

Neuro-Senosry
Other Middle Ear Conditions

- **Cholesteatoma:**
  - Most commonly affects the attic (=epitympanum) and antrum of the mastoid
  - Pars flaccida (top part of tympanic membrane) gets sucked in, expands, erodes surrounding tissue
  - May present with:
    - Chronically discharging, smelly ear, resistant to treatment
    - Conductive hearing loss: ossicles eroded
    - Complication: brain or mastoid abscess
  - Treatment: remove diseased bone

- **Otosclerosis:**
  - New bone formation fixes the footplate of stapes
  - Conductive hearing loss but ear looks normal
  - F > M, familial, ↑in pregnancy, menopause
  - 1:20 – 25,000, can be bilateral
  - Treatment: Stapedectomy (put in piston) or hearing aid

- **Tympanic sclerosis.** White plaques on ear drum. No consequence

- **Barotrauma:** from flying/diving. Bleeding and bruising around malleus. Will settle spontaneously

- **Haemotympanum:** Blood in middle ear. ?Temporal bone fracture. Battle’s Sign (of temporal fracture): bruising behind the pinna

**Ear Testing**

- **Voice Testing**
- **Tuning fork tests:**
  - **Rinne Test:** 512 Hz fork beside the ear. If conductive loss then bone conduction is better than air conduction. If sensorineural, air conduction best
  - **Weber Test:** Tuning fork on top of the head. Louder in affected ear if conductive loss, softer in affected ear if sensory loss

- **Pure Tone Audiometry:**
  - Can establish severity of hearing impairment and whether sensorineural or conductive
  - Measures thresholds across a range of frequencies. Threshold = lowest intensity that can be detected
  - Usually only test in range of conversational speech (250 Hz to 8 KHz)
  - Normal hearing is 0 – 20 dB (zero is based on population surveys)
  - Harder if child aged 3 – 5: need to play games etc

- **Auditory Brainstem Response (ABR):**
  - Detects evoked potentials in the brainstem in response to sound
  - Used for neonatal testing (reliable from full term), in older kids where behavioural responses are unclear and for testing the auditory nerve (eg acoustic neuroma – but MRI is gold standard, CT with contrast poorer)

- **Tympanometry:**
  - Measures compliance of middle ear
  - Normal is -100 to 100 daPa
  - Type A: normal (peak compliance over 0 daPa). If peak is low ?scarring or adhesions
  - Type B: flat curve (ie not compliant at any pressure).
    - Low volume type B: wax impaction or middle ear infusion
    - High volume type B: perforation or grommet
  - Type C: peak shifted to the left. Eustachian tube dysfunction/obstruction

- **Otoacoustic emissions:**
  - Test for cochlear function, eg in neonatal screening
  - Also for tinnitus: is it cochlear or non-cochlear

- **Paediatric testing:**
  - 0 – 3 months: referred from neonatal high-risk register. Need to correct (eg hearing aid implants) by 9 – 10 months otherwise speech impairment
  - 6 – 12 months: distraction testing – looking for head turning, etc
  - 1 – 2½ years: in a room with speakers
Hearing Loss

- See Hearing, page 905 for developmental delay resulting from hearing loss

**Congenital Sensorineural Deafness**

- Irreversible
- Pathology: problems with nerve or cochlear
- Profound hearing loss at birth: 2 per 1,000
- Most often detected by parents (ie believe them!)
- Aetiology: genetic or acquired, etc:
  - Idiopathic 60%
  - Genetic: most are spontaneous mutations rather than family history
  - Low birth weight
  - Infection (fairly rare now), eg Rubella, also toxoplasmosis, CMV, syphilis
  - Maternal drugs: eg aminoglycosides, alcohol
  - Lots of others, eg hypoxia, high bilirubin

**Sudden Onset Sensorineural Hearing Loss**

- = Uni/bilateral sudden onset within 3 days. May also get dizzy, tinnitus
- Could be inflammatory, infective, ototoxicity, acoustic neuroma (⇒ always investigate)
- Urgent specialist referral within 24 hours
- Spontaneous remission likely, poor prognosis if elderly, diabetic, vascular disease (Cochlear artery is an end artery – if blocked no collateral flow)

**Presbycusis**

- = Age related hearing loss, especially at higher frequencies
- Bilateral, symmetrical. May get recruitment (some sounds sound louder – eg toilet flushing, doing dishes)
- M > F, 24% of 64 – 74 year olds, 40% of over 75s
- May have ↓word discrimination: hard to help, ↑volume doesn’t help
- Aetiology: age, noise, hypertension, genetic predisposition
- Pathology: degenerative changes, eg of cochlea and also of central procession (this part won’t respond to ↑volume)
- Clinical: progressive deafness, ‘social’ deafness, especially 1 KHz, tinnitus. Often judged worse by spouse/partner
- Exclude: wax impaction, otosclerosis, Paget’s disease of the middle ear bones, acoustic neuroma
- Management:
  - Screen elderly people (eg questionnaires or audiometry)
  - Hearing aid: only ¼ who would benefit use one, although there are many barriers to use (including cost)
  - Speak facing the person, clearly, slowly, not too loud, paraphrasing sentences that aren’t heard rather than repeating them (also give this advice to spouse and caregivers),
  - Aids (telephone boosters, lights that flash when the doorbell rings, etc)
  - Rehabilitative services available through the Hearing Association

**Noise Induced Hearing Loss**

- Commonest cause of hearing loss < 60
- Usually industrial noise exposure: factories, builders, firearms, jack hammers
- Safe limit: 80 db for not more than 4 hours
- Classic damage at 4 & 6 KHz (ie higher freq) on audiogram. Usually bilateral
- Treatment: Prevention, hearing aids not much help

**Meniere’s Disease**

- Diagnostic triad: tinnitus (usually low pitched), deafness, vertigo, (+ feeling of aural fullness)
- Clinical: acute onset of triad, disabling vertigo (world spinning, vomiting) for 6 – 12 hours then low frequency hearing loss
- 30 – 55 years, M > F
- Stages:
  - Early: occasional attacks
  - Later: fluctuating low tone deafness
  - End stage: low tone deafness, imbalance but no vertigo
Pathology: endolymphatic hydrops: distension of endolymphatic space
Aetiology: unknown. ↑Production of endolymph
Diagnosis: possibly nystagmus, fluctuating SN loss
Treatment: Supportive, low Na diet (↓endolymph), thiazides, antivertigo, antiemetic and histamine medication

Acoustic Neuroma
- Progressive loss of hearing in one ear with tinnitus
- Not usually associated with ↓vestibular function – slow enough to compensate (ie CNS adjusts so world doesn’t seem on a tilt). But, everyone with acute vertigo should have a pure tone audiogram to screen for the (rare) possibility of acoustic neuroma
- MRI is definitive, CT is unreliable and should not be done

Aural Rehabilitation
- When hearing loss cannot be corrected, use hearing aids, listening devices and communication strategies
Abdominal Physiology

- Fluid into GI tract each day:
  - Drink: 2L
  - Saliva: 1L
  - Bile: 1 – 1½L
  - Stomach Secretion: 1 – 2 L
  - Pancreas: 2L
  - Small Bowel: 1L
  - 7 – 9 L per day into top end of small bowel

- Output of H2O in faeces = 150 – 200 ml in faeces. 7.5 L absorbed in small intestine. 1-3 L absorbed in Colon
- Normal stool is 70 – 80% water: held by fibre or in bacteria. ↑Stool H2O by 25 ml → diarrhoea. ↓By 25 ml → constipation

Abdominal History

- Top down approach ie start with swallowing/regurg problems and move inferiorly
- Abdominal Pain:
  - SOCRATES
  - Frequency and duration
  - Site and radiation: pancreas or peptic ulcer may radiate to the back, diaphragm to shoulder and oesophagus to the neck
  - Pattern: colicky pain is due to peristaltic movements against obstruction in bowel or ureters. Biliary pain usually lasts for hours (ie is not colicky)
  - Aggravating or relieving factors, including food, vomiting, defaecation, flatus, lying still in peritonitis
- Appetite and weight change:
  - Anorexia and weight loss ⇒ ?malignancy
  - ↑Appetite and weight loss ⇒ ?malabsorption
- Nausea and vomiting, ask about vomit (blood, bile, old food ⇒ outlet obstruction, etc)
- Heartburn and acid regurgitation
- Dysphagia: differentiate painful swallowing from actual difficulty
- Diarrhoea: check frequency and consistency. Can be:
  - Secretory diarrhoea: large volume
  - Osmotic diarrhoea: disappears with fasting
  - Abnormal intestinal motility
  - Exudative diarrhoea: with blood or mucus
  - Malabsorption: steatorrhoea
- Constipation: check what they mean. Check drugs, hypothyroidism, diabetes, etc. Is it recent (cancer can cause obstruction)?
- Mucus: ?IBS or rectal ulcer, fistula or villous adenoma
- Bleeding:
  - Haematemesis (vomiting blood)
  - Melaena (jet black stools)
  - Haematochezia (bright red rectal bleeding)
- Jaundice: also ask about dark urine and pale stools (→ obstructive jaundice)
- Pruritis: can be caused by cholestatic liver disease
- Abdominal swelling: also check ankles
- Lethargy: common in liver disease
- Drugs: especially NSAIDS
- Social history: alcohol, occupational exposure to hepatitis, travel, sexual and recreational drug history
- Also:
  - Any relationship of symptoms to: diet, envt (work, home, stress), menstrual cycle
  - Alarm symptoms
  - Localise symptoms
Disease process (infection, infl, immune, infiltrative)
- **Structural disease** (s + s according to specific disease, has specific test, med or surg rx)
- **Functional disease** (by def all tests are normal therefore dx by exclusion)

### Abdominal Exam
- Trying to filter symptoms for:
  - Upper vs. lower
  - Functional (motility) vs. structural (infection etc)
  - Alarm symptoms

### Periphery
- General:
  - Lie flat and comfortable (relaxed muscles)
  - General appearance:
    - Jaundice
    - Weight and wasting (weight them)
    - Skin: pigmentation (eg haemochromatosis)
  - Mental state: hepatic encephalopathy
- Hands for peripheral stigmata of abdominal disease (mainly liver):
  - Nails: Leuconychia (nail bed opacity in hypoalbuminaemia), clubbing in cirrhosis
  - Palms: Palmar erythema (reddened palms) in chronic liver disease, anaemia (from GI loss, malabsorption or chronic disease)
  - Dupuytren’s Contracture: thickening of the palmar fascia → permanent flexion, especially of the ring finger. In manual workers, alcohol, and familial
  - Hepatic flap: extend wrists and separate fingers for 15 seconds
- Arms:
  - Bruising:
    - Large bruises (ecchymoses) from clotting disorders
    - Small bruises (petechiae) from alcohol toxicity → ↓ platelets (also portal hypertension → splenomegaly → ↓ platelets)
  - Also muscle wasting, scratch marks, spider naevi (cirrhosis – usually alcohol, due to oestrogen excess)
- Face:
  - Eyes for jaundice, anaemia, or scleritis/iritis (associated with inflammatory bowel disease)
  - Bilateral swollen parotids due to fatty infiltration with ↑ alcohol
  - Smell of breath: fetor hepaticus (sweet smell) or alcohol
  - Ulceration (eg in Crohn’s) or candida in the mouth
  - Angular stomatitis: cracks at the corners of the mouth: causes include Vit B 6 and 12, folate and iron deficiency
- Neck and Chest:
  - JVP
  - Cervical lymph nodes and especially supraclavicular nodes (always bad)
  - Gynaecomastia: due to ↑ oestrogen to testosterone ratio (alcoholic effect on Leydig cells, or due to spironolactone (used to treat ascites)
- Examine chest:
  - Gynaecomastia
  - Spider naevi
  - Body hair

### Abdomen
- Regions:
  - Right & left hypochondrium, epigastrium
  - Right & left lumbar/mid-lateral region
  - Right & left iliac fossa, hypogastrium or suprapubic
- Why examine:
  - Enlarged organs
  - Abnormal masses (e.g. tumour or inflammation – abscess) & fluid (ascites)
  - Signs of peritoneal irritation (hurts with cough)
  - Hernia
• Inspection:
  - ?Abdomen moves with respiration (look from side on to view asymmetry ⇒ ?mass)
  - Scars: what were operations
  - Hernias - Hernial Orifices: Umbilical, Inguinal, femoral
  - Visible lumps/organs
  - Skin lesions/pigmentation (eg Shingles causes strange pains until it erupts)
  - Distension: Due to Fat, Fluid, Fetus, Flatus, Faeces, Filthy big tumour. Umbilicus is shallow or everted in ascites or pregnancy
  - Veins. Test direction of flow. In portal hypertension, flow is away from umbilicus (rare, = Caput Medusae). In IVC obstruction, flow is upwards
  - Striae: Ascents, pregnancy, recent weight loss, rarely Cushing’s Syndrome
  - Pulsitations: abdominal aorta. Visible in thin people. If fat then ?aneurysm

• Palpation:
  - Relax patient, use warm hands. Bend knees up if necessary to relax muscles
  - Gently all round: look at face – check for tenderness/peritonism, obvious lumps. Do most painful quadrant last. If tense, use their hand
  - Percuss before palpation for organs. Check for shifting dullness
  - More firmly: looking for organs, masses

• What to palpate for:
  - Liver:
    - Don’t usually feel in normal adult, may in child. Normal span in mid-clavicular line is 10 - 12 cm. Don’t measure on lateral side, right lobe hangs down in some giving appearance of bigger liver (Riedel’s lobe)
    - Describe as hard or soft, tender or non-tender, regular or irregular, pulsatile or non-pulsatile
  - Spleen: needs to be enlarged 3 or 4 times to palpate. Palpable spleen is ALWAYS bad. Start palpation inferior to the umbilicus
  - Kidney: if palpable either tumour or obstructed
  - Aorta: can nearly palpate in most people – key issue is width
  - Gallbladder: Murphy’s sign: lay fingers along costal margin, patient takes a deep breath and it hurts. Enlarged gallbladder is unlikely to be gallstones as chronic gallstones →fibrosis that can’t then expand. Instead, ?carcinoma of the head of the pancreas.
    - Also palpate for bladder, uterus
  - What to note: Site, size, shape, consistency, tender, pulsatile

• Signs of inflammation, infection or haemorrhage:
  - Tenderness: how severe is pain in response to pressure
  - Guarding: muscles resist pressure. Can be voluntary or involuntary (latter suggests peritonitis)
  - Rigidity: muscles tight
  - Rebound tenderness: push down surreptitiously then remove hand quickly – watch face for pain (peritonitis)

• Percuss for:
  - Liver
  - Spleen: unreliable
  - Kidneys: but overlying bowel makes this problematic
  - Bladder: supra-pubic dullness indicates upper border of an enlarged bladder or pelvic mass
  - Shifting dullness in ascites

• Auscultate:
  - Bowel sounds: just below umbilicus. Are either present or absent (increased or decreased meaningless)
  - Over liver, spleen, renal areas for rubs and bruits

• Groin: genitalia, lymph nodes, hernial orifices

• Rectal:
  - Observe for tags, haemorrhoids, pylonodal sinuses, blood, faeces colour
  - Feel for anal tone, masses or strictures in the rectum

• Legs: bruising, muscle wasting, oedema (check sacral as well)

**Causes of Splenomegaly**
- Chronic granulocytic leukaemia
- Malaria
- Lymphoma
- Myelofibrosis
Polycythaemia

Abdominal Exam – RP

Examination of the GIT

- Wash your hands.
- Introduce yourself to the patient, and ask permission to examine them.
- Expose the patient, and lie them flat.
- NB. Gastroenterologists will order the GIT exam: I Palp Perc A

**Inspection**

<table>
<thead>
<tr>
<th>Look around the bed</th>
<th>O2, drips, cigarettes, special foods, diabetic diet</th>
</tr>
</thead>
<tbody>
<tr>
<td>Look at the patient</td>
<td>Comfortable at rest, NG tube, jaundice, cachexia, dehydration</td>
</tr>
<tr>
<td>Look at the hands</td>
<td>Palmar erythema or pallor, Dupuytren's contracture, tendon xanthomata</td>
</tr>
<tr>
<td>Look at the nails</td>
<td>Clubbing (cirrhosis, lymphoma, IBD, Coeliac disease), leukonychia (hypoalbuminaemia), koilonychia (iron deficiency), Muehrcke's lines, Terry's nails (distal 80% - liver disease)</td>
</tr>
<tr>
<td>Look at the wrists</td>
<td>Pulse, asterixis</td>
</tr>
<tr>
<td>Look at the arms</td>
<td>Ask for BP; scratch marks (obstructive jaundice), spider naevi, bruising, needle track marks</td>
</tr>
<tr>
<td>Look at the eyes</td>
<td>Jaundice, anaemia, Kayser-Fleischer rings, xanthelasma</td>
</tr>
<tr>
<td>Look in the mouth</td>
<td>Ulcers, pigmentation, telangiectasia, fetor hepaticus, candida, angular stomatitis (Fe def), gums, leukoplakia, atrophic glossitis (vit B def), macroglossia (amyloidosis), Peutz-Jegher's syndrome (melanin deposits on lips + mouth – increased risk of GI malignancy)</td>
</tr>
<tr>
<td>Feel salivary glands</td>
<td>Supraclavicular – Virchow's and axillary (hold their right arm with yours and feel with left, and vice versa)</td>
</tr>
<tr>
<td>Sit next to the pt</td>
<td>For the rest of the examination</td>
</tr>
<tr>
<td>Look at the abdomen</td>
<td>Gynaecomastia, pulsations, obvious masses, telangiectasias, drain, catheter, scratch marks, spider naevi, striae, bruising, distension, masses, scars, Sister Mary Joseph nodule, Grey-Turner's/Cullen's sign, stomas, acanthosis nigricans, tattoos, skin changes (eg Campbell de Morgan spots), caput medusa</td>
</tr>
</tbody>
</table>

**Palpation**

| Light palpation | In all 9 segments of the abdomen (ask if there’s any pain first, and watch the patient’s face) |
| Deep palpation  | In all 9 segments of the abdomen, watching the face; feel for any masses |

**Organ examination**

| Feel for the liver | Starting in the right iliac fossa, asking the patient to breathe in each time you palpate |
| Feel for the GB   | Murphy’s |
| Feel for a AAA    | Above the umbilicus (the aorta divides below this point) |
| Feel for the spleen| Start in RIF unless pointed elsewhere by percussion; bimanual technique |
| Ballot the kidneys| Put one hand posteriorly in the flank, and ballot the kidney onto a hand positioned anteriorly |
| Auscultate kidneys| Posterior bruit = specific not sens; anterior bruit = sens not specific |
| Auscultatory percussion | Of bladder – steth just above symph – scratch from umbilicus down – sound intensifies over bladder |
| Examine lymph nodes| Supraclavicular (virchow's node – L enlarged node in gastric ca), axillary, inguinal |
| Test for appendicitis| McBurney’s = 1/3 from ASIS to umbilicus; Rovsing’s = pain in RLQ when LLQ palpated; Psoas sign = place hand over R knee + ask pt to raise thigh – increased pain suggests psoas irritation |

**Percussion**

| General percussion | Ask if pain anywhere. Topographic percussion to assess gas/mass + percussion tenderness |
| Percuss the liver  | Starting in the RIF until dull, then percuss out the upper border |
| Percuss the spleen | Castell's point = junction of ant axillary line + L subcostal margin – percuss continuously during insp + exp (normally tympanic – dullness in insp or exp = big spleen); Traube's space = triangle – AAL, 6th rib, costal margin – percuss during insp + exp (dull in insp or exp = big spleen) |
| Percuss the kidneys | Using fist to determine tenderness |
| Check for shifting dullness| With finger in the midline, move down the flank until percussion note becomes dull. Ask the patient to roll away from you – ascites is suggested if the note becomes resonant. Do both sides |
Auscultation

<table>
<thead>
<tr>
<th>Listen for bowel sounds</th>
<th>Up to three minutes. Can be normal, absent or tinkling (in obstruction)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Listen for bruits</td>
<td>Aortic, renal, iliac, femoral</td>
</tr>
<tr>
<td>Listen over RUQ + LUQ</td>
<td>RUQ: hepatic tumour(s)/AVM/tricuspid regurg; LUQ: ca pancreas/spleen vasc anomaly; friction rubs heard over RUQ or LUQ indicate infarcts or tumours</td>
</tr>
</tbody>
</table>

Final manoeuvres

<table>
<thead>
<tr>
<th>Examine the ankles for oedema</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Examine the hernial orifices (or say you would, as below)</td>
<td>Standing – cough, feel for expansile mass; can auscultate</td>
</tr>
<tr>
<td>Examine the external genitalia</td>
<td></td>
</tr>
<tr>
<td>Perform PR exam</td>
<td></td>
</tr>
</tbody>
</table>

I would complete my examination by....

- “I would like to examine the hernial orifices, examine the genitalia, perform a digital rectal examination, dipstick the urine, examine the stools and look at the observation chart (temperature, BP, sats) or growth chart if a child”

Abdominal Tests

Abdominal X-ray

- Gas:
  - Normal in colon and stomach, some in small bowel OK
  - Define colon: has haustrations – but don’t cross taeniae coli. Only part of bowel with faeces
  - If they have ulcerative colitis shouldn’t be bigger than 5cm – otherwise toxic megacolon
  - Transverse diameter of caecum shouldn’t be bigger than 9 cm otherwise risk of rupture
  - Small bowel: circularis goes right round. Max diameter 3 cm. Gas if obstructed, diarrhoea, ileus or swallowing gas due to pain
  - Gas under diaphragm = pneumoperitoneum
  - Can have gas in biliary tree (esp. after ERCP, or if fistula to bowel), and retroperitoneal from perforated 2nd part of duodenum
- Stripes:
  - Edges of psoas: demarcated against fat
  - Lateral abdominal wall: flank line is peritoneum. If exudate in the paracolic gutter then distance from the colon is increased
  - Renal outline: parallel to upper psoas
  - Edge of liver
  - Edge of spleen (not always seen)
- Stones:
  - Any extraosseous calcifications
  - Bladder, kidney, gallbladder
- Bones

Other Abdominal Tests

Endoscopy

- Complications: Mallory Weiss tear, perforation (1/2000), aspiration pneumonia (rare)

Ultrasound for Ascites

- Need 1 litre of fluid before it can be detected

Rectal Biopsy

- For ulcerative colitis, microscopic colitis, amyloidosis, cancer

Stool Test

- Occult blood
- Culture (for bacteria): would either be self-limiting or very sick
- Ova, parasites & giardia antigen: if high risk, repeat 3 times. Needs to be warm on arrival in lab
**Barium Enema**
- Make sure they got to the caecum (i.e. want to see contrast in the appendix or terminal ileum)
- Also need to know that bowel was clean enough for them not to miss anything

**Nutrition**
- Normal energy metabolism:
  - Adults need 25-30kcal/kg/day (~100-120kJ/kg/d) + glucose is preferred source of immediate energy (can be produced from CHO, fat or protein)
  - Glycogen lasts only 36-48hrs (500mg)
  - Typical diet = CHO 40-60% (4kcal/g – 17kJ); fat 20-45% (9kcal/g – 37kJ); protein 10-20% (4kcal/g – 17kJ)
- CHO metabolism:
  - Most ingested CHO broken down (amylases) to glucose for utilisation for all cells
  - RBCs and brain use glucose only
  - GNG + glycogenolysis used when needed
- Fat metabolism:
  - Hydrolysis → absorption → resynthesised as TAGs → TAG + apoprotein combination to form chylomicrons
  - transport to lymphatics → LPL releases FFA from TAG for entry into metabolising cells
  - Hydrolysis releases glycerol and FFA (converted into AcCoA for CAC)
  - During starvation, large amounts of FFA released and saturate CAC therefore KB formed
- Protein metabolism:
  - No body storage pool therefore need 0.8-1g/kg/d
  - Used for repair, synthesis, growth, energy
  - Up to 1/3 of body protein can be catabolised for energy
- Nitrogen balance:
  - Intake must = output (urine/faeces) for NB to occur
  - PNB = growth/rebuilding
  - NNB = catabolic states eg sepsis, trauma, burns, starvation
  - NB = (protein intake x 0.16) – (daily urinary N[urea] + 4g)

**Energy Metabolism During Starvation**
- **Immediate** use: liver glycogenolysis
- **Early** starvation: glucose produced by GNG using AA, glycerol + lactate
- **After a few days**: decreased metabolic rate + increased reliance on FFA (taken up by heart, kidneys and muscle directly) and converted to KB; lactate and pyruvate converted to glucose
- **Prolonged** starvation: brain adapts to using KB, decreasing the need for protein catabolism (Ig decreases therefore infection)
- In contrast, catabolic states eg sepsis, trauma, burns, **increase protein catabolism** by 50% or more due to hormones + cytokines; also see lipid oxidation and insulin resistance

**Assessment of nutritional status**
- Anthropometric measurements:
  - Height, weight, triceps skinfold thickness (approximates adipose) and mid-arm circumference (approx protein) can be compared to standard pop measurements
  - Body weight: below 90% of ideal indicates undernutrition
  - Comparing actual 24 hr urine Cr excretion to ideal excretion standardised for height or arm length
- Biochemical tests:
  - Albumin, transferrin, lymphocytes, delayed hypersensitivity skin tests to common Ag + NB reflect protein status
  - Rate of nutrition depletion:
    - Undernutrition progresses rapidly on intake of < 1000kcal/d (4000kJ)

**Nutritional requirements**
- Body also needs vitamins, trace elements, electrolytes and water
- Energy intake varies according to state of health/d, sex, age, activity

**Developmental Abnormalities**
- See Congenital Abnormalities, page 976
Oral Pathology

- Same pathology in the mouth as with skin, mucosa, nerves, blood vessels, etc. But also specialised stuff
- Teeth and Teeth forming tissue:
  - Genetic defects
  - Severe illness eg measles → bands on teeth
  - Tetracycline → discoloration
  - Vomiting, regurgitation (eg bulimia) → erosion
  - Cysts or tumours of teeth forming tissue (eg ameloblastoma)
  - Gums: lose more teeth through gum disease than caries. Immunosuppressive disease can lead to abnormal gums (eg leukaemia)
- Salivary glands:
  - Calcification in duct of major gland → blockage
  - Tumours/cysts
  - Recurrent infections: short/wide ducts → retrograde flow → infection with oral commensals
  - Post-radiotherapy to head and neck. Salivary tissue very sensitive → dry mouth
  - Drug induced dry mouth: made worse by anxiety, smoking, dehydration
  - Sjogren’s Disease: autoimmune attack of salivary and lacrimal glands
  - Dry mouth → rapid tooth decay (no buffering from saliva)
- Oral Mucosa:
  - Hyperkeratosis with hyperplasia or atrophy: looks white
  - Ulceration: lots of causes: eg trauma (new dentures, burns), herpes, **Aphthous ulcers** (= ulcers that form on the mucous membranes of the mouth or genitals; if recurrent then check ↓serum ferritin, hormonal cycle, stress, food allergy [eg benzoic acid in Coca Cola], heredity)
  - White lesions (due to thickened keratin layer):
    - **Lichen Planus**: white patches surround by red erosions
    - Lichenoid drug reactions
    - Malignant and premalignant (eg leukoplakia - white, erythroplakia – red). Eg squamous cell carcinoma. Related to smoking – 60 – 75% of white lesions go away if they stop

Oesophagus

Dysphagia

- =Difficulty swallowing
- Define level and whether progressive or intermittent
- History: time course, reflux symptoms, cough, asthma, chest infections, weight loss, pain
- Examination:
  - Lymphadenopathy
  - Chest signs: consolidation, effusion
  - Hepatomegaly
  - Ascites
  - Raynaud’s: connective tissue disorders (CREST syndrome)
- Investigations:
  - Barium swallow (video)
  - CT scan: staging malignancy
  - Endoscopy: assess mucosa, strictures
  - Manometry: assess motility
- Impaired oesophageal motility:
  - Fluids get through OK, **solids** the problem
  - Pharynx: **neurological diseases** causing failure of high pressure contraction
  - Cricopharyngeal sphincter: failure due to **cricopharyngeal spasm or pharyngeal pouch**
  - Oesophagus: failure of peristaltic wave due to diffuse **oesophageal spasm**
  - Cardiac sphincter: failure of opening due to **achalasia**
- Oesophageal obstruction:
  - **Fluids** also a problem
  - **Extrinsic compression**: thyroid, other neck mass, lymph nodes (Ca lung)
- **Carcinoma** of the oesophagus. Often diagnosed at advanced stage. Either **squamous** or **adenocarcinoma**. Diagnosis by endoscopy + biopsy +/- CT. Treatment – surgical reconstruction. Palliation: radiation + internal stent
- **Reflux stricture** of the lower oesophagus

### Oesophageal Tumours

<table>
<thead>
<tr>
<th>Oesophageal carcinoma</th>
<th>Type</th>
<th>Features</th>
<th>Risk factors</th>
<th>Pathology</th>
</tr>
</thead>
</table>
| Oesophageal adenocarcinoma | M>F  | Syr survival 20% | 1. Barrett oesophagus (ie chronic reflux oesophagitis)  
2. Smoking | 1. Glands invading SM (crossed BM)  
2. Mucin  
3. Desmoplastic reaction |
| Oesophageal SCC | More common | 1. Alcohol  
2. Smoking  
3. Diet (fungus contaminated + nitrosamine containing foods, also a/w vitamin def) | 1. Strictures  
2. Ulceration  
3. Intercellular bridges  
4. Keratin whorls  
5. Islands of invading squamous epi |

- **Symptoms & signs:**
  - Dysphagia: when disease advanced
  - Inability to swallow saliva
  - Pain
  - Weight loss, anaemia, lymphadenopathy, hepatomegaly
- **Investigations:**
  - Endoscopy: biopsy
  - Bloods: FBC (anaemia), ALP (metastases in liver or bone)
  - CT, MRI: localised tumours
- **Differential diagnosis:**
  - Benign stricture
  - Motility disorders, especially achalasia
  - Extrinsic compression of oesophagus (e.g. bronchial carcinoma)
- **Treatment:**
  - Adequate nutrition (enteral feeding tube if necessary)
  - Pain management
  - Surgery/radiotherapy: usually only palliative
- **Squamous cell carcinoma:**
  - 90 % of oesophageal cancer
  - Epidemiology: M > F 4:1, B > W, approx 5 per 100,000
  - Aetiology: dietary (fungal, nitrates, ↓leafy greens), oesophagitis (minor RF for SCC), alcohol, tobacco, genetics
  - Macroscopic appearance: Site: 50% middle, 30% lower, 20% upper. Early lesion a small grey-white thickening. Later: fungating tumour, ulceration, infiltration (may present as stricture)
  - Microscopic appearance:
    - Sheets of neoplastic squamous cells with intercellular bridges
    - Keratin whorls ⇒ well differentiated
    - Mitoses, necrosis, pleomorphism (as with all malignant tumours)
    - Invasion of mediastinal structures and lymphatics
  - Clinical outcome: Insidious (⇒ late presentation). 70% dead at one year
- **Adenocarcinoma of the oesophagus:**
  - 10% of oesophageal carcinomas. Arise in Barrett's mucosa
  - Elderly, mainly males
  - Macroscopic: mass or nodule
  - Microscopic: pleiomorphism, irregular gland formation

### Achalasia

- Failure to relax lower oesophageal sphincter (aetiology unknown)
- **Symptoms & signs:**
  - Dysphagia: with both **solids and liquids**
  - Intermittent chest pain
  - Regurgitation/reflux
  - Weight loss
Nocturnal cough (related to regurgitation & aspiration)

Investigations:
- Chest x-ray: dilated oesophagus
- Barium swallow: delayed passage through cardia, oesophageal dilation
- Endoscopy: may be normal, may be food in oesophagus (→ secondary oesophagitis)
- Manometry: impaired relaxation of lower oesophageal sphincter, absent peristalsis

Differential diagnosis:
- Benign or malignant stricture
- Malignancy at cardia

Treatment
- Medical: nitrates and calcium antagonists →↓sphincter pressure
- Balloon Dilation
- Botulinum toxin injection
- Cardiomyotomy
- Retrosternal pain may continue following treatment. May need H2 antagonist

Dyspepsia
- = Upper abdominal discomfort
- Includes bloating, fullness, early satiety, nausea, anorexia
- Chronic discomfort in the upper abdomen; related to eating (eg early satiety) – “indigestion”
- Distinct from reflux (heartburn, acid reflux etc)
- 42% of general pop c/o either dyspepsia or reflux

Causes:
- Peptic ulcer disease
- Atypical reflux
- Functional gut disorders (eg epigastric pain syndrome, post-prandial distress syndrome)
- Malignancy

Alarm features:
- Blood loss/anaemia symptoms
- Dysphagia
- Weight loss
- Age (i.e. new onset of symptoms at older age)

Hx:
- Alarm features (if so – endoscopy)
- Exclude non-gut pathologies (eg cardiac)
- Pain – SOCRATES
- Relationship to eating
- Lifestyle factors (eg lying down after eating, certain foods – chocolate etc, smoking, ETOH)

Ix:
- H. pylori – test and treat (seropositive pts receive anti-HP rx)
- Endoscopy
- Trial of therapy (eg PPI or H2 blocker or domperidone – prokinetic)

Rx:
- Test and treat (seropositive = triple therapy; seronegative = anti-secretory/pro-kinetic drugs eg domperidone)
- Alarm symptoms = gastroscopy
- Stop NSAIDs
- Exclude bilary colic, pancreas and heart pain
- Functional/idiopathic/essential dyspepsia = all investigations normal but still pain = up to 60% of dyspepsia.
- Increased visceral sensitivity, ?delayed gastric emptying, ?H Pylori gastritis
- Abdominal pain without significant pathology very common
- Ask about weight: if overweight – think reflux, if losing weight think cancer

Oesophagitis
- Caused by:
  - Reflux oesophagitis
  - Irritants (eg alcohol, tobacco)
Fungal or viral infection (in immunocompromised; candida + HSV)
- Eosinophilic (seen in atopic children/adolescents; dysphagia; >20 eosinophils (pink) per high power field)
- Systemic blistering diseases (rare)
- Radiation (eg for breast cancer) or cytotoxics
- Graft vs. host disease (affects whole GI)

**Gastro-Oesophageal Reflux Disease (GORD)**
- Includes reflux oesophagitis
- An acid and motility disease
- Caused by contact of refluxed gastric contents (acid and enzyme) with oesophageal mucosa
- Heartburn and regurg (reflux) most common symptoms
- Mechanisms for reflux:
  1. **Lowered sphincter pressure/incompetence:** Aggravated by large meals, acidic (e.g. citrus), fatty food, chocolate, smoking, peppermint, caffeine
  2. **↑Abdominal pressure:** effects right crus of diaphragm which acts like an external LOS: aggravated by obesity, straining, pregnancy, bending over

**Diagnosis:**
- **Therapeutic trial:**
  - If heartburn + acid regurg symptoms present and no alarm symptoms, a therapeutic trial of **lifestyle changes** and **antacids** should commence
  - **Alarm symptoms** (weight loss, nausea and vomiting, bleeding/anaemia, non-cardiac CP, hoarseness, nocturnal cough/choking, asthma) = gastroscopy
- If going to investigate, don’t treat in meantime: otherwise →↓inflammation (if any)
- **Endoscopy** most sensitive and specific: use after failure of therapeutic trial or if alarm symptoms. Biopsy only to exclude malignancy or Barrett's oesophagus. 50% are normal on endoscopy
  - Gold standard: 24 hour ambulatory pH monitoring
  - Lesions graded 1 (mild) to 4 (severe), 5 (metaplasia – Barrett’s). If Grade >= 3, then indefinite, significant acid suppression

**Alarm Symptoms:**
- Dysphagia
- Early satiety
- Night waking
- Abrupt onset
- Recurrent hoarseness
- ↑Severity
- Weight loss
- Vomiting blood
- Symptoms for the first time > 45 years or soon after any treatment
- Differential: peptic ulcer, gastric or oesophageal cancer, angina/IHD, hiatus hernia
- Macroscopic appearance: oedema, hyperaemia (redness), ulceration, white patches with candida
- Microscopic appearance:
  1. Intraepithelial eosinophils
  2. Neutrophils in the epithelium and lamina propria
  3. Regenerative and degenerative features of the epithelium (→ thickening)
  4. Ulceration

**Treatment hierarchy:**
- Aim is to control symptoms; heal oesophagitis and reverse/prevent complications
- Try **antacids** (will not cause healing of erosive disease; sucralfate enhances local mucosal resistance and has been shown to heal mild disease ) & **lifestyle changes first** (8-12/52 trial), try this first provided no alarm symptoms before progressing to H2RA or PPI):
  - No food/fluids for 2-3 hrs before lying down
  - Elevate head of bed (75-100mm) – extra pillows don’t work (need shoulders elevated too)
  - Lose weight if you’re a fatty
  - Restrict/avoid foods causing symptoms (eg coffee, alcohol, fruit juice, fatty foods, chocolate)
  - Avoid large meals
  - Avoid stooping
  - Stop noxious meds (**aspirin, NSAIDs** etc)
  - If using antacids, take after every meal and before bed
- Paracetamol for pain not aspirin
- High fibre diet: reduces straining → reduces reflux due to ↓intra-abdominal pressure (only helps if straining to start with)
- Prokinetics: improve oesophageal clearance and competence of LOS + accelerate gastric emptying; cisapride, metoclopramide or domperidone
- Antisecretory therapy:
  - H2 antagonists (OK for mild): reduce volume and acidity of gastric juice; healing after 8 – 12 weeks
  - PPI (more effective in severe): heals pts w moderately severe and severe d and prevents recurrent stricture formation; effective where H2RA have failed; omeprazole, lansoprazole, pantoprazole
- Nissen fundiplication (operation): also reduces hiatus hernia at same time

- Chronic reflux oesophagitis histology:
  - 1. Eosinophils
  - 2. Regenerative changes = thickened squamous epithelium (increased basal layer) +
  - 3. Elongation of papillae CT (submucosa)
- This eventually → gastric metaplasia → intestinal metaplasia/Barrett’s (goblet cells) → dysplasia

- Complications:
  - Barrett’s oesophagus: long-standing reflux → metaplasia: columnar changes above gastro-oesophageal junction. **Oesophageal inflammation-neoplasia process**: chronic inflammation (eg GORD) → metaplasia from squamous to gastric to intestinal (at junction b/w oesophagus + stomach - squamocolumnar) → dysplasia → invasive tumour
  - Ulceration, stricture (always biopsy strictures as some cancers present like this)
  - Adenocarcinoma

**Barrett Oesophagus**
- Post long-standing reflux
- Metaplasia from squamous → columnar epi (intestinal metaplasia)
- Acid mucin-containing goblet cells (stain blue) + red velvety mucosa
- Most important RF for oesophageal ADENOCARCINOMA (30-40x)
- **Barrett oesophagus with dysplasia** = dysplasia (gland crowding, increased cellularity, ↑N:C, hyperchromasia etc)
- Does not regress

**Hiatus Hernia**
- Common. May be asymptomatic
- Two types: sliding or rolling/para-oesophageal
- Symptoms:
  - **Sliding**: reflux, cardiac and pulmonary symptoms (mass in thoracic cavity).
    Sphincter above diaphragm
  - **Rolling** (paraoesophageal): sphincter below diaphragm but part of stomach above. See cardiac and pulmonary symptoms, dysphagia, hiccough, volvulus

**Stomach and Duodenum**

<table>
<thead>
<tr>
<th>Condition</th>
<th>Associations/aetiologies</th>
<th>Features</th>
<th>Path</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gastritis</td>
<td>1. H.pylori&lt;br&gt;2. Autoimmune&lt;br&gt;3. Toxic eg ETOH&lt;br&gt;4. NSAIDS&lt;br&gt;5. Chemical (reflux) gastropathy</td>
<td>Chronic ulcer due to exposure to excess acid</td>
<td>1. Inflammatory cells&lt;br&gt;2. H.pylori organisms&lt;br&gt;3. Chronic h.pylori can see intestinal metaplasia – goblet cells in stomach (blue staining)</td>
</tr>
<tr>
<td>Peptic ulcer disease</td>
<td>1. H.pylori&lt;br&gt;2. NSAIDS&lt;br&gt;3. Zollinger-Ellison syndrome (gastrin-producing tumour) - rare</td>
<td></td>
<td>1. Inflammation&lt;br&gt;2. Shallow ulceration&lt;br&gt;NB. malignant ulcers have raised, irreg, rolled or nodular edges (benign have smooth tapering edges)</td>
</tr>
<tr>
<td>Menetrier’s d</td>
<td>Fine print!</td>
<td>Hyperplasia of mucous cells</td>
<td></td>
</tr>
<tr>
<td>Gastric adenocarcinoma</td>
<td>1. H. pylori&lt;br&gt;2. Diet (nitrites, smoked + salted food, lack of fresh fruit/veg)&lt;br&gt;3. Smoking</td>
<td>Two types:&lt;br&gt;1. Intestinal&lt;br&gt;2. Diffuse signet ring cell (e-cadherin) –</td>
<td>Intestinal: gland invasion, desmoplastic reaction, cyto features of malignancy, mucin</td>
</tr>
</tbody>
</table>
Hereditary (e-cadherin mutation – signet ring cell morphology) can present as linitis plastica (diffuse thickened morphology). DSRC: cells don’t stick well tog; signet ring looking cells

GIST

Gastric lymphoma H. pylori

Leiomyoma Benign

Gastritis

- **Acute** gastritis:
  - Transient, acute, mucosal inflammation
  - Causes: NSAIDs, alcohol, chemotherapy, stress, shock, severe systemic infection
  - Macroscopic appearance: oedema, hyperaemia, superficial erosion
  - Microscopic appearance: neutrophils, sloughing, haemorrhage in the lamina propria

- **Chronic** gastritis:
  - Lost velvety appearance, flat (no folds)
  - Autoimmune type: Associated with antibodies to parietal cells (→ achlorhydria) and intrinsic factor.
    - Pernicious anaemia develops in 10%. Usually affects body of the stomach
  - **Helicobacter pylori** infection → hypertrophic gastritis: enlargement of rugal folds due to hyperplasia.
    - Several causes. Differential: lymphoma can also present with enlargement of rugae

Acute Ulcers

- **Stress** (physiological) ulcers: shock, burns, sepsis
- Due to mucosal hypoxia
- Usually heal quickly
- Appearance: multiple circular ulcers < 1 cm. Penetrate submucosa. Occasionally massive bleeding

Peptic (Gastric & Duodenal) Ulcer

**Symptoms & Signs**

- Gastric & duodenal usually indistinguishable clinically
- Gastric ulcer: epigastric pain worsened by food + helped by lying flat or antacids
- Duodenal ulcer: epigastric pain relieved by food + worse lying flat or antacids
- Uncomplicated: can be silent, epigastric pain after food, relived by antacids, and waking at night due to pain, weight change
- Complicated: haematemesis/melaena, vomiting, severe pain → pancreatitis or perforation (but 50% of patients with fatal complications present without ulcer pain), shock, anaemia, peritonitis

**Epidemiology**

- 10% of the population have one at some time in their lives
- M > F 3:1
- Genetic risk (50% twin concordance)

**Aetiology**

- Need mucosal injury
- H. Pylori infection. Damages D cells → ↑gastrin → ↑acid & pepsin → metaplasia + helicobacter damage → ulcer
- Smoking, alcohol, etc
- NSAIDs
- If neither H. Pylori infection nor NSAIDs then ulcer very unlikely
- Not due to ↑acid (except for Zollinger-Ellison syndrome)
- Macroscopic appearance: well demarcated, punched out, with radiating mucosal folds. Most <4 cm diameter
- Microscopic appearance – 4 layers/zones:
  - Exudative zone: fibrin, debris, neutrophils, etc
  - Necrotic zone: necrotic debris
  - Granulation tissue zone
  - Zone of fibrous tissue
Adjacent: blood vessel thickening, mucosal hyperplasia, chronic inflammation

*Helicobacter Pylori*
- Curved gram –ve rod organisms in gastric mucus
- From contaminated water
- 22% prevalence in Welly (test + scope strategy better – definitely is if prevalence <10%)
- Motile via flagella, burrows into mucus layer (corkscrew shape)
- Produces urease – neutralises acid and NH₄causes gastric injury
- ↑risk of gastritis, ulcers, adenoca, gastric lymphoma
- Two patterns seen:
  - **Antral**: when located in antrum will see high acid production and duodenal ulcer risk
  - **Pangastritis**: when in fundus will see lower gastric acid and gastric ulcer risk + adenocarcinoma risk
- Dx:
  - **CLO test** (tests for urease conversion into NH₄, giving a pH change + therefore a colour change)
  - Urea breath test
  - Faecal Ag test
  - Serology
- H. Pylori infection in 70-80% of gastric ulcers, 95% of duodenal
- Also associated with gastric adenocarcinoma and gastric MALT lymphoma (i.e. it’s a carcinogen)
- Lives beneath gastric mucus: pH of 5 – 7 (compared with 1 – 2 in stomach lumen)
- H. Pylori always gives gastritis, usually in the antrum, but usually asymptomatic. Eradication only of benefit if ulcer present
- Microscopic appearance: chronic atrophic gastritis. Chronic inflammatory infiltrate → gland atrophy over time, intestinal metaplasia of remaining glands

*Investigations*
- **Bloods**: FBC (anaemia), amylase
- Refer for endoscopy if > 45 years or alarm symptoms (See Gastro-Oesophageal Reflux Disease (GORD), page 237)
- At endoscopy check for H Pylori, CLO test from biopsy sample, or histology/culture, and biopsy from antrum of stomach. 1% of gastric ulcers are cancers – always biopsy – but ulcers don’t predispose to cancer
- Urease breath test (gold standard): swallow C¹³labelled urease and check for expired labelled CO₂. H. Pylori has Urease to turn urea → NH₂ + CO₂ (radio-labelled)
- CXR: subdiaphragmatic gas in perforation

*Differential*
- Pain: Reflux, gastric ulcer, gastric cancer, gallbladder disease, chronic pancreatitis, IBS
- Acute Severe Pain: acute pancreatitis, bilary colic, aortic dissection, MI
- Zollinger-Ellison syndrome: uncontrolled gastric acid secretion driven by ↑plasma gastrin released by a gastrinoma - 50% malignant → multiple peptic ulcers
- Crohn’s, Lymphoma, CMV
- Ulcers – malignant vs benign: malignant often have irregular edges, are large + can be haemorrhagic; benign = smooth rolled edge + smaller

*Treatment*
- If on NSAIDs: stop them. Normally curative
- Antacids
- H2 receptor antagonists: good healing over 4 – 8 weeks (ranitidine, cimetidine)
- PPIs: for unresponsive ulcers - superior to H2RA for healing and maintenance
- **Triple therapy** for H. Pylori:
  - 75% effective under normal conditions. Reinfection is rare (< 1%)
  - 2 weeks optimal – 7 days pretty good
  - pH has effect on antibiotic bioavailability: want to ↑pH (e.g. omeprazole)
  - Bismuth (De-Nol) + tetracycline & metronidazole + ranitidine, or
  - Clarithromycin & metronidazole + ranitidine, or
  - Amoxycillin + metronidazole + omeprazole
- Treatment of H. Pylori in non-ulcer dyspepsia has little effect. Only proven benefit of eradication is in ulcer disease and MALT lymphoma
- Always re-scope an ulcer to check healing. You want to be sure it’s not a cancer missed on histology (and PPIs will mask symptoms)

**Complications**
- Only time surgery is involved
- Haemorrhage: 2.5% of PU per year → occult, melaena or haematemesis → 10% mortality
- Perforation: 1% of PU per year, usually NSAID users
- Penetrating: pancreas, liver, biliary
- Obstruction: of pylorus due to chronic scarring/stenosis → functional obstruction

**Pernicious Anaemia**
- Symptoms & signs (due to anaemia or B12 deficiency):
  - SOB/lethargy
  - Sore tongue (glossitis in 50%)
  - Parasthesiae and gait disturbance (peripheral neuropathy), loss of proprioception/reflexes
  - Depression, impaired memory
  - Mild splenomegaly
- Investigations:
  - Bloods: macrocytic anaemia, leucopenia, hypersegmented neutrophils, ↑bilirubin, ↓serum B12
  - Schilling Test: < 10% urinary excretion of 58Co labelled B12, corrected when administered with intrinsic factor
  - Also serum gastrin measurement and endoscopy for gastritis
- Differential:
  - Dietary (e.g. vegan) or malabsorption (e.g. Crohn’s) deficiency of B12
  - Chronic H Pylori gastritis
  - 8% of pernicious anaemias develop gastric cancer
- Treatment: iv B12, loading dose then 1 mg every 3 months (watch for folate deficiency initially)

**Gastric Neoplasia**
- Symptoms & Signs:
  - ‘Ulcer-like dyspepsia’ lasting more than a few weeks in middle aged or older
  - Early satiety, fullness → small cancer in pylorus, large in body of stomach, extrinsic compression, or linitis plastica (infiltrates stomach so can’t distend)
  - Vomiting, haematemesis/melaena
  - Weight loss, malaise
  - Anaemia
  - Metastases: Knobbly enlarged liver, ascites, pleural effusion, left anterior axillary node (Virchow’s)
- Investigations:
  - FBC (anaemia), LFT (mets?)
  - Endoscopy: biopsy and assess obstruction
  - CT to assess metastases
- Differential:
  - Ulcer or non-ulcer dyspepsia
  - Reflux oesophagitis
  - Anaemia of other causes
  - Depression
- Types:
  - Benign Tumours:
    - Polyps: hyperplastic/inflammatory – 90%, Neoplastic/adenomatous – 10%
    - Stromal tumours: leiomyomas, etc
  - Gastric Carcinoma:
    - Epidemiology: high in Japan (due to diet → screening programme), China, ↓in Western world (better water → ↓helicobacter and better food preservation → ↓oxidised food which is carcinogenic).
      6/100,000. M > F
    - Aetiology: Diet (↑pickles, ↑smoked food, ↓green leafy vegetables), genetic, associated with chronic gastritis and adenomatous polyps, and helicobacter
    - Evolution: dysplasia → carcinoma-in-situ (confined to submucosa) → invasive
Macroscopic: early – thickening, hyperaemia. Go on to 1) ulcerating, fungating masses, rolled overhanging edge, 2) diffusely infiltrative (linitis plastica – “leather bottle stomach” – thickened wall and folds), 3) polyoid mass

Microscopic appearance: 1) Intestinal type: malignant glands, 2) Diffuse or gastric type: syngnet ring cells

Outcome: depends on stage not type. Metastasis to lymph nodes, peritoneum, liver, lungs

Treatment:
- Resection
- Chemotherapy for palliation only
- Symptomatic drug treatment

Coeliac Disease

- Chronic inflammatory disorder of GIT caused by lifelong immune response to dietary gluten
- Gluten sensitive enteropathy: sensitive to gliadin protein fraction in gluten (found in BROW: barley, rye, oats and wheat)
- Is a genetically predisposed AI condition
- Underdiagnosed ~ 80% remain undetected → leading to significant morbidity
- SI main target, systemic manifestations (skin, bone) common
- Patients with active disease have an increased risk of death however this returns to normal after 3-5 years on a GFD
- Coeliac predominantly an upper GIT disorder therefore Fe (absorbed in duo) can be decreased; vitB12 deficiency only if severe

Epidemiology

- At least 1% of pop: 1/100-1/300 worldwide (1/100 in NZ); more common in euro, less in Chinese
- Prevalence depends on population prev of HLA types; appears to be increasing
- F>M 2:1

Clinical

- Many pts have minimal symptoms or present atypically
- S & S:
  - Lassitude (weariness, listlessness)
  - Anaemia
  - Weight loss, anorexia, chronic diarrhoea, FTT
  - Fertility + gynae problems
  - Pain post meals
  - Extra-intestinal = short stature, pubertal delay, Fe def anaemia, dental enamel defects, neuropsychiatric disturbance

Types

- Classical (GI symptoms)
- Atypical (non-GI symptoms)
- Silent (no symptoms)

Differential

- Other causes of diarrhoea: e.g. Lactose intolerance, IBD, IBS
- Thyrotoxicosis (→ ↑ bowel motility)
- ↑ Ca

Diagnosis

- Characteristic histopathology (Modified Marsh score- infiltrative (lymphocytes) to atrophic pattern 0 - IV) changes in intestinal bx + clinical improvement in response to a GFD (+ positive serological tests)
- Serological tests: have a role in confirming coeliac + screening individuals at risk (anti-tTG, anti-endomysial Ab)

Screening Test

- For those with chronic/intermittent disease, FTT, persistent n + v, fatigue, recurrent abdo pain, weight loss, Fe def anaemia
- FDR, autoimmune thyroid disease, dermatitis herpetiformis, IBS, T1DM
- **IgA anti-tTG** is the best screening test
- IgG anti-deamidated gliadin peptide antibody test is a new test that may pick up further cases missed by IgA-anti-tTG

**Confirmatory Test**
- Endoscopy with duodenal bx
- If screening test is negative, pts with diarrhoea, weight loss or anaemia should still have duodenal bx

**Investigations**
- Bloods (FBC, CRP, U&E, LFT, Ca, Vit B12, folate, Fe, ferritin)
- Serology (endomysial Ab, tTG, IgA + IgG Ab, total IgA) if IgA low, can be a FN as % of pop have low IgA; **don't do anti-gliadin Ab, they're useless**
- Faeces (FOB, check for steatorrhoea, calprotectin)
- Duodenal bx

**Genetics**
- DQ2 and DQ8 are **necessary but not sufficient** for development of coeliac
- Also a/w class I + II HLA (A, B, DR, DQ); T2DM ~4% have coeliac
- FHx: FDR at increased risk – 20-30% if have HLA-DQ2 or DQ8+ (20-30% pop have DQ2 or DQ8 Ag)
- HLA types:
  - >99% of those with CD have HLA-DQ2 or DQ8 mutations
  - However, up to 30% of the normal pop will carry these genotypes therefore testing has a **high NPV but a low PPV**
  - HLA typing is not part of the routine testing for CD
  - Can be used to assist in dx of a case where serology + duo bx are not clear cut or to rule out CD in a pt already on a GFD + doesn't want to undergo a gluten challenge or for those who cannot undergo endoscopy + bx

**Pathogenesis**
- Activation of cell-mediated (Tcell) + humoral (Bcell) **immune response upon exposure to glutens** (prolamins + glutenins) of WBR in a genetically susceptible person; HLA-DQ2 found in 95%; remaining have HLA-DQ8
- Gluten absorbed + picked up by macrophages who present it to mucosal DQ2/DQ8 restricted Tcells – stimulates immune response
- **AutoAb to connective tissue surrounding smooth muscle** = endomysium is highly specific for coeliac – the Ab target is tTG; leads to mucosal inflammation + further Bcell activation
- A/w auto-Ab against tTG and others

**Pathology**
- 1. Subtotal villous atrophy
- 2. Crypt hyperplasia
- 3. ↑ intraepithelial lymphocytes
- Leading to abnormal small bowel mucosa and malabsorption. Primarily affects **distal duodenum**. In severe cases can extend to terminal ileum

**Sequelae**
- Cancer risk: 1.3:1; especially **lymphoma EATL** (enteropathy associated T-cell lymphoma) but untreated classical coeliac also ↑ risk for SI adenocarcinoma, oesophageal + oropharyngeal SCC
- Refractory disease: persistent symptoms, villous atrophy, failure to respond to GFD – **considered a low-grade intraepithelial lymphoma**

**Other Associated Conditions**
- Osteoporosis
- **Infertility** and period problems (may manifest for first time during preg)
- **AI conditions** occur 10x more frequently
- **Dermatitis herpetiformis** (erythematous macules, pruritis, symmetrical, 90% have no GI symptoms; 75% have villous atrophy; gluten sensitive)
- **Gallstones/reflux**: gastrin, motilin, CCK made in G cells on villi in duodenum therefore can develop reflux/HB and gallstones due to low production of these hormones therefore **GB + stomach do not empty properly**

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- **Lactase deficiency**: lactase made on brush border therefore can be a bit lactose intolerant also

**Management**
- Refer to dietician (GFD is low in fibre therefore need to eat a high-fibre diet w whole-grain rice, maize, veg etc)
- Complete GFD (Foods allowed: rice, corn, beans, buckwheat, milk/cheese, soybean, millet, sorghum; oats must be pure)
- May need vitamins
- May need DEXA
- Repeat endoscopy @ 6-12/12
- Screen FDR
- Maintaining + monitoring GFD:
  - CD serology become neg by 6-12/12 in those on GFD
  - Serology become pos w large transgressions of the GFD but not small
  - The best monitor of GFD is a dietician
  - Hx regarding adherence not as good as serology
- Follow-up:
  - Duo bx at 12/12 to document healing
  - Regular testing of nutritional indices recommended (FBC, iron studies, vit D, folate, vit B12, Ca)
  - Baseline bone densitometry w f/u if appropriate

**Other Malabsorption Syndromes**
- **Lactose Intolerance**:
  - Lactose intolerance very common: especially where dairy products are uncommon. Either *congenital* (rare), *acquired*, or *secondary to enteritis* (i.e. be careful with milk for several weeks after bad diarrhoea)
  - **Lactose breath test**: give lactose. Broken down by lactase. If ↓lactase then osmotic diarrhoea → rapid transit → early & large rise in H2 as lactose is broken down by bacteria (essentially undigested lactose produces high levels of hydrogen). Check with serial breath H2 measurements
- Tropical Sprue: enterotoxic E coli infection in visitors to the tropics. Affects distal intestine
- Whipple’s Disease: tropheryma whippelii (bacteria) infection. Obstruction to lymphatics causes malabsorption. Treat with erythromycin, otherwise death from systemic spread
- Abetalipoproteinaemia: genetic defect, unable to synthesise apoproteins

**Small & Large Bowel**

**Anatomy**
- **Bowel wall anatomy**: mucosa → *muscularis mucosae* (separates mucosa from SM) → submucosa → *muscularis propria* → serosa/adventitia
- NB BM surrounds each gland (doesn’t just separate mucosa from SM), LP fills rest of mucosa

**Pathology**

<table>
<thead>
<tr>
<th>SI conditions</th>
<th>Condition</th>
<th>Pathogenesis</th>
<th>Features</th>
<th>Path</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coeliac disease</td>
<td>Upon exposure to gliadin, tTG modifies the protein, and the immune system cross-reacts with the small-bowel tissue, causing an inflammatory reaction</td>
<td>Risk of lymphoma</td>
<td>1. Villous atrophy – flattening 2. ↑ intraepithelial lymphocytes (&gt;5/epi cell) 3. Crypt hyperplasia (big crypts, little villi)</td>
<td></td>
</tr>
<tr>
<td>Giardia</td>
<td>Protozoan parasite</td>
<td>Can cause villous atrophy</td>
<td></td>
<td></td>
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<tr>
<td>Ischaemic gut</td>
<td>MVD: strangulation → haemorrhage → venous drainage blocked but still arterial supply → necrosis</td>
<td>Gastric, duodenal or pancreatic mucosa</td>
<td>1. Congested blood vessels 2. Interstitial oedema 3. Sloughed epithelial cells</td>
<td></td>
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<tr>
<td>Meckel’s diverticulum</td>
<td>Remnant of vitelline duct (intestine to yolk sac) 80cm north of IC valve, 1-8cm long</td>
<td>Can lead to perf, fistula, ulceration, bleeding, intussusception, tumours</td>
<td></td>
<td></td>
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<tr>
<td>Intussusception</td>
<td>Mostly seen in &lt;5yrs Due to lymphoid hyperplasia or meckel’s or mass</td>
<td>Bowel obstruction or bleeding</td>
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<td><strong>Hirschsprung’s disease</strong></td>
<td>Absence of PS ganglion cells (due to failure of migration of neural cells) therefore no peristalsis</td>
<td>1:5000 congenital; M&gt;F Delayed meconium, distention</td>
<td>1. Dilated + hypertrophied proximal segment 2. Narrowed distal segment (no ganglion cells)</td>
<td></td>
</tr>
<tr>
<td><strong>Diverticular disease</strong></td>
<td>Acquired → low fibre diet → increased pressure → mucosal herniation</td>
<td>Sigmoid predominantly</td>
<td>Can lead to diverticulitis, bleeding, perf, abscess, fistula, peritonitis</td>
<td></td>
</tr>
<tr>
<td><strong>Colitis</strong></td>
<td>1. Infectious (campylobacter, salmonella, shigella, EHEC, CMV, c.diff) 2. Radiation induced 3. Ischaemic</td>
<td>Pain, diarrhoea, bleeding</td>
<td>1. Focal or diffuse inflammation 2. Cryptitis/crypt abscesses 3. CMV = big cells 4. Pseudomembranous → clostridium → mucosa dies + sloughs off</td>
<td></td>
</tr>
<tr>
<td><strong>Ischaemic colitis</strong></td>
<td>MVD, embolic (eg aorta), shock, vasculitis, volvulus, intussusception etc</td>
<td>&gt;50yrs Atherosclerosis, DM RFs</td>
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- Differentiating small and large bowel: large bowel has taeniae coli and haustra are not continuous around inside of lumen
- Type of colitis:  
  - Infective  
  - Collagenous  
  - Microscopic  
  - Pseudomembranous  
  - Acute & chronic irradiation  
  - Necrotising enterocoloitis  
  - Ischaemic  
  - Amoebiasis  
  - Crohn’s and Ulcerative
- Gut layers:  
  - Mucosa and muscularis mucosa  
  - Submucosa with lamina propria  
  - Muscularis propria (two layers)  
  - Serosa/adventitia
- Melanosis Coli: brown cells at base of crypts - lipofuscin from broken down organelles, correlated with laxative use, no impact

**Functional Motility Disorders**
- Upper GIT eg non-ulcer dyspepsia (post-prandial distress syndrome; epigastric pain syndrome)  
  - Epigastric pain syndrome = intermittent pain + burning localised to epigastrium at least once/wk, not relieved by pooing or farting, not localised to other abdo or chest regions, at least 3/12 w onset at least 6/12 prior

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*Gastro-Intestinal*
- **Post-prandial distress syndrome** = at least 3/12 w onset at least 6/12 prior of post-prandial fullness after ordinary-sized meals several times/wk OR early satiation preventing finishing regular meal

- **Lower GIT** eg **IBS**
  - **IBS** = at least 3/12 w onset at least 6/12 prior of recurrent abdo pain/discomfort a/w improvement w pooing +/OR onset a/w change in frequency (straining, urgency) of stools +/OR onset a/w change in form (d or const) of stools; passage of mucus, bloating
  - **IBS** extra-intestinal features (lethargy, urinary freq, urgency, nausea, dyspareunia, fibromyalgia etc)

- **Biliary tract eg SOD (sphincter of oddi dysfunction)**
  - Is a symptom complex of intermittent upper abdominal pain that may be accompanied by nausea and vomiting
  - There are two types of sphincter of Oddi dysfunction: 1) papillary stenosis and 2) sphincter of Oddi dyskinesia. Papillary stenosis is a fixed anatomic narrowing of the sphincter, often due to fibrosis. Sphincter of Oddi dyskinesia refers to a variety of manometric abnormalities of the sphincter of Oddi.

- **Awareness disorder**:
  - Functional GIT disorder a/w increased awareness i.e. some people are more hypersensitive to movement in their abdo – can be painful

### Ischaemic Bowel Disease

- **Distribution**:
  - **Vascular occlusion**: superior mesenteric
  - **Watershed lesions** → in between vascular territories (eg splenic flexure, rectum)

- **Transmural infarction**:
  - Pathogenesis: arterial **thrombosis, embolic** occlusion, venous thrombosis or **strangulation** and torsion
  - Macroscopic appearance: *red and intensely congested*. Subsequently gangrenous
  - Microscopic appearance: transmural necrosis, congested with blood, epithelium sloughed off, inflammation, perforation in 3 – 4 days
  - Clinical: severe pain, nausea, collapse, 50 – 75% die

- **Mucosal Infarction**:
  - Pathogenesis: **non-occlusive hypoperfusion** damaging only the inner layers due to shock, cardiac failure, etc
  - Macroscopic appearance: congested in patches or large areas. Mucosa haemorrhagic, oedematous, ulcerated
  - Microscopic appearance: Necrosis of mucosa, remainder OK
  - Clinical: *pain, bloody diarrhoea*, shock, potentially reversible

### Bowel Obstruction

**Presentation**

- **High small bowel**: mainly *vomiting*, less distension/pain, no constipation, more rapid onset
- **Low large bowel**: mainly *distension/constipation/pain*, evolves over days/week (‘sub-acute’)
- Visceral pain → poorly localised to either epigastric, peri-umbilical or subrapubic regions

#### Classification

- Small vs. large
- Complete vs. incomplete
- Open loop vs. closed loop
  - Open loop: mainly colicky pain – comes in waves. Either top end or bottom end still open
  - Closed loop:
    - Isolated loop → ↑peristalsis & ↑fluid → ↑intramural pressure → ↓capillary perfusion & compromised venous drainage → gangrene → perforation (rapidly fatal through sepsis and mass cytokine release)
    - Symptoms: quick (6 hours start to finish), constant severe pain that started colicky, ↑temperature & ↑pulse once infarction starts
    - X-rays & WBC may be normal
    - Differential diagnosis pancreatitis (do amylase)

#### Causes

- Intraluminal:
Cholecystoduodenal fistula → **gallstone ileus**. Gallstone moves from gallbladder to duodenum via fistula (→ air into biliary tree). Also following ERCP
- Bezoar: lump of stuff (e.g. hair) intermittently blocking ileocaecal valve

- **In the bowel wall:**
  - Crohn’s
  - Tb
  - Tumours of small bowel. (Less common) – lymphoma, carcinoid (neuro-endocrine), adenocarcinoma, melanoma secondaries

- **Outside wall:**
  - **Hernia** of small bowel, especially indirect inguinal or femoral *(always examine groin)*
  - **Adhesion** from previous surgery (look for scars): can take years to present acutely
  - **Small bowel volvulus:** malrotation of embryonic mesentery (can also be acquired, e.g. drugs) → easy rotation of mesentery
  - **Intussusception:** piece of bowel forced into distal section. Rare, *most common in kids* (2 months → 2 years). Especially around ileocaecal valve

- **Also in large bowel:**
  - Diverticular stricture and cancer (most common in sigmoid)
  - Volvulus: of any part of colon (especially sigmoid)
  - Distal obstruction can also cause ileocaecal valve to shut → closed loop obstruction. Caecum ischaemic first as biggest radius (Law of La Place)
  - **Pseudo-obstruction = ileus:** motility problem (esp. after recent surgery)

- **History:** bowel movements, previous surgery, weight loss
- **Exam:** dehydration (from vomiting) & distension
- **Treatment:**
  - **Rehydration:** crystalloid (i.e. saline) – only want to restore ECF (i.e. not dextrose)
  - **Nasogastric tube:** suck out stomach contents →↓vomiting & aspiration
  - **AXR + CXR**
  - **Urinary catheter:** monitor fluids
  - **Monitor creatinine:** if hypoperfusion → kidney failure
  - **FBC:** group & save
  - **Pain relief:** 10 mg im morphine or slow infusion. If dose is bad enough to need another then need surgery
  - If no scars & no hernias → surgery
  - If scars → may settle (if operate → more adhesions). Regular review

**Appendicitis**
- = Acute Suppurative Appendicitis
- Lifetime incidence = 6%
- Most common surgical emergency
- Incidence declining (?↑Hygiene +↓pathogen exposure)
- Gut organisms invade appendix wall after lumen obstruction
- If suspected then NBM. If no diarrhoea or vomiting then no immediate danger of dehydration
- If you diagnose it, or if you don’t, you’ll be wrong 50% of the time!

**Symptoms & Signs**
- Very difficult to diagnose – considerable variety in presentation
- **Fever:** 37.5 – 38.5. Typically low grade. Higher if perforated. Swinging fever more typical of an abscess
- **Pain:**
  - **Initially:** central abdominal colic (obstructed appendix and ↑lumen pressure – referred pain midgut)
  - Ball-valve relief of obstruction often leads to colicky pain
  - Once peritoneum inflamed: **constant RIF pain**
  - If perforated: generalised tenderness, maybe distension. If really sick, abdomen may not be hard
  - However, considerable variation – pain may stay central, may be situated elsewhere in abdomen
  - Lying on back and lying still, coughing hurts (peritonitis)
  - Push on right side (2/3 of the way from umbilicus to ASIS: **McBurney’s**)”
  - Push on left side → hurts more on right (Rovsing’s sign)
Evoking pain: cough or hop on right leg. In a child, look for tenderness and guarding – not rebound – won’t let anyone touch them after that.

- Systemic signs:
  - Kids: vague pain, off food (won’t eat favourite food), diarrhoea, vomiting
  - Elderly: shocked, confused, no pain
  - Anorexia, maybe vomiting
  - Constipation or diarrhoea
  - Tachycardia (not always)

- May be urinary symptoms and signs: especially in children with appendix in the pelvis – e.g. dysuria, white cells in urine (always do dipstick)

- Get children to blow out and suck in abdo to assess for peritonism

**Differential**
- Appendicitis may co-exist with acute tonsillitis, pneumonia, UTI or even gastro-enteritis
- Salpingitis in female, ECTOPIC pregnancy (do pregnancy test), food poisoning, diverticulitis, cholecystitis, perforated ulcer, cystitis, Crohn’s disease, inflammation of Meckel’s diverticulum (if operate and appendix OK, always check a metre up the small bowel), radiation of TORSION of right testis, strangulated inguinal hernia, pyelonephritis

**Pathology**
- **Pathogenesis:** Obstruction of the lumen (faecolith, tumour, worms) → ↑ intraluminal pressure → pressure ischaemia → bacterial invasion → inflammation → ↑ oedema → pop
- Macroscopic appearance: congested, dull, fibropurulent exudate on serosa, luminal abscess, gangrene, rupture
- Microscopic appearance: neutrophils IN mucosa, submucosa and muscularis propria, necrosis +/- abscess

**Treatment**
- If not sure, observe: it will get better or worse
- Supportive care: IV, NG, restore hydration
- Appendicectomy
- Metronidazole + cefuroxime (reduce wound infection)

**Children**
- Anatomical variations:
  - Typical site only 30 – 40% of time
  - PR: pain on right side → retrocaecal appendix (30%). Pain may radiate up right flank. May be no abdominal tenderness
  - Pelvic (23%). If in contact with bladder → sterile pyuria. If in contact with sigmoid → diarrhoea

  - Course accelerated:
    - Tiny lumen + ↑ lymphatic tissue, ↑ inflammation, perforate quickly
    - Dehydration, tachycardia and shock
    - Board-like abdomen after resuscitation

  - Treatment:
    - **Resuscitation first:** NG, IV, antibiotics
    - Operate when: ↑ urine output, ↓ temperature, ↓ pulse rate. Anaesthetics → vasodilation and cardiac depression → ↓ ↓ BP if not well hydrated

**Complications**
- Wound infection
- Perforation → peritonitis → infertility in girls (→ lower threshold for surgery in girls)
- Abscess
- Bowel obstruction (related to perforation → adhesions)

**Other Disorders of the Appendix**
- Mucocoele of the appendix: dilation of the appendiceal lumen by mucus duct hyperplasia (either benign or malignant)
- Pseudomyxoma peritonei: ‘Jelly Belly’. Mucinous cystadenocarcinoma invading the peritoneum, fills with tenacious semisolid mucus. Begins in appendix or ovary. Treated with serial resection + appendicectomy +/- oophorectomy
Ulcerative Colitis (UC)

- Chronic inflammation of colonic mucosa (only). Unknown aetiology

Epidemiology

- **More common** than Crohn’s
- 1 in 1500 in US. Rare in developing countries
- Peak incidence in 25 – 30 year olds
- Smoking is **protective**
- Risk in 1st degree relatives increases 15-fold
- F > M, W > B

Symptoms & Signs

- Diarrhoea if disease extends above rectosigmoid junction
- Mucus and blood per rectum
- **Urgency** to defaecate
- Abdominal pain, tenderness
- Relapsing-remitting in 65% patients
- If severe attack: fever, tachycardia, hypoalbuminaemia
- May have: erythema nodosum, arthropathy, aphthous ulcers in mouth and liver complications

Investigations

- Stool culture: exclude infectious
- Faecal calprotectin
- **Bloods**: ↑ESR and acute phase proteins
- Possible deficiencies: Fe, Hb, albumin, electrolyte abnormalities
- Sigmoidoscopy: red, raw, granular mucosa
- Colonoscopy & biopsy. Spreads from rectum to some point in colon.

Pathology

- Macroscopic appearance:
  - Begins in rectum and extends in continuity to left colon. 40 – 50% limited to rectosigmoid colon. 10% have pan-colitis, may also develop ‘backwash’ ileitis.
  - Mild: Erythema only. Severe: Mucosal haemorrhages and broad-based ulcerations (not deep though). Normal appearance during relapses
  - **Pseudopolyps**: islands of remaining, regenerating mucosa
- Microscopic appearance:
  - Mucosal inflammation only: mucosal ulcers
  - Neutrophils, plasma cells, histiocytes in lamina propria
  - *Crypt abscesses* (neutrophils in crypt) suggestive of UC rather than Crohn’s. May extend into lamina propria to produce ulcers
  - Chronically, mucosa becomes thin and atrophic
  - Distortion of crypt architecture, branching
  - Over time → dysplasia → flat carcinomas (cf raised in colorectal cancer)

Differential Diagnosis

- Microscopic (lymphocytic colitis), Collagenous colitis or Crohn’s colitis
- Differentiating b/w IBD + acute infectious colitis: abnormal tissue architecture seen in IBD, normal architecture but too many inflammatory cells seen in acute infection
- Irradiation proctitis
- Infection, IBS, or cancer
- CMV or herpes simplex in immunosuppressed patients

Complications

- **Anaemia** due to chronic blood loss
- **Toxic megacolon**: diameter of transverse colon > 5.5 cm. Acute dilation of colon due to loss of muscle tone → ↑gas → distension → vascular occlusion → necrosis. May rupture → peritonitis. Emergency
- ↑Risk of **colon carcinoma**. Key risk facts:
  - How long have they had it (main one): 1% at 10 years, 30% at 30 years. Require regular screening
How much bowel is affected: greatest in pancolitis. Minimal with only rectal involvement

How well controlled is the inflammation

Aggressive flat lesions, infiltrates quickly into lymphatics in submucosa

- Perforation
- Fibromuscular strictures (check to exclude malignancy)
- Strong association with PSC (pANCA positive)

**Treatment**

- Maintenance = 5-ASA (mesalazine/balsalazide) + immunosuppressants if severe UC (azathioprine, 6MP, cyclosporin)
- Acute flare = corticosteroids (PO prednisone/IV hydrocortisone) + antibiotics + mesalazine for mild distal colitis + cyclosporine
- Maybe TNF-α for refractory UC

**Crohn’s Disease**

- Chronic granulomatous inflammation of the gut

**Epidemiology**

- Incidence ↑. Peaks in 2nd to 3rd decade
- 1 per 1000 in UK
- F > M, W > B

**Symptoms & Signs:**

- Malaise, weight loss (65 – 75%), failure to thrive, malabsorption
- Diarrhoea (70 – 90%)
- Rectal bleeding (45%)
- Pain (50%, from inflammation, infection, obstruction, colicky from intermittent obstruction of terminal ileum)
- Perianal disease (50 – 80%)
- Anaemia, glossitis (due to malabsorption)
- Aphthous ulcers in mouth
- Erythema nodosum (painful red nodular lesions on shins), pyoderma gangrenosum (recurring skin ulcers – 10 cm), clubbing
- Asymptomatic periods for weeks-months
- Attacks may be precipitated by emotional/physical stress
- Risk factors: genetic, smoking, high sugar/low fibre

**Aetiology**

- G X E X immune X intestinal permeability
- Type 4 immune reaction: trigger unknown. Cause: ?immune hyper-reactivity
- Proposed agents: viruses, disordered immunologic response to ingested antigen
- Genetic susceptibility: 10-fold risk in first-degree relatives
- ⇒ Multifactorial → abnormal regulation of inflammatory mediators

**Investigations**

- Bloods: check for anaemia (including anaemia of chronic disease), malabsorption, inflammatory measurements, ↑ ESR and acute phase proteins
- Deficiencies: folate, iron, B12, etc, electrolyte abnormalities
- Culture/faecal calprotectin to exclude infective causes
- Sigmoidoscopy/colonoscopy + biopsy
- Upper GI endoscopy
- Barium contrast of small & large bowel: strictures, fistula, cobblestone appearance, skip lesions etc

**Differential**

- Ileal disease: Tb, Lymphoma
- Colonic disease: colitis (ulcerative, ischaemic, radiation, collagenous), infection (salmonella, shigella, campylobacter), cancer
- Malabsorption: lactose intolerance, coeliac disease
• Differentiating b/w IBD + acute infectious colitis: abnormal tissue architecture seen in IBD, normal architecture but too many inflammatory cells seen in acute infection

Pathology

• Location:
  ➢ 75% terminal ileum
  ➢ 50% also involves colon
  ➢ 25% colon only (predominantly right side)
  ➢ <5% oesophagus, mouth

• Macroscopic appearance:
  ➢ Skip lesions
  ➢ Transmural inflammation
  ➢ Thickened, inflexible (resembles rubber hose) with narrow lumen
  ➢ Thickened, fibrosed mesentery and enlarged regional lymph nodes
  ➢ Strictures, fistulas, abscesses
  ➢ Mucosa: varying degrees of erythema and oedema. Cobblestone mucosa

• Microscopic appearance:
  ➢ Submucosal and subserosal inflammation with only secondary mucosal involvement (ie glands may be straight, unaffected)
  ➢ Aphthous (= shallow) ulceration of the mucosa
  ➢ Lymphocytic infiltrate, fibrosis
  ➢ Multifocal granulomatous vasculitis
  ➢ Non-caseating granulomata (only 60%): can have some Langerhans giant cells (horseshoe pattern of nuclei around periphery of a giant cell), but usually granulomas poorly circumscribed

Treatment

• Aim: suppress activity, restore quality of life, prevent complications
• Diet: nutritional supplements. Malnutrition a real risk, → growth retardation in kids. May need enteral or TPN feeding for ‘Bowel Rest’ → ↓antigen load (controversial)
• Maintenance:
  ➢ 5-ASA – sulfasalazine/ascocol/pentasa (can use suppository for distal disease)
  ➢ Immunosuppressants (azathioprine, 6MP, methotrexate – CD only, cyclosporin)
  ➢ Stop smoking
  ➢ Maybe TNF-α blockers if refractory
• Acute flare:
  ➢ Corticosteroids PO pred, IV hydro
  ➢ ABs
• Cholestyramine: absorbs bile (normally absorbed in the terminal ileum) to stop it getting into the large bowel, where it causes irritation
• Surgery
• Monitor: inflammatory markers

Complications/Associations

• Episcleritis (reddened sclera)
• Stricture, obstruction, fistulas (to bowel, bladder, vagina)
• Malnutrition
• Large & small bowel cancer (5% at 10 years – ie small risk – not screened for)
• Ankylosing Spondylitis
• Pyoderma gangrenosum
• Iritis
• Arthritis

Comparison with Ulcerative Colitis

<table>
<thead>
<tr>
<th>Crohn’s</th>
<th>Ulcerative Colitis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Macroscope</td>
<td>Continuous</td>
</tr>
<tr>
<td>Skip lesions</td>
<td>Mucosa only affected</td>
</tr>
<tr>
<td>Transmural inflammation</td>
<td>Large bowel only</td>
</tr>
<tr>
<td>Thickened wall</td>
<td>Pseudopolyps</td>
</tr>
<tr>
<td>Often proximal to large bowel</td>
<td>Cobblestone appearance</td>
</tr>
</tbody>
</table>

Gastro-Intestinal
**Microscopic**
- Granulomas (only 60%, poorly formed – pale area with giant cells)
- Crypt architecture preserved (like a row of soldiers)
- Muscularis involved

**Complications**
- Minor cancer risk
- Fistulas, strictures, fissures

**Surgery**
- Recurs at anastamosis. Surgery for obstruction and abscess common

<table>
<thead>
<tr>
<th>UC</th>
<th>CD</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Lesion location</strong></td>
<td>Affects mucosa + submucosa (occasionally) See crypt abscesses commonly</td>
</tr>
<tr>
<td><strong>Epidemiology</strong></td>
<td>2-10/100000 (more common than CD) More common in Jews + less common in black American + Asian populations</td>
</tr>
<tr>
<td><strong>Immune cells</strong></td>
<td>Type 2 T-helper lymphocytes</td>
</tr>
<tr>
<td><strong>FHx</strong></td>
<td>FDR risk for UC is 2-5% Monozygotic twins = 20%</td>
</tr>
<tr>
<td><strong>Genes</strong></td>
<td>No known gene defect</td>
</tr>
<tr>
<td><strong>Environmental factors</strong></td>
<td>More common in high SES Smoking is protective Early appendectomy protective against later development of UC Luminal flora plays a role</td>
</tr>
<tr>
<td><strong>Mass</strong></td>
<td>Rare</td>
</tr>
<tr>
<td><strong>Perianal d</strong></td>
<td>V rare</td>
</tr>
<tr>
<td><strong>Abscess</strong></td>
<td>V rare</td>
</tr>
<tr>
<td><strong>Serology</strong></td>
<td>pANCA positive in 80%</td>
</tr>
<tr>
<td><strong>Rectal involvement</strong></td>
<td>Always</td>
</tr>
<tr>
<td><strong>Pattern</strong></td>
<td>Proximal diffuse extension from the rectum</td>
</tr>
<tr>
<td><strong>ileal involvement</strong></td>
<td>Rare, backwash ileitis in 10%</td>
</tr>
<tr>
<td><strong>Fistulas</strong></td>
<td>Exceptional</td>
</tr>
<tr>
<td><strong>Strictures</strong></td>
<td>Rare</td>
</tr>
<tr>
<td><strong>Granulomas</strong></td>
<td>V rare</td>
</tr>
<tr>
<td><strong>Goblet cell depletion</strong></td>
<td>Common when active</td>
</tr>
<tr>
<td><strong>Risk of ca</strong></td>
<td>High after 20 years</td>
</tr>
<tr>
<td><strong>Effective drugs</strong></td>
<td>Corticosteroids Cyclosporin</td>
</tr>
<tr>
<td><strong>Maintenance drugs</strong></td>
<td>5-ASA, AZA</td>
</tr>
<tr>
<td><strong>Presentation</strong></td>
<td>Bloody diarrhoea, pain, cramps, tenesmus</td>
</tr>
<tr>
<td><strong>Nutrient deficiency</strong></td>
<td>Common in CD due to malabsorption</td>
</tr>
<tr>
<td><strong>Dx</strong></td>
<td>Radiology, endoscopy, histology, clinical</td>
</tr>
<tr>
<td><strong>Hx</strong></td>
<td>Explore symptoms NSAID use, URTI or GIT infection Smoking (CD)</td>
</tr>
<tr>
<td><strong>Ix</strong></td>
<td>FBC, ESR/CRP, albumin, LFTs + serology, Fe + B12/folate def Stool microscopy + culture</td>
</tr>
<tr>
<td>Progress monitoring</td>
<td>Regular bloods, ESR/CRP, AXR</td>
</tr>
<tr>
<td>---------------------</td>
<td>----------------------------</td>
</tr>
<tr>
<td>Supportive rx</td>
<td>IVF w electrolytes depending on presentation</td>
</tr>
<tr>
<td>Nutritional support</td>
<td>Can eat normally and no dietary manipulation usually of benefit however adherence to 'elemental' diet (given in simplest formation eg pro as AA, CHO as glucose and fat as FA) can induce remission in small bowel CD</td>
</tr>
<tr>
<td>Drugs to avoid</td>
<td>Avoid anti-diarrhoeal meds (codeine etc) as they may precipitate TMC</td>
</tr>
</tbody>
</table>
| Active disease      | Corticosteroids PO pred, IV hydro ABs  
Mesalazine for mild distal colitis Cyclosporin  
5-ASA – mesalazine/balsalazide Immunosuppressants (azathioprine, 6MP, cyclosporin – for severe UC) |
| Maintenance         | Corticosteroids PO pred, IV hydro ABs  
5-ASA – sulfasalazine/asacol/pentasa (can use suppository for distal d)  
Immunosuppressants (azathioprine, 6MP, methotrexate – CD only, cyclosporin) Stop smoking |
| Perianal disease    | Metronidazole and ciprofloxacin |
| Refractory disease  | Infliximab |
| Fistulising disease | Infliximab |
| Surgery             | Done for uncontrolled severe d  
Rectum + entire colon taken, either permanent colostomy or ileo-anal pouch  
Abscess Refractory disease  
50% recurrence rate after – take 5-ASA compound long term Complications = malabsorption |
| Disease f/u         | Those in remission should have f/u every 6-12/12 including bloods etc  
R sided colitis has higher risk of cancer than L sided  
Colonoscopy surveillance every 1-2 years after 10 years of UC – low grade dysplasia requires 3/12 repeat  
No need for special colonoscopy surveillance in CD |
| Pregnancy           | Similar rate of preg to general pop  
Active d can cause spont abortions + prem deliveries  
75% of pts w inactive d at conception will remain inactive; those w active d will stay w active d  
Sulfasalazine OK to use during preg + breastfeeding but use folate  
Corticosteroids also safe  
AZA + 6MP should be stopped when conception takes places  
Methotrexate should be stopped  
Metronidazole is OK for short periods |
| Disease severity    | <4BM/d = mild d = PO 5-ASA  
5-8BM/d = moderate d = PO steroids  
>8 BM/d = severe d = IV steroids (stace notes = if >6BM/d + systemic signs = IV steroids) |

**Small Bowel Tumours**

- Benign: Polyps (Peutz-Jeghers), Juvenile Polyps, Adenomas, Stromal tumours
- Malignant:
  - **Carcinoid** tumours:
    - Tumours arising from neuroendocrine cells
    - Mainly midgut. Similar tumours occur in lungs, ovaries, biliary tree
    - Can release 5HT3 (carcinoid syndrome), gastrin (peptic ulcer), insulin (hypoglycaemia)
    - Macroscopic appearance: submucosal elevations, yellow/grey, infiltrative, ulceration, multiple
    - Microscopic appearance: Uniform cells, oval nucleus, fine chromatin, pink cytoplasm, neuroendocrine granules
    - Clinical: malignancy depends on site. Appendix and rectum better, ileal and colonic worse
  - **Carcinoid Syndrome**: due to excess serotonin. Occurs with hepatic metastases (liver efficiently removes 5HT from portal circulation) → flushed, wheezing, right sided heart failure, diarrhoea (↑motility), abdominal pain, oedema, skin lesions
  - **Lymphomas** of the GI tract:
    - Affects stomach, ileum, colon, jejunum. Arise in the gut, or spread there from elsewhere
    - 3 types: MALT, Sprue associated, and immunoproliferative small intestinal disease
    - Macroscopic appearance: plaque-like expansion of the mucosa → ulcerating, fungating mass, can → obstruction or perforation

Gastro-Intestinal 253
Microscopic appearance: tumour cells diffusely infiltrate the wall, cytologically resemble follicular lymphoma cells
Clinical outcome: prognosis depends on depth of invasion, size, direct extension

Adenocarcinoma: uncommon. Resembles those in the colon

Colorectal Cancer

Presentation
- Change in shape of stools significant (e.g. pencil shaped)
- Rectal bleeding/mucus
- Persistent changes in bowel habit
- Tenesmus: constant feeling of need to defecate, even after passing stool
- Weight loss
- Anaemia
- Abdominal or rectal mass in late presentation
- Hepatomegaly (from secondaries)
- **Left-sided CRC clinical:** present earlier, occult or frank blood, change in bowel habit, mucous, pain, perf
- **Right-sided CRC clinical:** iron-deficiency anaemia, frank bleeding, pain (obstruction less likely as stools less well formed + larger lumen)

Risk Factors
- Interaction b/w G X E
- Environmental factors: diet, lifestyle, smoking
- Family history
- Premalignant lesions

Family History and Colorectal Cancer
- Average risk = up to two 1st or 2nd degree relatives with bowel cancer at 55 or older (as long as on different sides of family). 98% of population
- Moderate risk = either one 1st degree relative diagnosed before 55 years, or two 1st or 2nd degree relatives on one side of family diagnosed at any age. 1% population. Refer for colonoscopy every 5 years from age 50 or 10 years younger than earliest diagnosis in family
- High risk = more than above, including FAP or identified high-risk mutation in near relative. <1% of population. Suggest genetic testing. Referral to plan appropriate surveillance
- Incidence has been declining since 1950’s (5.8% decrease in men, 12.9% decrease in women)
- People may not know family history: can they get death certificates of relatives

Pathology
- 7th decade; M>F for rectal ca but M=F elsewhere
- 70% found in rectosigmoid
- Environmental factors: low fibre diet (prolongs GI transit time – increasing time for carcinogen production), high animal fat (forms carcinogens)
- Genetic factors:
  - FAP (APC gene – Sq21): 100% risk
  - Familial CRC = 2+ first degree relative increases risk by 3x (k-ras mutations)
  - HNPCC: 50% risk if FDR affected
- **Most are sporadic** mutations – inherited ~ 10-15%

Polyps

<table>
<thead>
<tr>
<th>Polyps</th>
<th>Type</th>
<th>Clinical presentation</th>
<th>Features</th>
<th>Path</th>
</tr>
</thead>
</table>
| Non-adenomatous | Hyperplastic | Most asymptomatic, bleeding, bowel habit change, intussusception, passed PR, mucus production | • 90% of all polyps
• Benign, non-neoplastic mucosal hyperplasia
• 75% in rectosigmoid
• Sessile, multiple, <0.5cm
• Large or multiple polyps show weak ass w ca (ass w DNA microsatellite instability ca) | Serration – mucosal overgrowth |
Juvenile

Often auto-amputate and are passed PR

Caused by cystic dilation of glands

<table>
<thead>
<tr>
<th>Adenomatous</th>
<th>Tubular adenoma</th>
<th>Rectal bleeding, mucus secretion</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Adenomas &gt;75% villous elements (papillary projections)</td>
<td>1. Thrown into villous folds</td>
</tr>
<tr>
<td></td>
<td>10-15% of adenomatous polyps</td>
<td>2. Dysplasia (the distinguishing feature b/w adenomatous polyps as cf other polyps) – low or high grade (carcinoma in-situ)</td>
</tr>
<tr>
<td></td>
<td>Left colon</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Most likely to harbour ca</td>
<td></td>
</tr>
</tbody>
</table>

Familial adenomatous polyposis (Polyposis coli)

Same polyps as sporadic variety just >100 of them (usually 1000s)

Prox + distal disease

Autosomal dominant with high penetration – APC gene 5q21

Nearly all develop ca – prophylactic colectomy 20-25 yrs

= Any lesion which protrudes above the level of the surrounding mucosa

Hyperplastic polyps:
- 90% of all polyps, measure < 0.5 cm, mainly in rectosigmoid
- Benign, no premalignant potential
- “Dew drop” appearance, on top of mucosal fold
- Sessile (no stalk), often multiple, very common
- Microscopically: elongated crypts, goblet and absorptive cells, excess mucin

Adenomatous polyps:
- 10% of polyps
- Neoplasms: precursors of most colonic carcinomas. Normally removed as don’t know which will become invasive
- Malignancy related to size: <1.5 cm only 1% contains a carcinoma, > 1.5 cm 10% will contain a carcinoma in-situ. As long as it’s confined to the mucosa, there is no metastatic potential. If submucosal invasion then segmental resection
- Macroscopically: stalk (ie pedunculated)
- Microscopically: neoplastic glands, hyperchromatic, etc
- Tubular adenomas: Most common (75%), usually pedunculated, most common in left colon, M > F, 50% are solitary, continued colonoscopic follow-up necessary. Head has closely packed tubules/glands lined by non-differentiated neoplastic columnar cells. Stalk has normal colonic mucosa
- Villous adenomas: Papillary projections, larger, more likely to harbour carcinoma, sessile, 10 – 15% of adenomatous polyps, mainly rectosigmoid
- Tubulovillous adenomas: contain 25 – 75% of villous component. May secrete lots of mucous

Adenomatous polyp – cancer relationship:
- Negligible risk with hyperplastic/juvenile polyps
- 30-70% of villous adenomas become malignant
- All FAP become malignant
- Adenoma-carcinoma sequence: mutational activation (K-RAS, p53, 5q mutations are important ones) of oncogenes + inactivation of tumour suppressor genes (~4 mutations required)
- Distinguishing b/w adenoma + adenocarcinoma:
  - Invasion of BM and
  - Desmoplastic reaction (inflammation + fibrosis)

Juvenile polyps:
- Left side of large bowel of kids
- Cause rectal bleeding
- Grossly look similar to adenomas
- Microscopically not neoplastic. Cystically dilated mucous glands, inflammation of lamina propria, maybe ulceration
- Peutz-Jeghers Syndrome: polyp containing mucin filled cysts and smooth muscle in the lamina propria. No malignant potential. Maybe pigmentation in the mouth

Polyposis Syndromes
- Familial Adenomatous Polyposis (FAP):
  - 0.5% of all colorectal cancers.
Autosomal dominant, antioncogene mutation of APC gene

APC gene: 1 in 10,000 have mutation → 100s of adenomatous polyps appearing in 2nd or 3rd decade
Will develop carcinoma ⇒ prophylactic colectomy. APC gene also mutated in sporadic cancer

Hereditary Non-polyposis Colon Cancer (HNPCC):
A misnomer – there are polyps!
Doesn’t go through adenoma-carcinoma sequence
Aka Lynch Syndrome. 5% of non-FAP colorectal cancers. Patients often young with multiple tumours. 1 – 5% of all CR cancer
Aetiology = mutations in mismatch repair genes – microsatellite instability – unable to correct DNA base pair mismatch; autosomal dominant
50% risk if first-degree relative affected
Young (<40yrs), right sided, high grade tumours
Must meet ‘Amsterdam criteria’ to make HNPCC dx (3 or more family members, 2 successive generations, etc)
~20 polyps (adenomatous polyps – often villous) as cf. FAP which has hundreds
Gardner’s Syndrome: colonic polyposis, epidermoid cysts (skin), osteoid osteomas (benign bone tumours). High risk of carcinoma
Turcot’s Syndrome: colon polyps + brain tumours

Adenocarcinomas of the Colon

Epidemiology:
In US, 2nd only to lung cancer in cancer deaths. Much lower in third world (⇒ environmental factors)
Peak incidence in 7th decade (ie old), except APC and UC
70% in recto-sigmoid colon, rest all the way back to caecum
M:F is 2:1 for rectal, equal for right sided

Aetiology:
Adenomatous polyps (esp villous)
Ulcerative colitis
Familial adenomatous polyposis
Family History
Environmental factors: high incidence in Europe/North America, low in Asia/Africa. Urban > rural
Diet: high fat and low fibre (slower transit ⇒ ↑exposure to carcinogens)

Pathogenesis: ↑ loss of heterozygosity in genes involved in DNA repair, tumour suppression and oncogene activation. Either through ↑turnover due to mucosal damage ⇒ ↑risk of gene match failure or directly genotoxic mechanism
Presentation:
Left sided: annular encircling ⇒ napkin ring or apple core constriction. Signs of obstruction. Poorer prognosis despite earlier detection due to ↑invasion
Right sided: large fungating or sessile masses, necrotic areas, occult bleeding, anaemia, weight loss
May produce mucin, ulceration ⇒ blood loss
Doubling time of about 2 years
Macroscopic description: Early: may still appear to be a polyp or sessile. Later: obliterate precursor adenoma
Microscopic appearance: Most are moderately differentiated, irregular glands with pleiomorphic cells, usually lack mucin production. Mucinous carcinomas (10 – 15%) have pools of mucin, cleaves through tissue aiding spread (worse prognosis)
Variants: Adenosquamous carcinoma, small cell undifferentiated (rare), Ulcerative colitis ⇒ poorly differentiated colitis

Other Large Bowel Tumours
Lymphomas: Non-Hodgkin’s. Eg MALT
Gastrointestinal stromal tumours: arises from interstitial cells of cajal
Carcinoid tumours: most common in appendix and stomach. See Small Bowel Tumours, page 253
Mesenchymal tumours (eg leiomyomas – smooth muscle tumour): much less common

Diagnosis
Rectal exam
FOBT: sensitivity 50% and low specificity
Sigmoidoscopy picks up 40% (& take biopsy).
Colonoscopy: expensive, miss rate for cancer 2-3%
- CT colonography
- Double contrast barium enema: cheaper, miss rate for cancer 10 – 15%
- Check for dissemination: LFT, Abdominal CT, CXR (25% have metastatic disease at presentation)
- CEA

**Differential**
- Diverticular disease
- Inflammatory Bowel Disease
- Irritable Bowel Syndrome
- Rectal ulcer

**Treatment of Colorectal Cancer**
- No role for radiotherapy in colon (as cf rectum)
- Adjuvant chemotherapy:
  - Improves 5 year survival over surgery alone from 50 to 60/65% (but can’t predict who will benefit)
  - ↑Quality of life (side effects of cancer are pretty severe, chemo reduces these)
  - Given after surgery
  - Six months of 5FU
  - Currently given to:
    - Dukes C: All patients (C1 = Muscularis propria + lymph node, C2 = serosa + lymph node)
    - Dukes B2 (serosa): High risk groups, perforation, invasion of adjacent organs, diploid tumours
- Rectal cancer:
  - No serosa around rectum – cancer infiltrates straight into fat – harder to get clear resection margins
  - Radiation in rectal cancer good: but → impaired function and may irradiate small bowel → fibrosis
  - Try and predict who needs irradiation and do it pre-operatively
- Palliation: hospice + chemotherapy better quality of life than hospice alone
- Other targeted therapies and ablative (eg RFA ablation) techniques are coming to the fore

**Prognosis of Colorectal Cancer**
- Invade into serosal fat; metastasise to regional lymph nodes then to liver, lungs and brain. Rarely intraperitoneal spread
- Complications: obstruction, perforation, haemorrhage, fistulas
- Prognosis mainly related to stage (how far it’s spread), to a lesser extent the grade and location
- Pre-operative staging: ultrasound of liver, Xray of lungs
- Duke’s Post-operative staging:

<table>
<thead>
<tr>
<th>Duke’s staging</th>
<th>Level of invasion</th>
<th>5-yr survival</th>
<th>Modified by:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage A</td>
<td>Confined to mucosa</td>
<td>100</td>
<td></td>
</tr>
<tr>
<td>B1</td>
<td>Muscularis propria</td>
<td>65</td>
<td>1. Lymphovascular invasion</td>
</tr>
<tr>
<td>B2</td>
<td>Serosa</td>
<td>50</td>
<td>2. Perineural invasion</td>
</tr>
<tr>
<td>C1</td>
<td>MP + local LN</td>
<td>40</td>
<td>3. High mucin</td>
</tr>
<tr>
<td>C2</td>
<td>Serosa + apical LN</td>
<td>25</td>
<td>4. Emergency surgery</td>
</tr>
<tr>
<td>D</td>
<td>Distant mets</td>
<td>5</td>
<td>NB. Duke’s often not used now</td>
</tr>
</tbody>
</table>

- Wgtn Hospital uses APC staging (Australasian Pathologists): minor differences to Dukes
- 5 year survival = cured – unlikely to relapse after that

**Follow-up**
- Colonoscopy (e.g. initially rest of colon for 2nd primary, then every 3 years)
- Monitor tumour marker **CEA** (carcinoembryonic antigen). Also raised in a variety of other tumours & benign cancers. Not sensitive for early cancers (4% of Duke’s A). Neither sensitive nor specific

**Diverticular Disease**

**Aetiology & Epidemiology**
- ↓Dietary fibre → ↓stool weight and ↓colonic transit → ↑colonic pressure
- 50% in > 70 years
**Symptoms & Signs**

- Most asymptomatic
- Uncomplicated disease (Diverticulosis): non-specific tender sigmoid colon, cramping lower abdominal pain (esp. LIF), altered bowel habit (hard or ribbon like stools, e.g. due to stricture)
- Complicated disease (Diverticulitis): constant pain worse with movement, fever, shock, peritonitis, haemorrhage, guarding, palpable mass, ileus, distension, obstruction (= “Left sided appendicitis”)
- PR bleeding not usually concurrent with guarding

**Pathology**

- Diverticulosis: multiple out-pouchings or herniations (= diverticula) of the mucosa through the muscle wall of the bowel at the point where arteries penetrate the bowel wall
- Diverticulitis: inflammation of the diverticulum caused by obstruction of the neck, faecal impaction, constricted blood supply, infection from luminal flora
- Complications:
  - Abscesses → obstruction, bleeding due to erosion of blood vessels
  - Stricture from scarring

**Investigations**

- Bloods usually normal in uncomplicated disease: do FBC and LFT
- Complicated disease: inflammatory/infection markers (eg blood cultures if temp > 38 C)
- CT, ultrasound, colonoscopy

**Differential**

- Cancer
- Inflammatory bowel disease
- Drug induced colonic symptoms
- Abscess/perforation: pyelonephritis, perforated peptic ulcer, ischaemic colitis
- Haemorrhage: polyp, angiodysplasia, GI bleeding
- Stricture: radiation damage, ischaemic colitis, endometriosis
- Malabsorption: lactose intolerance, coeliac disease
- Infection: campylobacter, other infection

**Treatment:**

- Acute management:
  - Fluids (nil by mouth to rest gut)
  - For diverticulitis: antibiotics (eg cefuroxime and metronidazole). If really nasty then Gentamycin, Amoxycillin and Metronidazole
  - Usually settles with conservative management. If not, then resect affected colon:
    - Hartman’s procedure: Remove affected segment. Bring proximal bowel out to a colostomy. Temporarily close off distal segment
    - Reverse colostomy 3 months later
- Chronic management:
  - ↑Fibre, ↑fluids, ↑exercise
  - For constipation: bulking agents, lactulose
  - For pain relief: anticholinergics (ciclyclomine), antispasmodics

**Irritable Bowel Syndrome (IBS)**

- Very common (up to 15 – 20%)
- F > M

**Symptoms & Signs**

- Crampy lower abdominal pain relieved by defaecation or flatus, associated with change in stool frequency/consistency
- Diarrhoea (rarely at night) and mucus
- Distension, variable abdominal tenderness
- Nausea, heartburn, early satiety
- Urinary frequency
- Exacerbated by anxiety or stress
• Age < 50 years
• Feeling of incomplete evacuation
• But NO blood, weight loss or recent onset

**Diagnosis**
• A diagnosis of exclusion
• Continuous or recurrent symptoms for at least 3 months
• **Abdominal pain relieved by defecation** or associated with a change in bowel habit
• Irregular pattern 25% of time with 2 or more of:
  - Change in frequency (> 3 per day or < 3 per week)
  - Change in form (lumpy/hard/loose)
  - Change in passage (straining/urgency/feeling of incomplete evacuation)
  - Mucus
  - Bloating/distension

**Investigations**
• Exclude other conditions, e.g.:
  - **FBC**: anaemia and nutritional deficiency
  - **LFT**: exclude biliary colic
  - **Thyroid function**: exclude myxoedema (→ constipation) or thyrotoxicosis (→ diarrhoea)
  - **Colonic imaging** for new or different symptoms in > 40 years – exclude cancer/IBD
  - **Faecal fat**, breath test, lactose tolerance test

**Differential**
• Diagnosis of exclusion, so the differential is everything else
• Cancer, IBD, diverticular/coeliac disease, infection, diverticular disease, chronic pancreatitis, biliary/liver disease, peptic ulcer, motility disorder, bacterial overgrowth, laxative abuse, endometriosis, ovarian malignancy, thyroid disease

**Aetiology**
• Abnormal gut motility
• Enhanced visceral sensitivity
• Psychological/psychiatric disorder
• Food allergy/intolerance

**Treatment**
• Supportive, reassurance, stress reduction, ↑ fibre (RDI = 25 – 30 grams, average is 15), ↑ fluids (2 litres per day), ↑ exercise
• For constipation: bulking agents, lactulose
• For pain relief: anticholinergics (cyclomine), antispasmodics
• For confirmed diarrhoea: antimotility drugs (**loperamide**, codeine phosphate)
• If depressed then **antidepressants**

**Bacterial Overgrowth of Small Intestine**
• = **Aerobic G+ bacteria replaced by anaerobic G-**, esp. e coli & **Clostridium difficile** (toxin causes diarrhoea)
  - often in a blind loop of bowel, or in the small bowel which usually has low bacterial load
• Symptoms & Signs:
  - Diarrhoea, abdominal pain, weight loss
  - Steatorrhoea, anaemia, ataxia/neuropathy (due to B12 deficiency – bacteria eat it all)
• Investigations:
  - Blood: check for anaemia, B12, folate
  - Schilling test
  - Stool test
  - Duodenal aspiration and biopsy
• Differential:
  - Coeliac disease
  - Chronic pancreatitis
  - Crohn’s disease
  - Infections: campylobacter, Giardia, AIDS enteropathy

**Gastro-Intestinal** 259
Breath tests: ↑H2 after lactulose, etc

Aetiology
- Motility disorders
- ↑Bacteria: e.g. ↓stomach acid (hypochlorhydria)
- Impaired immunity

Treatment:
- High protein diet, vitamin supplementation, stop antibiotics
- Antibiotics: Metronidazole 400 mg TD, Ciprofloxacin 500 mg BD, or vancomycin

Pseudomembranous Colitis
- Acute diarrhoeal illness following broad-spectrum antibiotics
- Overgrowth of Clostridium difficile
- Macroscopic appearance: pus erupting from glands (like little volcanoes, cauliflowers)
- Microscopic appearance: superficial necrosis of epithelium and crypts, ↑↑mucus/pus over the surface

Diarrhoea
- = Acute Enterocolitis
- Normal bowel habit:
  - Frequency = 3/d – 3/w
  - Form = Bristol stool chart
  - Amount = ~250g/d
  - Absence of blood, pain, tenesmus
- Diarrhoea definition:
  - The abnormal passage of loose or liquid stools more than 3/d and/or a volume of stool > 200/250g/d
  - Chronic diarrhoea = as above for > 4/52 (although Wyeth says 2/52)
- Diarrhoea types:
  - Secretory diarrhoea means that there is an increase in the active secretion, or there is an inhibition of absorption. There is little to no structural damage eg cholera
  - Osmotic diarrhoea occurs when too much water is drawn into the bowels. This can be the result of malabsorption (e.g., pancreatic or coeliac d), in which the nutrients are left in the lumen to pull in water
  - Exudative diarrhoea occurs with the presence of blood and pus in the stool eg IBD or e.coli
  - Motility-related diarrhoea is caused by the rapid movement of food through the intestines (hypermotility). If the food moves too quickly through the gastrointestinal tract, there is not enough time for sufficient nutrients and water to be absorbed eg hyperthyroidism or diabetes
  - Inflammatory diarrhoea occurs when there is damage to the mucosal lining or brush border, which leads to a passive loss of protein-rich fluids, and a decreased ability to absorb these lost fluids eg bact/viral/IBD
  - Dysentery – generally, if there is blood visible in the stools, it is not diarrhoea, but dysentery. The blood is trace of an invasion of bowel tissue eg shigella, salmonella
- Diarrhoea DDx:
  - Functional = irritable BS
  - Inflammatory
  - Infective (usually acute) (noro, rota, campylo, salmonella, shigella, giardia, EHEC, staph)
  - Malignancy
  - Diverticular disease
  - Malabsorption
  - Hyperthyroidism
- Functional disease/irritable BS:
  - Age <45
  - Normal basic investigations
- NB. ↑f does not = diarrhoea; eg someone going 6-7/d could just be pushing out pebbles – not ↑ liquidity
- Hx:
  - What is normal for them?
  - R/o alarm symptoms (weight loss, blood, anaemia)
  - Tenesmus, pain etc
  - Steatorrhoea
  - FHx (ca, IBD)
  - Previous surgery (eg resections = malabsorption)
  - ETOH/drugs (including ABs)
  - Travel

Gastro-Intestinal
• Exam:
  - Extraintestinal manifestations
  - Abdominal mass
  - PR

• Ix:
  - Bloods (FBC, ESR/CRP, Coeliac serology, Fa studies, LFTs [alb, pro], U & E, Ca\(^{2+}\), vit B12, folate, TSH)
  - Faeces (culture, calprotectin – indicates inflammation; fat measurement), FPE is a good test for pancreatic dysfunction
  - Breath test for fat malabsorption (\(^{14}\)C triolein may serve as an alternative to faecal fat collection)
  - Endoscopy (sigmoidoscopy, colonoscopy; pts < 45 w chronic d should undergo sigmoidoscopy in the first instance as diagnostic yield differs little from use of colonoscopy )
  - Radiology (SBFT, enteroclysis, MRI enterography; SI imaging reserved for cases where SI malabsorption suspected + distal duo histo is normal; \(^{99m}\)Tc HMPAO labelled white cell scanning is a non-invasive technique to examine intestinal inflammation – as useful as SBFT in assessment of terminal ileal CD)
  - Capsule studies (useful for occult bleeding)

**Infectious Diarrhoea**

• Symptoms & Signs:
  - Dysphagia (e.g. Candida)
  - Flatulence, colic, distension, diarrhoea (watery, fatty, bloody)
  - Vomiting
  - Fever

• Investigations
  - Blood: eosinophilia, HIV
  - Faecal microscopy, parasitology, culture
  - H2 breath test
  - Endoscopy/Colonoscopy +/- biopsy

• Pathology: red, oedematous bowel (all look the same), microscopically non-specific inflammation

• Differential:
  - Drug induced diarrhoea: laxatives, magnesium compounds, diuretics
  - Severe alcohol intake
  - Diabetic autonomic neuropathy
  - IBD
  - Malabsorption: coeliac, lactose intolerance, lymphoma, pancreatitis, bilary/liver disease

• Management:
  - Rehydration
  - Investigate cause
  - Monitor complications: anaemia (due to haemorrhage), septicaemia, perforation, appendicitis
  - Strict food hygiene
  - Avoid milk → ↓secondary hypolactasia
  - Antibiotic treatment

**Infectious Agents**

<table>
<thead>
<tr>
<th>Infectious diarrhoea</th>
<th>Type I</th>
<th>Type II</th>
<th>Type III</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mechanism</td>
<td>Non-inflammatory (enterotoxin)</td>
<td>Inflammatory (mucosal invasion + infl, cytotoxin)</td>
<td>Penetrating</td>
</tr>
<tr>
<td>Location</td>
<td>Proximal SI</td>
<td>Distal SI + colon</td>
<td>Distal SI (terminal ileum)</td>
</tr>
<tr>
<td>Illness</td>
<td>Watery diarrhoea, cramps, bloating</td>
<td>Dysentery (bloody d., crampy abdo pain), malaise, fever</td>
<td>Enteric fever (fever, abdo pain, constipation, splenomegaly, leukopenia)</td>
</tr>
<tr>
<td>Diagnosis</td>
<td>No faecal WBCs</td>
<td>Faecal WBCs</td>
<td>Blood culture positive for salmonella typhi</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Organism</th>
<th>Type</th>
<th>Features</th>
<th>Clinical</th>
<th>Diagnosis</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Salmonella typhi</td>
<td>Type III</td>
<td>As above</td>
<td>Incubation = 2-5d S &amp; S as for Type II</td>
<td>Selective culture of stool sample</td>
<td>● Child/pregnant = erythromycin</td>
</tr>
<tr>
<td>Campylobacter jejuni</td>
<td>Type II</td>
<td>● Zoonosis – often contaminated undercooked chicken  ● Guillain-Barre syndrome can occur 2-3 weeks after</td>
<td></td>
<td></td>
<td>● Adult = ciprofloxacin ● F &amp; E replacement</td>
</tr>
</tbody>
</table>

Gastro-Intestinal
<table>
<thead>
<tr>
<th>Organism</th>
<th>Type</th>
<th>Description</th>
<th>Incidence</th>
<th>Treatment</th>
<th>Notes</th>
</tr>
</thead>
</table>
| *Salmonella* spp                              | Type II | - S. *typhimurium* commonest foodborne d  
- S. *spp* commonest infectious agent causing foodborne d (meat, poultry, eggs, dairy)  
- Asymptomatic carriage \~ 4/5/2 | 1-3d | Selective culture of stool sample |  
- ABs not indicated  
- prolongs asymptomatic carriage  
- F & E replacement |
| *Yersinia enterocolitica*                     | Type II | - Zoonosis – undercooked contaminated pork  
- Reactive polyarthritis may occur in 10-30% of HLA-B27 positive adults  
- Oocysts can persist for long periods  
- Cattle are reservoir  
- Non-bloody d | S & S as for Type II – see enterocolitis | Selective culture of stool sample |  
- Child = cotrimoxazole  
- Non-preg adult = ciproflox  
- F + E replacement |
| *Shigella* spp                                | Type II | - Human only reservoir of infection – person to person transmission  
- Highly infectious; S. Sonnei and flexneri common NZ spp  
- Young cattle reservoir, can survive in envt for long periods  
- Mucosal invasion + infl + cytotoxin (verotoxin) – same as shiga toxin  
- WBC bind verotoxin and disseminate it from GIT to blood  
- Endothelial cells susceptible to verotoxin and thrombosis occurs  
- Haemolytic uraemic syndrome (HUS) in 5-10% - haemolytic anaemia with TCP and RF | 1-2d | Selective culture of stool sample |  
- Child = cotrimoxazole  
- Non-preg adult = ciproflox  
- F + E replacement |
| *EHEC – enterohaemorrhagic e. Coli*           | Type II | - Most EHEC belong to O157:H7  
- Young cattle reservoir, can survive in envt for long periods  
- Mucosal invasion + infl + cytotoxin (verotoxin) – same as shiga toxin  
- WBC bind verotoxin and disseminate it from GIT to blood  
- Endothelial cells susceptible to verotoxin and thrombosis occurs  
- Haemolytic uraemic syndrome (HUS) in 5-10% - haemolytic anaemia with TCP and RF  | 1-8d | Selective culture of stool sample |  
- Supportive as ABs may increase HUS risk  
- F + E replacement |
| *Clostridium difficile*                       | Type II | - Common post AB therapy 3-29% (15% with ß-lactams, 25% with clindamycin) – ABs wipeout normal microflora (e.g. bacteroides fragilis) +  
- C.diff is normal commensal in neonates/infants but <3% of adults – transmitted via hands of health workers/envt sources (soil, water)  
- C.diff also produces exotoxins (toxin A & B) that disrupt intercellular junctions \rightarrow infl | 5-10d after AB therapy | EIA (enzyme immunoassay) in stools |  
- Stop ABs where appropriate  
- Metronidazole tds/7d or vancomycin for severe cases  
- 1. F & E replacement |
| *Giardia lamblia* (protozoa)                  | Type I | - Ingestion of contaminated water with giardia cysts – leading to trophozoite colonisation of SI | 1-2weeks | EIA for giardia antigen  
Microscopic ID of cysts/trophozoites |  
- Metronidazole tds/5d  
- F & E replacement |
| *Cryptosporidium hominis* (protozoa)         | Type I | - Cattle are reservoir  
- Oocysts can persist for long time in envt  
- Outbreaks a/w contaminated H₂O | 2-10d | EIA for crypto Ag  
Oocyst detection using immunofluorescent assay or modified ZN stain |  
- No anti-crypto drug available  
- F & E replacement |
| Rotavirus | Type I | - RNA virus, commonest cause of severe gastro in children <5, can be fatal  
- Viral replication in villous epithelium of SI  
- Non-structural glycoprotein (NSP4) enterotoxin | Inc = **1-3d**  
S & S as for Type I  
+ n & v & fever | EIA for rotavirus Ag  
F & E replacement |
| --- | --- | --- | --- | --- |
| Norovirus | Type I | - RNA virus (calicivirus)  
- Outbreaks common  
- Faecal-oral contamination – foods  
- Mechanism unknown, jejunal bx = intact epi, shortened MV, widened intercellular spaces | Inc = **1-2d**  
As for rotavirus | PCR for noro RNA  
F & E replacement |
| E.coli (ETEC, EPEC, EAEC); vibrio cholera – Type I | | | | |
| Bacterial enteroinvasive: | | | | |
| - Campylobacter Jejuni  
  - Poultry  
  - Haemorrhagic colitis  
  - Erythromycin (used to be ciprofloxacin but it’s been put in chicken feed →↑resistance) | | | | |
| - Escheria Coli  
  - Enterotoxic subspecies  
  - Travellers diarrhoea | | | | |
| - Salmonella/Shigel: Poultry | | | | |
| Bacterial enterotoxins: | | | | |
| - Vibrio Cholerae | | | | |
| - Staph Aureus: Food poisoning (eg cream buns) | | | | |
| - Clostridium Botulinum | | | | |
| - Some subtypes of E Coli | | | | |
| Protozoa: | | | | |
| - Giardia  
  - Trophozoites reside mainly in duodenum, also small bowel  
  - Cysts in faeces  
  - Small bowel diarrhoea → diarrhoea during night (large bowel ‘sleeps’) | | | | |
| - Entamoeba histolytica: causes amoebic dysentery (colitis) | | | | |
| - Cryptosporidium:  
  - Common in kids  
  - Is chronic in immunocompromised  
  - No effective antibiotic treatment | | | | |
| Constipation | | | | |
| - = Infrequent bowel action (ie > 3 days) or difficult/painful defecation | | | | |
| - Affects 3% in young adults → 20% in elderly | | | | |
| Physiology: | | | | |
| - Muscular movements: segmentation mixes bowel contents. Peristalsis moves it along. Mass movements occur once or twice a day (usually after a meal)  
- Faecal mass in rectum → internal anal sphincter opens by reflex. External sphincter remains contracted voluntarily, but will tire quickly → leakage  
- Defaecation requires relaxation of external sphincter, pelvic floor muscles and abdominal straining  
- Motility affected by sympathetic (→↑segmentation) and parasympathetic (→↑peristaltic and mass movement) system, hormones, fibre, acid pH, lactobacilli  
- Age related changes: mucosal atrophy (→↓mucus), muscular atrophy, etc | | | | |
| Assessment: | | | | |
| - History: What do they mean? Frequency, stool consistency, presence of blood/mucus, ease of evacuation, onset of symptoms, and drug history, exercise  
- In elderly screen for risk factors: ↓fibre following changed diet or false teeth, can’t shop or prepare food, ↓physical activity → ↓transit time, dehydration, neurological disease (eg diabetic neuropathy)  
- Exam: systemic disease, abdominal exam and perianal sensation | | | |
Investigations: Usual, plus blood tests to exclude anaemia, hypothyroidism and electrolyte abnormality

Consider:
- Diet
- Drugs
- Obstruction
- Neuro disorders
- IBS
- Depression

Management
- Review medication, eg:
  - Opioids
  - Anticholinergics (eg antihistamine, antiemetics)
  - NSAIDs
  - Serotonin antagonists
  - Phenothiazines
  - Tricyclic antidepressants
- **Bowel retraining.** Try during high motility periods – first thing in the morning and after meals. Exercise to improve abdominal muscles
- **Adequate fibre and fluid and exercise**
- **Laxatives:**
  - **Hydrophilic bulk forming agents,** eg Normacol, Metamucil. Must also take adequate water. Not useful in palliative care (patients are too sick to eat it)
  - **Osmotic agents,** eg lactulose or sorbitol → not broken down in small bowel → ↑osmotic gradient → ↑water content. Take 1 to 2 days to act. Safest agent in the long term
  - **Stool softeners and lubricants.** Take 1 to 3 days to act. Act as detergents to increase water penetration and thus softening of the stool. Eg docusate agents, Coloxyl (a detergent effect → breaks up stool, may be hepatotoxic) and lubricants. Oil based lubricants (eg paraffin) can affect vitamin and drug absorption and be aspirated
  - **Stimulants and irritants** → ↑peristalsis and net fluid secretion. Eg Senna. Take 6 to 12 hours to act. Stimulates the myenteric plexuses to produce peristalsis. Avoid irritant laxatives unless impaction, severe muscle weakness. Long term use of laxatives causes constipation by damaging the nerve supply of the gut
  - Locally acting agents eg glycerol suppository at peak motility time. Can have osmotic and irritant agents
  - Investigational agents such as cisapride (prokinetic agent)
- Rectal Laxatives:
  - For faecal impaction
  - On exam will either have a loaded rectum or ballooning of the rectum (dilated distally ⇒ impacted further up)
  - Types:
    - Glycerine suppositories: soften stool by lubrication and osmosis
    - Bisacodyl (Dulcolax) suppositories: Causes peristalsis
    - Sodium Phosphate enemas
    - Oil Enemas

Fibre
- **Dietary Fibre:** the undigested and unabsorbed polysaccharide (cereal, fruit, vegetable) that remains at the end of the small bowel. Contains cellulose and non-cellulose polysaccharides, lignin, gums and waxes
- Worth a trial in constipation, IBS (esp. with constipation) and non-ulcer dyspepsia of dysmotility type
- Get good 24 hour dietary history
- Intake from cereal source is 4 or 5 times greater than fruit or vegetables. It is also less fermented in large bowel
- Ideal level = 30g/24 hours. Usual NZ adult approx. 15 g/24 hours
- 20 g of fibre in 6 tablespoons of bran, 2 Weetbix or 4 large thick slices of whole meal bread
- Suggestions for use:
  - **Increase SLOWLY** (i.e. aim for a full bowl of All bran in 2-3 months): otherwise bloating, distension, gas
  - Take fibre every day
  - Necessary amount is not a weight – but the amount necessary to keep stools soft
  - Drink lots of water (2 L per day is recommended)
  - Will increase gas (fibre promotes bacterial growth): take stairs not lift!
Other Bowel Diseases

- Collagenous colitis:
  - Chronic or episodic watery diarrhoea
  - F > M, 30 + years, autoimmune association
  - Macroscopic appearance: looks normal at colonoscopy
  - Microscopic appearance: subepithelial hypocellular collagen band (prevents H2O absorption)

Anorectal Problems

- Haemorrhoids:
  - Dilated veins beneath the submucosa → bleeding from overlying mucosa
  - Don’t cause pain unless prolapsed or thrombosed
  - Can cause itchiness
  - Treatment: injection with sclerosant (eg almond oil), banding (but infection and bleeding risk), infra-red coagulation

- Rectal Prolapse:
  - Self-limiting in kids, in elderly due to weakened pelvic floor (childbirth or denervation)
  - Treatment is surgical, faecal incontinence improved in half

- Rectal Cancer:
  - Majority can be felt on digital examination
  - Adenocarcinomas
  - Presentation: bleeding and tenesmus, rarely pain
  - Treatment: local excision or resection

- Fissures:
  - Vertical tear in anoderm. 90% posteriorly
  - Acute or chronic
  - Vicious circle: tight internal anal sphincter → tear → reflect spasm → constipation → further tearing
  - History: severe pain and bleeding on defaecation
  - Associated with high resting anal pressure
  - Treatment: high fibre diet, lots of H2O, local analgesic cream, GTN paste (relaxes sphincter) (all conservative), limited internal sphincterotomy

- Abscesses and fistulae:
  - Infection of tiny glands emptying at dentate line
  - Infection can burrow into perianal fat or ischiorectal fat
  - Drainage may result in anal fistula

- Pruritis Ani (itchy anus):
  - Usually worse at night
  - Causes by anal or dermatological conditions
  - Anal: haemorrhoids, keyhole deformity, pinworm infection, anal warts and cancers
  - Dermatological: Bowen’s disease, Paget’s disease of anus, eczema
  - Treatment: avoid strong steroid creams, avoid itching, and drying carefully

- Anal Cancer:
  - Uncommon. Spreads to inguinal glands
  - Can be adenocarcinoma, basaloid carcinoma (this and next two caused by HPV 16 and 18), squamous carcinoma, muco-epidermoid carcinoma, anal melanoma
  - Related to HPV (as with cervical cancer) → anal intraepithelial neoplasia
  - Risk factors as for cervical cancer (number of partners, age of first intercourse, etc)
  - Above dentate line – endodermal origin → adenocarcinoma
  - Below dentate line – ectodermal origin → squamous or basal cell carcinoma or melanoma

- Anal warts: condylomata acuminata. Caused by HPV 8 and 11. Usually an STD

- Perianal suppurration

- Angiodysplasia (submucosal proliferation of vessels – associated with age and aortic stenosis)
GI Bleeding

<table>
<thead>
<tr>
<th>Upper GI bleeding</th>
<th>Lower GI bleeding</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peptic ulcer</td>
<td>Diverticulitis</td>
</tr>
<tr>
<td>Gastritis</td>
<td>Colitis – infectious or inflammatory</td>
</tr>
<tr>
<td>Mallory-Weiss tear (in mucous membrane of oesophagus due to vomiting, coughing etc)</td>
<td>Large bowel tumour/polyp</td>
</tr>
<tr>
<td>Oesophagitis</td>
<td>Haemorrhoids</td>
</tr>
<tr>
<td>Oesophageal or gastric ca</td>
<td>Anal fissure</td>
</tr>
<tr>
<td>Drugs – NSAIDs, anticoagulants, SAIIDs</td>
<td>Angiodysplasia (AVM)</td>
</tr>
<tr>
<td>Haemangiomia</td>
<td>Bleeding disorders</td>
</tr>
<tr>
<td>Bleeding disorders</td>
<td>Blood from upper GI bleed</td>
</tr>
<tr>
<td>Swallowed blood from nosebleed</td>
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</tbody>
</table>

- **Coffee ground**: modified by gastric juices – signifies UGIB
- **Haematemesis**: suggests more acute bleeding
- **Melaena**: can be UGIB or LGIB

**Physiological Response to Blood Loss**

- **Acute response**: *BR mediated* therefore increased TPR, HR, contractility, and consequently BP
- **Kidney response**: *RAAS activation* – leading to increased TPR, increased aldosterone + thus NaCl + H2O
- **Heart response**: *atrial BR* decrease the release of ANP
- **Thirst**: activation of RAAS + decreased ANP contributes to thirst response

**Upper GI Haemorrhage**

- From above the ligament of treitz/duodenal-jejunal flexure
- **Symptoms/Signs**:
  - **Haematemesis** (either fresh or coffee ground appearance): check not coughing it up. Can check vomit with urine dipstick for blood
  - **Melaena** (black/sticky foul smelling stools): stomach denatures haemoglobin → black. So no melaena if bleed is distal to the proximal small bowel. Exclude iron tablets, bismuth preparations & Guinness
  - Rectal bleeding (*haematochezia*): brisk bleeding for this to occur!
  - **Anaemia**: tired, pale, breathless, faint (brain struggles to compensate if PO2 <60 mmHg)
  - Hypovolaemia: carotid bodies → sympathetic →↑HR & peripheral vasoconstriction; ↓renal perfusion → ↑renin → ↑angiotensin (vasoconstriction) → ↑aldosterone (H2O retention); ↑ADH → thirst and H2O retention. If serious hypovoleamia: postural hypotension, cold & clammy, confused, thirsty, weak pulse & tachycardic, ↓urine output
  - Check stridor: tumour compressing trachea – expiratory wheeze
- **History**:
  - Always ask about CV and respiratory history, and when they last ate, in case surgery is needed
  - **Medications**: NSAIDs (if so, then steroids further increase risk), anticoagulants
- **Investigations**:
  - Bloods: anaemia, reticulocytes, group & hold, U &Es, LFTs (varices), clotting (either poor liver function or Warfarin → bleeding)
  - Endoscopy (can do biopsy)
  - Barium swallow (not so good)
- **Causes**:
  - Ulcers (35-50%)
  - Oesophagitis (8-15%)
  - **Varices** (5-10%)
    - Portal HTN → portosystemic anastamoses (b/w azygous system + portal system) + splenomegaly
    - 15-30% of those with PHTN get v, ~20% of these bleed
    - Only 40-50% of pts with UGIB + known varices will have bled from varices (therefore look for other causes)
    - Bleeding implies cirrhosis + PHTN
    - Hypotension will lead to further ischaemic injury of hepatic cells therefore important to control bleeding very early
    - Site of bleeding = lower 2-3cm of oes (site of perforating veins)
    - Colour signs – “cherry red spots” + “blue signs” are more likely to bleed
>12mmHg portal P (i.e. **12mmHg P above IVC P**) required for active bleeding (normal portal P <5mmHg; portal HTN >10mmHg)

- Banding will cause ulcers therefore use PPI in conjunction; need multiple bandings to rx
- Rx:
  1. **RESUS**
  2. **Terlipressin** (shuts down splanchnic circ therefore ↓ P in varices; is an ADH analogue therefore vasoconstricts; octreotide/SST can be used also)
  3. **Banding**
  4. **Ballooning** if in ED - *sengstaken-blakemore tube* – used in emergency
  5. **Sucralfate** (antacid) or H2RA to prevent stress-induced ulcers (not for use in acute bleeding)
  6. **TIPS**
  7. **Surgery**
  8. Also rx with AB (**cef + met**) as infection kills in variceal bleeding – decreases death rate
  9. **Secondary prevention of variceal bleeding** = banding + BB

- Natural hx:
  - 75-85% stop spontaneously
  - 25% re-bleed (mortality 30%)
  - Mallory-Weiss tears (15%)
  - AVMs/malignancies
  - Other causes: gastritis (e.g. alcoholic), malignancy (check for masses, lymph gland enlargement, organomegaly)

- Causes of small bowel bleeding (eg if no upper or lower cause found):
  - **Vascular lesions** (angiodysplasia, telangiectasia)
  - **Ulceration** (CD, NSAIDs – terminal ileum + caecum prone to NSAID injury)
  - **Tumours** (GIST, lymphoma, carcinoid)
  - Under 25: Meckel’s diverticulum
  - 30–50: Small bowel tumour
  - Over 50: angiodysplasia

**Lower GI Haemorrhage**

- Symptoms/Signs:
  - Blood in/with stool. Colour indicates site: if bright red → 95% of pathology **distal to splenic flexure** (usually anus & rectum)
  - Pain on passing motions → anal fissure (haemorrhoids don’t cause pain unless prolapsed)
  - Anaemia
  - Angina (in elderly with CHF, anaemia → angina due to ↓O2 → ↑heart work)
  - Check: Meckel’s diverticulum – lined with gastric mucosa
- Family Hx: colorectal cancer/inflammatory bowel disease
- Rectal Exam (Always do abdominal exam as well)
  - Look first: skin tags → Crohn’s, sentinel tags → chronic anal fissure
  - Digital examination: if acute fissure this will be very painful (→ give up)
  - Rigid sigmoidoscope: in 2/3 can only see rectum
- Investigations: rectal exam, sigmoidoscopy, colonoscopy, barium enema, bloods (anaemia, reticulocytes)
- Causes:
  - Anatomical (eg **diverticular disease**: brisk bleeding with sudden onset)
  - Vascular (angiodysplasia)
  - Inflammation (IBD)
  - Infectious
  - Neoplastic (polyp/ca)
  - Haemorrhoid (blood coats bowel motion with drops after motion passed)
  - Post-polypectomy bleeding
  - Anal fissure

**Treatment of Major GI Haemorrhage**

- Resuscitate:
  - NS 2L
  - **Plasma expander** (4% normal serum albumin (NSA), dextran)
  - Blood:
    - Shock = clinical picture of profound hypovolemia plus SBP < 100mmHg
    - Indications for transfusion = **postural hypotension** (↓15mmHg), shock, or Hb < 100g/L
If meet any of the criteria for shock then transfer to ICU: postural hypotension > 15 mmHg fall, tachycardia > 100, systolic BP < 100.

Check thirst/urine output (insert catheter)
Max O2

Monitor resus:
- ECG/pulse rate
- Oximetry
- CVP +/- art line for BP
**Urinary catheter** for output (40-50mL/hr = adequate organ perfusion)

**Bloods**: group and hold (don’t crossmatch until sure you need it), ABG, Hb, baseline creatinine before renal failure, ↑urea – may be due to breakdown of blood in gut, check platelets, INR & APTT for liver disease, bleeding disorders, warfarin OD)

Investigations:
- FBC, coags, U & E, cross match, ABGs
- ECG, CXR
- Endoscopy (Gastroscopy (more a dx test rather than a therapeutic tool); colonoscopy – the procedure of choice in evaluating pt with acute LGIB)
- Labelled RBC (NM scan)
  - Detects **active bleeding** at rates of 0.1-0.5mL/min and is more sensitive but less specific than angio
  - Either technetium sulphur colloid or $^{99m}$Tc pertechnetate-labeled RBCs; imaging performed at 30m intervals for up to 24hrs
- Angiography
  - Detects active bleeding at rates of 1mL/min
  - Overall yield of angio for detection of GI bleeding source ranges from 40 – 78%; v specific though (100%)
  - Used when bleeding source not IDed on colonoscopy

**Treatment**:  
- Resus first
- Endoscopy:
  - Clips
  - Adrenaline injection
  - Sclerotherapy for varices
  - Argon
- Medical:
  - PPI
  - **HP eradication** (triple therapy – amoxy, clarithromycin, omeprazole)
  - **Propranalol** for variceal bleed when bleeding controlled
  - IV terlipressin for varices
- TIPS:
  - = Transjugular intrahepatic porto-systemic shunt
  - If variceal bleeding continues despite sclerotherapy/banding + terlipressin
  - Used for complications of PHTN (refractory variceal bleed, ascites, hepatorenal syndrome); Budd-Chiari syndrome etc

**Angiodysplasia** (Rx w contact thermal probes)

65% will spontaneously stop → resuscitate/transfuse and investigate less urgently

Indications for surgery:
- Failure of conservative treatment
- In shock, rebleed, etc
- Consider if > 6 units of blood needed over 24 – 48 hours

**NB.** mortality rates for LGIB = <5%; UGIB = 2%
Liver Disease

Liver Anatomy/Physiology
Anatomy:
- **Lobes**: division according to topography - right, left, caudate, quadrate
- **Segments**: functional division according to arterial and portal blood supply and bile drainage
- **Dual blood supply**: portal vein, hepatic artery; prevents against infarction
- **Blood drainage**: hepatic veins

Histology:
- **Lobule**: Basic organization unit
- Structure bounded by the portal triads (tracts) and oriented about a central vein
- Hepatocytes within the lobule are arranged in plates (1 cell thick)
- **Sinusoids** intervene between the hepatic plates
- **Portal triads** (tracts) - hepatic artery branch, portal vein branch, bile duct

Functions of the Liver
- Conjugation & excretion of bilirubin; production of bile acids
- CHO metabolism: glycogenolysis, GNG, glycogenesis
- Protein metabolism incl albumin, coag factor, lipoprotein synthesis
- Ammonia → urea
- Metabolism of steroids, ETOH
- Metabolism + excretion of drugs
- Filtration + removal bacteria + other debris from blood
- Vit D etc etc etc

Assessment

Presentation
- Found coincidentally when clinically well (e.g. medicals)
- Family screening e.g. abnormal irons, HBV
- Non-specific illness and found to have abnormal LFT: ?alcohol, medicines, viral, jaundice, liver/biliary disease
- Is it acute, chronic, acute on chronic, or a failing chronic

Aetiology

- **Acute** hepatitis:
  - Viral: A, B, C, D, others
  - Toxic:
    - Drugs
    - Poisoning (eg alcohol)
- **Chronic** hepatitis:
  - Viral: B, C, B + D, CMV
  - Toxic:
    - Drugs
    - Chronic Alcohol
  - Autoimmune
  - Metabolic:
    - Alpha-1-antitrypsin
    - Wilson’s disease
    - Haemochromatosis
  - **Fatty liver**: Obesity, NiIDDM, Drugs, alcohol

History

<table>
<thead>
<tr>
<th>Liver disease</th>
<th>Pre-icteric phase</th>
<th>Icteric phase</th>
<th>Medical hx</th>
<th>Risk factors for LD</th>
<th>Fx</th>
<th>Meds</th>
<th>Lab tests</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Malaise; nausea, vomiting; HA; dislike of fatty foods, sex, ETOH; fever; chills;urticaria; rash; polyarthralgia/arthritis; abdo pain; dark urine</td>
<td>Jaundice, dark urine, pale poos; decreased fever, may feel better; pruritis</td>
<td>Surgery; CHF; UC/CD; preg; HIV; halothane recently; TPN</td>
<td>Contact w jaundice/hepatitis people; sexual orientation; travel; diet (shellfish); tattoos; ethnic group (HBV in asian, maori, Pl); HCW; transfusion; IVDU; drugs; ETOH</td>
<td>Anaemias, jaundice (eg Gilbert’s), Wilson’s, haemochromatosis, gallstones, ETOH, AI disease</td>
<td>Phenothiazine, isoniazid, alpha-methyldopa, OCP, paracetamol, ABS (fluclox, clavulonic acid)</td>
<td>LFTs, FBC, INR (if platelets low, can indicate hypersplenism secondary to portal HTN – can be seen in HCV)</td>
</tr>
</tbody>
</table>

- Surgery: e.g. cholecystectomy
- Heart disease: congestive heart failure
- Pregnancy
- HIV positive, sexual orientation
- Contact with hepatitis: family, sexual
- Travel: malaria, parasites
- Hepatitis infection risk: tattoos, body piercing, health care worker, transfusion, IVDU, unsafe sex
- Alcohol → acute alcoholic hepatitis
- Ethnic group
- Medications – ALWAYS ASK ABOUT DRUGS
- Family History: e.g. anaemias, Gilbert’s syndrome, haemochromatosis, gallstones, alcoholism, autoimmune disease, Wilson’s disease (copper)
- Symptoms: itch, urine and stool colour, anorexia/weight loss, nausea/vomiting, yellowing of skin

Liver Function Tests (LFTs)

- True tests of liver function are rarely done: NH3, bile acids, coagulation studies, excretion studies
- Investigations:
  - Bloods:
    - Bilirubin
    - LFTs: AST, ALT, ALP, GGT
    - Total protein, albumin
    - Tests can be widely variable for the same condition
    - Other: Coagulation studies, ammonia
    - Special tests: α1 antitrypsin, α-fetoprotein, hepatitis markers, specific autoantibodies, 1gs, caeruloplasmin
    - Any liver disorder may → ↑ferritin (also an acute phase protein)
Also test for other causes of liver disease: HBV, HIV, iron studies (ferritin), immune liver disease (↑ANA)

- Imaging: ultrasound +/- CT, MRCP, ERCP. Ultrasound and CT have high false negatives for biliary
- Percutaneous transhepatic cholangiogram – PTC
- Liver biopsy the gold standard

Aim to decide if liver disease is present, is progressing or is severe

**Chemical Path's Take on LFTs**

- **Transaminases** (ALT + AST):
  - ↑ by damage to hepatocytes (eg necrosis):
    - Common: viral hepatitis, alcoholic liver disease, NASH, meds toxicity/OD, CHF
    - Also ↑ in haemochromatosis, AI hepatitis, A1ATD, Wilson’s
- **ALP & GGTP**:
  - Found mainly in bile ducts
  - ↑ by disorders damaging/obstructing the ducts ie cholestasis:
    - Extrahepatic: stones, tumour → jaundice
    - Intrahepatic: toxicity, tumour → jaundice less likely
    - Cirrhosis, PBC, PSC, sarcoid
  - ↑ ALP:
    - Physiological: growth, #s, pregnancy
    - Liver disease: primary cholestatic disease, secondary cholestasis due to hepatocellular disease
    - Bone disease: malignancy, hyperPTism, vit D deficiency, CRF
    - Miscellaneous: hyperthyroidism, familial, intestinal disease (eg coeliac), drugs eg phenytoin
- **GGTP**:
  - Doesn’t actually correlate well with ETOH consumption (ie can be normal)
  - May be used as a marker but is not specific
  - Not tested routinely in Wellington any more, hard to determine upper point of reference interval
  - But some evidence of GGT as a RF for CVD + CKD
- **Albumin + protein**:
  - Albumin T1/2 = 3/52 + is ↓ in chronic disease or very severe prolonged acute disorders → ↓ not liver specific
  - Globulins change little in acute LD but gamma globulins ↑ in chronic LD as a polyclonal immune response
- **Bilirubin**:
  - Jaundice is a clinical dx, usually seen when bili > 40umol/L (~ twice normal)
  - Is a breakdown product of Hb + carried unconjugated to the liver by albumin
  - Unconjugated = indirect = not water soluble
  - Liver conjugates with glucaronic acid = direct → excreted in bile
- **LFTs: what to test?**
  - No guidelines, although asymptomatic testing is inappropriate
  - AST (found in RBC, muscle, heart etc) is less liver specific than ALT but when elevated more than ALT, indicates severe damage (eg ETOH cirrhosis) therefore both together can be useful
  - ALP + GGT together indicate cholestasis but individually not entirely useful
- **Risk factors in those without primary clinical features of LD:**
  - DM or metabolic syndrome
  - Suspicion of excessive ETOH abuse
  - Hepatotoxic drugs
  - AI disorders
  - IBD
  - Haemochromatosis
  - Ca
  - HD
- **The tired pt, when to test:**
  - BPAC recommends LFTs be done in pts under 50 years presenting with tiredness only if there are risk factors
  - LFTs recommended for tiredness at any age lasting > 1/12

**Evaluating LFTs:**
- Practically useful to roughly categorise into:
  - 1. Hepatocellular or
  - 2. Cholestatic or
**Gastro-Intestinal**

---

**3. Mixed pattern**

- Think of common disorders first
- BPAC suggest 3/12 LFT f/u interval in an asymptomatic low risk individual if original result < 3x ULN, then full IX if transaminases remain ↑; immediate IX if 3 x ULN

**Cases:**

- 24 y/o woman, tired, mild resp infection. GP thought she was slightly jaundiced + bili was 40umol/L but normal other LFTs. She was iron deficient but felt better after a month of Rx + bili is now 25umol/L → **Gilbert’s syndrome**
- 25 y/o male undergoes routine tests for insurance medical. Not jaundiced, normal exam and hx. Bili = 29umol/L (RR <20umol/L) but normal other LFTs → **Gilbert’s syndrome**
- 51 y/o male general health check. LFTs ordered. Bili = 15. ALP = 75U/L. ALT = 80U/L (twice normal). Other tests normal. Appropriate follow up? → **repeat test, do hx + exam**
- 28 y/o man feeling unwell for 1/52, aches, vomiting, itching, dark urine, pale faeces, jaundice. Bili 315, 253 direct. ALP 227. GGTP 332. ALT 2774. AST 1574. Normal protein → needs **immediate full IX + admission**
- Need to test INR + NH3
- 6/7 later he was green/yellow + bili ↑ to 549! Albumin + total protein had ↓, hepatitis serology –ve
- LFTs slowly improved by still not quite normal, immune markers negative except low titre ANA
- Bx → chronic hepatitis → likely AI hepatitis → azathioprine with good response
- 32 y/o female non-specifically unwell. LFTs normal except ALP 140 (UL = 90) → could be any of the causes of ↑ALP
- 24 y/o female with T1DM with ALP 150. Drinks significant ETOH but GGTT normal. Abdo bloating + wt loss, protein + albumin low, Fe + vitamin deficient → **coeliac disease**
- 62 y/o man lost 8kg in 1yr. Feeling anorexic + nauseous + lost more weight. Fe def anaemia. Bili 18. ALP 890. GTG 760. TP 59, Alb 32 → **colorectal liver mets**

**Autoantibodies in liver disease:**

- ANA + SMA in AI hepatitis, 50-70%
- AMA in PBC, 90%
- p-ANCA in PSC, 80%

**Things to exclude:**

<table>
<thead>
<tr>
<th>Disease</th>
<th>Clues</th>
</tr>
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<tbody>
<tr>
<td>ETOH related</td>
<td>Hx, AST/ALT &gt;1, MCV, high GGT</td>
</tr>
<tr>
<td>Hep C</td>
<td>Risk factors, anti-HCV +ve, HCV PCR +ve</td>
</tr>
<tr>
<td>Hep B</td>
<td>Risk factors, HBs +ve</td>
</tr>
<tr>
<td>Other viral</td>
<td>Probability eg EBV, +ve serology</td>
</tr>
<tr>
<td>Drug-induced</td>
<td>Meds hx, temporal relationship</td>
</tr>
<tr>
<td>Haemochromatosis</td>
<td>FHx, iron studies</td>
</tr>
<tr>
<td>AI hepatitis</td>
<td>ANA, SMA, LMK</td>
</tr>
<tr>
<td>PBC</td>
<td>AMA, IgM, more cholestatic, women</td>
</tr>
<tr>
<td>Wilson’s disease</td>
<td>FHx, copper, c’plasmin, younger</td>
</tr>
<tr>
<td>PSC</td>
<td>A/w IBD, p-ANCA</td>
</tr>
<tr>
<td>A1ATD</td>
<td>FHx, A1AT level, genotype</td>
</tr>
</tbody>
</table>

**Non-alcoholic fatty liver disease:**

- Spectrum of liver disease from **steatosis through steatohepatitis to cirrhosis** (identical to alcoholic LD but no hx)
- NAFLD a/w **metabolic syndrome** (central obesity, insulin resistance, T2DM, HTN, hyperuricaemia, dyslipidemia)
- Defined as **fat accumulation exceeding 5-10% by weight**, estimated practically as % of fat laden hepatocytes
- NASH implies micro + macrovesicular steatosis, lobular inflammation + fibrosis
- NASH is accepted as < 20g/d or < 14units/week where a unit is 10g of ETOH
- Prevalence = 20-30% have excess liver fat, 10% of these meet criteria for NASH, up to 30% of those with NASH develop fibrosis/cirrhosis
- ↑ ALT is usually the first enzyme ↑
- Older age, obesity, DM are predictors of fibrosis; insulin resistance (ie MS) is an important factor in steatosis + possibly NASH + cirrhosis
- NAFLD accounts for ~ 70% of all cases of cryptogenic chronic hepatitis
Natural hx: debate re whether someone with incidentally ↑ liver enzymes but asymptomatic has a disease

Treatment is weight loss, exercise + possibly metformin

Only bx can confirm/exclude the dx + determine severity of necrosis, inflammation, fibrosis

Bx may be done after failure of LFTs to normalise after 3-6/12 of lifestyle intervention

Key points (ie ignore the above!):
  - NAFLD encompasses a spectrum from simple hepatic steatosis to NASH + cirrhosis
  - NASH implies micro + macrovesicular steatosis, lobular inflammation + fibrosis
  - NASH is accepted as < 20g/d or < 14 units/week
  - RF: DM, obesity, older

Insulin resistance is the hallmark of NAFLD to the extent that in its absence the dx is unlikely

Dx of NASH requires confirmation of IR, exclusion of other forms of LD + histology

Other causes of steatohepatitis: ETOH, drugs (amiodarone, tamoxifen, methotrexate), Cu toxicity, jejunoileal bypass, rapid profound weight loss, TPN, a- or hypobetalipoproteinaemia

Metabolic syndrome:
  - Group of related abnormalities that ↑ risk of developing CVD
  - Abdominal obesity, dyslipidaemia, HTN, IR, proinflammatory state, defined by 3 or more of:
    1. WC >102cm in men + >88cm in women
    2. Triglycerides > 1.7mmol/L
    3. HDL <1.04 in men + 1.29 in women
    4. BP > 130/85
    5. FG 6.1 – 6.9mmol/L (ie IFG)

Risk of CVD ↑ 3-fold; DM 5-fold

Rx: diet, weight loss, exercise, possibly metformin

Other causes of cholestasis: ETOH, drugs (amiodarone, tamoxifen, methotrexate), Cu toxicity, jejunoileal bypass, rapid profound weight loss, TPN, a- or hypobetalipoproteinaemia

Liver Disease Assessment

Test abnormalities

Non-hepatic causes

GGT Pancreatic disease, ETOH, COPD, RF, DM, MI, anti-epileptics, AAbs
ALP Growth, pregnancy, paget’s d, bone #/secondaries, Hodgkin’s, hyperparathyroidism
ALT/AST Coeliac, TB, sarcoid, AB, hypothyroid, addison’s, toxic paracetamol dose, cocaine, CHF, muscle disorders
Bilirubin Haemolysis, blood transfusion, sepsis, rifampicin, ribavirin

Patterns of LFT abnormalities

Cholestasis ↑ ALP, GGT, bilirubin Drug hx, preg, PBC, PSC (pANCA +ve in 80%), liver mets, sarcoid; need to fractionate bili, US, ERCP
Hepatocellular ALT > AST (this ratio in injury normal LFTs) Fatty liver, ethnicity, viral hepatitis, AI hepatitis (ANA, SMA, LKM), drug OD (paracetamol), hepatic ischaemia/infarct
Hepatocellular AST > ALT Severe liver disease: ETOH, Wilson’s, NASH, liver malignancy, severe chronic
Three questions to answer:
- Is there liver cell death?
- Is there cholestasis?
- Is liver cell function normal?

**Is there liver cell death – inflammation and hepatonecrosis?** Check:
- **Bilirubin:** in acute hepatitis will be 50:50 direct and indirect
- Raised aminotransferases predominate
- **If AST > ALT** think severe **cirrhosis, liver malignancy, alcohol.** In normal hepatitis ALT > AST
- In acute injury, transaminases rise in proportion to degree of necro-infl (acute viral hepatitis, paracetamol tox etc) but NOT in others (end stage liver cirrhosis, chronic viral hep)
- **Ischaemic liver injury + acute viral hepatitis cause massive ALT/AST rise** but in ischaemia the ALT quickly falls and LDH rises once blood supply restored
- Degree of transaminase elevation depends on timing of sampling relative to insult
- ALT only comes from hepatocytes; AST from RBCs, muscle, hepatocytes
- Peak ALT values:
  - HAV = 800-1000
  - HBV = 1000-1500
  - HCV = 300-800
  - Alcoholic hepatitis = <300
  - BACE (HBV – HAV – HCV – ETOH)
  - If v high, consider ischaemia, drugs + other viruses
- **Common liver causes:**
  - **NASH** (fatty liver): probably the most common cause of mildly elevated LFTs, especially if obese, Type 2 diabetes and hyperlipidemia
  - **Acute/chronic viral hepatitis**
  - **Genetic haemochromatosis**
  - **Autoimmune hepatitis**
  - Less commonly: antitrypsin deficiency and Wilson’s disease
- **Causes of abnormal LFTs other than Liver disease:**
  - Diseases of other organs affecting liver, e.g. RA
  - Medicines, alcohol, tonics, remedies, poisons
  - Congestive heart failure → hepatic congestion
  - AST: also produced by:
    - Muscle: If normal ALT and ↑AST then do a CK for muscle breakdown
    - Blood: Haemolysis

**Is there cholestasis (impaired bile flow)?**
- Liver can remove 5 * normal bilirubin from circulation (i.e. large functional reserve)
- Cholestasis usually refers to obstruction within the liver
- ‘Obstructive Jaundice’ ⇒ major ducts
- Bile salts are 90% reabsorbed in the terminal ileum. They emulsify fats. Bile also contains cholesterol, phospholipids and bilirubin (reabsorbed → urobilinogen → urine)
- If left or right hepatic duct blocked, other side of liver will be sufficient to keep bilirubin normal
- Diffuse partial obstruction to prox bile ducts (PSC) or unilateral complete obstruction will cause GGT/ALP rise but normal bili
- GGT released in inflammation: usually in parallel with ALP in obstruction; if ↑GGT and ALP then ALP is from the biliary tree
- Microscopic biliary epithelial canalicular damage (eg flucloxac or clavulonic acid; stone; ca) will cause cholestasis
- GGT is sensitive but not specific – NPV is high
- Conjugated (direct) bilirubin is proportionate to the degree of failure of excretion (intrahepatic cholestasis) or obstruction to the flow of bile (extrahepatic cholestasis)
- Early marker of cholestasis is rise in total bile acid level and useful for dx of early cirrhosis, PBC, cholestasis of pregnancy, OCP, cholestatic drug reactions
- **Gilbert’s = increased unconjugated bili (due to impaired conjugation) with normal GGT; 5% of pop have it; jaundice increases on a low fat diet** (unconjugated increases as not conjugating it for fat breakdown)
- In haemolysis the unconjugated bili fraction is high as are reticulocytes, but haptoglobin is low
- Common:
  - Biliary obstruction: gallstones
  - Drug hepatotoxicity
  - Neoplasms (e.g. head of pancreas)
- Less Common:
  - Primary biliary cirrhosis
  - Primary sclerosing cholangitis
  - Sarcomiosis
  - Autoimmune cholangiopathy
- Other causes of ↑ALP:
  - ALP from bone and cholangiocytes (biliary epithelium). Excreted in urine, but saturated kinetics → ↑serum level
  - Physiological:
    - Bone: Growth and fractures. High in puberty
    - Pregnancy (placental)
    - Benign ↑ with age
- Bone disease: Paget's, malignancy, renal failure, hyperparathyroidism, Rickets
- GI tract can also produce ALP, e.g. Crohn's
- Miscellaneous: hyperthyroidism, familial benign, transient of infancy

- Is liver function normal?
  - Are detoxification, synthesis, and glucose management working? Has a large functional reserve. Check:
    - Bilirubin: is it conjugated?
    - Albumin: is the liver producing protein?
      - Albumin T1/2 = 14-21/7 – ↓ in chronic hepatocellular disease
      - Also varies with nutritional and metabolic conditions/states
    - Prothrombin time (INR):
      - Is it producing coag factors + undertaking vit K carboxylation? (shorter T1/2 than albumin)
      - Give vit K + retest 12-24 hrs later – will improve if obstruction but won’t if hepatocellular dysfunction; >2 = chronic LD
      - Factors 2, 5, 7, 9, 10
- Tests in cirrhosis:
  - Liver function tests very variable:
    - Quiescent phase: normal or minor ↑ in LFT
    - Active Phase: ↑ in ALT and AST when necrosis is dominant
  - Causes: idiopathic, alcohol, chronic active hepatitis, primary biliary cirrhosis, haemochromatosis, Wilson's disease, α1 antitrypsin deficiency
  - Other examples of Liver Function tests:
    - ↑↑ALT and ↑↑AST: viral hepatitis, paracetamol OD
    - ↑ALP and ↑ bilirubin in a 12 year old with vomiting: Gilbert's syndrome (↑ bilirubin when fasting), ALP normally raised at this age
    - ↑ Bilirubin, ↑ ALP, ↓ Albumin + neuro signs → ? Wilson's disease (very rare)
    - ↑ Bilirubin, ↑ ALP, ↓ Albumin + abnormal electrophoresis → ? ↓ α1 antitrypsin

- Total Protein
  - Normal Ranges:
    - Total Protein: 60 – 80
    - Albumin: 34 – 46
    - Globulin Gap = TP – albumin ~ 20 (> 40 or < 20 is likely to be abnormal)
  - Examples:
    - 55 year old man, ↓ albumin (23), normal protein (70) ⇒ ↑ Ig (common in cirrhosis)
    - 14 year old, ↑ cholesterol, ↓ protein 45, ↓ albumin 20 ⇒ nephrotic syndrome
    - 58 year old man with diabetes, protein 94, albumin 56 ⇒ dehydration (don't get albumin > 50 without dehydration)
    - 40 year old post-op, protein 26, albumin 11 ⇒ dilution. Took blood downstream of iv line
    - 46 year old, enlarged nodes, protein 50, albumin 33 ⇒ ↓ globulin gap ⇒ ? immunocompromised/lymphoma
    - 60 year old, pneumonia, protein 70, albumin 22 ⇒ acute phase + maybe ↑ Ig
    - 50 year old, recurrent abdominal pain, protein 55, albumin 27 ⇒ pancreatitis → malabsorption
38 year old, SOB, rash, protein 86, albumin 34 \( \Rightarrow \) sarcoidosis or SLE

10 year old, lifelong recurrent chest infections, protein 70, albumin 40 \( \Rightarrow \) immunodeficiency: IgA deficiency

- **Differentials:**
  - **Hypoproteinaemia:**
    - 1. *Haemodilution*: poor iv therapy, drip arm, SIADH, pregnancy
    - 2. ↓*Albumin*: ↓*synthesis* (liver disease, malabsorption, malnutrition), losses (renal, gut, skin), non-specific (eg acute illness)
    - 3. ↓*Ig*: primary or secondary immunodeficiencies. Only IgG deficiency is enough to show up as low protein or on electrophoresis
    - NB. Low albumin + high globulins can give normal TP
  - **Hyperproteinaemia:**
    - 1. *Haemoconcentration*: dehydration, haemostasis
    - 2. ↑*IgG* (↑ in other globulins rarely have an impact on TP):
      - Monoclonal: *myeloma*, *lymphoma*, macroglobulin, MGUS
      - Polyclonal: liver disease, infection, autoimmune, sarcoidosis
    - Oligoclonal: between mono & polyclonal; almost any acute or chronic condition

**Electrophoresis**

- Bands: albumin, α1 antitrypsin, haptoglobins (α2 band), transferrin, complement, Ig
- Three indications:
  - 1. To detect deficiency of α1 antitrypsin
  - 2. To detect monoclonal antibody band
  - 3. To reveal immunosuppression
- Cannot be used to quantify protein subfractions \( \Rightarrow \) if wanted, need to ask specifically for these
- Monoclonal Gammaglobulinaemia of Uncertain Significance (MGUS)
  - Benign, but potential for malignant transformation (eg to Myeloma): 5% at 5 years, 25% at 15 years
  - \( \Rightarrow \) need to follow up over time
  - See Monoclonal Gammopathy of Undetermined Significance, page 487

**Jaundice**

- For neonatal jaundice, see Jaundice, page 925
- Visible when bili 40-60mmol/L
- May rise in haemolysis, cholestasis, hepatitis, impaired liver function
- Jaundice – key questions:
  - Is it pre-hepatic = indirect bili; haemolysis, inadequate conjugation
  - Is it cholestatic (obstructive) = dark urine, pale poos, pruritis, cholestasis refers to intrahepatic obstruction (PBC, PSC, cholestatic hepatitis – some drugs) or obstructive jaundice (duct obstruction – IH + EH)
  - Is it painful = SOCRATES
  - Is the pt taking drugs?
- Causes:
  - Unconjugated hyperbilirubinaemia:
    - Overproduction: Intravascular or extrahepatic haemolysis
    - ↓Hepatocellular uptake: drugs, sepsis, starvation
    - ↓Hepatocellular conjugation: *Gilbert’s* syndrome, neonatal jaundice, drugs, diffuse hepatic disease
  - Conjugated bilirubinaemia (cholestatic jaundice):
    - Impaired hepatocellular secretion: various syndromes, duct stricture, biliary cirrhosis, steroids
    - Hepatocellular cholestasis – impaired secretion plus liver injury as well: viral infection, drugs, alcohol
    - Extrahepatic obstruction: stones, carcinoma, strictures and congenital atresia

**Pathology**

- See WebPath for histology pictures with explanation
- Normal histology:
  - Divided histologically into lobules. The center of the lobule is the central vein. At the periphery of the lobule are portal triads
Functionally, the liver can be divided into three zones, based upon oxygen supply. Zone 1 encircles the portal tracts where the oxygenated blood from hepatic arteries enters. Zone 3 is located around central veins, where oxygenation is poor. Zone 2 is located in between.

- Cords of hepatocytes between sinuses running from portal tract to central vein
- Zone 3 (perivenular) more sensitive (eg to drugs) than zone 1 (periportal)

**Patterns of liver injury:**
- Hepatocyte accumulation
- Hepatocyte necrosis/apoptosis
- Inflammation
- Regeneration
- Fibrosis

**Clinical syndromes of liver injury:**
- Hepatic failure (acute and chronic)
- Cirrhosis
- Portal hypertension
- Jaundice/cholestasis
- Malignancy

**Acute hepatitis:**
- Inflammation of the liver: no cause implied
- Macrophage appearance: mildly enlarged, tender liver. Flu like symptoms.
- Jaundice, itching
- Microscopic appearance:
  - Diffuse liver cell injury with lobular disarray: loss of normal radial array
  - Focal necrosis of hepatocytes with hepatocyte regeneration (mitotic figures, variation in cell size)
  - Portal inflammation: lymphocytes & macrophages. Eosinophils with drugs
  - Bile stasis: variable (often absent), due to disruption of canaliculi, greenish
  - NO fibrosis

**Chronic hepatitis:**
- If longer than 6 months then chronic — otherwise acute (unless chronic signs — e.g. spider naevi)
- Chronic active and chronic persistent hepatitis reflect different disease activity but caused by the same agents
- Chronic persistent hepatitis:
  - Benign and self-limiting, following acute hepatitis and lasting several years
  - Inflammation limited to portal triad (lymphocytes, macrophages and plasma cells)
  - Architecture preserved, NO fibrosis, no hepatocyte necrosis
- Chronic active hepatitis:
  - Progressive hepatic necrosis and fibrosis, potentially leading to cirrhosis
  - Clinical course variable. 5 year survival 25 – 50%
  - Marked portal inflammation extending into lobules
  - Piecemeal necrosis (= interface hepatitis = periportal necrosis): ‘nibbling away’ at hepatocytes around portal tract by lymphocytes → necrosis
  - Bridging necrosis: creating portal-central or portal-portal tracts
- Hepatitis B: ground glass hepatocytes – large, uniform cytoplasm filled with viral protein
- Hepatitis C: fatty degeneration, bile duct lesions and portal tract lymphoid aggregates/follicles
- **Fulminant Hepatitis:**
  - Very rare. Onset to death in 2 – 3 weeks (massive necrosis) to 3 months (submassive failure)
  - Causes: **Viral** (60%), **drugs/chemicals** (30%, eg paracetamol poisoning), numerous other minor causes
  - Macroscopic appearance: all/most of liver destroyed. Red, limp, wrinkled capsule. Mushy red
  - Microscopic appearance: Zonal (2,3) or complete necrosis, liquefaction of hepatocytes, little inflammation
- **Inflammatory diseases of the liver - i.e. hepatitis:**
  - **Definition:** hepatitis = inflammation + hepatocellular injury / necrosis
  - **Inflammation:** some etiologic clues provided by inflammatory cell type and distribution of the inflammation within the lobular (portal, periportal, or lobular)
  - **Hepatocellular injury / necrosis:** variable in extent and severity
- **Acute hepatitis:**
  - **Definition:** Inflammation and hepatocyte injury / death in patients with clinical, biochemical, or serologic evidence of hepatitis for less than 6 months.
  - **Aetiology:** vast majority of cases are viral (HAV, HBV, HCV) drug, including alcohol, some herbal products
- **Chronic hepatitis:**
  - **Definition:** Inflammation and hepatocyte injury / death in patients with clinical, biochemical, or serologic evidence of hepatitis for **greater than 6 months**.
  - **Aetiology:** vast majority of cases are viral (HBV, HCV), others (autoimmune hepatitis, Wilson’s disease, drug-related)
- **Alcohol-related liver disease** (old term: alcoholic liver disease):
  - Ethanol is a potent hepatocellular toxin
  - Morphologic features - variable:
    - **Steatosis:** intracytoplasmic accumulation of fat within hepatocytes
    - **Hepatitis:** hepatocytes necrosis; infiltrate of neutrophils, “Mallory hyaline” within the hepatocytes (intracytoplasmic accumulation of precipitated cytokeratin filaments)
    - **Fibrosis:** especially around central vein – “sclerosing hyaline necrosis”
- **Non-alcohol-related fatty liver disease:**
  - Morphologic features
    - Similar to those of alcohol-related liver disease
    - Distinction from alcohol-related liver disease must be made on **clinical grounds**
- **Cirrhosis:**
  - **Definition:** diffuse process characterized by fibrosis (scar) and the conversion of the normal hepatic architecture into regenerative nodules
  - **Cirrhosis** = regenerative nodules + fibrous bands (aka: bridging fibrosis)
  - General points
End-stage result of chronic injury to the liver
- The chronic injury can be to hepatocytes (e.g. hepatitis B, ethanol abuse, hemochromatosis) or the biliary tract (e.g. primary biliary cirrhosis, primary sclerosing cholangitis)
- The chronic injury heals with fibrous bands (scar) and regenerative nodules (architecturally abnormal - lack the organized architecture of lobules)

Physiologic results
- Portal hypertension
- Compromise of the synthetic and metabolic capacity of the hepatocytes to varying degrees

Management of Acute Hepatitis
- Avoid strenuous physical activity while jaundiced, increase slowly afterwards
- Best rest only if unwell
- No corticosteroids
- Perhaps reduce fat, abstinence from alcohol
- Care with personal hygiene
- Follow liver tests until normal

Progression of Chronic Hepatitis
- Acute hepatitis (inflammation/cell death) → regeneration → resolution or chronic hepatitis, which may → fibrosis (the necessary step for progression to liver failure) → disordered architecture → cirrhosis
- Assessing Liver Biopsy:
  - Is there inflammation around the portal tract (= portal triad: bile duct + portal vein + hepatic artery)? 'Limiting plate' surrounds portal tract. Monocytes migrate through this and cause piecemeal or interface hepatitis. If it extends to another portal tract then called bridging necrosis
  - Is there inflammation/necrosis out in the lobule → intralobular or focal necrosis
  - Are there inflammatory cells in the portal tract → portal inflammation
  - How much scar tissue/fibrosis is there?
  - Knodell index scores each of these to generate a Hepatitis Activity Index (HAI). Score out of 22
    - Grade = inflammation score (periportal = piecemeal/interface; confluent; intralobular/focal; portal) out of 18
    - Stage = fibrosis score out of 4
- Child-Pugh Classification of liver function/failure:
  - Sum of scores for encephalopathy, ascites, bilirubin, albumin, INR, nutrition
  - Subjective measures
  - Scoring system for cirrhosis/end stage liver disease (ESLD)

<table>
<thead>
<tr>
<th>Score</th>
<th>5 year survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade A</td>
<td>&lt;= 6</td>
</tr>
<tr>
<td>Grade B</td>
<td>7 – 9</td>
</tr>
<tr>
<td>Grade C</td>
<td>&gt; 9</td>
</tr>
</tbody>
</table>

- MELD (model for ESLD) and PELD (paeds model for ESLD): use objective measures

Fatty Liver Disease
- Both NAFLD and alcoholic liver disease are fatty liver diseases

NAFLD – Non-alcoholic Fatty Liver Disease
- Types:
  - Steatosis
  - Steatohepatitis (NASH)
- Often asymptomatic
- Usually associated with metabolic derangements – obesity, insulin resistance, diabetes
- See hepatomegaly – occasionally right sided pain
- AST/ALT elevated in 90% - ratio < 1
- Death from metabolic syndrome consequences or cirrhosis
- Histology:
  - Steatosis (lipid deposits: micro + macrovesicular)
  - Ballooning degeneration
  - Mallory-hyaline inclusions (but these are more characteristic of ETOH changes)
Inflammatory cells
Fibrosis

Alcoholic Liver Disease

- Short term ingestion of 80g (8 standard drinks; 1 = 10g) → reversible steatosis
- Daily intake >80g for prolonged periods → risk of severe hepatic injury
- Only 10% alcoholics get cirrhosis though:
  - Women > men
  - Strong family association
  - Co-morbid conditions (eg Fe overload, viruses)

Alcoholic Steatosis (Fatty Liver):

- Pathogenesis: ↑ synthesis of TAGs + ↓ fatty acid oxidation + ↓ formation/release of lipoproteins → fat in lymphocytes
- Macroscopic appearance: large, pale, liver with soft greasy cut surface
- Microscopic appearance: Micro and macro-vesicular types. Intracytoplasmic droplets coalescing to fill the cell, may rupture (no inflammation before rupture). Perivenular fibrosis
- Outcome: Liver function may be normal. If no fibrosis then can be cleared
- Fatty liver can also be caused by toxic, metabolic and hypoxic conditions, and occurs in malnourished kids in the third world

Alcoholic hepatitis:

- Acutely following heavy drinking
- Often superimposed on fatty change or cirrhosis
- Microscopic appearance:
  - Similar to viral hepatitis
  - Liver cell necrosis and inflammatory infiltrate
  - Mallory bodies (alcoholic hyaline): intracytoplasmic collection of cyto-skeletal proteins. Looks like candy floss
  - Fibrosis

Alcoholic Cirrhosis:

- Causes 60 – 70% of cirrhosis. Most of the rest is viral
- Only 10% of alcoholics get cirrhosis
- Requires daily alcohol of > 60 gm (6 standard drinks; 1/3 bottle of spirits)
- Macroscopic appearance:
  - Initially large, fatty, micronodular (liver cells regenerating between fibrosis)
  - Progresses to small, non-fatty, macronodular (>10 mm) liver. Often micro-macro nodular presentation
- Microscopic appearance:
  - Early: delicate portal-central fibrosis, fatty parenchyma
  - Late: enlarged nodules surrounded by broad fibrous bands (with signs of liver failure). Bile retention within nodules
- Immediate causes of death: hepatic coma, GI bleed, infection, hepatocellular carcinoma, head injury → subdural haematoma

Alcohol also → pancreatitis (see Pancreas, page 297)

Viral Hepatitis

- Causes:
  - Prime target is the liver: Hep A, B, C, D, E
  - May affect liver secondarily: EBV and CMV

Risk of chronic hepatitis:

- HAV = 0%
- HBV = 10%
- HCV = >80%
- HDV = 5%
- HEV = 0%

Distribution of cause of acute hepatitis (e.g. ALT > 1000) in Auckland: A - 25%, B - 25%, EBV - 25%, C - 5 – 10%, some CMV

Chance of transmission from needle-stick injury: HBV – 30%, HCV – 3%, HIV – 0.3%
- Clinical course: variable – from asymptomatic to fulminant/fatal
- Common symptoms:
  - Malaise, weakness, lethargy
  - Flu like illness: tiredness, fever, myalgia
  - Anorexia, nausea, vomiting (especially Hep A)
  - Jaundice (uncommon)

<table>
<thead>
<tr>
<th>Virus</th>
<th>Transmission</th>
<th>Features</th>
<th>Complications</th>
<th>Diagnosis</th>
<th>Treatment/Prevention</th>
</tr>
</thead>
<tbody>
<tr>
<td>HAV</td>
<td>Contaminated food/water via faecal/oral route</td>
<td>Inc = 2-6weeks Most likely H.V. to cause anorexia + nausea</td>
<td>Rare No chronic carriage</td>
<td>Acute = IgM AntiHAV in blood Past = IgG AntiHAV in blood</td>
<td>HAV vaccine – need booster at 1yr Dead whole virus vaccine NB. cannot distinguish vaccine immunity from natural infection</td>
</tr>
<tr>
<td>HBV</td>
<td>Blood and other body fluids (via sex – most common, perinatally, needle-sharing/stick)</td>
<td>Inc = 2-6months</td>
<td>1. Chronic carrier state (10-15%) 2. Chronic hepatitis (persisting ALT) 3. May progress to cirrhosis or 4. Hepatocellular carcinoma</td>
<td>Order of appearance (palindrome!): 1. HBsAg 2. HBe 3. IgM &amp; IgG Anti-Hbc 4. Anti-HBe 5. Anti-Hbs</td>
<td>Recovery from HBV when loss of HBsAg &amp; appearance of Anti-HBs (but never actually clear the virus) HBV: IgM Anti-Hbc Carrier: HBsAg Infective: HBe Past infection: IgG Anti-Hbc Vaccine immunity: Anti-Hbs</td>
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<tr>
<td></td>
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<td></td>
<td>Acute HBV: IgM Anti-Hbc Carrier: HBsAg Infective: HBe Past infection: IgG Anti-Hbc Vaccine immunity: Anti-Hbs</td>
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<td></td>
<td>NB. Best test for active HBV is HBV DNA test – more sensitive than HBe (from Stace)</td>
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<td></td>
<td></td>
<td>Monitoring: 1. Test HBsAg monthly until negative 2. If still positive at 6/12 test for HBsAg/6/12 until 2yrs post acute illness 3. Presence of HBe in blood correlates with presence of whole HBV virions and reflects pts infectivity (indicates active infection)</td>
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<td></td>
<td>Pre-core mutant strains of HBV: Some strains unable to express HBe even though active replication occurring in liver</td>
</tr>
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<td></td>
<td>ALT &gt; 50IU/L &amp; positive HBV DNA PCR indicate pre-core mutant strain</td>
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<td></td>
<td></td>
<td>Antivirals: Entecavir – nucleoside analogue Lamivudine (resistance can occur) Adefovir (for lamivudine resistant strains)</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Prevention: HBV vaccine at 0, 1, 6/12 Interpretation of HBV tests:</td>
</tr>
<tr>
<td></td>
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<td></td>
<td></td>
<td></td>
<td>Monitoring: No evidence of infection HBsAg carrier HBsAg past infection</td>
</tr>
<tr>
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<td></td>
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<td></td>
<td>HBC not part of HBV vaccine therefore can distinguish between natural infection &amp; vaccine protection</td>
</tr>
</tbody>
</table>

Gastro-Intestinal 282
<table>
<thead>
<tr>
<th>Virus</th>
<th>Description</th>
<th>Transmission Criteria</th>
<th>Symptoms</th>
<th>Diagnosis</th>
<th>Treatment</th>
<th>Protection/Vaccination</th>
</tr>
</thead>
<tbody>
<tr>
<td>HDV</td>
<td>Defective virus - can only replicate in the presence of HBV (needs HBsAg as an outer coat); same transmission criteria as HBV</td>
<td>1. Acute HDV on acute HBV seen (usually seen in IVDU) 2. Chronic HDV in chronic HBV carriers</td>
<td>Acute HDV: severe &amp; progressive chronic hepatitis</td>
<td>IgG Anti-HDV test</td>
<td>HBV vaccine confers protection against HDV</td>
<td></td>
</tr>
<tr>
<td>HEV</td>
<td>Contaminated food/water via faecal/oral route</td>
<td>Inc = 4-6 weeks  V. uncommon in NZ</td>
<td>HEV infection in pregnancy has high mortality rate (20%)</td>
<td>IgM Anti-HEV</td>
<td>No vaccine available</td>
<td></td>
</tr>
<tr>
<td>EBV</td>
<td>Via respiratory droplets  See atypical mononuclear cells on blood film</td>
<td>Excreted in urine and saliva – children principle infection source</td>
<td>5% of cases may progress to hepatitis</td>
<td>Acute primary infection: IgM Anti-VCA (virus capsid antigen)  Past infection: Anti-EBNA (Epstein-barr nuclear Ag)</td>
<td>No vaccine available</td>
<td></td>
</tr>
<tr>
<td>CMV</td>
<td>Excreted in urine and saliva – children principle infection source</td>
<td>Acute CMV hepatitis occurs mostly in immunocompromised (transplant pts, prem neonates)</td>
<td>Acute CMV: IgM Anti-CMV, detection of CMV DNA in body fluids by PCR  Past CMV: IgG Anti-CMV</td>
<td>No vaccine available</td>
<td></td>
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</tr>
</tbody>
</table>

**Hepatitis A**
- Infectious hepatitis
- 25 – 33% of clinical cases of hepatitis
- Especially in kids, normally mild
- Transmitted by food (especially raw shell fish) or contaminated water
- Viraemia lasts 7 days after onset of jaundice. Don’t get virus in the blood (or only transiently). It’s a gut bug
- Symptoms: arthralgia, weight loss, fatigue, low grade fever, loss of appetite, abdominal pain
- Diagnosed by IgM Anti-HAV & ?exclusion of HBV
- Treatment: supportive, dietary restriction, rest, no alcohol. Notifiable disease
- Post exposure prophylaxis with ISG (immune serum globulin) for contacts
- Vaccination:
  - Havrix 1440: 99% immunity after 1 month. One dose im. Booster after 6 – 12 months gives longer-term immunity. Inactivated HAV
  - Especially for travellers, sewage workers, health and childcare workers
  - Can’t distinguish natural immunity from vaccine immunity (IgG Anti-HAV in both)

**Hepatitis B**

**Epidemiology**
- 350 million with chronic infection, >75% of these Asian
- 30% of chronically infected die prematurely from the disease
- In NZ, approx. 50,000 carriers. Chinese 10%, Maori 5.4%, PI 4.4%, European 0.43%
- Transmission:
Body fluids (blood, semen), including transfusion & contaminated needles
Mother to baby (vertical transmission): 95% risk of infection – **vaccinate at birth and give Anti-HBs** – immune globulin
Organ transplant
Child to child (horizontal transmission). Must get into blood – e.g. grazes, stubbed toes. Very resilient virus. Children are most likely to have asymptomatic seroconversion

**Diagnosis**
- ALT elevation to **1000-1500** (usually higher than for Hep C)
- **Viral antigens:**
<table>
<thead>
<tr>
<th>Antigen</th>
<th>Antibody</th>
</tr>
</thead>
<tbody>
<tr>
<td>Surface</td>
<td>HBsAg</td>
</tr>
<tr>
<td>E (fraction of core)</td>
<td>HBeAg</td>
</tr>
<tr>
<td>Core</td>
<td>HBcAg (never in blood)</td>
</tr>
</tbody>
</table>
- Acute Viral Hepatitis due to HBV with recovery:

*Jaundice*

**Progression**
- Incubation 45 – 180 days

**Screening:**

<table>
<thead>
<tr>
<th></th>
<th>Anti-HBc</th>
<th>HBsAg</th>
<th>Anti-HBs</th>
</tr>
</thead>
<tbody>
<tr>
<td>No infection</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Vaccinated</td>
<td>-</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>Carrier</td>
<td>+</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>Past infection: non infectious</td>
<td>+</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>Past infection: low infectivity, silent carrier</td>
<td>+</td>
<td>-</td>
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</tr>
</tbody>
</table>

- Normal virus called ‘wild type’. Also **pre-core mutant HBV virus – doesn’t produce E antigen** but will still be HBV-DNA +ive
• Symptoms:
  ➢ Incubation: can be up to 6 months or longer
  ➢ Minority of first episodes are symptomatic
  ➢ If symptoms occur: *malaise, anorexia, nausea, jaundice*. Coincide with appearance of Anti-HBc antibody in serum

• Acute HBV infection leads to:
  ➢ 10% **chronic infection** (‘carrier’ is a misnomer) due to ineffective immune response. 90% of infected newborn infants, 25% in young children, and 2% adults. 25% of ‘carriers’ develop **chronic active hepatitis** and **cirrhosis**, and 50% have **hepatocellular carcinoma** peaking in the 5th decade
  ➢ 65% transient subclinical infection → 100% recovery
  ➢ 25% acute hepatitis → 99% recover, 1% → fulminant hepatitis

• Stages of illness:
  ➢ Immune tolerant stage (mainly babies): no hepatitis even though circulating virus. HBsAg, HbeAg in blood
  ➢ Immune activation → ↑ALT
  ➢ If chronic: called chronic lobular hepatitis (CLH) or chronic active hepatitis (CAH). 6% will clear it per year.
  Key issue is how much fibrosis has occurred before clearance. See **ground glass hepatocytes + bridging necrosis**
  ➢ First stage of clearance: E antigen seroconversion. ↓HBeAg and ↑anti-HBe (was there previously – but used up too rapidly to detect. As HBeAg ↓, residual anti-HBe ↑)
  ➢ Second stage: S antigen seroconversion

**Vaccination**
• Most effective means of control: vaccination: Engerix B. 85 – 90% efficacy
• Yeast derived subunit vaccine.
• Number of notifications has dropped from 400 to 100 since introduction in 1988
• Suspension of synthetic HBsAg
• Doses at 0, 1 and 6 months → immune levels of Anti-HBs in 92%
• Check for seroconversion 2 months later
• Booster every 2 – 3 years if high risk

**Treatment**
• **Entecavir** – nucleoside analogue
• Lamivudine:
  ➢ Resistance can occur
  ➢ Purine nucleoside analogue: inhibits DNA polymerase. Potent inhibitor of HBV replications
  ➢ As safe as placebo, no interactions, excreted unchanged
• Adefovir (for lamivudine resistant strains)
• IFN (boosts IS – therefore hepatitis can get worse – care needed)
• Each year of treatment:
  ➢ 17% HBe seroconversion (30% if concurrent interferon)
  ➢ 15% get YMDD mutant → ↑ALT and ↑HBV DNA again. But these also seem to seroconvert in time
• Eligibility:
  o If ALT > 2 * normal
  o Pre & post liver transplant
  o HIV and HBV co-infection (plus multi drug therapy for HIV as well)
• Risk of Hepatocellular carcinoma – related to length of time as a carrier

**Hepatitis C**
• An **enveloped ssRNA virus** (used to be called non A non B). 6 geneotypes identified
• Damage is caused by immune response – not virus

**Presentation**
• Incubation to onset of symptoms average 7 weeks (range 3 – 20)
• HCV RNA detectable within 1 – 3 weeks of exposure. Rises rapidly to $10^6$ – $10^8$ per ml
• Only 1/3 have symptoms. Clinical illness (if any) lasts 2-12 weeks
• ALT elevation to 300 – 800 (less than HBV)
• 50% go on to chronic infection (ie higher than Hep B)
• May present with end stage liver disease (e.g. may present for first time with variceal bleeding)
Hepatocellular carcinoma found in 1/3, test with ultrasound. Evidence that interferon for 6 months ↓ risk of HCC

**Risk Factors**
- NZ prevalence: 0.47%
- Low infectivity: mainly transmitted by blood
- Transfusion
- **IV drugs** (40-60% of cases)
- Sexual contact (very low risk)
- Maternal transmission to neonate in 5% of maternal infection (ie low risk)

**Viral Serology**
- **Acute HCV**: Anti-HCV doesn’t appear for 3 months. Can do PCR. **Exclude** HAV, HBV, EBV, and CMV
- **Chronic HCV**: Anti-HCV antibody
- Indications for HCV test:
  - Chronic hepatitis (raised ALT over 6 months)
  - History of Non-A, Non-B hepatitis but at least 3 months after acute infection
  - At risk groups: IV users, haemophiliacs
  - Donors: blood and organs
- Indications for HCV RNA test. Test if indeterminate Anti-HCV results, diagnosis in neonates and monitoring of interferon therapy
- 80% of chronically infected have persisting viraemia

**Tests**
- LFTs: bilirubin, albumin
- FBC: platelets
- APTT/INR
- Anti HCV antibodies
- PCR for HCV RNA
- Ultrasound for size (& to guide biopsy)
- Biopsy → degree of fibrosis → prognosis
- Exclude: Hep A, Hep B, Iron studies, ANA

**Progression**
- If self-limited HCV RNA undetectable and ALT back to normal in 1 – 3 months
- Wide spectrum: 1/3 persistently normal ALT. Majority fluctuating ALT (immune system active and causing hepatocyte death). ALT height doesn’t correlate with histological severity. Acute – ALT 10 times normal
- Non-hepatic manifestations: arthritis, dry membranes, lichen planus (white plaques in mouth), glomerulonephritis, cryoglobulinaemia, porphyria cutanea tarda (PCT – blisters on skin)

**Prognosis**
- Contributing to progression:
  - Alcohol → ↑ fibrosis
  - HBV
  - Age at infection - younger have longer period of time with infection
  - Mode of acquisition: transfusion worse (?greater viral load)
  - Genotype of virus: effects interferon treatment. Type 1 → severe disease and poor response to interferon
Management

- ↓Alcohol
- Have liver biopsy before commencing drug treatment. Also, intravenous drug users should have drug free urines (otherwise risk of reinfection)
- Need strong motivation/compliance
- **Interferon** - best for:
  - High ALT
  - Disease < 5 years
  - Non-cirrhotic
  - Not genotype 1
  - Low viral load
  - No history of depression (interferon can cause this)
  - Causes flu like symptoms: ↓appetite, fever, myalgia. Largely resolves after 1-2 weeks. Given it up-regulates the immune system can also cause ↑autoimmune diseases (e.g. thyroid)
  - On its own only 15% are PCR negative 6 months after completing treatment
- Combination Interferon/Ribavirin:
  - **Ribavirin is teratogenic:** contraception needs to be VERY reliable
  - Purine nucleoside analogue
  - Stored and transported in red cells. Dose dependent haemolysis → monitor Hb and reticulocytes
  - Only useful in addition to interferon
  - After 3 months, 35% non-responders. 65% complete responders. For genotypes 2 & 3 most of these go on to be sustained responders
- Transplantation:
  - Hep C most common indication
  - Recurrent (usually mild) infection of graft
  - Survival: 65% at 5 years

Other Viral Hepatitis

**Hepatitis D**

- Defective virus that can only replicate in the presence of HBV infection (requires HBsAg as a viral coat)
- Common in Middle East, Pacific Islands
- Clinical:
  - Acute D on Acute B: in IV drug users. Often severe/fulminating
  - Chronic D on Chronic B: endemic in many parts of the world. Perinatal transmission
- Complications: chronic hepatitis more common in HBV carriers who are also infected with HDV
- HBV vaccination also protects against HDV

**Hepatitis E**

- Faecally transmitted: contaminated food and water
- Epidemic in India, China, Russia, parts of Africa
- Higher mortality than HAV, up to 20% in pregnant women
- Test for IgM-specific antibody

**Epstein Barr Virus**

- 1% of infections present as acute viral hepatitis, with significant elevation of ALT (mild ↑ALT in most cases)
- See Epstein Barr Virus, page 820

**Cytomegalovirus (CMV)**

- See Infectious diseases chapter

**Tumours of the Liver**

- Can see:
  - Non-neoplastic (focal nodular hyperplasia)
  - Benign (haemangioma, adenoma)
  - Malignant (HCC, mets)
• **Metastases** are the most common

**Hepatocellular Carcinoma**

• Epidemiology:
  - M:F 2.4:1
  - 1/3 most common ca on worldwide basis
  - Geographic variations (chronic HBV + HCV infection in SE Asia, Japan, China, Africa)
  - 80% of all liver primary cancer
  - Third world: 40% of all cancer, age 20 – 40
  - Western world – incidence sharply increasing

• Clinical associations:
  - Chronic **viral** infection
  - Chronic alcoholism
  - NASH
  - Hereditary haemochromatosis
  - A1ATD

• Pathogenesis:
  - **Hepatitis B + C**: commonest where carrier state begins in infancy; HBV – 27% lead to HCC, HCV 75%
  - **Cirrhosis**: chronic regenerative activity; macronodular > micronodular
  - Fungal **toxins**: aflatoxin, mycotoxin
  - Thorium dioxide (old contrast)
  - Anabolic steroids
  - Will see ↑ alpha-feto protein

• Macroscopic appearance: Either large, unifocal mass, multifocal widely distributed nodules, or infiltrative cancer. Yellow-white masses, occasionally bile stained

• Microscopic appearance:
  - Well differentiated: trabeculae and acini of malignant cells, large irregular nuclei, bile pigment, cytoplasmic inclusions
  - Anaplastic: giant cell, small cell, spindle cell

**Cholangiocarcinoma**

• Arises in **intrahepatic** biliary tree
• Associated with **parasitic** infestation (ie 3rd world)
• Microscopic appearance: **well to poorly differentiated adenocarcinoma**. Malignant ductules in a dense stroma
• Clinical: ill defined upper abdo pain, malaise, fatigue, enlarged nodular liver, poor prognosis due to late presentation

**Rarer Cancers**

• Angiosarcoma: malignant tumour of blood vessels. Haemorrhagic appearance in liver. Associated with vinyl chloride (ie plastics manufacture) and arsenic
• Hepatoblastoma: In infants, can be epithelial or mixed, recapitulates foetal liver

**Non-Neoplastic Nodules**

• Focal nodular hyperplasia:
  - Generally accepted to be a **hyperplastic (regenerative) response to hyperperfusion** by the characteristic anomalous arteries found in the center of these nodules
  - Common
  - See characteristic **stellate scar** pattern grossly

**Benign Tumours of the Liver**

• **Bile duct adenoma**: “von Myenberg complex”, 1 cm pale nodules composed of small ducts in fibrous tissue. Incidental finding at surgery
• **Liver cell adenoma**:
  - Associated with **oral contraceptives, pregnancy**, anabolic steroids. Rupture can lead to massive haemorrhage (eg in pregnancy)
  - Appearance: soft-yellow bile stained well-circumscribed nodules. Sheets and cords of polygonal cells, lack normal architecture – no portal tracts. No features of malignancy
• **Haemangioma**: common, composed of masses of blood vessels that are atypical or irregular in arrangement and size
• Other: Cavernous haemangioma, biliary cysts

**Cholestatic Liver Diseases**
• Cholestasis = arrest or marked reduction in bile secretion or flow
• Functional secretory disturbance of hepatocytes +/or obstruction at any level in pathway from canaliculi to duodenum
• *Intrahepatic/extrahepatic* cholestasis but often mixed

**Vanishing Bile Duct Disease**
• Neonate = bile duct atresia:
  ➢ Panbiliary disease
  ➢ Progressive *necroinflammatory destruction* of bile ducts beginning in the *extrahepatic* system
  ➢ Begins *in-utero* or in the *perinatal* period
  ➢ Presents with progressive jaundice
  ➢ Need liver bx to dx
• Adults:
  ➢ PBC
  ➢ PSC
  ➢ Liver allograft rejection
  ➢ GVHD

**Ascending Cholangitis**
• *Suppurative inflammation* within the bile ducts with bile stasis
• Caused by obstruction, treated with drainage
• Common organisms are *enteric*: E Coli, Klebsiella, Enterobacilli

**Primary Sclerosing Cholangitis**
• Autoimmune destruction of *intra* and *extra* hepatic bile ducts
• M:F = 2:1
• 70% associated with *ulcerative colitis* (5% UC sufferers get PSC) and HLA types
• See cholestasis w *pANCA* (80-90%)
• Insidious presentation like PBC – *elevated ALP*
• *Cirrhosis and liver failure* within 5 years; 7% develop cholangiocarcinoma
• Radiology helpful in dx
• Microscopic appearance: *onion skin fibrosis* around *intrahepatic* ducts
• Rx: liver transplant

**Primary Biliary Cirrhosis**
• Autoimmune destruction of medium sized *intrahepatic* ducts
• F:M = 6:1, middle aged females
• *Insidious onset*: pruritis, fatigue, steatorrhoea, vit D malabsorption
• See ↑ALP + GGT
• See anti-mitochondrial Ab (*AMA*) + IgM
• Give *ursodeoxycholic* acid (UDCA) – bear bile
• *Focal inflammatory destruction of bile ducts*, no primary inflammation in stroma → ducts reduced in number → green bile plugs in canaliculi → bile *infarct and portal-portal fibrosis* → *cholestasis and cirrhosis*

**Other**
• Secondary biliary cirrhosis: scarring following obstruction and ascending cholangitis
• Disappearing bile ducts: *Autoimmune, Graft vs. Host, Liver allograft rejection/post transplant* – all due to *lymphocytic destruction of biliary epithelium*

**Other Liver Diseases**
• Toxic: drugs, alcohol

*(although mildly pleiomorphic)*
• Fatty liver: obesity, diabetes, drugs, alcohol
• Drugs: e.g. flucloxacillin (and other antibiotics) can cause intrahepatic cholestasis

**Haemochromatosis**

• Bronzed diabetes: triad of micronodular cirrhosis, diabetes mellitus, and skin pigmentation (iron stimulates ↑melanin)
• Affects liver, pancreas, heart, gonads. Also causes osteoarthritis and diabetes
• **Primary/idioopathic/genetic:**
  - Common **autosomal recessive,** often silent until 6th decade: usually males (5:1) 40 – 60 years.
  - First presentation often seen in asymptomatic folk w ↑ferritin + FHx
  - European population – mutation (C282Y) in HFE gene -6p. Gene product HFE regulates Fe absorption by enterocytes – mutation causes overaccumulation of 0.5 – 1g per year
  - Homozygous 0.45%, heterozygous 11% - most common genetic disorder in humans BUT low penetrance
  - Homozygotes: 65 – 100% will have iron overload. Heterozygotes have elevated ferritin but no disease
  - Die from hepatocellular carcinoma, cardiac disease, liver failure
  - Iron accumulates in the cytoplasm of liver cells (lots of black dots), also in pancreas, endocrine glands, skin, myocardium, joint linings
  - Microscopic appearance: Initially golden brown periportal ferritin deposits in hepatocytes. Later Kupffer cells become loaded. **Non-inflammatory cirrhosis.** Pearl stain: stains iron blue
  - **Tests:**
    - Measure serum Fe, transferrin, % sats (abnormal if >55%), serum ferritin (abnormal if >200ug/L in women/350uG/L in men)
    - Hepatic Fe count
  - **Monitoring:**
    - If transferrin > 45% or serum ferritin > 300 ng/ml then liver biopsy if > 39 years
    - **Hepatic Iron Index** = hepatic iron concentration/age. Normal < 1.9 mmol/gm/yr
    - If cirrhosis for > 10 years then screen for hepatocellular carcinoma every 6 or 12 months. If picked up clinically then too late
    - Screen for α-feto Protein (tumour marker), or inject lipiodol into hepatic artery → preferentially taken up by HCC → hypodense on CT
    - Treatment of HCC: resection or liver transplantation. Chemo ineffective
  - **Advanced organ changes:**
    - Liver – enlarged → cirrhosis
    - Pancreas – chronic pancreatitis
    - Joints – arthritis
    - Testes – testicular failure
    - Heart – damaged myocytes
    - Skin – bronze colour
  - **Treatment of haemochromatosis:** if **regular venesection** before organ damage then normal life expectancy. Regular initial venesection to ↓↓iron load, then venesection very 3 – 6 months

• **Secondary (called Fe overload)** rather than haemochromatosis:
  - Chronic transfusion overload
  - Ineffective erythropoiesis (eg thalassaemia, liver disease, high iron intake)
  - Iron first in Kupffer cells, later in hepatocytes
  - Cirrhosis unusual

**Vascular Disease of the Liver**

• Post-hepatic disease:
  - Right sided heart failure:
    - Enlarged, tense, tender liver
    - Marked centrilobular congestion and haemorrhagic necrosis: ‘nutmeg liver’ – lacy pattern with dark and light areas
  - **Cardiac Sclerosis:**
    - Less common complication of heart failure
    - A peri-venular fibrosing reaction following long-standing congestion
    - Rarely causes ↑portal pressure
Hepatic Vein Thrombosis (Budd Chiari Syndrome):
- Hepatic congestion from obstruction to blood flow due to occlusion of hepatic veins or IVC
- Associated with anything causing hypercoagulability: polycythaemia vera, pregnancy, oral contraceptives, hepatocellular carcinoma
- Appearance: swollen, red liver, congestion, veins containing thrombi


Pre-hepatic disease: Portal vein obstruction due to cancer, peritoneal sepsis, pancreatitis, surgery, cirrhosis

Gilbert’s Syndrome
- Normal variant in 2-7% of the population
- Intermittent ↑ indirect (unconjugated) bilirubin + jaundice due to ‘defective’ uptake and conjugation of bilirubin by liver
- Manifests in adolescence/early adulthood
- Exacerbated by low fat/low calorie diet (e.g. when gastroenteritis; unconjugated increases as not conjugating it for fat breakdown). Use this to test: fast and see if it increases. Also worse when ill due to other causes (may present as a red herring)
- Bilirubin rarely as high as 85umol/L (fluctuates between 20-50umol/L); normal GGT
- Complex genetic basis
- Diagnosis usually by exclusion although genetic test now available (gene test for UGT1A1*28)
- Is totally benign

Neonatal Liver Disease
- Extrahepatic Biliary Atresia: destructive inflammation of bile ducts → cirrhosis
- Neonatal Hepatitis: non-specific idiopathic response to neonatal hepatic insult (eg virus). Giant cell transformation of hepatocytes, chronic inflammation around portal tracts, focal necrosis and lobular disarray

Wilson’s Disease
- Rare (1/30,000) autosomal recessive: accumulation of dietary copper in liver, brain, eye
- Mutation in ATP7B gene, impaired copper excretion into bile
- Presentation 6-40 years with acute/chronic liver disease, neuropsychiatric or parkinsonian features
- See:
  - Fatty changes
  - Acute hepatitis or chronic hepatitis (fatty change + Mallory bodies)
  - Cirrhosis
  - Kayser-Fleischer rings (brown ring – see right)

Alpha-1 Antitrypsin Deficiency
- Autosomal recessive
- A1AT is a protease inhibitor glycoprotein secreted by hepatocytes + lung epithelial cells + phagocytes; preferred target is neutrophil elastase
- Major role in lung is to protect connective tissue from neutrophil elastase
- ↑ as an acute phase protein
- → inhibits proteases released by neuts during inflammatory responses
- Genetics:
  - PiMM wild type – 90% of the population have this
  - Only liver disease if < 10% normal function (ie ZZ allele).
  - Z is bad, M is normal, S is mildly impaired. Only 10% of ZZ get chronic liver disease. MZ probably has no disease association
  - 7 – 10% of the population have a variant associated with mild/moderate deficiency
- Abnormal A1AT accumulates in cells as cytoplasmic globules → cell death → fibrosis
- Lung disease (40%) is more common than liver disease (10%) in ZZ
- Clinical: neonatal hepatitis, or can remain silent into adulthood when presents with cirrhosis, HCC or premature emphysema
- Treatment: liver transplant, smoking cessation, limit EtOH
End Stage Liver Disease

**Cirrhosis**
- **Final common pathway** for many chronic injuries to the liver
  - Chronic hepatitis, drugs, alcoholic hepatitis, NASH, metabolic disorders (wilson’s, A1ATD), cholestatic + biliary disease (vanishing bile duct diseases), vascular diseases
- Diffuse hepatic fibrosis with irregular regeneration of surviving hepatocytes to form nodules
- Disruption of normal vascular arrangements → portal hypertension
- Micronodular and macronodular forms

**Hepatic Failure**
- Conjugated jaundice
- Fatigue, muscle wasting, bruisability
- ↓ Platelet count (reliable early indicator of cirrhosis)
- ↓ Synthesis: notably of albumin
- Fluid retention, ascites, spontaneous bacterial peritonitis
- Coagulopathy: ↓ synthesis of 2, 5, 7, 9, 10
- Hyperammonaemia → metabolic encephalopathy
- Gynaecomastia (steroid hormones not metabolised)
- Hepatocellular carcinoma

**Hepatorenal Syndrome**
- Renal failure in patients with liver failure → ↑ urea and creatinine
- Rapid decline in renal function secondary to cirrhosis/acute LF
- Decreased liver function causes changes in splanchnic circulation therefore blood flow and tone in kidneys is deranged
- RF is a consequence of these changes in blood flow
- Blood is hyperosmolar but urine sodium is low
- Treat with albumin infusion + vasoactive drugs e.g. octreotide, midodrine

**Hepatic Encephalopathy**
- Metabolic derangement of the brain: only mild morphologic changes (eg oedema)
- See Delta waves on EEG
- Flapping tremor
- Grade 1 – altered mood, confusion, 2 – drowsy, disorientation, ataxia, 3 – marked confusion, sleepy, obey simply commands, 4 - coma

**Encephalopathy**
- Nitrogenous products made in GIT normally removed in liver – screwed in ESLD therefore enceph
- Also, ↑ protein intake therefore ↑ chance of enceph
- Try to avoid constipation (lactulose) and to avoid sedatives
- Graded from 1-4 (4 = coma; 1 = altered mood; 3 = able to follow simple commands1)
- Rx:
  - **General** (assess cardiac, resp, neuro)
  - **Weigh** (daily)
  - **Fluid intake** (0.75-1.5L/d) (care with IVF; if Hb low, give blood)
  - **Diet** (high calorie intake, do not restrict pro, night time snack, no added salt ~60-80mmol Na/d)
  - Do not treat enceph prophylactically
  - Avoid/care with sedatives, diuretics, electrolytes (K), laxatives
  - Baseline bloods
  - **Screen for infection** (urine, blood, ascites – TREAT ON SUSPICION)

**Portal Hypertension**
- Diagnosed clinically: if cirrhosis, ascites and varices assume portal hypertension. Can confirm with Doppler ultrasound
- Causes:
  - Post-hepatic: vascular outflow obstruction (Budd Chari Syndrome)
  - Intrahepatic: cirrhosis
  - Prehepatic: portal vein occlusions
- Portal pressure = hepatic vein P – systemic venous P (IVC P)
- Normal portal P <5mmHg
• Portal HTN >10mmHg
• Varices bleed at >12mmHg

Consequences:
  ➢ Portosystemic shunts: varices (oesophageal, rectal, umbilical, spontaneous)
  ➢ Spontaneous bacterial peritonitis
  ➢ Ascites: ↓ albumin synthesis, ↑ portal pressure, ↑ hepatic lymph formation and renal retention of sodium and water
  ➢ PHTN gastropathy (dilated veins around stomach bleed → anaemia)
  ➢ Splenomegaly w hypersplenism

• Treatment of varices:
  ➢ See GI bleeding
  ➢ Complicated by hypo-coagulopathy secondary to liver failure (do INR and APPT)
  ➢ Band oesophageal varices lower down: collapses them further up. Varices are asymptomatic until eroded by acid or increased pressure from vomiting
  ➢ Emergency therapy for bleeding varices:
    o Terlipressin (shuts down splanchnic circ therefore ↓ P in varices; is an ADH analogue therefore vasoconstricts); octreotide/SST can be used also
    o Balloon tamponade
    o Resuscitation
    o Then emergency endoscopy with sclerotherapy (takes several iterations) or banding, or TIPS/surgery (portal/caval shunt)
  ➢ Maintenance treatment:
    o Use non-specific B-B eg nadalol/propranalol → ↓CO due to ↓HR
    o Sucralfate (an Al carbohydrate): 1 gm 1 hr ac QID - surface protective effect to stop ulcers over sclerosed varices

Ascites
• Rx w low salt + low H2O diet + spironolactone or paracentesis
• Careful not to make them too dry too fast
• Tense ascites = massive ascites, often refractory, needs therapeutic paracentesis
• Transudate = low protein/alb = SAAG (serum alb:ascites alb gradient) >11 in PHTN therefore need pleural fluid aspirate for dx
• Therapeutic paracentesis – take off 5L therefore need to give alb ~ 40g to ensure fluid doesn’t move from IV space to refill the interstitium
• Infection/SBP:
  ➢ See SBP as low protein ascites therefore low Ig in ascitic transudate
  ➢ Bact translocated across gut into peritoneum + into vasc system
  ➢ Rx w cefotaxime + thereafter w norfloxacin
  ➢ Kupffer cells stuffed + shunts (anastamoses) allow bact passage around the body

Nutrition
• Malnutrition is common in chronic liver disease due to ↓ absorption and ↓ synthesis
• Survival depends on nutrition
• Anorexia, prob eating pro, fluid + salt intake issues
• Liver crap + GNG + glycogenolysis, esp at night therefore proteolysis + catabolic state etc = have a sweet meal before bed
• Na retention as PHTN causes ascites therefore ↓ circ volume + RAAS activation = use spironolactone to rx
• Hyponatremia also occurs – too much H2O (free H2O retained in LD) = restrict fluid intake
• Give ↑ fat and ↓ CHO to combat hyperglycaemia resulting from insulin resistance
• If encephalopathy, then low protein diet, antibiotics to decrease bacterial ammonia production and lactulose (↓ transit time & metabolised by bacteria → ↑ H+ which converts NH3 to less absorbable NH4)

Gallbladder and Bile Ducts
• Cholecystitis = inflamed gallbladder (eg due to stone impacted in gallbladder or cystic duct). Acute or chronic
• Cholangitis = bile duct infection: RUQ, pain, jaundice & rigors
• Choledochoolithiasis = gallstones in common bile duct
• Cholecystolithiasis = gallstones in gallbladder
• Bile:
- GB concentrates bile 10-fold by removing H2O
- Bile salts produced by breakdown of chol + are detergents allowing absorption + digestion of fats

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<tr>
<th>Biliary + Pancreatic Conditions</th>
<th>Presentation</th>
<th>Cause</th>
<th>Path</th>
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</table>
| Acute cholecystitis             | 1. RUQ steady pain, radiates to R shoulder, back  
2. N & V  
3. Fever  
4. Increased WCC, mild inc bili +ALT/AST | ● Gallstones → obstruction → increased intraluminal P → P necrosis → infection  
● Can see acalculous acute chole due to biliary stasis (major surg, sepsis, severe trauma etc) | Macro: enlarged, red to black, pus, thick-walled, cholesterolosis (yellow flecks)  
Micro: acute infl – oedema, WBC, congestion (dilated vessels), necrosis |
| Chronic cholecystitis           | Repeated attacks of acute cholecystitis | Repeated acute attacks or localised ischaemia due to P of stone against wall | Macro: thickened wall  
Micro: chronic infl cells, fibrosis, muscle hypertrophy, rokitansky-aschoff sinuses (sinuses of dead spaces – herniation due to ↑P), porcelain GB |
| GB mucocele                     | Occurs when cystic duct becomes obstructed – mucus builds up | | |
| GB carcinoma                    | ● Associated with chronic inflammation (due to stones); or chronic infection; IBD; GB polyps  
● Most are adenocarcinoma, can see SCC | | |
| Cholangiocarcinoma              | 1. Obstructive jaundice, pale stools, dark urine  
2. N & V, wt loss  
3. Elevated LFTs | ● Ass w chronic infl – PSC, chronic parasitic infection, IBD, chemical exposure  
● Mostly adenocarcinoma, rarely SCC | Patterns: 1. Nodules within wall 2. Diffusely infiltrative 3. Polypoid |
| Acute pancreatitis              | 1. Sudden onset intense epigastric abdo pain, radiating to back, relieved by leaning forward  
2. N & V  
3. Shock  
4. Fever  
5. Signs: tachy, tender, guarding, distension  
6. Elevated amylase + lipase (leaks out into circ) | I GET SMASHED  
Idiopathic, gallstones, ETOH, trauma, scorpion, metabolic d, steroids, hyperlipidemia/hypercalcaemia, ERCP, drugs  
Enzymes released + activated, causing:  
1. Acinar cell injury  
2. Duct obstruction  
3. Stuffed up IC transport of enzymes | Macro: 1. Variegated areas of red-black haemorrhage  
2. Yellow fat necrosis  
3. Peritoneal 'chicken broth' fluid  
4. Resolution = fibrosis, calcification, pseudocyst  
Micro: 1. Proteolytic destruction parenchyma  
2. Necrosis + haem  
3. Necrosis of fat by lipolysis  
4. Acute inflammation |
| Chronic pancreatitis            | 1. Chronic abdo pain, intermittent attacks  
2. Steatorrhoea  
3. Malabsorption | 1. Intraductal plugging + obst  
2. ETOH: direct toxic effects on acinar cell → release of cytokines → collagen production induced  
3. Ischaemia from obstruction + fibrosis | Macro: Atrophy + fibrosis – looks 'woody', dilated ducts, calcifications |
| Pseudocyst                      | Collection of necrotic, haemorrhagic material rich in pancreatic enzymes, enclosed by wall of granulation tissue; takes > 4 weeks to develop – therefore not an acute collection | | |
| Pancreatic carcinoma            | ● Syr survival <5%  
Age, high fat diet, smoking, DM, | | |

Gastro-Intestinal 294
Pancreatic endocrine tumours (islet cell)

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<td>1.</td>
<td>Beta cell tumours most common (functioning = insulinomas); 10% malignant</td>
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<tr>
<td>2.</td>
<td>Alpha cell tumours (functioning = glucagonomas)</td>
</tr>
</tbody>
</table>

**Cholelithiasis**

- Gall stones
- If bile is supersaturated with cholesterol $\rightarrow$ crystals precipitate

**Cholesterol stones**:
- $85\%$ of stones
- Incidence: Northern European ancestry, ↑age, female, obesity (fair, fat, female, forties, FHx)
- Caused by supersaturation of the bile with cholesterol $\rightarrow$ precipitation around bits of junk (eg epithelium)
- Appearance: either pure pale yellow and radiolucent, or mixed grey ‘gravel’ $\rightarrow$ more dangerous as can squeeze through cystic duct

**Pigment/bilirubin stones**:
- $15\%$ of stones
- Aetiology: Asian, haemolysis, alcoholic cirrhosis, biliary infection, ↑age
- Excess unconjugated bilirubin forms insoluble precipitates with Ca $\rightarrow$ calcium bilirubinate
- Appearance: small, jet black and ovoid

**Mixed stones**

**Cholesterolosis**: yellow flecks due to foamy macrophages gobbling up cholesterol

**Complications**: cholecystitis, pancreatitis, choledocholithiasis, ascending cholangitis, GB mucocele, gallstone ileus

**Cholecystitis**

**Biliary Colic**

- Symptoms:
  - Gives a colicky pain $\rightarrow$ waves of intense pain every 10 – 20 minutes with little pain in between. Patient is restless $\rightarrow$ can’t get comfortable in any position (as opposed to cholecystitis below)
  - May be mild tenderness on examination
- Pathogenesis:
  - Impaction of stone in the cystic duct
  - No inflammation of the gall bladder (yet)
- Investigations:
  - Plain xray (mainly to exclude other causes of an acute abdomen $\rightarrow$ eg obstruction, perforation, etc)
  - Diagnosis by US $\rightarrow$ looking for a thickened wall on the gall bladder and filling defects in the ducts
  - CT the best modality for looking for stones
- Management:
  - IV fluids (may not have been drinking, may need to be nil-by-mouth if they go to surgery)
  - Bloods: FBC, U&Es, LFTs, Amylase, Clotting factors, Group & Hold, ESR/CRP
  - Urine: UTI/pregnancy
  - Pain relief + antiemetics
  - Antibiotics
  - Antispasmodics (eg Buscopan) for colic

**Acute Cholecystitis**

- Most dangerous common complication of cholelithiasis
- Clinical presentation: acute abdomen. Symptoms may be obscured by the predisposing condition
- $90\%$ caused by impaction of stone in the neck: calculus acute cholecystitis. If no stones then acalculous cholecystitis (usually vasculitis)
- ↑Inflammation due to ↑pressure, chemical irritation, and secondary infection
Macroscopic appearance: enlarged (bigger than chronic), tense, covered by fibrin, contains turbid bile or pus. Wall is thick and oedematous and the mucosa is red or green-black (gangrenous cholecystitis, due to ↓blood flow secondary to ↑pressure)

Microscopic appearance: acute inflammation, congestion, abscess, necrosis

Symptoms:
- 70% stones are asymptomatic. If symptomatic there is a 30% 5 year risk of complications requiring surgery
- Uncomplicated: severe constant epigastric/RUQ pain, lasting several hours, radiating to back, maybe nausea/vomiting. It hurts to move or breathe so patient lies still. Local peritonitis (very tender). If impacted then inflammatory component (fever, ↑WBCs)
- Complicated:
  - Fever, abdominal pain, nausea, vomiting: indicating acute cholecystitis
  - Fever, pain, jaundice: acute cholangitis (Charcot’s triad)
  - Abdominal and back pain, collapse, vomiting, hypotension: acute pancreatitis

Investigations:
- Murphy’s sign: Lay 2 fingers on RUQ. Patient inspiration → pain. No pain on LUQ
- Gallstones often incidental finding on ultrasound or x-ray (if calcified – only 10% radio-opaque)
- Ultrasound picks up 98% of gallbladder stones but only 50% of common bile duct stones. More can be inferred from a dilated duct (> 6 mm)
- Serum amylase: if > 1000 IU/L → acute pancreatitis
- ALP & bilirubin
- WBC count → cholecystitis
- Antimitochondrial antibody tests → exclude primary biliary cirrhosis

Differential:
- Obstructive Jaundice: pancreatic neoplasm, cholestatic hepatitis
- Biliary colic: pancreatitis, oesophagitis, peptic ulcer, IBS
- Ascending Cholangitis

Treatment:
- If acute, nil by mouth, pain relief, IV antibiotics (e.g. cefuroxime)
- Usually settle with conservative treatment (wait 2 days and see). Then schedule for elective cholecystectomy 6 week later (once inflammation settled down)
- Surgical Options:
  - ERCP
  - Lithotripsy
  - Laparoscopic cholecystectomy
  - Percutaneous transhepatic cholangiogram gallbladder cannulation (PTC)
- Long term:
  - No relationship with high-cholesterol diet. Avoid obesity
  - Drugs: bile acid treatment – dissolve small cholesterol stones

Chronic Cholecystitis
- ?Aetiology: no infective or inflammatory agents
- Macroscopic appearance: normal to enlarged gallbladder with stones and a fibrous thickened wall
- Microscopic appearance: chronic inflammation, fibrosis and muscular hypertrophy. Rokitansky-Aschoff sinuses: herniations through submucosa. Lipid laden macrophages extend into the lamina propria
- Symptoms: heartburn, belching, intolerance of fatty foods, discomfort. Can be found in people without gallstones ⇒ symptoms not specific

Ascending Cholangitis
- AKA bacterial hepatitis = Infection of the biliary tract
- Signs of acute cholecystitis plus sweats and rigors
- Very sick! Infection in the obstructed biliary tree
- Rapid systemic septic complications (fever, hypotension, shock, RF, DIC)
- Need to decompress quickly
- Lab = Increased WCC, left shift, cholestasis, blood culture positive (gram –ve eg e.coli)
- See Charcot’s triad:
  - RUQ pain
  - Fever
  - Jaundice
- Rx:
Urgent IV ABs (ciprofloxacin) + resus
IVF, electrolyte replacement
Urgent decompression (ERCP, PTC)
Treat other complications

Often accompanies obstruction due to gall stones
Also following ERCP (probe introduces gut bacteria into the ducts which are normally sterile)
Can be rapidly fatal – have low threshold for treatment
Rare differential Mirrizi Syndrome: no stone in the common duct but its compressed by adjacent inflamed gallbladder

Mucocoele of the Gallbladder
Cystic duct becomes obstructed. Trapped bile is absorbed and gallbladder fills with mucus

Tumours
Benign tumours:

- Adenomas and papillomas: project into the lumen. Benign overgrowths of epithelium
- Adenomyoma: nodule at the gallbladder tip composed of smooth muscle around benign ductules

Malignant:

- Carcinoma of the gallbladder:
  - Uncommon: 0.5% of cholelithiasis patients
  - Associated with gallstones and inflammation
  - Presentation: insidious until late. Abdo pain, jaundice, anorexia, weight loss, nausea. 1% 5-year survival
  - Macroscopic appearance: at fundus and neck. Either infiltrating or fungating type. At discovery usually involve liver, bile ducts and portal nodes
  - Microscopic appearance: 95% adenocarcinoma (can be poorly differentiated), 5% squamous cell carcinoma (from squamous metaplasia)

- Carcinoma of the bile ducts and ampulla = cholangiocarcinoma:
  - Tumour markers = CA19.9 (sens = 89%) + CEA (spec = 86%); CT has 82% sens + 80% spec
  - Uncommon, associated with chronic inflammation, parasites, ulcerative colitis
  - Presentation: obstructive jaundice, pale stools, nausea, ↑LFTs. Differentiate from obstruction due to stones. Poor prognosis
  - Macroscopic appearance: papillary fungating mass + intraductal nodules + diffuse infiltration → obstruction. Periampullary tumours have better prognosis
  - Microscopic appearance: adenocarcinoma, occasionally squamous cell

Pancreas

Acute Pancreatitis
Inflammation in pancreas and peripancreatic tissues (sometimes with haemorrhage and necrosis)

Causes
90% caused by either (grog or gravel):

- Gallstones blocking the ampulla (60%)
- Alcoholic (more chronic than acute) (30%). Pathogenesis unclear - ?duct obstruction

Also: trauma, ERCP, drugs

Types:

- Interstitial or oedematous pancreatitis: mild, self-limiting
- Acute haemorrhagic (necrotising) pancreatitis: severe

Pathogenesis
Activation of pancreatic enzymes → cellular injury, release of enzymes and cytokines → ischaemia. Secondary bacterial infection possible. May also follow ERCP – catalysts from duodenum activate pancreatic enzymes while still in the pancreatic duct

Macroscopic appearance:

- Variegated: blue-black haemorrhage, yellow-white fat necrosis
- Peritoneal ‘Chicken-Broth Ascites’: layer of clear fat floating on turbid liquid – lipase has digested abdominal fat
- With resolution: fibrosis, calcification, pseudocysts
Microscopic appearance: If mild, periductal inflammation. Proteolytic destruction of the pancreatic substance. Necrosis of blood vessels → haemorrhage

Presentation
- Upper abdominal** constant** (i.e. inflammatory) pain + lumbar back pain
- Nausea, vomiting
- Peritoneal irritation, ileus
- Jaundice, especially in gallstone induced
- Tachycardia
- Signs (due to haemorrhagic fluid in the extra peritoneal space):
  - **Cullen’s Sign**: Discolouration around the umbilicus
  - **Grey-Turner’s Sign**: Discolouration around the flanks
- If severe:
  - Shock: enzymes into blood, acute peritonitis, massive inflammation
  - Respiratory failure, circulatory failure
- Complications: **shock**, ARDS, acute renal failure, abscess, duodenal obstruction

Investigations
- **↑**Serum or urine amylase. Height of amylase does not correlate with severity. Other conditions may cause raised amylase. **↑**Lipase
- Also possibly **↑**glucose, **↑**WBCs, **↑**creatinine, **↓**calcium, **↑**faecal elastase
- CXR to exclude gastrointestinal perforation (air under diaphragm)
- Ultrasound/ERCP, ALT and bilirubin to check for stones
- CT to determine extent of inflammation/necrosis. Use contrast – necrotic tissue doesn’t light up as it’s not perfused
- Also FNA

Differential
- Abdominal catastrophe: perforation, ectopic pregnancy, infarction, ruptured aneurysm, obstruction, appendicitis
- MI
- Acute cholecystitis

Progression
- Most fully recover in 4 – 6 days with **IV fluids, O2, analgesia**
- If severe, up to 50% mortality. Treat for renal, cardiac and respiratory failure. Surgery for infected necrosis
- Treat cause: e.g. ECRP + sphincterotomy, later cholecystectomy, alcohol abstinence, etc
- Supportive treatment: IV fluids, pain relief, inotropic support if ↓BP or renal hypoperfusion despite fluids

Chronic Pancreatitis
- = **Replacement of pancreatic tissue by fibrosis**, often with calcification, sometimes with duct dilation and stones
- May result in chronic pain, relapsing acute pancreatitis, exocrine or endocrine deficiency

Causes:
- Alcohol (60 – 80%) → duct obstruction by protein rich secretions
- Obstruction (10%)
- Idiopathic (10%)
- Genetic factors
- Hypercalcaemia and Hyperlipidaemia
- Congenital anomalies of duct
- Following acute pancreatitis of any cause

Symptoms
- Abdominal pain, weight loss, diarrhoea/steatorrhoea, diabetes mellitus (late complication – islet cells are the last to fail), acute pancreatitis

Investigations
- As for acute, plus check chronic differentials (e.g. ulcer, GORD)
Blood glucose, GTT

Pathology

- Chronic calcifying pancreatitis:
  - In alcoholics
  - Macroscopic appearance: throughout lobules of pancreas, hardened foci of calcification
  - Microscopic appearance: atrophy of acini, fibrosis, chronic inflammation. Dilated ducts and atrophic epithelium

- Obstructive pancreatitis
  - Due to choledolithiasis
  - Affects periductal regions, mainly head of the pancreas
  - Ductal epithelium better preserved

Treatment:

- Exocrine/endocrine replacement
- Analgesia
- Surgery: duct dilation, resection of diseased portion

Pancreatic Tumours

Symptoms

- Weight loss, anorexia, lethargy
- Pain
- Jaundice (70%)
- Pruritis (itching)
- Diabetes mellitus

Investigations

- FBC: anaemia, sepsis
- LFTs: to confirm obstructive jaundice
- Ultrasound
- ERCP or CT
- Ca19.9

Differential

- Obstructive jaundice
- Hepatic jaundice
- Cachexia: gastric, colorectal or ovarian cancer
- Other pancreatic disease

Types

- Pseudocysts (don’t have epithelial lining so not a true cyst – not neoplastic):
  - Congenital (rare) or acquired
  - Solitary cyst 5 – 10 cm diameter, contains serous, turbid fluid
  - Associated with pancreatitis, especially alcoholic
- Benign tumours: rare. Serous cystadenoma (elderly women), solid cystic tumour (young women)
- Carcinoma of the pancreas:
  - Epidemiology:
    - 5% of cancer deaths
    - Usually fatal, 90% die within one year, 5 year survival 1 – 2%
    - Associated with smoking, fatty diet, chemical carcinogens
    - M > F, B > W, 60+
  - Presentation:
    - Often perineural invasion (travels along nerves) → difficult pain
    - Affecting head: obstructive jaundice
    - Affecting tail: weight loss, liver metastases
  - Macroscopic appearance: 60% head (most pancreatic tissue is there). Grey-white tumour with infiltrative margins. Extends to duodenum, liver, nodes, etc
  - Microscopic appearance: 90% adenocarcinoma, 10% adenosquamous. Other rare types
- Treatment: palliative most commonly. Stenting or ERCP for duct compression
- If resection possible:
  - For body/tail: distal pancreatectomy – usually need to remove spleen as well
  - For head: pancreaticoduodenectomy (*Whipple* operation)
- Other tumours: benign or malignant endocrine tumours (insulinoma, gastrinoma)
Renal and Genitourinary

- References: Renal Medicine handout, General Medicine Run, and Prof Delahunt’s pathology handout
- See also Renal Disease in Children in Children, page 968

Anatomy

History

- Exposure to nephrotoxic medication (i.e. pre-renal or intrinsic renal failure)
- Risks of renal artery atherosclerotic disease
- Volume depletion → pre-renal
- Rash = allergic interstitial nephritis
- Bone pain in elderly → multiple myeloma → acute renal failure

Renal Physiology

- Function of kidneys:
  - Maintenance of fluid and electrolyte balance
  - Excretion of metabolic wastes
  - Excretion of acid
  - Endocrine (calcitriol, erythropoietin)
- Allows regulation of a daily intake of:
  - Water: 1 – 20 litres
  - Sodium: 5 – 500 mmol
  - Potassium: 20 – 200 mmol
  - Protein: 30 – 150 g
- Fluid dynamics:
  - Kidney’s receive 20 – 25% of cardiac output
  - GFR maintained by autoregulation (tubuloglomerular feedback: ↓ flux past MD eg ↓BP → afferent arteriole dilation + renin release → efferent art constriction → ↑GFR) but dependent on glomerular pressure and renal blood flow
  - Normal urination: 1 ml/kg/hr (down to 0.5 ml/kg/hr OK)
  - Urine output of 1 – 2 litres/day
- Tubule function:
  - Proximal tubule:
    - 70-90% Na, H2O, Cl, K
    - Reabsorption of glucose, AAs, + HCO3
    - Filtrate remains isotonic

Renal and Genitourinary
Loop of Henle:
- Countercurrent exchange for filtrate dilution
- Important for the control of urine concentration

Thick descending limb:
- Fluid equilibrates with interstitium
- Permeable to water + Na

Thin ascending limb:
- Permeable to Na, urea etc
- Impermeable to H2O
- Established hypotonic filtrate + hypertonic interstitium

Thick ascending limb:
- Solute actively transported
- Tubule fluid more dilute

Distal tubule:
- Hormonal regulation of Na control – aldosterone
- Excretion of acid + K
- Urine concentration/dilution - ADH

Hormones:
- Intra-renal:
  - Renin-angiotensin system: ↓Na/hypotension (past MD/JGA) → ↑renin → ↑angiotensin II → vasoconstriction + ↑aldosterone + thirst → ↑afterload (arterial vasoconstriction) + ↑preload (venous vasoconstriction + ↑aldo) + SNS activation
  - Prostaglandins: vasodilating, control glomerular blood flow, natriuretic and diuretic

- Extra-renal (and acting on the kidneys):
  - Aldosterone: stimulated by angiotensin II and ↑K → Na reabsorption
  - ADH: controlled by both volume and osmotic stimuli → ↑water resorption
  - Atrial and brain natriuretic proteins (ANP/BNP): volume overload → natriuretic and diuretic

- For hypo/hypernatraemia, potassium and acid-base balance, see Electrolytes, page 155

Assessment of Renal Function

Urinalysis
- Should:
  - Avoid early morning specimen
  - Be a clean voided midstream specimen
  - Should be delivered fresh to the lab or refrigerated
  - Advise on method of collection

- Dipstick:
  - Blood: indicates bleeding in the urinary tract or free haemoglobin or myoglobin
  - Proteinuria: sensitive to protein – but use 24 hour urine to quantify, or spot check with protein:Cr ratio in morning urine. Urine protein is normally albumin. Hyaline and granular casts and Bence Jones Proteins don’t test +ve for protein
  - Glucose: diabetes, pregnancy, sepsis, tubular damage or low renal threshold
  - Nitrates ⇒ UTI

- Microscopy:
  - Blood: should be less than 8 x 10⁶ cells per litre (no more than 3RBC/hpf)
    - Normal morphology suggests bleeding from the lower urinary tract: calculi, infection, neoplasia
    - Dysmorphic cells suggests glomerular bleeding: glomerulonephritis and vasculitis (including endocarditis). Microhaematuria can be seen in either nephrotic or nephritic. Macro haematuria is normally nephritic
  - WBCs indicate infection (>2WBC/hpf; >5 x 10⁶/L), less commonly renal tuberculosis, renal stones and papillary necrosis
  - Eosinophils ⇒ interstitial nephritis
  - Casts:
    - Hyaline casts: just protein, no cellular elements and may be normal (especially concentrated urine)
Granular casts: **degenerative cellular** material – usually tubular cells → pathology

Red cell casts: **glomerular bleeding** → usually active GN

White cell casts: **pyelonephritis**, interstitial nephritis or glomerulonephritis

**Glomerular Filtration Rate (GFR)**

- Marker of renal excretory function
- **Determined by intra-glomerular pressure**, which in turn is determined by the difference in **vascular tone between afferent and efferent arterioles**. Maintained by autoregulation except when blood pressure is very high or very low

**Creatinine:**
- Waste product from muscle breakdown
- **Filtered** at the glomerulus + **not** reabsorbed, but a small amount is **secreted** from the tubules (ie GFR less reliable at small urine flows)
- Affected by **muscle mass, protein intake and age** (i.e. Cr can be the same in two individuals, yet GFR might be completely different) → poor indicator of renal function. Serial measurements helpful
- Normal Creatinine < 0.110 mmol/L (110 µmol/L)

Use **Cockcroft-Gault formula** (don’t need to try and remember):

\[
GFR(\text{mL}/\text{sec}) = \frac{(140 - \text{age}) \times \text{body weight(kg)} \times 0.85(\text{female})}{50 \times \text{serum creatinine(micromol/L)}}
\]

- Normal is > 1.5 ml/sec (> 90 ml/min)
- Use total body weight but recognise it overestimates if obese
- Or collect 24 hour urine and compare to plasma concentration with **UV/P**
- Can measure with radionuclides (**DTPA scan**)
- **eGFR** what is used now (complicated formula – do not need to know, lab performs this)
  - Not accurate above 60ml/min
  - Not accurate for obese, very young or very old
  - Not validated for Asian, PI, Maori

**Other**

- Urine protein/creatinine ratio:
  - Spot urine sample used
  - Measures protein concentration
  - Detects **total protein** (as cf UACR)
  - 100mg/mmol equates to around 1g/d (significant proteinuria = >45mg/mmol)

- Urine albumin/creatinine ratio:
  - The total protein-to-creatinine ratio does not detect microalbuminuria
  - Albuminuria is a more sensitive marker than total protein for chronic kidney disease due to diabetes, hypertension, and glomerular diseases therefore **UACR** is the better choice

- Volume assessment:
  - Lying and standing BP
  - JVP
  - Change in weight
  - Oedema, etc (tissue turgor, LOC, MM, CR, HR, UO)

- Tubular function: test concentrating ability with fluid deprivation and ADH administration
- Urinary acidification: give ammonium chloride and then measure urinary pH
- Also consider blood tests: Ca, PO4, FBC, complement, autoantibodies, etc
- NB. Urea is not a marker of kidney function – used rather as a marker for toxins in the blood

**Renal Imaging**

- See contrast nephropathy for info on contrast
- **Plain X-ray**: shows radio-opaque renal stones (**80% are**) not uric acid stones (eg Gout). Methodology:
  - Gas:
    - Should see gas in **stomach + colon** (not really in SI)
    - Abnormal if in:
      1. **Biliary tree**
      2. **Peritoneum: pneumoperitoneum**
      3. **Bowel wall**
      4. **Retroperitoneum**
      5. **Renal tract**
Renal colic/pancreatitis → focal ileus
Emphysematous pyelonephritis → gas in kidney
Emphysematous cystitis → gas in bladder

- **Stripes:**
  - Of normal visceral outlines, and
  - Find the psoas muscle and move out parallel to this to find the kidneys
  - Assess size: length of kidney = length of 3 verteabrae + disc spaces. Up to 2 cm variation in size between kidney's OK

- **Stones:** check course of ureters: lie anterior to psoas (follow transverse processes), anterior to sacro-iliac junction, around pelvis, into bladder (NB. Bladder stones can be very large!)

- **Bones:** renal osteodystrophy, etc

**Intravenous urogram** (Plain film + contrast) = IVU = IVP (Intravenous pyelogram)
- Superceded by CT
- Gives anatomical and functional information
- Shows renal contours, presence of scarring, reflux nephropathy, obstruction
- Depends on renal uptake of the contrast. Little use if significant renal impairment (eg CR > 200)

- **Phases and interpretation:**
  - Control →
  - Nephrogram phase (1 minute post injection): renal contour, position, equal in intensity? →
  - Pyelogram phase (5 minutes): see major and minor calyces and bladder →
  - Post micturition phase: look for normal voiding

- **Antegrade and retrograde pyelography:** direct injection of contrast into the renal pelvis or the ureter

- **MCU:** Fill bladder with contrast and image following micturition. For assessment of vesico-ureteric reflux in children

**Ultrasound:**
- Good first-line option
- All pts with newly diagnosed renal failure should undergo renal US as an initial assessment
- For renal size and contour
- Shows hydronephrosis – but may not show the site of obstruction. Reasonable view of renal masses and cysts
- Poor imaging of ureters
- Will see **acoustic shadowing** behind stones
- Scarring: asymmetric indentation of renal outline. If young → ?reflux. If older → ?ischaemia

- **CT:** for complex cysts, masses, renal colic and **stones**.
- Modality of choice for stones. 5 mm slices:
  - ↑Sensitivity
  - No contrast risk (mortality 1 in 40,000)
  - Can sort out differentials of colic (eg appendicitis) on CT that you won’t see on IVP
  - Stone filling the whole of the renal calyces = staghorn calyx (in recurrent infection and alkaline urine)

**Nuclear medicine studies:**
- Renogram for assessing function of each kidney, avoids nephrotoxic contrasts
- Especially good for renal artery stenosis and obstruction
- A normal renogram shows an initial perfusion phase, a secondary renal uptake phase, and an excretory phase
- **DTPA:** eliminated almost entirely by filtration → used to show obstruction
- **Mag3: secreted** by tubules
- **DMSA:** is retained by the cells of the PT therefore highlights proximal tubules. Good for showing **renal scarring**, eg reflux nephropathy – preferred IX for diagnosing reflux nephropathy

**Arteriography:** Renal artery stenosis

**Renal Biopsy**

- Under local
- Indications: acute renal failure, nephrotic syndrome, heavy proteinuria or haematuria, alterations in renal transplant function
- Only if histology will influence management
- Major contraindication: bleeding tendency (check FBC and clotting first)
- Complications: bleeding and development of a perirenal haematoma (eg in amyloid disease when rigid arterioles won’t contract following bleeding)
- Risk of serious complications < 1% (fistula, haematoma, infection, surgery, etc)
Presentation of Kidney Disease

- This section outlines how kidney diseases present. A variety of kidney diseases present symptomatically in a variety of different ways. The major underlying diseases are described in the following section of Kidney Diseases, page 316
- Other presentations of kidney disease:
  - **Hypertension**: common symptom of chronic renal failure of any cause
  - See Renal Osteodystrophy in Increased Bone Resorption, page 409
  - See Urinary Tract Pathology, page 329

Nephritic Syndrome

- = **Proliferative glomerulonephritis**
- Presentation:
  - Urinary sediment: **haematuria, RBC casts + dysmorphic RBCs** (dysmorphism implies glomerular pathology as cf normal/isomorphic RBCs which imply tubule pathology)
  - Varying degrees of **proteinuria**
  - **Oliguria** → fluid retention
  - **Oedema** (especially facial)
  - **Azotemia**: renal impairment/ARF → ↑Cr, electrolyte disturbance
  - Hypertension
- Histology: Large glomeruli (diffuse changes of predominantly mesangial cells), polymorphs and black deposits on epithelial side of BM, can occasionally lead to crescents (ie lots of cell proliferation compared with Nephrotic Syndrome ⇒ rapidly progressive glomerulonephritis)
- Possible causes:
  - Post-infectious GN
  - Rapidly progressive GN
  - Mesangio-capillary/mesangioproliferative GN
  - Systemic disease
  - Maybe IgA GN

Nephrotic Syndrome

- = **Non-proliferative glomerulonephritis**
- Presentation:
  - Marked **proteinuria** (may make urine frothy) > 3 g/day
  - **Hypoalbuninaemia → oedema**: generalised, insidious onset, may be periorbital in the morning, legs in the afternoon. If gross then ascites and pleural effusion
  - **Hypercholesterolaemia** (↑ lipoproteins as liver ↑ protein production)
  - Renal function is generally preserved. But may retain Na and H2O. May ↑ plasma volume
  - If polyuria then ⇒ tubular and interstitial damage as well
- Pathogenesis: common end point of a variety of disease processes that alter the permeability of the basement membrane
- Possible causes (first 3 reasonably common in adults, Membranous is perhaps the most common):
  - Minimal change GN
  - Membranous GN
  - Focal Segmental GN
  - Maybe IgA and mesangiocapillary
  - (Diabetes, amyloidosis (eg multiple myeloma), drugs but these are not considered nephrotic syndrome)
- Management:
  - Minimal change: very responsive to steroids. The rest need something stronger (eg cyclophosphamide) and commonly ⇒ renal failure over time
  - Fluid restrict
  - Monitor and treat BP
  - Salt restricted, high protein diet
  - Oral diuretics + K (beware hypovolaemia ⇒ pre-renal failure)
- Complications: lose Antithrombin III protein as well as albumin ⇒ renal vein (and other) thrombosis.
  - Prophylactic anticoagulation
- Cause and Pathology:
  - Tumor carcinomas ⇒ MN; lymphoma ⇒ MCD
  - Heroin, other drugs heroin ⇒ FSGS; gold, penicillamine ⇒ MN/FSGS
Infectious (see “HAS” below)
Systemic (see “LAD” below)
Lupus → MN
Amyloidosis, myeloma variable
Diabetes mellitus Kimmelsteil-Wilson lesions
Hepatitis → Hep B → MN; Hep C → MPGN
AIDS → FSGS collapsing variant
Syphilis → MN

When secondary causes are ruled out, think of the primary (idiopathic) causes of nephrotic syndrome:
FSGS: increasing and most common cause in urban settings and in patients of African descent
Membranous (MN): most common cause overall; more prominent in elderly patients
Minimal change disease (MCD): most common in children, #3 in adults
Membranoproliferative glomerulonephritis (MPGN): can present as nephritic or nephrotic syndrome

Acute Renal Failure

= Abrupt reduction in GFR → ↑ plasma urea & creatinine (↑ nitrogenous waste products) and (usually)
↓ urine volume (oliguria < 400 ml/day, anuria < 100 ml/day). If ↑↑ urea but only ↑ Cr then ? dehydration or catabolic state
Assess severity using Cockcroft-Gault equation (see page 303). Normal clearance >= ~ 100 ml/min
Due to acute damage to any part of the kidney or renal tract
Usually Acute Tubular Necrosis but always consider differentials
The majority of episodes of ARF are due to prerenal failure and intrinsic renal failure (ATN) due to ischaemia and nephrotoxins
ARF is not a single disease entity, it is a syndrome caused by many different diseases and/or mechanisms
ARF is often encountered as a complication in seriously ill patients who have complex medical problems
ARF is frequently observed in the intensive care unit setting and contributes significantly to increased patient morbidity and mortality

Clinical Approach to the Diagnosis of ARF

Once recognised ARF, next step is to treat metabolic consequences → hyperkalemia, metabolic acidosis etc
Can then move on to thinking about the underlying cause
Is it “ARF” or “acute-on-chronic renal failure” (ie is there pre-existing renal impairment)?
Is there pre/renal/post renal failure:
天鹅是不是有它的身体部位
Is there renal tract obstruction?
天鹅是不是有它的身体部位
Is there a reduction in effective ECF volume?
天鹅是不是有它的身体部位
Is there renal parenchymal disease other than ATN?
Has there been a major vascular occlusion?

ARF Overview

ARF commonly results from hypotension leading to hypoperfusion of vital organs
Some of this is preventable. At risk patients can be easily identified and observed closely
Acute renal failure carries a high mortality (around 50% unselected cases)—so it is better to prevent it than try and treat it
ARF is either the development of oliguria (less than 400 ml/day or less than 0.5 ml/kg/hr for two hours if catheterised) or an ↑ Cr
Half of all ARF is nonoliguric
At medical school you learn the standard list of prerenal, renal, and postrenal causes of acute renal failure. In reality, acute renal failure is nearly always caused by prerenal problems. Nine in 10 peri-operative renal failures is prerenal. Primary renal disease, like glomerulonephritis, is uncommon. Postrenal disease, like obstruction, occurs occasionally.
The most common scenario is a period of hypoperfusion leading to acute tubular necrosis. The outer medulla of the kidney is relatively hypoxic because of its high workload and therefore prone to injury
The various urine tests that you learn about, which may point towards renal or prerenal causes of acute renal failures are not helpful, because in hospital the cause is usually obvious and many patients are on diuretics which makes the urinary sodium values difficult to interpret
Luckily, treatment of acute renal failure is relatively simple. There are five steps:
天鹅是不是有它的身体部位
1. Treat a high potassium first (> 6.5 mmol/l)
2. Correct hypovolaemia with successive fluid challenges
3. If you have corrected volume depletion, but there is still hypotension causing hypoperfusion, then invasive monitoring, vasoactive drugs, and intensive care are required.

4. Exclude obstruction with an ultrasound scan as soon as possible and insert a urinary catheter.

5. Look at the drug chart and stop all the poisons. Antihypertensive drugs may also need to be omitted.

- Dipstick the urine (before catheterisation) and screen for infection. Involve the renal team in complex cases or if abnormal urine dipstick.

- Frusemide (as well as dopamine) has no effect on improving renal function. Frusemide is helpful once the patient is filled but remains oliguric and therefore at risk of becoming overloaded.

- Renal replacement therapy is indicated in volume overload, worsening metabolic acidosis, or resistant hyperkalaemia.

- Always stop non-specific NSAIDs and ACEi in any patient who is admitted with volume depletion—for example, diarrhoea, vomiting, bleeding, severe sepsis—or hypotension. This is because angiotensin converting enzyme inhibitors act on the afferent arteriole and non-steroidal anti-inflammatory drugs act on the efferent arteriole. The combination of volume depletion and the action of these drugs severely reduces glomerular filtration rate. In cirrhosis and congestive cardiac failure where prostaglandins are recruited to increase renal blood flow, non-steroidal anti-inflammatory drugs are more potent.

**Drugs the Kidney Does Not Like**

- **Any that are renally excreted** the kidney is not fond of when sick (tend to accumulate + can cause toxic effects [not necessarily at the kidney level])

- **NSAIDs** (→↓vasodilating PGs)

- **Metformin**: ↑ risk of lactic acidosis – contraindicated in chronically impaired kidneys + ARF

- **Allopurinol** – excreted through kidneys

- **Digoxin** – excreted through kidneys etc etc etc

**Pre-renal ARF**

- ↓ in glomerular perfusion in absence of structural kidney damage

- Kidney usually autoregulates – but can’t cope with extremes

- Can’t interpret results if patient has had recent diuretics

- If prolonged → ischaemic damage → loss of medullary gradient and reabsorbing capacity → dilute urine

- **Causes:**
  - **Volume depletion**: Usually GI loss, but also renal loss, burns, haemorrhage
  - **Cardiac failure** → ↓renal perfusion
  - Systemic vasodilation: sepsis or antihypertensives
  - Reno-vascular disease: renal artery stenosis
  - Alteration to intra-renal haemodynamics i.e. vasoconstriction in kidneys, e.g. due to NSAIDs (→↓vasodilating PGs), ACE inhibitors (→↓efferent arteriolar tone →↓intraglomerular pressure)

- Intense reabsorption of salt and water leads to:
  - Low volume of urine, high osmolality (> plasma), but low urine Na (usually < 20 mmol/l)
  - ↑ Urine to plasma ratio of creatinine and urea
  - Urea is re-absorbed preferentially to creatinine at low urine flows therefore plasma urea to creatinine is increased
  - Hyaline casts: aggregates of urine protein if low urine flow

- **Kidneys try to compensate by:**
  - Vasodilating afferent arterioles (via ↑PGs)
  - Activation of RAAS → ↑BP and vasoconstricts efferent arterioles in an effort to try and ↑ GFR

- **Management:**
  - Rapid fluid resuscitation
  - Correct underlying disorder (eg inotropes)
  - Monitor intravascular volume and watch for ATN

- NB. In those with CKI undergoing surgery, ensure well hydrated especially in the fasting period prior to surgery

- Also, ensure any potentially damaging meds are stopped as BP ↓ ++ during surgery therefore UO ↓ therefore ↑ toxicity of drugs

**Intrinsic (Renal) Acute Renal Failure**

- **Possible presentations:**
  - Oliguria (rather than anuria)
  - Nephritic syndrome: haematuria, hypertension, oliguria +/- oedema
  - Proteinuria: excludes pre and post-renal
Hypertension: intrinsic renal disease → ↑BP, pre-renal → ↓BP
Systemic features of disorders causing intrinsic failure (eg fever, arthralgia, skin rash, vasculitis etc)

- Due to:
  - **Acute Tubular Necrosis** (most common cause): See page 317 (ischaemia, toxic, obstructive)
  - **Acute Interstitial Nephritis**: See page 318
  - **RPGN**: urine chemistry midway between pre-renal acute renal failure and acute tubular necrosis - ↑urine to plasma ratios for osmolality and creatinine, and Na between 20 – 40 mmol/L. See page 318
  - **Vascular** (large or small vessel renal vascular disease)
  - Nephrotoxins
  - Other tubular diseases (eg myeloma)

- Investigations:
  - Urinalysis: cells, casts, protein
  - US: ↑echogenicity
  - Renal biopsy
  - Also blood tests to exclude specific causes: ANA, ANCA, complement, CK, etc

**Post-renal Acute Renal Failure**

- Presentation:
  - **Complete anuria**: most pre-renal and intra-renal failure is oliguric. But partial obstruction may give moderate tubular dysfunction → osmotic diuresis → polyuria
  - Normal urinalysis: no proteinuria or casts, any blood (eg from stones, cancer) will be normal not dysmorphic
  - Specific diseases pre-dispose: eg diabetes and analgesic use → papillary necrosis → bits fall off and cause obstruction. See Acute Papillary Necrosis, page 318

- Due to obstruction:
  - Usually in urethra: bladder stones or tumours. Prostate usually chronic
  - If at ureteric level must be bilateral to lead to severe kidney failure or obstruction on one side and a poor functioning kidney on the other
  - **Extrinsic obstruction** due to eg retroperitoneal fibrosis following radiotherapy, haematoma etc
  - → ↑tubular pressure → ↓glomerular filtration
  - Usually obvious from history, confirm with:
    - Ultrasound of kidneys for hydronephrosis
    - CT to determine the level of the blockage

**Diagnostic Evaluation**

- Need to do a complete hx, exam:
  - Assess BP
  - Assess oedema (including pulmonary)
  - Assess JVP
- Urinalysis (dipstick, sediment analysis, urine chemistry)
- Blood tests (U + E – serial measurements)
- Evaluate for obstruction (US)
- Renal US +/- other special Ix (e.g. bx, CT etc)

**Investigations in Acute Renal Failure**

<table>
<thead>
<tr>
<th></th>
<th>Pre-renal</th>
<th>ATN</th>
<th>RPGN</th>
<th>AIN</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urine Osmolality</td>
<td>&gt;500</td>
<td>&lt;350</td>
<td>300-400</td>
<td>300-400</td>
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<tr>
<td>Urine Na</td>
<td>&lt;20</td>
<td>&gt;40</td>
<td>20-40</td>
<td>20-40</td>
</tr>
<tr>
<td>Urine/Plasma urea</td>
<td>&gt;10</td>
<td>&lt;10</td>
<td>Intermediate</td>
<td>Intermediate</td>
</tr>
<tr>
<td>Urine/Plasma creatinine</td>
<td>&gt;40</td>
<td>&lt;20</td>
<td>Intermediate</td>
<td>Intermediate</td>
</tr>
<tr>
<td>Fractional excretion of Na</td>
<td>&lt;1</td>
<td>&gt;3</td>
<td>&lt;1</td>
<td>&gt;1</td>
</tr>
<tr>
<td>Urine Sediment</td>
<td>RBC</td>
<td>Occasional</td>
<td>+</td>
<td>+++</td>
</tr>
<tr>
<td></td>
<td>WBC</td>
<td>Occasional</td>
<td>Occasional</td>
<td>++</td>
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<tr>
<td></td>
<td>Granular casts</td>
<td>Occasional</td>
<td>++</td>
<td>+</td>
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<td></td>
<td>Epithelial casts</td>
<td>+++</td>
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<td></td>
<td>RBC casts</td>
<td>+++</td>
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<tr>
<td></td>
<td>WBC casts</td>
<td>Occasional</td>
<td></td>
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</tr>
</tbody>
</table>

* Renal and Genitourinary 308
Renal and Genitourinary

- Fractional excretion of Na = \( \frac{\text{Urine Na} \times \text{Plasma Cr} \times 100}{\text{Plasma Na} \times \text{Urine Cr}} \)
- Renal biopsy is rarely needed to differentiate causes of renal failure, mainly in RPGN

**Management**

- Treat **cause**
- Optimise **volume status** + haemodynamic status
  - Give fluids if not looking overloaded (to get them peeing)
  - If still oliguric/anuric, give frusemide
  - If still oliguric/anuric, dialyse
- Monitor for ↑K⁺ - if hyperkalemia (especially >6mmol/L), give:
  - **Insulin** + dextrose – shifts K⁺ into cells
  - IV Ca²⁺ gluconate - stabilises cardiac membrane and forms complex with K⁺ (only lasts 30min)
  - Resonium – binds K⁺ and removes it from the body (through GIT)
  - Salbutamol – shifts K⁺ into cells (but is arrhythmogenic)
- **Dialysis**
  - **ECG** = flattening of P waves, broadening of QRS complex, tall tented T waves
- Treat pulmonary oedema → ?dialysis
- **Monitor fluid balance and electrolytes** (serial U & Es) carefully
  - If overloaded → diuretics and fluid restrict
  - If dry → fluids (“better to be wet and wise than dry and dead”)
- Can use forced alkaline diuresis to prevent renal tubular obstruction by uric acid or methotrexate
- Can use forced alkaline diuresis to prevent renal tubular obstruction by casts in rhabdomyolysis
- **Avoid nephrotoxic drugs** (including contrast – can use hydration +/- N-acetylcysteine to reduce risk of contrast nephrotoxicity)
- **Supportive treatment:**
  - Identify and treat the underlying cause (ie correcting prerenal and postrenal factors)
  - Optimise cardiac output and renal blood flow by correcting fluid imbalances and using inotropes if indicated
  - Review medications: stop nephrotoxins; administer drugs in doses appropriate for their clearance
  - Monitor for acute complications eg hyperkalemia, acidosis, pulmonary oedema
  - Prevent/treat infectious complications (expert nursing care of catheters and skin)
  - Provide early nutritional support
- **Initiation for renal replacement therapy:**
  - **Indications for acute dialysis:**
    - Volume overload
    - Refractory hyperkalaemia
    - Metabolic acidosis
    - Symptoms & signs of severe uraemia
    - Drug overdose with dialysable toxin
  - **Choice of therapy:**
    - Individual preference
    - Availability of local resources
    - Haemodynamic stability of the patient
  - **Options:**
    - Intermittent haemodialysis
    - Continuous therapy (CVVH, CAVH, etc)
    - Peritoneal dialysis
  - The optimal timing for the initiation, method, and dosing of RRT remains uncertain

**ARF – Course and Prognosis**

- The course of ischaemic and nephrotoxic ATN can be divided into 3 phases:
  - Initiation
  - Maintenance
  - Recovery
- Return to normal renal function is the usual outcome (if the patient survives)
In-hospital mortality rates exceed 50% in patients requiring RRT for ARF, esp in critically ill ICU patients with multi-organ failure complicating sepsis

- Extreme ischaemia can induce bilat. renal cortical necrosis & irreversible renal failure (<5% of ARF cases)

**Contrast Nephropathy**

- Contrast is water soluble and **iodine based**
- CN is an important cause of iatrogenic acute renal impairment:
  - An acute impairment of renal function following exposure to radiographic contrast materials for which alternative causes have been excluded
  - >25% increase in serum creatinine within 48-72 hours of contrast administration
- Contraindications:
  - eGFR < 40
  - Previous **allergy** to contrast
  - Myeloma
- Risk factors:
  - *Pre-existing renal impairment*
  - **Diabetes** mellitus
  - ↓ in effective arterial volume (CHF, dehydration, nephrosis, cirrhosis)
  - High doses of contrast
  - Concurrent use of nephrotoxic drugs (NSAIDs, ACEIs)
- Features:
  - Deterioration in renal function within 24-48 hours of contrast administration
  - Creatinine generally peaks 2-3 days post exposure
  - Returns to baseline within 7-10 days
  - Typically mild, reversible, short duration and nonoliguric
  - Usually medically manageable, but occasionally renal failure requiring short-term or even chronic dialysis is a well recognised outcome
  - Associated with increased hospital morbidity and mortality
  - True incidence unknown
- Pathogenesis:
  - Direct renal tubular epithelial cell toxicity
  - Renal medullary ischaemia
- Prevention:
  - Consider alternative imaging modalities
  - Identify high-risk patients in advance of planned contrast studies
  - Minimise contrast volume (<125mls)
  - Minimise volume depletion
  - Avoid repetitive contrast studies
  - The most important preventive strategy is **peri-procedural hydration** (N-acetyl cysteine may be renoprotective in some studies)
  - Use nonionic/low osmolality contrast agents in high risk patients. (A meta-analysis showed low osmolality media were only statistically significantly less nephrotoxic in the subgroup of patients with renal impairment)
  - Instruct high-risk patients not to take **metformin** for at least 48 hours post contrast
  - In high-risk patients, check renal function 48-72 hours post contrast

**Rapidly Progressive Glomerulonephritis**

- See GN section on RPGN
- Ensure early recognition (haematuria, red cell casts in urine sediment, features of systemic inflammation)
- An important cause of ARF developing outside hospital
- Early recognition and diagnosis crucial as immediate treatment may prevent the development of ESRF
- Immunology and **renal biopsy** essential
- Treatment usually involves **immunosuppression** and occasionally plasma exchange

**Chronic Renal Failure**

- See also:
  - Adult Polycystic Kidney, page 323
  - Wegener’s granulomatosis, Microscopic Polyarteritis, and Henoch-Schonlein Purpura, Vasculitis, page 444
- = Reduction in renal function for > 6 months
Causes:

- Diabetes Mellitus (diabetic nephropathy) 50%
- Glomerulonephritis 25%
- Hypertension (vascular disease) 10%
- Polycystic Kidney Disease 6%
- Reflux Nephropathy 2%
- Analgesic Nephropathy < 1%
- Miscellaneous 7%
- Uncertain diagnosis 7%

Miscellaneous causes include: stone disease, interstitial nephritis, amyloidosis, myeloma, lithium toxicity, obstructive uropathy, renal cell carcinoma, post-partum failure

Stages:

- Normal
- I = GFR >90ml/min/1.73m² with proteinuria or haematuria
- II = GFR 60-90 with proteinuria or haematuria (NB. Elderly often have GFR in this range with no proteinuria/haematuria – quite normal)
- III = GFR 30-60
- IV = GFR 15-30
- V = GFR < 15 (including dialysis)

Symptoms:

- Earlier: nausea, anorexia, lethargy, itch, nocturia, impotence
- Later: oedema, SOB, chest pain (from pericarditis), vomiting, confusion, fits

Signs of ESRF:

- Pallor, nail changes (Lindsay’s nails – 50/50), bruising, uraemic breath, tachypnoea, pericardial rub, HTN, confusion, seizure etc

Treatment:

- Treat primary disease
- Aggressively lower BP (ACEi)
- Treat proteinuria (ACEi)
- Address anaemia, Ca, PO4, PTH, nutrition issues
- Address vascular risk factors
- Avoid nephrotoxic drugs
- Educate re potential for dialysis
- Palliate, dialysis, transplant

Diabetic Nephropathy

- See also Diabetes Mellitus, page 133
- Occurs in both type 1 and 2 (type 2 can present with DN)
- Takes 5-20 years to develop
- 50% will develop DN
- Associated with other microvascular complications (e.g. neuropathy + retinopathy [retinopathy + nephropathy often coexist])

Definitions:

- Overt diabetic nephropathy = proteinuria > 500 mg/day in the absence of other renal disease
- Microalbuminuria:
  - Albumin excretion 30 – 300 mg/day (= 20 – 200 μg/minute). Concentration is not relevant – it is the amount excreted per unit time. Albumin is more specific for nephropathy than total urine protein (normal protein < 150 mg/day – mainly from tubular cells). Normal dipstick not sensitive enough at this level. Random early morning urine is dependent on concentration
  - Urinary albumin:creatinine ratio is a useful screening test
  - Marker for endothelial damage elsewhere. Strong association with retinopathy, IHD, etc
  - Prognosis for a diabetic with microalbuminaemia is worse than for HIV!

Natural history:

- Type 1 Diabetes:
  - Not usually evident until after 10 – 15 years of disease. If none by 25 years then nephropathy unlikely
  - Once overt nephropathy starts, progresses to ESRF over 5 – 7 years
  - Initial hyperfiltration in about 50% of diabetics (↑GFR by about 25 – 50%). Over time this reduces and hypertension ensues
- Type 2 Diabetes: similar progression to ESRF once overt nephropathy
- For both:
Renal and Genitourinary

- Development of microalbuminuria (20-200µg/min – 30-300mg/d)
- Progression to overt proteinuria (>300mg/d)
- Deterioration in renal function
- Both follow a predictable course

- Pathology:
  - ↑Intra-glomerular pressure, glomerular hypertrophy, deposition of advanced glycosylation end products
  - Glomeruli:
    - Glomerulosclerosis: nodular (Kimmelstiel-Wilson) or diffuse (late)
    - Mesangial thickening with deposition of eosinophilic material
    - GBM irregularly thickened
  - Arterioles: show evidence of subintimal arteriosclerosis and hyalinisation
  - Interstitium: tubular atrophy and fibrosis

- Look for other renal pathology if:
  - No retinopathy
  - Active urinary sediment
  - Rapid onset nephrotic syndrome
  - Type 2 diabetes

- Management:
  - Anti-hypertensives:
    - All effective
    - ACE inhibitors are best at ↓protein and ↓intra-glomerular pressure and therefore are first-line
    - May delay progression to proteinuria even in normotensive patients
    - Aim to lower blood pressure by as much as possible without creating hypotensive symptoms. Also calcium antagonists (diltiazem and verapamil → ↓proteinuria)
    - Aim for 130/85 in those with no proteinuria; 120/75 in those with
  - Glycaemic control: HBA1c < 8.5% delays progression in early phases – not later (glycaemic control not particularly effective)
  - ACEi/ARBs: as above. If cough then use ARBs
  - Avoid nephrotoxins
  - Protein restriction: limiting intake may reduce progression. High intake → ↑intraglomerular pressure and hyperfiltration
  - Dialysis: worse prognosis than non-diabetics due to concurrent IHD. Peritoneal dialysis better if CVS instability
  - Transplant: best prognosis in the absence of CV disease. Disease can recur in the graft 5 – 10 years later
  - NB. Up to 30% of insulin is metabolised by the kidneys therefore sugar control can paradoxically improve with worsening renal function (and therefore need to reduce dose)

- Other renal complications:
  - Urinary tract sepsis. Should be treated even if asymptomatic
  - ↑Risk of pyelonephritis
  - Papillary necrosis. May → macroscopic haematuria or ureteric obstruction
  - Autonomic neuropathy → neurogenic bladder → infection/obstruction
  - Contrast nephropathy: always hydrate aggressively

Vascular Disease

- HTN, along with other vascular risk factors can lead to ischaemic nephropathy

See:

- Minimal proteinuria (as cf with DN – therefore can distinguish between the two)
- Bland sediment
- Other vascular disease
- Thinned cortex on US
- Bx: glomerulosclerosis with interstitial fibrosis, arterial hypertrophy (a more prominent feature than DN)

Treatement:

- ↓BP
- ↓vascular risk factors
- Avoid nephrotoxins
**Renal Artery Stenosis**

- Needs to be >70% to have haemodynamic consequences
- Autoregulation of afferent and efferent glomerular arterioles normally manages intraglomerular pressure, but **with severe RAS, the glomerulus is dependant on high systemic pressure to get perfusion of the glomerulus**
- RAS → accelerated hypertension as RAAS activated to ↑ NaCl + H2O due to ↓ flow past the MD
- Treatment with ACEi/ARBs blocks the AII mediated efferent vasoconstriction therefore lowering intraglomerular pressure and ↓ GFR therefore → Do not use with single kidney or bilateral disease
- Treatment:
  - Treat BP
  - Treat other vascular risk factors
  - Angioplasty/stent (although aim to treat with medication first as disease can recur + meds less invasive) – only do this if **rapid changes seen**

**Systemic Lupus Erythematosus**

- Autoimmune disease characterised by skin, kidney, joint, serosal membrane + blood vessel inflammation
- Renal involvement common:
  - Clinically apparent in around 50%
  - Histologic lupus nephritis in 100%
  - 5% present with a renal syndrome
- Due to nephritogenic autoantibodies (eg against the GBM) and immune complex deposition
- Presentation:
  - Usually heavy proteinuria, nephritic syndrome or RPGN
  - Test for **SLE antibodies** (see Blood Tests in Inflammatory Arthritis, page 429)
  - Most patients have ↓ complement
- Histology:
  - Mimics anything!
  - Most severe: diffuse proliferative glomerulonephritis with crescents i.e. RPGN
  - Common: membranous pattern, tubulo-interstitial damage
  - Immunofluorescence (IF): extensive deposition of IgG and C3, also C1q, IgA, IgM and fibrin
- See also Systemic Lupus Erythematosus, page 439

**Reflux Nephropathy**

- See also UTIs in Children, page 334
- Most common cause of end-stage renal failure in children, **secondary to vesico-ureteric reflux + infection in infancy**
- May not appear till adulthood (ie slowly progressive)
- See pressure effects on tubules and abnormal development of kidneys + further scarring from infection episodes
- Associated with higher rates of UTI
- Lesser grades spontaneously resolve
- CKD develops between **20 and 60**
- Diagnosed antenatally or following childhood UTI
- Investigations:
  - Renal cortical **scarring** on ultrasound or DMSA scan
  - IVU may show clubbing of calyces
  - Biopsy: chronic interstitial disease with secondary focal glomerulosclerosis
- Treatment: aggressive blood pressure control (reimplantation in childhood); prophylactic AB not useful

**Thrombotic Microangiopathy**

- Includes Haemolytic Uraemic Syndrome (HUS), Thrombotic Thrombocytopenic Purpura (TTP) and HELLP Syndrome of Pregnancy (Haemolysis, elevated liver enzymes and low platelets)
- Presentation:
  - Microangiopathic haemolytic anaemia, low platelets and renal and neurological manifestations
  - Renal involvement: haematuria and proteinuria, renal failure in 40 – 80%
- Investigations: Blood film → marked fragmentation of red cells, Coomb’s test –ive
- Treatment: 90% response to **plasmapheresis** with or without corticosteroids
**Multiple Myeloma**
- See Multiple Myeloma, page 486
- BM infiltrate of plasma cells, monoclonal gammopathy in serum; Bence Jones light chains in urine
- Renal involvement is a common feature of MM and heralds a worse prognosis
- Damage due to light chain or amyloid deposition
- Usually presents with heavy proteinuria but also with ARF
- Many forms of renal disease associated with myeloma (cast nephropathy, interstitial nephritis, amyloid deposition, hypercalcemia)

**Amyloidosis**
- A dysproteinaemia that usually presents renally with nephrotic syndrome
- Types:
  - Primary amyloidosis: idiopathic or associated with myeloma. Amyloid protein is part of the Ig light chain. Poor prognosis
  - Secondary amyloidosis: deposition of a different form of protein. Associated with chronic inflammatory or infective conditions (eg Rheumatoid arthritis, Tb, etc)
- Particularly affects glomerular capillary walls, seen with Congo Red Stain

**Complications of Chronic Renal Failure**

**Uraemia**
- = Symptom complex associated with severe, near end-stage renal failure (ie GFR < 20 mls/min)
- Leads to:
  - Accumulation of uraemic toxins
  - Anaemia
  - Hyperparathyroidism
  - Metabolic acidosis
- Common symptoms (NB some of these may be due to anaemia alone):
  - CNS: fatigue, weakness, malaise, ↓concentration, restless legs, insomnia, myoclonic jerks, seizures
  - GI: anorexia, nausea, vomiting, gastritis
  - Blood: anaemia, platelet dysfunction (→ bleeding)
  - CVS: hypertension, oedema, pericarditis
  - Skin: pruritis, pigmentation
  - Endocrine: hyperlipidaemia, hypogonadism (→ infertility and amenorrhoea), impotence
- Investigations:
  - Serum creatinine and urea: markers of uraemia but also affected by malnutrition and muscle mass
  - Creatinine clearance: overestimates GFR in severe renal failure as some Cr is secreted in the tubule
  - Albumin: marker of malnutrition and key prognostic factor
  - Ca, PO4 and PTH: markers of renal osteodystrophy (see Increased Bone Resorption, page 409)
  - HCO3: degree of metabolic acidosis
  - Anaemia due to ↓erythropoietin (but exclude other causes, eg ↓Fe or folate)
- Management:
  - Protein restriction (but beware malnutrition)
  - Alkali supplementation (eg HCO3) to control acidosis
  - Aggressive blood pressure control
  - Fluid restriction if pulmonary oedema
  - Anaemia management
  - K restriction and avoiding K ↑ drugs
  - Dialysis if these measures fail to control symptoms/signs. See Renal Replacement Therapy, page 326

**Anaemia**
- Normocytic, normochromic
- Develops progressively as GFR ↓ below 60ml/min/1.73m²
- Universal in patients with end-stage renal failure (except that it’s less common in polycystic disease)
- Secondary to erythropoietin deficiency, plus also ↓RBC survival
- Also ↓Fe and folate due to dialysis
- BM reveals erythroid hyperplasia
- Management:
- **Synthetic erythropoietin + Fe**: very effective, including ↑well-being, exercise tolerance, ↓LV hypertrophy, etc. Most are Fe deficient, so need supplementation (maybe iv). Complications: worsening hypertension
- Maybe blood transfusion: effective but only temporary benefit. Complications: Fe overload, development of cytotoxic antibodies (→ problems for future renal transplant)

**Secondary Hyperparathyroidism**
- See Parathyroid, page 145
- Pathogenesis:
  - ↓1,25 (OH)2D3 [calcitriol] from kidneys → ↓Ca absorption and ↑PTH [25 hydroxylation occurs in liver]
  - Renal failure → ↓PO4 excretion → ↑serum PO4 → ↑PTH
  - As PO4 ↑, blood Ca decreases (precipitates with PO4) → stimulates ↑PTH (will see in most patients with GFR < 50 mls/min)
  - PTH causes Ca release from bones (leads to ↓ bone Ca + ↑ blood Ca – metastatic calcification) + ↑ PO4 excretion
  - Therefore steady state is normal Ca + PO4 but high PTH and thinning bones; as GFR worsens, PO4 ↑ + pruritis etc sets in
- Presentation:
  - *Pruritis* (?soft tissue deposition of calcium phosphate)
  - *Bone pain* due to calcium resorption
  - Restless legs
- Management:
  - Early replacement of *calcitriol* (but watch for hypercalcaemia) + Ca
  - Phosphate reduction: ↓dietary intake and PO4 binders:
    - Calcium carbonate (binding agent in the gut → ↓absorption)
    - Magnesium hydroxide
    - Aluminium hydroxide
  - If these don’t control the ↑PTH without causing ↑Ca, then parathyroidectomy (→ hypocalcaemia and requirement for ongoing calcitrol)

**Nutrition**
- ESRF suppresses appetite and is a state of catabolism
- **Protein restriction** preserves renal function:
  - Lowering protein intake protects against the development of glomerular scarring (glomerulosclerosis)
  - This effect is mediated, in part, by changes in glomerular arteriolar resistance, leading to a reduction in intraglomerular pressure and decreased glomerular hypertrophy
- Need to consider Na + K intake
- Need to consider diabetes
- Need to consider fluid intake
- Need a dietician!

**Drugs**
- Many drugs or their metabolites are filtered, secreted or metabolised by the kidneys → **therefore need dose reduction** (as they accumulate)
- Protein binding can be altered in CKD e.g. digoxin, phenytoin
- Some drugs are direct toxins to the kidney
- Drugs are the commonest cause of interstitial nephritis (ABs, omeprazole, NSAIDs)
- Some drugs do not do the job as well and the benefit:risk profile changes (eg statins, warfarin)
- CKD pts are on many drugs, be careful of interactions

**Other Complications**
- Hyperphosphataemia
- Vascular disease
- Chronic fluid overload → LV hypertrophy and ↑ BP

**Specific Nephrotoxins**
- Aminoglycosides eg gentamicin
- Amphotericin
• **NSAIDs**: → ↓PGs which vasodilate afferent arteriole → vasoconstriction + ↓GFR. Compounded risk if already dehydrated, elderly, etc
• **ACE inhibitors.** Acute renal failure following introduction of ACEi → ?renal artery stenosis: already reduced renal flow, ACEi → ↓ aldosterone → ↓ efferent arteriole vasoconstriction → precipitous fall in GFR as ACE is blocked
• All radio-contrasts: ↓risk in at risk patients by maintaining hydration with a saline drip
• Chemotherapy: eg Cisplatin

**Rhabdomyolysis**
- From trauma (eg crush injury), *status epilepticus, acidosis, etc*
- Injury to skeletal muscle cells resulting in leakage of cellular components into blood/urine
- →↑CK+
- → Renal failure due to combined effect of nephrotoxic effect of myoglobin, hypovolaemia and aciduria; life-threatening hyperkalaemia, hypovolaemia through *pooling of fluid in damaged muscle*, ↑PO4 + uric acid, MA, hypocalcaemia + DIC
- Urinalysis is +ve for blood but no RBCs on microscopy. Urine is dark brown
- An aside; causes of ↑CK =
  - Cardiac muscle = MI, cardiomyopathy, myocarditis
  - Skeletal muscle = trauma (crush esp), ischaemia, surgery
  - Exertion = marathons etc
  - AI = polymyositis, vasculitis etc
  - Inborn errors of metabolism
  - Metabolic = vit D def etc
  - Toxins
  - Other = heat stroke etc
  - Infection

**Kidney Disease**
- Glomerular BM = podocyte foot processes, shared BM, fenestrated capillaries
- Mesangial cells → produce mesangial matrix, support the BM, have contractile properties to allow or disallow blood flow during physiological changes; can proliferate when Ag-Ab complex deposited in BM

<table>
<thead>
<tr>
<th>Non-neoplastic kidney disorders</th>
<th>Nephritic syndrome</th>
<th>Nephrotic syndrome</th>
<th>IgA nephropathy</th>
<th>RPGN</th>
<th>Membranoproliferative</th>
</tr>
</thead>
</table>
| **Clinical features**           | 1. Haematuria      | 1. Proteinuria (charge) | 1. Essentially doesn’t quite fit either the nephritic or the nephritic syndrome | Rapidly progressive | 5-10% of idiopathic nephrotic syndrome
|                                 | 2. RBC casts       | 2. Hypoalbuminaemia | 2. See asymptomat ic haematuria | See haematuria and proteinuria | See membranous and mesangioproliferative changes
<p>|                                 | 3. Proteinuria (leaky) | 3. Oedema          | | | |
|                                 | 5. HTN             |                   | | | |
| <strong>Causes</strong>                      | PSGN (post infectious) | 1. Minimal change d (children) | IgA nephropathy (autoimmune) against mesangium | Anti-GBM disease (eg Good-Pasture syndrome if lungs involved too) or post infectious |
|                                 | Membranous (can be seen in HBV/HCV) | 2. Membranous | | | |
| <strong>Light microscopy</strong>            | 1. Glomerulus is hypercellular = proliferation of cells | 1. Glomerulus is normocellular BM/capillary loops appear thickened | 1. Increased mesangial matrix (as IgA deposited here) | Crescent formation (proliferation of BC in response to injury) | Proliferation of mesangial and endothelial cells + inflammatory cells GBM thickened |</p>
<table>
<thead>
<tr>
<th>Immuno-fluorescence</th>
<th>deposition</th>
<th>2. Increased overall cellularity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lumpy bumpy, granular appearance</td>
<td>Fine granules outlining the BM</td>
<td>Large <strong>MESANGIAL IgA</strong> deposition (not IgG as for GN)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1. Linear, ribbon-like pattern</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2. No fluorescence where crescent is</td>
</tr>
</tbody>
</table>

| Electron microscopy | 1. Subepithelial humps | 1. Thickened **GBM** Electron dense immune deposits |
|                    | 2. Swollen endothelial cells | 3. Intervening ‘spikes’ of matrix of BM in between deposits |
|                    |                          | Large IgA deposits adjacent to mesangial cells |
|                    |                          | 1. No evidence of immune deposition |
|                    |                          | 2. Linearly thickened BM |

### Renal Stones (Nephrolithiasis)

- **Symptoms:**
  - Loin pain → stone in kidney
  - **Colic** anywhere from **loin to groin** (may just be the tip of the penis) → stone in ureter
  - UTI, haematuria, obstruction

- **Risk factors:**
  - Low urine output (→ drink lots)
  - **Hypercalcaemia:** hyperparathyroidism, sarcoïd, neoplasia, Addison’s, Cushing’s, hyperthyroidism, Li, could be just due to ↑Vitamin D in summer
  - **Hyperoxaluria:** high levels of oxalate in chocolate, tea, rhubarb, spinach
  - Hypocitraturia
  - Hyperuricosuria

- **Investigations:**
  - MSU: RBC, UTI, protein, pH (stones like acid urine)
  - Plain X-ray of kidneys, ureters and bladder
  - Blood: U&Es, urate, Ca, PO4, HCO3

- **Management:**
  - Pain relief: NSAIDS (but care with ↓renal flow) or morphine
  - ↑Fluid intake
  - Sieve urine to catch the stone for analysis
  - If obstruction or infection → urgent urologist referral

### Tubulointerstitial Diseases

- Involve tubules and renal interstitium (not glomerulus)

### Acute Tubular Necrosis (ATN)

- **Ischaemic:**
  - **Patchy** areas of tubular necrosis (proximal convoluted tubules and straight segments of the loop of Henle) and thinning of epithelial brush border
  - **Loss of basement membrane** → scarring, loss of architecture → permanent loss
  - Regeneration if not too severe

- **Toxin-mediated** (e.g. **aminoglycosides**, radio-contrast agents, heavy metals, arsenic, solvents, **myoglobinuria** from muscle damage):
  - Necrosis is **continuous** not patchy
  - **No loss of basement membrane** → epithelium can **regrow** down the nephron → resolution
• Leads to:
  - **Intra-tubular obstruction** → ↓GFR. Glomeruli and vessels generally normal
  - **Hyaline casts** from cellular debris
  - Reduction in sodium reabsorption & loss of medullary concentration gradient → inability to concentrate urine → isoosmolar urine with Na > 20 mmol/L
• Management:
  - Fluid restrict
  - Correct electrolytes
  - Nutrition
  - Avoid nephrotoxins
  - Dialysis if:
    - Severe hyperkalaemia
    - Pulmonary oedema/severe hypertension
    - Symptomatic uraemia
    - Progressive uraemia with oliguria
    - Severe refractory metabolic acidosis
• Lasts 1-2 weeks, followed by gradual improvement in serum urea and creatinine, and diuresis (due to reduced medullary gradient) – monitor to avoid hypokalaemia and hypovolaemia
• Prevent preoperatively by maintaining hydration → maintained renal blood flow. No clear benefit from mannitol, dopamine, frusemide, etc

**Acute Papillary Necrosis**
• Diabetes
• Also in urinary outflow obstruction → ↑pressure in renal pelvis → ↓perfusion

**Acute Interstitial Nephritis (AIN)**
• = Intense, often patchy, interstitial inflammatory infiltrate of lymphocytes & monocytes
• Presentation:
  - Similar to RPGN
  - Also skin rash, fevers, eosinophilia of urine
• Glomeruli normal but may be tubular necrosis
• ↓GFR due to tubular obstruction and altered intra-renal haemodynamics
• Generally drug-induced (e.g. penicillins - especially amoxycillin, and cephalosporins) – sometimes with infections & systemic diseases. Also NSAIDs – but after months of exposure & severe proteinuria
• Symptoms: 1 – 2 weeks after exposure (ie delayed hypersensitivity): fever, maculopapular rash, eosinophilia, arthralgia, flank pain
• Urine has pyuria, mild haematuria and mild proteinuria
• Treatment: withdraw drug +/- steroids

**Acute Pyelonephritis**
• Caused by suppurative infection: E coli, Proteus, Klebsiella, Enterobacter
• From ascending UTI or haematogenous spread of infection (eg septicaemia)
• See Urinary Tract Infections, page 330

**Chronic Pyelonephritis**
• Not a disease, but a description of what happens to the kidney – it becomes dilated and replaced by fat
• Causes:
  - Recurrent infection
  - Obstructive uropathy
  - Vesicoureteric reflux (especially in kids with malformed vesicoureteric valves. Present in puberty with renal failure – subclinical before that)
  - Kidney stones (→↑infection)

**Glomerulonephritis**
• See also Presentation of Kidney Disease, page 305

**Overview**
• Variety of conditions → inflammatory changes in the glomeruli
• If severe enough to cause crescent formation → rapidly progressive glomerulonephritis (see page 321)
In general, GN is caused by stimulation of the immune system, leading to inflammation within the glomerulus and other components of the renal parenchyma. Some forms predominantly present in one way, but any form can present in any way. Common presentations are:

- Nephritic Syndrome
- Nephrotic Syndrome
- Acute Renal Failure
- Chronic Renal Failure
- Asymptomatic haematuria or proteinuria
- Hypertension

Either:
- Primary: limited to the kidney
- Secondary: part of a more widely disseminated immune process

Systemic diseases that may present as GN:
- Lupus nephritis: deposits of immune complexes everywhere within the glomerulus
- Arteritis: microscopic polyarteritis or Wegener’s granulomatosis
- Amyloid: nephrotic syndrome or renal failure. Histology with Congo Red Stain
- Diabetes (but not actually considered a nephrotic syndrome)
- Hypertension

Terminology:
- Proliferative: extra cells – proliferation of endogenous glomeruli cells
- Exudative: infiltration by neuts
- Diffuse: involves all glomeruli
- Focal: involves only some glomeruli
- Global: involves the whole glomerular tuft
- Segmental: involves only part of the glomerular tuft

Approach: consider potential underlying causes for GN in history-taking (drugs, autoimmune conditions, infection)

Adverse prognostic factors: male, smoker, interstitial fibrosis, hypertension

Diagnosis:
- Urinalysis: haematuria + proteinuria; blood morphology and casts
- Blood Pressure
- Urine protein:creatinine ratio to determine actual protein excretion (proteinuria as diagnosed by urinalysis only measures qualitative presence of protein [concentration], not quantitative amount of protein)
- Renal function tests: Cr, urea, electrolytes, albumin
- Other bloods: ANA (connective tissue disorders), ANCA (anti-neutrophil cytoplasmic antigen ⇒ Wegener’s Granulomatosis), Anti-dsDNA (⇒ SLE), anti-GBM, complement, ASO (anti-streptolysin O antibodies)
- Throat cultures if appropriate
- Ultrasound: exclude obstruction, looking for normal or slightly enlarged kidneys, echogenic (dark on US ⇒ ↑fluid)
- CXR: if Goodpastures Syndrome, Wegener’s Granulomatosis suspected
- Renal biopsy – only way to distinguish between types of GN

Histology. May see:
- Glomerular epithelial cells usually have interdigitating foot processes. If they swell, ↓gaps between them ⇒ proteinuria
- Mesangial cells (supporting framework) are the first to react to injury and the last to return to normal

Management
- Treatment:
  - Prompt referral
  - Keep BP < 145/90
  - Specific treatment
  - Monitor renal function

Clinical and Lab Features
<table>
<thead>
<tr>
<th>Proteinuria</th>
<th>Haematuria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asymptomatic</td>
<td>Nephrotic</td>
</tr>
<tr>
<td>Minimal Change</td>
<td>++ +</td>
</tr>
<tr>
<td>FSGN</td>
<td>+++</td>
</tr>
<tr>
<td>Membranous</td>
<td>+++</td>
</tr>
<tr>
<td>Post-Infectious</td>
<td>+</td>
</tr>
<tr>
<td>RPGN</td>
<td>+</td>
</tr>
<tr>
<td>IgA</td>
<td>+++</td>
</tr>
<tr>
<td>Mesangio-capillary</td>
<td>+</td>
</tr>
</tbody>
</table>

**Non-Proliferative GN**

- = nephrotic syndrome presentation
- = leaky filter (ie basement membrane)

**Types:**
- Minimal change disease
- Focal segmental glomerulosclerosis
- Membranous glomerulonephritis

**Minimal Change Disease**

- Presentation:
  - Usually *nephrotic syndrome*, with severe oedema, uncommonly have hypertension and 10% have microscopic haematuria
  - Commonly after an *URTI*
  - Boys > girls
  - 90% of childhood nephrotic syndrome, 30% of adult nephrotic syndrome
  - Renal function normal, unless it deteriorates secondary to hypovolaemia
  - Weak association with Hodgkin’s Disease

- Investigations:
  - Light Microscopy (LM): glomeruli are normal
  - Immunoflorescence (IF): negative
  - Electron Microscopy (EM): *fusion + effacement of foot processes*, no deposits

- Management:
  - Kids: natural history unpredictable:
    - 90% of kids respond to 8 weeks of *steroids*. If they relapse, respond to steroids again (eg triggered by intercurrent illness). No renal failure but complications of treatment
    - 10% become steroid dependent or resistant → use *cyclophosphamide/cyclosporin*
  - Steroids less effective in adults, but still reasonable response rate

**Focal and Segmental Glomerulosclerosis (FSGS)**

- Presentation:
  - Usually *nephrotic*, can be nephritic
  - Usually microscopic haematuria
  - Accounts for 10% of nephrotic syndrome in *adults* (usually younger adults)

- Can be primary (idiopathic) or secondary (previous disease causing scarring eg HUS, toxins, genetic)

- Investigations:
  - LM: *focal/segmental sclerosis* of the glomerular tufts. May be ↑mesangial matrix, interstitial fibrosis and tubular atrophy
  - IF: weakly positive for IgM and C3 (due to protein leak rather than deposition)
  - EM: no deposits but see segmental sclerosis

- Management:
  - Poor prognosis: 50% have a five year renal survival
Some response but frequent relapse to steroids

Membranous Glomerulonephritis

- Presentation:
  - Nephrotic syndrome, also asymptomatic proteinuria
  - Microscopic haematuria, hypertension, renal impairment
  - 30% of adult nephrotic syndrome, most commonly middle-aged
- Usually idiopathic, but 25% secondary to underlying disease, including:
  - Lung or colon cancer (< 10% or adults presenting with Membranous GN)
  - Infections: hepatitis B, malaria
  - SLE
  - Drugs: penicillamine, gold, high dose captopril
- Investigations:
  - Is autoimmune – but no antibody you can measure
  - LM: thickened, irregular capillary loops, spikes in BM with silver stain
  - IF: granular deposition of IgG and C3
  - EM: subepithelial deposits
- Prognosis: variable – 30% progress to end-stage, 30% improve, and the rest retain stable renal function but with ongoing proteinuria
- Treatment: steroids or cytotoxics for the progressive group

Proliferative GN

- Presentation = nephritic syndrome
- Types:
  - Post-infectious GN
  - RPGN
  - Systemic disease (e.g., SLE, Wegener’s, Good-Pastures)

Post-Infectious Glomerulonephritis

- = acute diffuse proliferative GN (acute = neutrophils; diffuse = all glomeruli; proliferative = ↑cells)
- 8 – 14 days following Group A β-haemolytic strep infection of throat or skin, also IE, osteomyelitis, etc
- Cultures usually negative, strep serology (ASO) may be helpful
- Presentation: usually nephritic, may be rapidly progressing → acute renal failure
- Biopsy: usually in adults to rule out a crescentic rapidly progressive GN:
  - LM: mesangial and endothelial cell proliferation + neutrophils. Crescents if severe
  - IF: usually +ive for granular IgG and C3 deposition
  - EM: subepithelial humps
- Treatment: supportive, NOT immunosuppressive. Treat culture-positive family members with penicillin
- Prognosis: slow recovery, mild residual impairment in a few

Rapidly Progressive Glomerulonephritis

- What is it:
  - A description not a diagnosis
  - = Acute renal failure secondary to glomerular disease generally with a nephritic presentation
  - Any form of GN can present in a rapidly progressive form. Generally caused by immune-mediated diseases
- ~ Crescentic glomerulonephritis (marker for severe RPGN):
  - = Cellular proliferation in glomeruli, and crescent formation
  - Pathogenesis of crescents: rupture of the basement membrane → fibrin leaks into Bowman’s space, macrophages recruited, epithelioid cells form a crescent. Leads to scarring and fibrosis of glomeruli
- Presentation:
  - Nephritic presentation. Nephrotic range proteinuria is rare
  - ↓GFR but tubular function OK so Na/H2O reabsorbed → oedema
  - Systemic features of immune mediated diseases: myalgia, arthralgia, fever, etc
- Investigations:
  - Urine chemistry midway between pre-renal ARF and ATN
LM: extensive proliferation of cells, numerous crescents, generally without polymorphs

IF:
- Granular IgG and C3 ⇒ immune complex mediated (Post strep, Lupus, etc)
- Linear IgG ⇒ Goodpastures
- None ⇒ pauci-immune

Due to:
- **Immune complex mediated GN:**
  - Post-infectious GN: e.g. post-streptococcal (rarely crescents, dialysis rarely needed) also staph. See page 321. Has granular IgG plus neutrophils
  - Lupus Nephritis, see page 313. Has granular IgG (plus IgA, IgE, etc)
  - Others, including vasculitis
- **Anti-glomerular-basement membrane diseases** (Goodpasture’s syndrome): See page 321
- **Pauci-immune:** (ie no evidence of immune deposits, probably cell mediated immune problem):
  - Wegener’s Granulomatosis: Causes GN, URTI, LRTI, non-caseating granuloma, CANCA is highly specific, -ive immunoflourescence, typically older patients. See also Wegener’s Granulomatosis, page 446
  - Microscopic polyarteritis (also joints)

- Prognosis dependent on **% of crescents**
- Treatment: **immunosuppressive** (iv methylprednisolone, cyclophosphamide) +/- dialysis

**Goodpasture’s Syndrome**

- GN +/- pulmonary involvement (ranging from pulmonary infiltrate on x-ray to frank haemoptysis)
- Pathogenesis: antibodies against an antigen in the GBM and pulmonary tissue
- Biopsy: crescents + linear immunoflourescence (only GN to show linear IF) on the basement membrane
- Can measure serum anti-GBM antibody
- Treatment: **immunosuppression** (steroids, cyclophosphamide) +/- plasmapheresis
- See also Miscellaneous Lung Diseases, page 131

**Asymptomatic Haematuria GN**

**Mesangial IgA disease (Berger’s Disease)**

- **Most common form of GN.** Common cause of recurrent haematuria in young men. Usually more benign
- Presentation, either:
  - Macroscopic haematuria +/- URTI (= Synpharyngetic haematuria)
  - Asymptomatic microscopic haematuria picked up on dipstick testing
  - Nephrotic levels of proteinuria are rare
- Biopsy:
  - LM: mesangial cell proliferation + ↑ matrix formation
  - IF: mesangial deposits of IgA and C3
  - EM: mesangial deposits
- Prognosis: only 15 – 20% progress to end-stage renal failure – these are more likely to have proteinuria, hypertension and impaired renal function at presentation
- No effective treatment. Consider immunosuppressive treatment if rapidly progressive, else treat hypertension
- Similar to Henoch-Schonlein Purpura – both IgA mediated diseases but HSP is more widespread, causing purpura (especially buttocks and ankles) and abdominal pain (which may ⇒ GI bleeding)

**Crossover Between Proliferative/Non-Proliferative GN**

- Overlap between proliferative + non-proliferative (ie some nephritic syndrome + nephrotic syndrome characteristics)
- Mesangioproliferative GN

**Mesangiocapillary (Membranoproliferative) GN**

- 50% present as Nephrotic Syndrome
- Either idiopathic (primary) or secondary (immune-mediated)
- Biopsy:
  - LM: cellular expansion of the mesangium. ‘Twin track’ BM
  - EM: subendothelial deposits or deposits within the BM
Hypertension
- **Histologic changes**: intimal fibrosis, hyaline deposition, downstream infarction → progressive scarring, granular surface
- Need to aggressively treat hypertension in people with other risk factors for kidney disease (e.g., diabetes)
- See Hypertension, page 47

Congenital Abnormalities
- Aplasia: absence of a kidney
- Hypoplasia: usually unilateral, secondary to obstruction of the ureter in utero
- Horseshoe Kidney:
  - 1 in 500
  - Work normally
  - Altered renal flow: ureter has to flow over the kidney → predisposition to recurrent UTI

Hydronephrosis
- Dilation of renal pelvis due to:
  - Renal pelvis:
    - Obstruction (at pelvis/pelvicoureteric junction) by stones, clot, sloughed papilla
    - Extrinsic compression (mass)
  - Ureter:
    - Intrinsic: obstruction due to stones, mass, scarring
    - Extrinsic: mass, pregnancy
  - Bladder:
    - Obstruction due to tumour, stone
    - Reflux
    - Neurogenic
  - Prostate:
    - BPH
    - Mass
    - Prostatitis
  - Urethra: stricture, posterior urethral valves
- See:
  - Blunted fornices (where pyramids indent into minor calyces) on IVU/CT
  - Dilated renal pelvis/ureter
- Leads to renal failure due to:
  - Chronic interstitial nephritis (as do other things): leucocyte invasion.
  - Atrophy of the collecting ducts and distal tubule (which are relatively hypoxic compared to the glomerulus). However, if the tubule goes, the glomeruli scleroses = lose whole nephron

Cystic Renal Disease

<table>
<thead>
<tr>
<th>Cystic Renal Disease Overview</th>
<th>Adult polycystic kidneys</th>
<th>Infantile polycystic kidneys</th>
<th>Cystic renal dysplasia</th>
<th>Medullary sponge kidney</th>
<th>Simple cortical cyst</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adult polycystic kidneys</td>
<td>Renal + other organ cysts; kidneys enlarge ++</td>
<td>Involves cortex + medulla</td>
<td>Developmental disorder in metanephric differentiation where the metanephric blastema + ascending ureteral bud fail to join (normally do so to form nephrons)</td>
<td>Dilated collecting ducts</td>
<td>Dilation of a single nephron</td>
</tr>
<tr>
<td></td>
<td>End result = RF + HTN</td>
<td>Associated with congenital hepatic fibrosis</td>
<td>Cystic structures emerge</td>
<td>Asymptomatic</td>
<td>Asymptomatic but can grow large + rupture</td>
</tr>
<tr>
<td></td>
<td>Autosomal dominant; 1 in 500</td>
<td>Incompatible with life</td>
<td>Results from obstruction of urinary outflow tract (e.g., stenosis or atresia) which leads to cystic dilatation</td>
<td></td>
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</tbody>
</table>

Adult Polycystic Kidney
- **Autosomal dominant**: PKD1 loci on chromosome 16 (worse), PKD2 on chromosome 4 (better)
- 1 in 500
- Multiple cysts in both kidneys cause compressive damage to surrounding tissue
• Pathogenesis:
  ➢ Whole nephron blows up → squashes other nephrons (pressure effect) → progressive renal failure
  ➢ Cystic lesions in other organs: liver, pancreas, lung (and association with intracranial berry aneurysms)
• Pathology:
  ➢ Round cysts
  ➢ Bumpy surface
  ➢ Areas of haemorrhage + calcification
• Presentation:
  ➢ Present with hypertension around age 50 → IHD, CVA
  ➢ Vary in severity and onset – 50% develop ESRF by 60yrs
  ➢ Usually only moderate proteinuria, but can see HTN, pain, bleeding
  ➢ Kidney’s can get very large → impair respiration
• Diagnose with US or CT at around age 25-30
• Treatment: slow progression through aggressive blood pressure control

Infantile Polycystic Kidney
• Autosomal recessive
• In mild forms that escape renal failure, is associated with congenital hepatic fibrosis
• Pathology:
  ➢ Elongated cysts
  ➢ Smooth surface

Cystic Renal Dysplasia
• AKA multicystic renal dysplasia
• Due to obstruction of urinary outflow tract prior to the union of metanephric blastema and the ascending ureteral bud
• → disordered kidney development
• Contains bone, smooth muscle, etc but is not a tumour

Simple Cortical Cyst
• 50% of those over 50 have a renal cyst
• Dilation of a single nephron, usually to 5 mm – 1 cm. Most people usually have 3 or 4
• Usually asymptomatic
• If very large:
  ➢ Can rupture → urinary peritonitis
  ➢ Can haemorrhage
  ➢ Can have a mass effect on surrounding parenchyma
• As cf complex renal cyst (see septations, blood flow on Doppler etc)

Other
• Acquired cystic disease (consequent to dialysis)
• RCC: can have cystic components
• Infection: Tb and hydatids can present as cystic dilation on US
• Medullary Sponge Kidney: rare. Dilated collecting ducts

Lab Diagnosis of Cystic Disease of Kidney
• In correlation with imaging
• Often may not need tissue dx (eg simple cortical cyst)
• Can assess via:
  ➢ FNA
  ➢ Partial/complete nephrectomy
  ➢ Post-mortem
Renal Tumours

Renal Adenoma/Papillary Adenoma
- Most people have one or two
- Associated with renal scarring
- < 5 mm diameter
- Papillary architecture
- No clear cells (if there are then malignant)

Other Benign Renal Tumours
- **Renal Oncocytoma:**
  - Have **oncocyes:** cells with abundant mitochondria (pink and granular) – tired epithelial cells
  - Grossly form a **stellate scar** (central fibrosis – looks like spokes of a wheel radiologically)
- Renal fibroma
- Angiomyolipoma: composed of fat, smooth muscle and thick blood vessels. Associated with Tuberous Sclerosis
- Juxtaglomerular Cell Tumour: Very rare, benign but causes malignant hypertension

Renal Cell Carcinoma
- 75% of renal epithelial tumours in adults
- Annual incidence 3/100,000
- Risk factors: smoking, obesity, hypertension, unopposed oestrogen
- 3% familial, Von Hippel-Lindau disease (rare genetic disorder characterized by visceral cysts, benign masses, + potential for malignant transformation in multiple organ systems. Hallmarks = development of retinal and CNS hemangioblastomas, pheochromocytomas, multiple cysts in the pancreas and kidneys, + increased risk for malignant transformation of renal cysts into carcinoma)
- Clinical features: haematuria, back pain, abdominal mass. Often metastasised before diagnosis
- Histology:
  - **Clear Cell Renal Cell Carcinoma:**
    - 80% of RCC
    - Metastasise up the renal vein to the heart → emboli → cannonball metastasis of the lung
    - Sheets of clear cells (clear cytoplasm)
    - See haemorrhage, necrosis, sometimes can be cystic
    - 3p25 deletion diagnostic feature
  - Papillary RCC: Better prognosis, 10%
  - Chromophobe RCC: Better prognosis, large cells, abundant cytoplasm, small dark nucleus
  - Sarcomatoid RCC: Highly malignant, highly anaplastic

Transitional Papillary Cell Carcinoma
- Present with painless haematuria
- Can cause hydronephrosis, flank pain, and renal colic from clots
- Peak in 6th – 7th decade, M > F
- Derived from epithelium of renal pelvis
- Associated with smoking, analgesic abuse, azo dyes
- Often associated with transitional cell carcinoma of the bladder and ureter

**Nephroblastoma (Wilms’ Tumour)**
- Very aggressive, presents with **abdominal mass** with or without haematuria. Pain and intestinal obstruction can occur
- 50% present < 3 years, 90% < 10 years, rare in adults
- Derived from metanephric blastema
  - Dark with scant cytoplasm
  - **Triphasic histology**: epithelial cells, stromal cells, blastema
- Now around 80% cure
- Associated with syndromes:
  - WAGR: Wilms, aniridia, genital anomalies and mental retardation
  - Denys Drash Syndrome: gonadal dysgenesis, nephropathy
  - Beckwith-Wiedemann syndrome

**Dermoid Cyst/Cystic Teratoma**
- From germ-line cells
- See skin, cartilage, teeth etc
- If well differentiated = benign = mature cystic teratoma
- If poorly differentiated = malignant = immature cystic teratoma

**Lab Diagnosis**
- Urine cytology
- FNA
- Core bx
- Nephrectomy – partial or complete

**Renal Replacement Therapy**
- For end-stage renal failure, characterised by:
  - Severe uraemia
  - Resistant pulmonary oedema
  - Uraemic pericarditis
  - Severe hyperkalaemia
  - Metabolic acidosis
  - Anaemia
  - Renal osteodystrophy
- Usually required if:
  - Cr is **500 – 1000 μmol/L** (depending on patient’s size)
  - Urea > 35 mmol/L
  - GFR < 10 mls/min
- Wherever possible, the type of treatment is open to patient preference with the aim of home self-care
- Types = peritoneal dialysis; haemodialysis; transplantation; palliative care

**Preparation of Patients for RRT**
- Dependent on early referral
- Pt education is crucial
- Need timely access placement (fistula/Tenckhoff catheter)
- Need to assess for transplant potential

**Indications to Initiate Maintenance Dialysis**
- Ideally patients should commence dialysis prior to the onset of these complications:
  - Pericarditis
  - Fluid overload/pulmonary oedema refractory to diuretics
  - Accelerated hypertension poorly responsive to antihypertensive medication
  - Progressive uraemic encephalopathy or neuropathy
  - A clinically significant bleeding diathesis attributable to uraemia
  - Persistent nausea and vomiting
Renal and Genitourinary

- Biochemical deterioration (eg creat >1000; urea >36; GFR <10ml/min/1.73m²)
- Objective evidence of malnutrition

**Principles of Dialysis**
- **Fluid removal** (ultrafiltration)
- **Solute (toxin) removal** (diffusion + convection)
- Solute and fluid move across a semi-permeable membrane between the blood and dialysate (fluid which contains a buffer solution + electrolytes at concentrations to allow efficient transfer during dialysis)

**Principles of Diffusion in Dialysis**
- Replaces excretory function of the kidney
- Residual kidney function reduces dialysis requirements – but this usually ‘dries up’ over the first few years on dialysis
- Blood is exposed to dialysis solution across a semi-permeable membrane → movement of low molecular weight proteins by:
  - Diffusion
  - Ultra-filtration and convection due to pressure gradient carrying compounds passively in fluid

**Haemodialysis**
- Dialyser or ‘kidney’ is a semipermeable membrane with blood flowing on one side and dialysate fluid flowing in the opposite direction
- Fluid and solute removal is by 2 processes:
  - **Diffusion** – solute movement across the membrane determined by pore size and characteristics and concentration gradients (ie solute moves down a concentration gradient)
  - **Convection** – fluid and solute movement across membrane determined by hydrostatic pressures
- Indicated for:
  - Acute dialysis
  - Weight > 100 kgs
  - Patient preference
- Contraindicated:
  - Profound hypotension: dialysis takes half a unit of blood out of the vasculature through the machine → further hypotension
  - Cardiac failure: intermittent nature of dialysis (every 2nd or 3rd day) → accumulating fluid in between times then rapid reduction in fluid. If heart function is dependent on pre-load, then a rapid reduction in circulating fluid → frank failure
  - Inability to establish long term vascular access: a particular problem with diabetics with vascular disease
- **Procedure**: 3 times a week for 5 to 6 hours, with a dialysis machine, dialysis membrane and dialysate (buffer/electrolyte solution).
- Access is via an arteriovenous fistula at the non-dominant wrist. There are other options if this fails. Vascular access can thrombose, stenose, become infected, lead to high-output failure, etc
- Complications:
  - Hypotension
  - Muscle cramps
  - Bleeding: due to blood loss in dialysis and the anticoagulation necessary to stop clotting in the machine
  - Arrhythmias: due to rapid changes in electrolytes
  - Infections: mainly staph in patients with temporary or tunnelled catheters
- CVVHD = **continuous veno-venous haemodialysis** (used when BP too low for normal dialysis)

**Peritoneal Dialysis**
- **Dialysate introduced into the peritoneal cavity**, with diffusion across the peritoneal membrane
- Less efficient so requires longer period of dialysis. Good for dialysis while still some kidney function remaining. Easier to learn and lower cost than haemodialysis
- **Solute removed by diffusion** from capillaries down concentration gradients
- Fluid removal by osmotic drag by a high glucose concentration in PD fluid
- Indicated if:
  - Severe cardiac disease: maintains more stable fluid levels in the body
Renal and Genitourinary

- Elderly or frail patients
- Diabetic patients
- Patient preference

- Contraindicated if:
  - Previous extensive abdominal surgery: requires adequate peritoneal membrane
  - Greater than 100 kgs: not efficient enough

- Types:
  - Continuous ambulatory peritoneal dialysis: 4 to 5 exchanges each day, each of 2 – 2.5 litres
  - Automated peritoneal dialysis: machine automatically exchanges through the night (9-15L; good for kids and people who work through the day)
  - NB. Glucose concentrations vary – those on RRT are fluid restricted (usually 1L/day) and weigh themselves daily. Extra weight = extra fluid, therefore an ↑ glucose concentration given to attract/pull off more water

- Complications:
  - Inadequate dialysis
  - Tenckhoff catheter problems
  - Infection at the exit site and peritonitis (abdominal pain and cloudy dialysis fluid). Usually staph.
    Intraperitoneal antibiotics. If G−ve then intra-abdominal pathology
  - Membrane failure
  - Hydrothorax
  - Hyperglycaemia: glucose is used in the fluid to encourage filtration
  - Malnutrition

Renal Transplantation

- Treatment of choice. If successful, provides full excretory and hormonal function
- 95% of patients and 85% of grafts survival at 1 year. Half-life of a graft ~ 13 years
- Not considered if significant co-morbidities
- Requires ABO compatibility (O = universal donor; AB = universal recipient) and negative cross-match (T + B cells)
- Tissue typing matches for deceased donor allocation
- Types:
  - Cadaveric transplantation: donor and recipient must be ABO compatible with a negative direct cross match test (ie no recipient antibodies which might cause acute rejection). Expected kidney survival = 10-15yrs
  - Live donor transplants: 25% of transplants. Donor must be investigated to ensure good renal function.
    Good results due to well donors and better preparation of recipients. Expected kidney survival = 15-20yrs
- Life-long immunosuppressive therapy is required, using cyclosporin, mycophenolate and prednisone.
  Combination therapy allows ↓ doses → ↓ complications
- Technical problems = graft thrombosis/haemorrhage, ureteric stricture, lymphocele, delayed graft function
  → ischaemic ATN
- Early post-transplant complications = fluid/electrolyte problems, pain, DVT/PE, infectious complications, SE from anti-rejection meds
- Acute rejection: oliguria, ↑ Cr, fever and swollen graft. May only be picked up biochemically. Most likely within the first 3 months, but can occur at any time. Treated with high dose corticosteroids
- Long term complications:
  - Infections due to immune compromise, including opportunistic infections, eg CMV, EBV, PCP. Prophylaxis during the first 3 months common
  - Malignancy: ↑ skin squamous cell, lymphoma, cervical and Kaposi’s Sarcoma – not breast, lung or colon

Cardiovascular Disease and CKD

- At all stages of progressive kidney disease, cardiovascular problems are the most important cause of death - amongst both patients on dialysis and recipients of renal transplants
- A reduced eGFR (<45mls/min) is associated with an increased risk of CV events and death
- CVD mortality in ESRF is 10-20 x higher than in the age-matched general population
- The overall mortality rate after renal transplantation is lower than among patients receiving dialysis

Ureter

- Congenital abnormalities:
Renal and Genitourinary

- Double/bifid ureters
- Megaureter
- Hydroureter
- Usually present with UTIs
- May have abnormalities elsewhere

- Ureteritis:
  - Associated with generalised UTI
  - May be caused by stones lodging the ureter
  - Rarely caused by Tb

- Transitional Cell Carcinoma:
  - Transitional between squamous and glandular epithelium. Tumours typically papillary/frond like
  - Similar histology to renal and bladder TCC
  - Infiltrates early to retroperitoneum with poor prognosis

### Urinary Tract Pathology

#### Kidney – congenital conditions

<table>
<thead>
<tr>
<th>Condition</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aplasia</td>
<td>Absence of kidney</td>
</tr>
<tr>
<td>Hypoplasia</td>
<td>Mini kidneys</td>
</tr>
<tr>
<td>Horseshoe kidney</td>
<td>Lower or upper poles fail to divide</td>
</tr>
</tbody>
</table>

#### Kidney – cystic renal disease

<table>
<thead>
<tr>
<th>Condition</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adult polycystic kidneys</td>
<td>Renal + other organ cysts; kidneys enlarge ++</td>
</tr>
<tr>
<td>Infantile polycystic</td>
<td>Involves cortex + medulla</td>
</tr>
<tr>
<td>Cystic renal dysplasia</td>
<td>Developmental disorder in metanephric differentiation where metanephric blaste</td>
</tr>
<tr>
<td></td>
<td>ma (one of the structures giving rise to kidney) + ascending ureteral bud fail</td>
</tr>
<tr>
<td></td>
<td>to join (normally do so to form nephrons)</td>
</tr>
<tr>
<td></td>
<td>Cystic structures emerge</td>
</tr>
<tr>
<td></td>
<td>Results from obstruction of urinary outflow tract (eg stenosis or atresia)</td>
</tr>
<tr>
<td></td>
<td>leads to cystic dilatation</td>
</tr>
</tbody>
</table>

#### Kidney – infection

<table>
<thead>
<tr>
<th>Condition</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>TB</td>
<td>Cheesy caseous necrosis</td>
</tr>
</tbody>
</table>

#### Kidney – other

<table>
<thead>
<tr>
<th>Condition</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hydronephrosis</td>
<td>Dilated renal pelvis due to distal obstruction eg BPH, stones, cancer etc</td>
</tr>
</tbody>
</table>

### Tubulointerstitial disease

<table>
<thead>
<tr>
<th>Condition</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute tubular necrosis</td>
<td>1. Shock: ischaemic; see patchy necrosis of tubules; loss of BM with scarring</td>
</tr>
<tr>
<td></td>
<td>2. Toxic: due to heavy metals + solvents; continuous necrosis of tubules with</td>
</tr>
<tr>
<td></td>
<td>no loss of BM therefore heals without scarring</td>
</tr>
<tr>
<td>Acute papillary necrosis</td>
<td>See:</td>
</tr>
<tr>
<td></td>
<td>1. Swollen kidneys</td>
</tr>
<tr>
<td></td>
<td>2. Tubule epithelium destroyed</td>
</tr>
<tr>
<td></td>
<td>3. Interstitial oedema</td>
</tr>
<tr>
<td>Interstitial inflammation</td>
<td>Can see passage of papillae in urine!</td>
</tr>
<tr>
<td>Acute pyelonephritis</td>
<td>Suppurative infection (e.coli, proteus, klebsiella, enterobacter)</td>
</tr>
<tr>
<td>Chronic pyelonephritis</td>
<td>Due to: recurrent UTI, obstruction, VUR, kidney stones</td>
</tr>
</tbody>
</table>

### Renal tumours

<table>
<thead>
<tr>
<th>Condition</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Renal adenoma (papillary)</td>
<td>Benign, &lt;5mm, associated with renal scarring, absence of clear cells, papillary architecture</td>
</tr>
<tr>
<td>Oncocytoma</td>
<td>Benign, eosinophilic oncocyttes (cells with abundant mitochondria)</td>
</tr>
<tr>
<td>RCC</td>
<td>Rochester classification:</td>
</tr>
<tr>
<td></td>
<td>3/100000 annual incidence</td>
</tr>
</tbody>
</table>
1. **Clear cell RCC** = most common, sheets of clear cells (pale – full of glycogen), mets via renal vein, 3p deletion – associated with von hippel-lindau syndrome

2. Papillary RCC
3. Chromophobe RCC
4. Sarcomatoid RCC = derived from other renal malignancies by metaplasia to stromal type tissue

Prognosis depends on: RV invasion, symptomatic disease, stage, grade

- Smoking related
- 3% familial
- Derived from PCT cells
- Clinical: haematuria, back pain, mass
- Gross: orange appearance, haemorrhage, cyst formation, irregular or well circumscribed, variegated
- Renal vein involvement key prog factor → RCC most likely to give cannonball spread to lungs

**TCC (urothelial CC)**

- Derived from renal pelvis epi
- Grows as a papillary structure (good prog) but later infiltrates medulla (bad prog)

**Nephroblastoma (Wilm’s)**

Childhood malignancy; derived from metanephric blastema

Triphasic histo:
1. Epithelial cells in tubules
2. Stromal cells
3. Blastema (this forms the substance of the kidney)

**Angiomyolipoma**

- Benign but can spout haemorrhage
- Composed of fat, smooth muscle, + dilated BVs

20% of pts have tuberosclerosis

**Juxtaglomerular cell tumour**

Benign, secretes renin

Can cause malignant HTN

**Ureter – congenital abnormalities**

Double/bifid ureters
Megaureter
Hydronephrosis

Can see multiple UTIs

**Ureter – inflammation**

Ureteritis
Associated with generalised UTI, rarely TB

**Ureter – tumours**

TCC

As for renal + bladder TCC; infiltrates early to retroperitoneum

Poor prognosis

**Bladder – infections**

Acute cystitis

Interstitial cystitis

Usual elderly pts

Micro: ulcerative chronic cystitis

?viral aetiology

**Bladder – tumours**

TCC

- As for other TCC
- Papillary tumour later infiltrates bladder
- Carcinoma in situ = non-papillary high grade variant, 50% invade in 5yrs, difficult to diagnose + treat as less obvious at cystoscopy

RF: azo dyes, smoking

S + S: painless haematuria (terminal)

Rx: if invasion = cystectomy; no Invasion = local resection (TURBT)

Screening: urine cytology for those at risk

**SCC**

Schistosoma invokes squamous metaplasia

Poor prognosis

**Rhabdomyosarcoma**

- Seen in childhood
- Rhabdomyoblasts (skeletal muscle) – look like tadpoles
- Aggressive if not treated – responds to chemo

**Urinary Tract Infections**

**Definitions**

<table>
<thead>
<tr>
<th>Bacteriuria</th>
<th>Presence of bacteria in urine (normal = sterile)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Significant bacteriuria</td>
<td>Exceeding the number expected from contamination (&gt;10^5)</td>
</tr>
<tr>
<td>Pyuria</td>
<td>&gt;= 10 leucocytes/cu.mm</td>
</tr>
<tr>
<td>Asymptomatic bacteriuria</td>
<td>Significant bacteriuria without clinical symptoms</td>
</tr>
<tr>
<td>Cystitis</td>
<td>Syndrome of lower UTI involving bladder = dysuria, frequency, sometimes supra-pubic tenderness</td>
</tr>
<tr>
<td>Acute pyelonephritis</td>
<td>Syndrome of upper UTI involving kidney = fever, flank pain/tenderness, sometimes dysuria, urgency, frequency, significant bacteriuria</td>
</tr>
<tr>
<td>Uncomplicated UTI</td>
<td>Infection in a structurally + neurologically normal UT</td>
</tr>
<tr>
<td>Complicated UTI</td>
<td>Infection in UT with functional or structural abnormalities = renal calculi, IDC, pregnancy, children</td>
</tr>
</tbody>
</table>

Renal and Genitourinary
UrosepsisClinical evidence of UTI + two or more of: temp > 38, HR > 90, RR > 20, PaCO₂ <32mmHg, WCC > 12 or < 4

Clinical Syndromes

- Uncomplicated UTI in women
- Uncomplicated acute pyelonephritis
- Asymptomatic bacteriuria
- Complicated UTI
- UTI in males

Diagnosis

- UTI is present when bacteria are multiplying in the urinary tract
- 95% of the time, a single bacterial species is responsible
- Urine culture necessary in pregnancy, DM, atypical presentation, recurrent attacks, or non-response to treatment
- Tests:
  - MSU
  - CSU (catheter urine)
  - SPA (suprapubic aspiration)
  - Microscopy: the above specimens are tested for: WBC, RBC, protein, glucose, ketones, nitrates, pH, sp gr

Pathogenesis

UTI Pathogenesis

<table>
<thead>
<tr>
<th>Ascending route</th>
<th>Haematogenous route</th>
<th>Host defences</th>
<th>Parasite + virulence factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Important for women due to short urethra</td>
<td>Infection of renal parenchyma with subsequent abscess formation = staph aureus commonly</td>
<td>Urine chemistry (pH)</td>
<td>Most UTIs = e.coli (O serotypes)</td>
</tr>
<tr>
<td>Uropathogens colonise vaginal introitus</td>
<td>Urine flow</td>
<td>Urine</td>
<td>Adhere to vaginal + uroepithelial cells via:</td>
</tr>
<tr>
<td></td>
<td>Urinary tract mucosa (cytokines)</td>
<td>IgA + tamm-horsfall protein prevent adherence</td>
<td>o Presence of p fimbrae (esp in pyelonephritis)</td>
</tr>
<tr>
<td></td>
<td>IgA</td>
<td>Inflammatory response</td>
<td>o Presence of type I fimbrae (esp in cystitis)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Resistance to serum bactericidal activity</td>
</tr>
</tbody>
</table>

Major Organisms

- E.coli 75-90%
- Staph saprophyticus 5-15%
- Other enteric organisms eg enterobacter faecalis, enterococcus, klebsiella, proteus (these MOs more commonly seen in recurrent UTIs esp in presence of structural abnormalities (VUR – vesicoureteral reflux, neurogenic bladder)
- Proteus mirabilis (and klebsiella, enterococcus and pseudomonas) – may → infection stones (produces urease → urine more alkalotic → precipitation of struvite stones: magnesium ammonium phosphate)
- Pseudomonas especially if catheterised or nosocomial infection

Investigations

- Dipstick: under-rated
  - Nitrites (produced by an enzyme in most infectious bacteria which breaks nitrates down to nitrites) ⇒ presumptive diagnosis
  - If no leukocytes, nitrates, protein or blood then no infection. ie high negative predictive value. Positive predictive value only about 30 – 40%
  - Culture should be done (ie not just dipstick) in pregnancy, diabetics, atypical presentations recurrent attacks and non-response to treatment
- Urine microscopy:
  - Some RBC and WBCs are normal
  - Look for casts, crystals, bacteria. Absence of bacteria not significant (treat empirically)
  - If RBC > WBC then ?stone
- Culture:
  - Bacteruria ⇒ 10⁵ colony forming units (cfu) per ml of urine. However, this was set using morning samples in young women via catheterisation ⇒ not much value.
• In kids, a much smaller number may be significant, especially if:
  o In a boy
  o Obtained by catheter. In a supra-pubic aspirate any growth is important
• Most UTIs are caused by a single bug. If multiple organisms then contaminated sample. Bugs can grow in transit \(\rightarrow\) send to lab straight away or refrigerate
• Antibiotic sensitivity: if multi-resistant then usually from Asia where antibiotics are freely available
  • Haematuria in 50% - but if asymptomatic \(\rightarrow\) ?bladder carcinoma or IgA disease (Berger’s disease)
  • Intravenous pyleogram / urogram (same thing)

**Microbiology**

<table>
<thead>
<tr>
<th></th>
<th>GP</th>
<th>Hospital</th>
</tr>
</thead>
<tbody>
<tr>
<td>E Coli</td>
<td>80%</td>
<td>40%</td>
</tr>
<tr>
<td>Coag –ive Staph (eg saprophyticus)</td>
<td>7%</td>
<td>6%</td>
</tr>
<tr>
<td>Proteus</td>
<td>6%</td>
<td>15%</td>
</tr>
<tr>
<td>Klebsiella</td>
<td>3%</td>
<td>12%</td>
</tr>
<tr>
<td>Enterococcus</td>
<td>3%</td>
<td>15%</td>
</tr>
<tr>
<td>Pseudomonas</td>
<td>1%</td>
<td>6%</td>
</tr>
</tbody>
</table>

• Hospital acquired are more antibiotic resistant
• Pathogenesis: bacterial adherence
  • Uropathic strains: fimbriae – microbial adhesions. Different types in different bugs, and different densities of receptors in hosts \(\rightarrow\) genetic predisposition
  • Catheter adhering strains:
    o Tightly adherent \(\rightarrow\) none grown from urine
    o Thick layer of ‘biofilm’ forms in lumen of catheter containing bugs. Antibiotics can’t penetrate \(\rightarrow\) change catheter
    o Risk factors: ↑ duration of use (but regular changing makes it worse), female sex, absence of systemic antibiotics, catheter care violations
    o Prevention: avoid catheterisation, lots of fluid, alternative method for bladder drainage (eg condom catheter), closed, sterile bladder drainage, appropriate aseptic technique at insertion

**Adults**

<table>
<thead>
<tr>
<th>Risk factors for UTI + natural history</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Male</strong></td>
</tr>
<tr>
<td><strong>All ages</strong></td>
</tr>
<tr>
<td>• Uncircumcised</td>
</tr>
<tr>
<td>• Uro surgery</td>
</tr>
<tr>
<td>• Catheterisation</td>
</tr>
<tr>
<td>• Previous UTI</td>
</tr>
<tr>
<td>• Neurogenic bladder</td>
</tr>
<tr>
<td>• Renal transplantation</td>
</tr>
<tr>
<td><strong>Adults</strong></td>
</tr>
<tr>
<td>• Insertive anal intercourse</td>
</tr>
<tr>
<td>• Lack of urination after sex</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td><strong>Elderly</strong></td>
</tr>
<tr>
<td>• BPH</td>
</tr>
<tr>
<td></td>
</tr>
</tbody>
</table>

• Epidemiology:
  • More common in women, older people, and long term care
  • 20% in women 65 – 75, 3% of men
• Definition: Lots of terms with subtle variations in meaning: UTI, bacteruria, bladder bacteruria, asymptomatic, etc, etc
• Presentation:
  • Acute symptomatic urinary infection = urgency, frequency and dysuria (pain on urination). NB urgency and frequency may be unrelated to infection (eg bladder instability)
  • In elderly may present atypically: delirium, falls, immobility
  • Cloudy urine, dark urine (volume depletion), and smelly urine are all normal!
  • Asymptomatic bacteruria = 2 consecutive positive cultures without symptoms attributable to the urinary tract
• Classification:
Uncomplicated: normal urinary tract and normal renal function

Complicated if:
- Abnormal urinary tract: eg calculi, reflux, obstruction, paraplegia, catheter, prostatitis, etc
- Impaired host defences: immunosuppressed, diabetes, etc
- Impaired renal function
- Virulent organism (eg Proteus)
- Male

Causes of dysuria:
- Urinary tract infection +/- vaginitis
- Vaginitis (Candida albicans, trichomonas vaginalis, gardnerella vaginalis)
- STDs
- Other: trauma, urethral syndrome

Treatment

<table>
<thead>
<tr>
<th>UTI ABs</th>
<th>Indications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Uncomplicated cystitis</td>
<td>(adult, non-pregnant woman with no anatomical defect)</td>
</tr>
<tr>
<td></td>
<td>Trimethoprim once daily (od) for 3 days OR Nitrofurantoin qds for 3 days NB. Follow up cultures to determine AB sensitivities</td>
</tr>
<tr>
<td>Complicated cystitis</td>
<td>(male adults, pregnant women)</td>
</tr>
<tr>
<td></td>
<td>Nitrofurantoin qds for 10 days OR Cefaclor tds for 10 days</td>
</tr>
<tr>
<td>Children (are a complicated cystitis by definition)</td>
<td>Gentamicin od IV OR Cefuroxime tds IV Need MCU + US</td>
</tr>
<tr>
<td>Pyelonephritis</td>
<td>Gentamicin once daily IV OR Cefuroxime tds IV</td>
</tr>
</tbody>
</table>

Cystitis:
- Short-course, renally excreted drugs preferred
- Single dose or 3d course most common
- Amoxycillin + trimethoprim have ↑ resistance
- Nitrofurantoin can be used in low dose in those with normal renal function
- Quinolones – very effective but resistance also a problem

Pyelonephritis:
- 7-10d oral if uncomplicated (as above)
- Parenteral if vomiting – gentamicin or 3’gen cephalosporin

Prophylaxis:
- Consider if recurrent infections, eg low dose nightly antibiotics for 3 – 6 months, post-coital antibiotics
- Bladder emptying at night and after intercourse
- Topical oestrogen cream if post-menopausal
- Adequate fluid intake (> 2 litres per day)

Men:
- If unknown cause - referral to urologist for kidney scan (e.g. stone)
- Always do urine culture in addition to antibiotics
- Do swab if discharge

Asymptomatic bacteriuria:
- If uncomplicated, then observe
- If diabetic, then treat
- If pregnant, then higher risk of pyelonephritis + perinatal morbidity:

Avoid trimethoprim (1st trimester) + quinolones
Will often need prophylactic treatment

Complications: ascending infection → renal scarring → hypertension, etc

Urethral syndrome
- No bacteria isolatable
- Can be chlamydia (need to do right test)
- Can become very sensitive after a number of infections (general inflammation)
Renal and Genitourinary

- Acidic urine will hurt more if inflamed → drink lots (dilute urine) and Uracil
- More common in older women

**Catheter-Associated UTIs**

<table>
<thead>
<tr>
<th>Clinical</th>
<th>Pathogenesis</th>
<th>Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>35-40% of hospital-acquired infections</td>
<td><strong>Unsterile insertion</strong> therefore introduced during catheterisation</td>
<td>Risk of infection increases with time catheter is in place</td>
</tr>
<tr>
<td>Most asymptomatic or fever + lower abdo pain</td>
<td>1. Enter via external surface of catheter</td>
<td>1. Only treat bacteriuria in symptomatic pts (<strong>change catheter + AB</strong>)</td>
</tr>
<tr>
<td>Common source of gram-neg bacteremia in hospital pt</td>
<td>2. Enter drainage system by contamination of bag</td>
<td>2. Ensure good fluid intake to decrease chance of infection</td>
</tr>
</tbody>
</table>

**UTIs in Children**

- **Epidemiology:**
  - UTI is common:
    - Males usually have them in their first year, for girls it’s ongoing
    - By age 7, 9% of girls and 2% of boys will have had at least one episode
  - Caused by E coli in over 80% of cases. Others are associated with complicated UTIs or long term antibiotic therapy (eg Candida)
  - Of 1000 kids with UTI:
    - 400 have vesico-ureteric reflux, 100 have renal scars, 10 will develop premature hypertension (eg in older childhood or pregnancy), end stage renal failure in 1
    - 10 – 20 will have obstruction due to urethral valves, VUJ or PUJ obstruction
    - Greatest risk usually kids < 4 and especially in first year of life
- **Risk factors for UTI:**
  - Previous infection
  - Normal anatomy but functional problem: e.g. VUR (in child, sibling or parent)
  - Structural abnormality: e.g. urethral stenosis/stricture (more common in boys – congenital, trauma or inflammation)
  - Vulvoanitis from poor perineal hygiene
  - Incomplete or infrequent voiding
  - In first year of life, uncircumcised male is 10 times that of circumcised
  - Sexual abuse: only 2% of patients investigated for sexual abuse have UTI as a symptom. UTI without other indications (lesions, bleeding, bruising) is very unlikely to be sexual abuse
  - Antibiotics: disrupt normal peri-urethral flora → predispose to infection
  - Constipation a risk factor: ask about this
  - Indwelling catheter
- **Risk factors for VUR:**
  - Children with UTI (30 – 40%)
  - Siblings affected
  - Antenatal dilation of the urinary tract (8 – 22%)
  - No evidence that prophylaxis → ↓ renal scars (controversial)
- **Always have appendicitis** as differential diagnosis: can have white cells in urine with appendicitis where appendix is in the pelvis (or elsewhere)
- **Symptoms are highly variable:**
  - 0 – 2: Fever/hypothermia (?sepsis), lethargy, poor feeding, diarrhoea, vomiting, abdominal distension, failure to thrive
  - 2 – 5: fever, rigors, vomiting, diarrhoea, colic, abdominal pain, some dysuria, offensive urine, haematuria, weak urine stream
  - 5 – 12: fever, rigors, abdominal pain (⇒ upper tract infection), dysuria, frequency, urgency, incontinence, haematuria
  - If systemic illness then ↑ likelihood of pyelonephritis as well as cystitis. If under one, can have pyelonephritis without systemic signs ⇒ if UTI under age 1 then presume Pyelonephritis
- **Diagnosis:**
  - Urine bag:
Wash genitalia before application, then apply over genitalia.
Test with urine dipstick. If positive, obtain definitive sample with catheter or supra-pubic aspiration (SPA).
Do not routinely send bag specimens for culture. Boys have 93% false positive.

**Catheter:**
- For children who can’t void on request and where the bladder is in the pelvis (SPA won’t work).
- Uncomfortable. Discard first few mls.
- Growth > 10⁶/litre suggest infection.

**Supra-pubic aspirate:**
- If child too young to obtain an MSU.
- Gold standard: any growth suggests infection (but beware contamination with skin commensals).

**MSU:** discard first few mls.

**Exam:**
- Often normal, other than fever.
- Do **blood pressure**, search for loin, abdominal and supra-pubic tenderness.
- Inspect spine and external genitalia, and brief neuro exam of the lower limbs.
- Check and plot growth.

**Management:**
- Admit for IV antibiotics if:
  - Neonate or immunocompromised.
  - Shocked.
  - Vomiting frequently (ie oral antibiotics won’t stay down).

- Hospital treatment:
  - Bloods: FBC, blood cultures, electrolytes and Cr. If toxic, consider LP and glucose.
  - Antibiotics: **Amoxycillin 50 mg/kg/6hr (max 2g)** (for enterococcus) and **gentamicin 2.5 mg/kg/8hr** (if older than 1 week and normal renal function) to cover everything else.
  - Discharge on oral antibiotics to take total treatment to 10 – 14 days. Then prophylaxis until follow-up.
  - Repeat urines to check it’s cleared.
  - Follow-up:
    - US within, say, 12 hours: checking for obstruction and kidney size. Poor sensitivity for reflux.
    - If <1 years then MCU (for reflux → risk of scarring) + delayed DMSA scan (eg after 6 months, look for filling defects → renal scarring).
    - If >1 years then delayed DMSA.
    - If reflux, then prophylactic antibiotics until out of nappies and 6 months since last UTI.

- Oral antibiotic treatment:
  - Don’t give antibiotics unless a definitive urine specimen has been obtained.
  - Antibiotics standard treatment:
    - **Cotrimoxazole 200/40mg in 5 ml, 0.5 ml/kg bd 5 days** (= trimethoprim + sulphamethoxazole – less concern about allergy in kids).
    - Amoxycillin 15 mg/kg tds po (max 500 mg) for 5 days.
    - Augmentin 15 mg/kg tds po (max 500 mg) for 5 days.
    - Prophylaxis in children with recurrent infection is common – but duration, drug and dose all remain variable. **Cotrimoxazole 200/40mg in 5 ml, 0.25 ml/kg po od**.
    - Repeat urines at conclusion of antibiotics to check it’s cleared.
    - Referral to urologist:
      - Boys: always refer for confirmed UTI, especially if circumcised.
      - Girls: At least repeat urines after first UTI to check cleared. Refer after second UTI.

**Bladder**

**Interstitial Cystitis**
- Usually elderly patients.
- Urine sterile.
- If severe then intractable pain with ↓bladder capacity.
- Microscopy → ulcerative chronic cystitis.
- ?Viral aetiology.
Bladder Tumours

**Transitional Cell Carcinoma**

- Classic association with *azo dyes* (clothing, plastics, batteries) and *smoking*
- Present with *painless haematuria*, often *terminal* (end of stream; ALWAYS investigate painless haematuria)
- Develop as a flat carcinoma-in-situ → papillary tumour → infiltrates
- Can see calcification of bladder on AXR

**Architecture:**

- Noninvasive:
  - Papillary
  - Sessile (in situ)
- Invasive:
  - Invasive papillary
  - Invasive sessile

**Dx:**

- Urine cytology using 2nd voided urine sample – mid morning, on consecutive days
- Will see cytological features of malignancy
- Histology: from either transurethral resection or cystectomy

**Management:** regular scraping it out until pathology says its metastatic then cystectomy

*Other Bladder Tumours*

- **Squamous cell carcinoma:** common in Egypt due to *Schistosoma* (parasite). Early infiltration
- Adenocarcinoma: Rare. Resembles large bowel adenocarcinoma. Derived from urachal remnant
- **Rhabdomyosarcoma:** In childhood. Aggressive but responds to chemo

**Urinary Incontinence**

- Bladder pressure > urethral pressure = flow of urine
- 8-34% of community dwelling older people. Women 1.5 to 2 times rate of men
- Only 25–50% with urinary incontinence seek medical help

**Physiology**

- Bladder fills at 25 – 125 ml/hr. Low pressure maintained by reflex arc → detrusor muscle inhibition
- Conscious sensation to void at 250 – 350 ml, normal capacity 400 – 600 ml
- Micturition co-ordinated by pontine micturition centre → parasympathetic nerves → S2 to S4 → relaxation of urethral sphincter muscles + contraction of detrusor until < 30 ml left in bladder. *Inhibition* of pontine centre → voiding

**Age related changes:**

- ↑Uninhibited detrusor contractions
- **Benign prostatic hypertrophy** in men → urinary outflow obstruction → urinary retention
- ↓*Oestrogen in women* → ↓urethral sphincter function
- Miscellaneous: ↓bladder capacity, ↑residual urine, ↑nocturnal urine production

**Causes**

- **Transient** causes of incontinence:
  - D: Drugs (diuretics, anticholinergic side effects → ↓detrusor contraction, sedatives) and delirium (↓executive function)
  - R: Retention of urine (eg prostate hypertrophy → retention → bladder pressure sphincter pressure)
  - I: Immobility (arthritis, etc), *inflammation* of bladder or vagina (asymptomatic bacteriuria), *impaction* of faeces
  - P: Polyuria (Diabetes, heart failure)
- **Overactive detrusor**: = detrusor instability
- **Urge** incontinence
Spontaneous contraction when attempting to inhibit voiding (eg stroke, prostate disease) → frequency, nocturia, urgency, urge incontinence

= Bladder instability – common → Urge incontinence

Usually no pathology found

Incompetent sphincter:

- Stress incontinence
- If normal bladder then Genuine Stress Incontinence (GSI)
- In small portion of men with prostate surgery, in women more complex (childbirth trauma, ↓oestrogen, prolapse etc) → momentary loss of small volume of urine with ↑intra-abdominal pressure (eg cough)
- Occurs in the absence of detrusor activity. Upper urethra slips through the pelvic floor
- Caused by childbirth, surgery, menopause (→ atrophy of urethral epithelium), masses, prolapse, pregnancy, etc

Overactive sphincter: anticholinergics, neural damage or prostate problems → retention → overflow incontinence

Overflow incontinence: due to over-distended bladder (without detrusor activity)

Reflex Incontinence: involuntary loss due to abnormal spinal reflex activity without the desire to void

Assessment

- History: Screen all elderly people. ‘Have you ever lost control/wet yourself?’ Impact on function, proximity to toilets, fluid intake, medications, etc
- Exam: neurological, esp. sacral nerve lesions, signs of stroke. Rectal exam (eg sphincter tone, faecal impaction, prostate - although large prostate size does not correlate to urethral obstruction), in women cough induced urine leakage, mobility, eyesight, cognition
- Investigations: urinalysis to exclude infection, exclude polyuria due to diabetes, urodynamic investigations (measuring micturition pressure and volume)

Management

- Stress incontinence: pelvic floor exercises, α agonists, oestrogen, surgery
- Detrusor overactivity: bladder retraining, bladder relaxants (oxybutynin: anti-cholinergic), remove obstruction
- Overflow/retention: surgery to remove obstruction, intermittent/permanent catheter
- Other: schedule toileting, pads, etc

Male Genitourinary

Prostate

Anatomy & Physiology

- Normally 20 – 30 g. Grossly enlarged can be 500g
- Prostate can become infected, hyperplastic or malignant
- Produces seminal fluid to bulk up semen + thus facilitate sperm transport
- PSA is produced for the ejaculate where it liquifies the semen in the seminal coagulum and allows sperm to swim freely
- Used to be described in lobes. Now described in zones:
  - Anterior zone
  - Transition and central zone: main site of benign hyperplasia
  - Peripheral zone: main site of malignancy. Next to rectum – can palpate on PR
- PR exam:
  - Even if normal, don’t ignore ↑PSA. Cancers can be small or diffuse, or anterior, in an already large prostate → PR isn’t sensitive
  - Nodularity can be detected on PR. This is due to desmoplasia (fibrous reaction) – usually to a slower infiltrating cancer

Prostatitis

- Acute:
  - Gonorrhoea most common cause: pain, discharge, haematuria, tender on PR
  - May be infarction secondary to hyperplasia compressing blood supply
- Granulomatous:
  - Tb (rare)
Fungal (only immunocompromised)
- Leakage of prostatic secretion into interstitium post surgery
- Resolving prostates (hard, knobbly prostate, ↑PSA, mistaken for malignancy). Suspect post surgery, but still need biopsy

**Benign Nodular Hyperplasia**
- **75% of men > 75**
- Not benign if not treated: → hydronephrosis → kidney failure → death!
- Testosterone → 5α-DHT + 17β-oestradiol (converted by 5α-reductase)
- As we age, plasma testosterone ↓ but is concentrated in prostate therefore ↑ conversion to 5α-DHT which stimulates:
  - 1. **Stromal AND**
  - 2. **Glandular** hyperplasia in **CENTRAL** zone
- Morphology: **nodular proliferation of ducts**, mainly in the central zone
- **Histology:**
  - Epithelial nodules
  - Fibrosis
  - Chronic inflammation
  - Focal infarction
  - Concretions
  - See two basal layers of nuclei stacked on top of each other
- **Consequences:** hypertrophied bladder trabeculae + hydronephrosis + renal failure
- **Management:**
  - 5α-reductase inhibitors (eg finasteride)
  - α1-blockers (**tamsulosin**)
  - TURP (retrograde ejaculation + risk of impotence and incontinence)

**Prostatic Carcinoma**
- Occurs in **25% of males over 70 years** (more if include indolent central or transition zone tumours)
- 6% mortality in males (~600/yr in NZ)
- 98% are adenocarcinoma occurring in the **PERIPHERAL** zone (**Prostate cancer = Peripheral; BPH = central**)
- **Key histological features:**
  - Single cell basal layer in duct epithelium
  - Prominent nucleolus + other cytological features of malignancy
  - Lots of small glands
- **Prognosis related to Grade:**
  - Using **Gleason score**: determine where the cancer is the most prominent (primary grade) and where it’s next most prominent (secondary grade)
  - Scored from 1 to 5 for each area
  - The **Gleason score** is the sum of the primary and secondary grades
  - The total score can be anything from a 2 (1 + 1) [but never actually see this in practice] to a 10 (5 + 5)
- **Examination:** PR → may appear hard and irregular (desmoplasia)
- Spreads to:
  - Pelvic lymph nodes via **perineural infiltration**
  - Bone
- **PSA:**
  - <4 generally is normal but really should be <2 for those under 50
  - Is elevated in both BNH + prostate ca
  - Useful when measured over time – **dynamic measurement (PSA velocity)**, one-off measurements are less useful
  - Increasing levels over time likely = ca
  - Some high grade ca are PSA negative therefore need DRE!
  - Useful for f/u post TURP
- **Management:**
  - Stage the cancer (using **NM** for bone mets; CT for LN spread)
  - Treatment depends on age + stage:
    - TURP
    - Radiotherapy
Renal and Genitourinary

- Radical prostatectomy (selected on basis of tumour bulk and grade (not if very high grade – will already have metastasised). 50% have complications (impotence, incontinence)
- Brachytherapy with caesium
- Orchidectomy

Workup of Obstruction from Enlarged Prostate

- Severe obstruction → retention, bladder stones, renal failure

- Investigations:
  - Cr: checking renal function
  - K and Na: checking renal failure
  - Blood gases for metabolic acidosis
  - PSA
  - Ultrasound: look for distended bladder and hydronephrosis
  - ECG if ↑K: if ECG changes or if K high then may need anti-arrhythmic
    - Prolonged PR interval, flattened P wave
    - Peaked T waves
    - Broad QRS complex

- Management:
  - CATHETERISE: should see K and Cr resolve over a day (depending on remaining renal function)
  - If high K, then calcium gluconate, then insulin + glucose

- Complications of obstruction:
  - Enlarged bladder: hyperplasia of detrusor muscle fibres, ↑space between trabeculated fibres
  - ↑Back pressure in ureter → hydronephrosis
    - ↓Filtration → ↑Cr
    - ↓Function of tubular epithelium due to poor perfusion → ↓active transport of K
    - Acidosis

- Moral: Must act on a distended bladder to protect the kidney

Prostate Cancer Screening

- Notes prepared for Public Health Test. Does PSA meet the 6 criteria for a good screening test? Source: Readings on Closed Reserve

- Is it an important health issue:
  - 2nd leading cause of cancer death in men in the US. In NZ, 800 cases and 400 deaths per year
  - A disease of the very old. 1% < 55 years, 65% > 75 years. Would reducing incidence lead to decline in all-causes mortality?

- Is there a suitable test: PSA test + digital rectal exam. PSA test is reasonably good at detecting pathology, and sensitivity is improving (currently ~ 80% → would miss 20% of TP)

- Is the natural history well understood:
  - Wide variety of cancers: from the slow growing, indolent sort to very aggressive
  - Need long enough asymptomatic duration to allow screening at reasonable intervals
  - Screening likely to detect indolent cancers (length bias)
  - Incidence of prostate cancer has increased dramatically since opportunistic screening introduced → treating many cancers that would have remained harmless (ie would die WITH cancer but not BECAUSE of cancer)

- Does treatment at the asymptomatic stage confer positive benefits over later treatment:
  - No firm evidence that radical prostatectomy is better than conservative treatment for asymptomatic cancers
  - For Grade I and II cancers, evidence that conservative treatment is at least reasonably effective
  - Risks of prostatectomy: 30-day mortality of 0.5% + significant levels of ongoing incontinence and sexual dysfunction
  - Assuming 4% rate of detection from screening, 1 in 5000 will die, 1 in 81 will be incontinent, and 1 in 36 will have sexual dysfunction as the result of the screening
  - Conclusion: Screening is good at detection of pathology, but don’t yet know if treatment is beneficial in net terms

- Infrastructure and cost: of lesser relevance until it can be demonstrated that screening is clinically effective
### Penis

#### Penis/scrotum/testes pathologies

<table>
<thead>
<tr>
<th><strong>PENIS</strong></th>
<th><strong>SCROTUM</strong></th>
<th><strong>TESTES</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Epispadias</strong></td>
<td>Urethra opens on <strong>dorsal</strong> surface</td>
<td><strong>Fournier gangrene</strong></td>
</tr>
<tr>
<td><strong>Hypospadias</strong></td>
<td>Urethra opens on <strong>ventral</strong> surface</td>
<td><strong>Scrotal carcinoma</strong></td>
</tr>
<tr>
<td><strong>Phimosis</strong></td>
<td>Unretractable foreskin</td>
<td><strong>TB</strong></td>
</tr>
<tr>
<td><strong>Paraphimosis</strong></td>
<td>Gross swelling of foreskin when not replaced after catheterisation</td>
<td><strong>Torsion</strong></td>
</tr>
<tr>
<td><strong>Condyloma</strong></td>
<td>Warts of penis</td>
<td><strong>Hydrocele</strong></td>
</tr>
<tr>
<td><strong>Erythroplasia of Queyrat</strong></td>
<td>Bowen’s d of the penis – SCC in situ, presents as erythroplasia (redness)</td>
<td><strong>Cysts of vestigial structures</strong></td>
</tr>
<tr>
<td><strong>Penile cancer</strong></td>
<td>Often SCC, more often CIS</td>
<td><strong>Spermatocele</strong></td>
</tr>
<tr>
<td><strong>Fractured penis</strong></td>
<td>Damage to erect penis – EMERGENCY (to 1 corpus cavernosum)</td>
<td>Needs urgent drainage of haemorrhage</td>
</tr>
<tr>
<td><strong>Urethral carcinoma</strong></td>
<td>Can be SCC or TCC</td>
<td></td>
</tr>
</tbody>
</table>

- For congenital malformations and paediatric presentations see Penis, page 974
- Epispadias: abnormal opening of urethra on ventral surface
- Fractured Penis: Rupture of corpus cavernosum during erection
- Condyloma: Genital wart. Usually flat. Associated with HPV
- Erythroplasia of Queyrat (= Bowen’s disease): non-invasive cancer of the penis. Premalignant condition. Starts in coronal sulcus
- Squamous cell carcinoma: Very rare, ↑ risk if not circumcised. Early spread to lymph nodes but doesn’t disseminate widely

### Scrotum

- Steatocystoma: benign sebaceous cysts, hereditary
- Fournier’s gangrene: Ischaemic necrosis. Little collateral flow to the scrotum so occlusion → domino effect. Treatment: debridement
- Squamous cell carcinoma

### Testes

- For Torsion and Hydrocoele, see Testes, page 973
- Testicular micro:
  - Tubules = germ cells (spermatogonia etc) + **sertoli** (support) cells
  - Interstitium = **leydig** cells (testosterone)

### Infection

- Epididymo-orchitis:
  - Bacterial infection: E Coli, Klebsiella, Proteus
- In adults also Gonorrhoea
- Usually self-limiting → antibiotics
- Key differential: torsion. If in doubt, emergency referral and Doppler US to assess blood flow

**Primary Orchitis:**
- Mumps, Tb, tertiary syphilis
- Rare

**Other**
- Spermatocoele: *dilation of a cord of epididymis*: common benign small lump on testis. Translucent to torch
- Haematocoele: *haemorrhage into tunica vaginalis or tunica albuginea* (rugby injury, bleeding disorder)

**Testicular Tumours**

<table>
<thead>
<tr>
<th>Tumour</th>
<th>Features</th>
<th>Macro/micro</th>
<th>Tumour marker</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Germ cell tumours (95%) – seminomatous vs non-seminomatous</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Seminoma</strong></td>
<td>Tumour of immature germ cells – “germ cell tumour”</td>
<td>Late mets, lymphatogenous spread</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Teratoma</strong></td>
<td>&lt;14 yrs = benign; &gt;14 yrs = malignant (mets to para-aortic LNs)</td>
<td>Early mets, lymphatogenous spread (lung, brain etc)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Yolk sac tumour</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Embryonal carcinoma</strong></td>
<td>Highly malignant</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Choriocarcinoma</strong></td>
<td>May develop in hydatidiform mole (non-viable fertilised egg) or from diff of germ cells</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Non-germ cell tumours</strong></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td><strong>Leydig cell tumour</strong></td>
<td>Will see precocious puberty (as overproduction of testosterone)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Sertoli cell tumour</strong></td>
<td>May present with gynaecomastia + precocious puberty</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Lymphoma</strong></td>
<td>Seen in older males, often bilateral</td>
<td></td>
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</tr>
</tbody>
</table>

- Incidence 3.5/100,000
- 3% bilateral
- 7% associated with undescended testis
- **Testicular biopsy not done** as can cause spread of tumour cells into **inguinal lymphatics** (surgery also done via inguinal region, not scrotum, for the same reason)
- **Cryptorchidism:** ↑ risk of testicular cancer – doesn’t matter which test was undescended – risk is increased for cancer in **both** testes
- **Non-seminomatous** germ cell tumours:
Infants/children: behave more **benignly** + tumours are generally **pure** – one type only

Adults: behave more **malignantly** + are **mixed** types

**Germ cell tumours:**

- Derived from germ cells
- Always found in the **midline** (pinealoma, retroperitoneal, thymoma, dysgerminoma etc)
- **Dysgerminoma:** ovarian tumours that are histologically identical to seminomas
- All have the **same macro/micro appearance** (loosely cohesive, large polygonal cells, lymphocytes)
- 95% of testicular tumours
- Peak in 15 – 34 year olds
- Painless swelling of the testis
- **Seminoma:**
  - 40% of testicular tumours
  - Gross: lobulated pale tumour mass
  - Micro: Undifferentiated germ cells + ↑ lymphocytes. Aggressive. Metastasise to inguinal and para-aortic nodes
  - Treatment: Orchidectomy via inguinal region (never via scrotum → different lymphatic drainage. Also never biopsy suspected testicular cancers). Very responsive to radiotherapy

- **Teratoma:**
  - 30% of testicular tumours
  - All can recapitulate ectodermal, mesodermal and endodermal tissue
  - Benign teratoma: More common in ovary than testis. 3% chance of malignant change. Mature tissues (usually skin elements – epidermis, hair follicles, etc)
  - Malignant teratoma: metastasise to para-aortic lymph nodes (especially neural cells – very aggressive). Gross appearance – lots of variety. Treatment: chemo +/- radiotherapy. Chemo stimulates cells to mature → still malignant but slower growing → excision of affected lymph nodes
  - **Embryonal carcinoma:** poorly differentiated, resembles adenocarcinoma. Highly malignant. May express tumour marker **alpha-fetoprotein**
  - **Choriocarcinoma:** Placental tissues (resembles hydatidiform mole). Expresses βHCG → positive for pregnancy test. Contains highly malignant syncytiotrophoblast and cytotrophoblast cells. Responds well to chemotherapy
  - Mixed tumours: Teratoma and seminoma

**Sex cord/stromal tumours:**

- **Leydig tumours:** 90% benign. Small brown mass. Present with overproduction of testosterone: precocious puberty or gynaecomastia in post-puberty. Can produce androgens, oestrogen or corticosteroids
- **Sertoli cell tumours:** Rare. 90% benign. Within seminephrous tubules of the testis. Local infiltration

**Lymphoma:** Older males, often bilateral, poorly differentiated and poor prognosis

Testicular tumours present relatively young, lymphoma in older men

---

*Renal and Genitourinary*
<table>
<thead>
<tr>
<th></th>
<th>Testicular Torsion</th>
<th>Epididymo-orchitis</th>
<th>Testicular Cancer</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Pain</strong></td>
<td>Acute, sudden onset. 30% have lower abdo pain</td>
<td>Usually develops over a day or so</td>
<td>Usually painless – but 30% have diffuse pain or ‘dragging sensation’</td>
</tr>
<tr>
<td><strong>Scrotum</strong></td>
<td>↑ oedema and erythema on affected side</td>
<td>↑ oedema and erythema on affected side</td>
<td>Testis enlarged. 15% have scrotal inflammation</td>
</tr>
<tr>
<td><strong>Palpation</strong></td>
<td>Testis enlarged, exquisitely tender, may ride high</td>
<td>Epididymis usually enlarged</td>
<td>Lump detected in body of the testicle</td>
</tr>
<tr>
<td><strong>Age</strong></td>
<td>Usually babies and pubescent boys. Can occur in 20s and 30s</td>
<td>Usually in 19 – 40 year olds</td>
<td>Peak incidence age 25 – 35, but as young as 15</td>
</tr>
<tr>
<td><strong>History</strong></td>
<td>May have had previous short acute episodes. Sometimes recent trauma</td>
<td>Sexual activity. UTI</td>
<td>History of undescended testis or family history</td>
</tr>
<tr>
<td><strong>Urinary symptoms</strong></td>
<td>90% have normal urinalysis</td>
<td>Dysuria, frequency, urgency, only 10% have discharge</td>
<td>Few in early stages</td>
</tr>
<tr>
<td><strong>GI symptoms</strong></td>
<td>Nausea in 1/3. 30% complain of abdo pain</td>
<td>Can be nausea/vomiting</td>
<td>Can be caused by mets</td>
</tr>
<tr>
<td><strong>Temperature</strong></td>
<td>Usually normal</td>
<td>May have fever</td>
<td>Usually normal</td>
</tr>
<tr>
<td><strong>Cremasteric reflex</strong></td>
<td>Diagnosis confirmed by absence, not excluded by presence</td>
<td>Present</td>
<td>Present</td>
</tr>
</tbody>
</table>

### Non-neoplastic Testicular Lesions

<table>
<thead>
<tr>
<th>Non-neoplastic testicular lesions</th>
<th>Condition</th>
<th>Features</th>
</tr>
</thead>
<tbody>
<tr>
<td>Torsion</td>
<td>Haemorrhage; seen in children more commonly</td>
<td></td>
</tr>
<tr>
<td>Varicocele</td>
<td>Collection of dilated veins in spermatic cord</td>
<td></td>
</tr>
<tr>
<td>Hydrocele</td>
<td>Fluid accumulation around testis in the TV – looks like a cyst – can transilluminate with torch</td>
<td></td>
</tr>
<tr>
<td>Tuberculous epididymitis</td>
<td>Cheesy caseous necrosis</td>
<td></td>
</tr>
<tr>
<td>Granulomatous orchitis</td>
<td>Auto-immune; granulomatous inflammation of seminiferous tubules but non-caseating</td>
<td></td>
</tr>
</tbody>
</table>
Terminology
- Varus = deformity/angulation (of distal segment) towards the midline
- Valgus = deformity/angulation away from the midline
- Genu = knee
- Cubitus = elbow
- Coxa = hip
- Pes = foot
- Cavus = abnormally arched
- Planus = flat
- Talipes = congenital deformity in which the foot is twisted out of shape or position (e.g., equinus)
- Ankylosis = joint fusion secondary to a pathological process (usually inflammation)
- Arthrodesis = surgical joint fusion

Quick Schema
- **PPTA SAW** (PC, pain, trauma, associated symptoms – fatigue/weight loss/fever/eye problems/raynaud’s, stiffness, ADLs, walking tolerance)

**Presenting Complaint**
- Pain, Loss of Function, Deformity
- Onset of presenting complaint:
  - Time: sudden, gradual
  - Mechanism: accident (etc), spontaneous

**Pain**
- SOCRATES
- Exacerbating and mitigating factors:
  - Movement
  - Position
  - Climatic conditions
- Day/night
- Sleep loss

**Trauma**
- HISSS
- How (mechanism): direct/indirect, fall, twist, running etc
- Immediate disability: unable to walk, limp etc
- Swelling: immediate, later, extent etc
- Sensation or sound: crack, break, pop, “felt like I dislocated it” etc
- Symptoms now: giving way, locking, catching etc

**Associated/Additional Symptoms**
- Fatigue
- Weight loss
- Fever
- Night sweats
- Eye problems
- Skin problems
- Raynaud’s (painful, cold fingers)
- Incontinence/perianal numbness/leg weakness/gait disturbance

**Stiffness**
- Early morning
- After inactivity
Walking Tolerance
- Including walking aids
- Up stairs etc

Treatment
- Analgesics (ask about efficacy and dose)
- Alternative therapy
- Rest/physiotherapy
- Surgical operations

Past History
- Cancer
- Relevant diseases and operations
- Fitness for anaesthesia

Social
- Occupation (Including work loss)
- Sports
- Domestic status
- Home environment

General Examination
- GIPMON
- Gait
- Inspect:
  - Posture
  - Symmetry
  - Shape changes
  - Scars
  - Swellings
  - Skin changes/rashes
  - Muscle wasting
- Palpate:
  - Temperature
  - Swellings
  - Tenderness
  - Crepitus
- Move:
  - FROM – active and passive
  - Restriction –mild, moderate, severe
  - Ligament stability
  - Special tests
- Operation/Function:
  - Functional assessment of joint
- Neurovascular assessment:
  - Pulses
  - Sensation
  - Power
  - Reflexes

Background
- Diaphysis = shaft of long bone
- Metaphysis = wider portion of long bone adjacent to epiphyseal plate
- Physis = growth plate
Radiology

- Check name and date
- Check quality and that film covers the pathology you want

Rules of 2

- **ALWAYS** take 2 views at 90%
- Include 2 joints: one above and one below:
  - Especially in paired bones of arm and leg. If there is a fracture with shortening, there will also be dislocation
  - Need to assess rotation relative to joint
- Sometimes need to X-ray 2 times. Eg May not see a scaphoid fracture until 10 – 14 days later (will see with a bone scan after ~ 24 hrs)
- Sometimes need to do opposite side to get a good idea of normal – especially if dealing with a complicated joint in a child with lots of epiphyseal plates around. Don’t do it routinely due to ↑ radiation

Describing a Fracture

- **WWTDAA** (what would the dog ask angela?)
- **Which** bone
- **Where** on the bone:
  - Intra or extra-articular
  - For a femur it can be **intracapsular vs extracapsular**, capital (through the head), subcapital (below the head), transcervical (through the neck), intertrochanteric, supracondylar, at the junction of the proximal and middle thirds, etc
  - Diaphysis: mid-portion or shaft of a long bone. Outer cortex and inner medulla
  - Epiphysis: ends of long bones
  - Metaphysis: rapidly growing trabecular bone adjacent to the growth plate
- **Type**: see below section on fractures
- **Displacement**:
  - Are the two ends aligned? Range from 0 to 100% displaced, and direction of displacement
- **Angulation**:
  - In degrees, of the # site
Musculo-skeletal, Rheumatology and Plastics

- Degree and direction. Described as the distal relative to the proximal portion when in the anatomical position. Medial is varus, lateral is valgus.

- **Associated** symptoms: eg
  - Neurovascular status
  - Compound wound (eg may see air in soft tissue)
  - Compartment syndromes
  - Foreign bodies, etc

- Types of joint injury:
  - Sprain: tearing of ligaments
  - Subluxation: partial loss of congruity of the articular surfaces
  - Dislocation: complete loss of congruity of the articular surfaces
  - Fracture-dislocation

- Of bone, only periosteum has nerve fibres therefore # pain is felt initially but not later (as periosteum dies)
- NB of joints, only capsule has nerve fibres therefore this is the source of pain in arthritis, not bone as joints contain no periosteum

**Types**

- **Greenstick**: only the convex side of the injured cortex is disrupted, transverse fracture. Only in kids (*higher collagen content and less mineralisation*). Can also present as:
  - Bowing of a long bone
  - Torus/buckle: fracture around the epiphysis if the force was along the axis of the bone

- **Transverse**: force at 90% to bone ie direct blow (⇒ also soft tissue injury). Stable when reduced

- **Oblique**: force at 90% while weight bearing (net vector is oblique). Slips out of reduction

- **Spiral**: rotatory force – twisting. Don’t need big force

- **Comminuted** (>2 pieces)

- **Epiphyseal**: described by Salter-Harris Classification: from I to V (most complex). II most common (break through epiphysis with a small chip of bone)

  - Intra-articular
  - Segmental: 2 breaks separated by a section of normal bone. Big force required
  - Stress: fractured bone trying to heal itself and refracturing, etc. May be visible on X-ray, will be visible as a hot spot on bone scan

- **Avulsion**: ligament tears off bone

- **Crush**: direct compression of cancellous bone may cause its trabeculae to collapse

- **Pathological**: bone weakened by disease

- Simple or compound (bone communicates with air). If compound then Gustilo Classification from I (minor) to III (extensive)

**Clinical Findings**

- Swelling (haematoma + oedema)
- Deformity
- Abnormal mobility
- Crepitus
- Skin integrity may be breached
- Vascular perfusion + neuro function should be evaluated

**Management of Fracture of the Extremities**

- General # priorities:
  - Resuscitate
  - Reduce
  - Stabilise

- **FRIAR**:
  - first aid
  - reduction
  - immobilisation
  - active movement
  - rehabilitation

- Immediate assessment:
  - *Straighten* any displaced fracture to allow adequate blood flow
  - Examine for fractures
- Examine for dislocations
- Compartment syndromes
- Look for vascular injuries: Hard to assess for vascular injuries when SBP is less than 90 mm Hg
- Look for nerve injuries

Goals of fracture management:
- **Upper limb**: restore function (alignment less important as ROM eg shoulder can compensate for malalignment)
- **Lower limb**: obtain and maintain alignment → restore alignment, angulation, rotation and length

Principles:
- Reduce severe deformity as soon as possible if it is causing soft-tissue or neurovascular compromise
- Open fractures → antibiotics
- Assess for conservative or surgical treatment
- Management is a tension between immobilising it long enough to enable union, and short enough to stop stiffening/arthritis of immobilised joints

Methods:
- **Reduction**:
  - By manipulation, traction or open reduction
  - Longitudinal traction which disimpacts any interlocked fragments + reversal of the forces causing the deformity
- **Immobilise**:
  - However, casting → muscle atrophy, stiff joints, OA, DVT
  - Methods = external splints (POP etc; should generally immobilise the joint above + below), continuous traction (of # surrounded by soft tissue), internal or external fixation
  - If it involves joint articulations (ie intra-articular): ORIF (especially if displaced) so that early movement can occur, otherwise secondary OA
  - Internal fixation: plates, nails (Kuntscher) or wires (Kirschner)
  - External fixation: screws into bone with external bracing; indicated for open or infected #s
- **Active movement and rehabilitation**:
  - Starts immediately after treatment – pt asked to move the injured part as much as the method of fixation allows
  - Slight movement helps to stimulated union, ↓ disuse osteoporosis, ↓ muscle atrophy, ↓ joint stiffness
  - External splints should be removed as soon as clinical evidence of union + programme of active exercises (physio) implemented

Rules for manipulation to obtain closed reduction:
- If you manipulate, then re-xray now
- Review early (eg after 1 week). Can’t re-manipulate after this should that be necessary

Indications for ORIF:
- Failure to obtain or maintain closed reduction, or where closed reduction has high failure rate (eg fractured neck of femur)
- **Intra-articular fracture** (especially if > 1mm displacement after reduction). Failure to operate leads to:
  - Short term: irritant effect of synovial fluid → non-union
  - Long term: pain, arthritis, instability
- Arterial compromise
- Open fracture [first aid = cover wound in sterile dressing soaked in NS or iodine; IVABs + tetanus]
- Pathological fracture
- Multiple injuries
- Segmental fracture

Risks of surgery:
- ↑ Soft tissue damage
- ↓ Wound healing
- Anaesthetic risks
- But potentially quicker recovery

**Healing of Fractures**
- Assessment of union of a fracture:
  - Clinical:
    - Absence of tenderness on direct pressure over the # site
    - Little or no pain when # site is stressed by angulation or rotation
Absence of movement at the # site

- Radiological:
  - No evidence of a gap at the # site + continuity of bone trabeculae across it

Stress fractures occur in:

- The elderly with osteoporosis
- Metabolic bone disease
- Very active runners/sports people (eg tennis, squash)
- *Never* in kids

Factors improving remodelling:

- Young age
- Long bones (for example, cf carpal bones)
- Close to growth plate
- If angle is in the principle direction of movement (ie posterior or anterior angulation of the radius, given this is in line with flexion and extension of the wrist)

Factors impairing healing:

- Movement (too much)
- Non-union
- Infection
- Poor blood supply
- Comminuted

Rule of thumb for fracture healing:

- Children generally unite in half the time taken in adult #s
- Upper limb: 4 – 6 weeks (kids at shorter end, adults at longer end, etc)
- Ankle: 6 weeks (close to a joint so want to mobilise early)
- Tibia and femur: up to 12 weeks
- Other specific times for some fractures

When to mobilise:

- Stable fractures should be mobilised soon
- Unstable fractures should be stabilised before mobilising

Patient advice:

- If the limb distal to a cast ever goes blue, becomes painful or tingles, *elevate it for ½ an hour and if no improvement return immediately* (not the next day). Remove cast and assess for improvement. If no improvement then urgent opinion
- When to start mobilising

Complications of Fractures

- Joint stiffness: *Cartilage requires motion for nutrition*. If held in one position → risk of cartilage deterioration
- Haemorrhage:
  - From bone marrow, periosteum + surrounding soft tissues = can cause ↓ blood volume
  - General rules: pelvis → 2-3L; femur → 1-2L; tibia/humerus → 0.5-1L
- Infection in open fractures:
  - → Osteomyelitis, slow union and increased chance of refracture
  - Clinical: history of open fracture or operation on closed fracture. Wound inflamed. Systemic signs of fever
  - Treatment: all open fractures require prophylactic antibiotics and excision of devitalised tissue. If acutely infected, surrounding tissues should be opened and drained + antibiotics
- Compartment Syndrome:
  - *Elevated pressure in an enclosed space* (eg muscle compartment) can irreversibly damage the contents of that space
  - 30mmHg of pressure is sufficient to occlude capillary flow even though arterial flow might still be possible (therefore a palpable pulse does not rule it out)
  - Major causes: processes constricting the compartment or ↑ the contents of the space:
    - Compressive bandages
    - Tight cast
    - Haemorrhage and oedema after fracture
    - Closure of fascial defects
  - More commonly seen in *tibial* #s
- If patient has *more pain than would be expected post #* → evaluate immediately for CS
- Muscles once infarcted are replaced by inelastic fibrous tissue (eg Volkmann’s Ischaemic Contracture of the forearm compartment after humeral supracondylar fracture). *Most sensitive test is passive extension*
of the muscles. Can still have arterial flow through the compartment while muscles are becoming ischaemic

- **Signs and symptoms** (The 6 p′s i.e.):
  - Pain: due to muscle ischaemia (in the first 10 min); often on passive stretching of muscles
  - Paraesthesia: due to nerve ischaemia (in the first hour)
  - Pallor: due to skin ischaemia (usually occurs late)
  - Pulselessness
  - Paralysis
  - Palpable tenseness

- **Diagnosis**: clinical; pressure > 30 – 40 mmHg (using needle manometer etc) and/or MRI
- **Treatment**: remove bandages, etc, consider decompression with a fasciotomy if pressure high, with wound left open for 5 days

- **Delayed union**: presents as pain + movement at fracture site with stress
- **Normal union times**

<table>
<thead>
<tr>
<th></th>
<th>Upper Limb</th>
<th>Lower Limb</th>
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<tbody>
<tr>
<td>Callus Visible</td>
<td>2-3 weeks</td>
<td>2-3 weeks</td>
</tr>
<tr>
<td>Union</td>
<td>4-6 weeks</td>
<td>8-12 weeks</td>
</tr>
<tr>
<td>Consolidation</td>
<td>6-8 weeks</td>
<td>12-16 weeks</td>
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- If these times prolonged “delayed union” is likely
- **Causes**: severe soft tissue damage, inadequate blood supply, infection, insufficient splintage, excessive traction
- **Clinically**: site tender, painful if subjected to stress, x-rays still show visible line
- **Treatment**: needs to be reviewed if no bridging callus by 3 months. Need internal fixation and bone grafting

- **Non-union**:
  - Non-union is likely if delayed union is not treated
  - Presents as non-painful movement at the fracture site
  - **Causes**: too large a gap (bone missing, muscle in way), interposition of periosteum, infection, excessive movement
  - **Clinical**: painless movement at fracture site. X-ray shows smooth and sclerosed bone ends or excessive bone formation
  - **Treatment**: not all cases need treating eg scaphoid, otherwise fixation and bone grafting necessary.

- **Malunion**:
  - When *bone fractures join in an unsatisfactory position* i.e. unacceptable angulation, rotation or shortening
  - **Aetiology**:
    - Failure to reduce a fracture adequately
    - Failure to hold reduction while healing proceeds
    - Gradual collapse of comminuted or osteoporotic bone
  - **Signs and symptoms**: usually obvious eg. Unusual bone alignment, x-ray
  - **Treatment**:
    - If detected before union complete angulation may be corrected by wedging of plaster
    - Forcible manipulation under anaesthetic
    - Osteotomy if union complete and deformity severe

- **Avascular Necrosis**:
  - **Aetiology**:
    - Rare
    - Focal subchondral infarction → collapse of necrotic segment → joint deformity → arthritis
    - Common in bones that derive most of their blood supply from the medullary cavity
    - Mainly femoral head, also knee, scaphoid, head of talus
    - Gross: infarct is yellow, opaque and chalky with rim of hyperaemic fibrous tissue
  - **Causes**:
    - Trauma (eg subcapital fractured neck of femur)
    - Secondary to corticosteroid treatment
    - Nitrogen embolisation in divers (Bends → Caisson disease)
    - Sickle cell disease
    - Alcoholism
    - SLE
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Infective endocarditis
Radiation
Diabetes mellitus

Signs and symptoms:
Joint stiffness
Pain in or near joint
Local tenderness
Restricted movement

Pathology:
Macro: wedge of necrotic bone – pale + collapse
Micro:
Viable articular cartilage
Dead bone – empty lacunae
Dead adipose tissue in the marrow space

Complex regional pain syndrome (CRPS):
Reflex sympathetic dystrophy or Sudeck’s atrophy, presents at intervals of days or weeks after injury as:
Disproportionate pain
Abnormal sensation (dysaesthesia)
Joint stiffness, thickening of soft tissues, sweating, loss of hair
Seen most in the hand (exquisitely tender)
Preventable by holding wrist + digits in positions of function + elevation of the part + early active exercises

Other complications of fractures:
Venous thromboembolism + PE: at risk due to immobility, leg injury, etc
Nerve damage
Skin necrosis
Pressure sores and plaster sores – where skin is pressed directly onto bone
Fat embolism: typically day 3 – 10. Either fat from marrow or something else. Clogs capillaries on right side of heart + if PFO can cause brain injury. Sudden SOB, hypoxia, maybe confusion. Immediate ICU management
Osteoporosis
Myositis ossificans: heterotopic bone (bone development in abnormal areas) – can be seen in muscles. More commonly in elbow
Fracture blisters: due to elevation of superficial layers of skin by oedema – can be sometimes prevented by firm bandaging

Blood Transfusion
What do you know already?
What do you want to know/get from this?
The options are:
Not having a transfusion: risks are much greater than from having a transfusion
Having a transfusion
There are no substitutes for blood products (RBCs, plasma, platelets)
What it is: giving blood or a product made from blood into a vein
Where it comes from: unpaid voluntary donors in NZ; collected sterile + screened for disease (HBB/HCV/HIV/syphilis) + blood type
What types: RBC for anaemia or bleeding; platelets for bleeding; FFP/cryoprecipitate for replacing clotting factors
The risks are very small:
Minor allergic reaction/rash in 1-2%
Major reaction 1/100,000
HCV/HIV much less than 1 in a million; HBV 1 in 100,000
Never seen a case of CJD in NZ from transfusion
BT have a high level of safety
Check understanding + allow questions

Surgery Complications
General: failure, infection, bleeding, damage to surrounding structures (nerve damage, blood vessel damage, bony injury/#), DVT/PE, different limb length, foreign bodies left, burns, allergy, stiffness of joints
Joint replacement: failure to implant, knocking/clicking sounds, dislocation of joint, residual pain
Osteoarthritis (Hip or Knee)
- OA is a wear and tear disease. Basic components of a joint are bone, cartilage, bone. In OA, the cartilage layer is worn away over time (general wear and tear, idiopathic, post trauma) causing changes in the underlying bone. Pain, stiffness and restriction of movement
- **Non-weight bearing** exercises, **weight loss** (↓ forces through the joint and can preserve the joint for longer), **analgesia**, walking aids, physio/OTs, appropriate footwear/inserts
- Aim to delay **surgery** for as long as possible – due to potential complications (see above; ie surgery carries with it risks + therefore it should be a last resort)

Carpal Tunnel Syndrome
- Due to compression of median nerve in carpal tunnel – get tingling and pain in distribution of nerve
- Pain usually worse at night or on repetitive movements
- Associated with pregnancy, obesity, DM
- **Mx:** wrist splint at night, carpal **steroid injection** (symptom relief), may need surgical decompression (straightforward surgery – 20min day case, LA, small incision)

Gout
- Causes of increased urate: hereditary, diet, alcohol (beer), diuretics, leukaemia (tumour lysis), renal impairment
- Precipitated by trauma, surgery, starvation, infection, diuretics (thiazides)
- **Prevention:** **avoid prolonged fasts**, **alcohol excess**, **purine rich foods** (e.g. meat and seafood), **weight loss**, low dose aspirin (↑ urate), use long-term allopurinol
- **Mx** acute attacks: strong NSAID (e.g. indomethicin) or colchicine if can’t use NSAID. Steroids (oral, IM, intra-articular) may be effective

X-ray Interpretation
- **OA:** joint space narrowing, subschondral sclerosis/cysts, osteophytes (usually in DIP joints of hand + the 1st CMP joint, and all weight bearing joints (+C5-6: fulcrum for head)
- **RA:** joint space narrowing, **erosions**, periarticular **osteopenia**, **fusiform soft tissue swelling** around joints (distribution opposite to OA e.g. MCP and PIPs + symmetrical distribution of other joints)
- **Gout:** **para-articular erosion with over hanging edges** (pathognomonic), soft tissue swelling, normal joint space/bone density, DIPJ
- #: WWTDAA

Cast
- **Patient advice:**
  - If the limb distal to a cast ever goes blue, becomes painful or tingles, elevate it for ½ an hour and if no improvement return immediately (not the next day). Remove cast and assess for improvement. If no improvement then urgent opinion
  - When to start **mobilising**

Management of Back Pain
- What have you tried so far?
- **Mechanical BP:**
  - Prevention
  - Rest, warmth, simple analgesia
  - Physio
  - Spinal support or brace
  - Epidural injection
  - Surgery
- **Conservative:**
  - 80 – 90% of back pain resolves in 4 – 6 weeks
  - **Firm** bed (eg a board underneath)
  - **No slouching**, education on how not to stress back
  - **Analgesia** (→ break cycle of muscle spasm)
  - No bed rest, early return to work
  - Warmth, analgesics
  - Promote self care and responsibility →↓dependence

Musculo-skeletal, Rheumatology and Plastics 352
Stay active. Eg swimming. But may need to modify normal activities. Lift carefully, wear low heeled shoes, chair which helps good posture, pillow between knees at night, walking, cycling, swimming

Exercises only help with symptoms – don’t affect recovery time

Physio – but not while acutely sore

Manipulation may help in the first month

Advice on prevention

Check-ups at 1, 4 and 6 weeks (ACC guidelines)

If not improved after 2 weeks, consider X-ray, referral, etc

Chronic pain:

Maybe weight loss

Avoid sitting for prolonged periods (discs under ↑ pressure when sitting)

Other treatment:

Sciatic pain: epidural steroid injection

Surgery: remove disc protrusion, decompression or stabilisation

Osteoporosis

Osteoporosis is a condition in which bone loss exceeds bone formation, with a resultant loss of calcium and protein from the bones. This causes the bones to become excessively thin making them weak, brittle and more likely to break. There are usually no symptoms of osteoporosis until a bone breaks. Treatment and prevention will normally focus on lifestyle changes and medications to boost bone density.

There is no single cause of osteoporosis but there are many risk factors. These include:

Older age (>50 years)

Female gender

Thin build

Physical inactivity

Family history of osteoporosis

Smoking

Excessive alcohol or caffeine consumption

Low dietary calcium intake

Low levels of vitamin D

Long-term use of some medications eg: corticosteroids, thyroid medications, epilepsy medications

Deficiency of oestrogen in women eg: post-menopausal, irregular periods, surgical removal of the ovaries, early menopause (before the age of 40 years)

Some medical conditions

Signs and Symptoms:

There are usually no symptoms of osteoporosis until a bone breaks. For this reason it is often referred to as a “silent disease”. Fractures of the wrist, hip and spine are common in osteoporosis. The fractures can be very painful and can lead to disability and loss of independence.

Diagnosis:

A full medical history, including signs, symptoms and family history will be taken.

Bone density testing is usually undertaken using dual energy x-ray absorptiometry (DEXA). This is a specialised x-ray scanning technique that emits only very low levels of radiation

The density of bone is measured at different locations (usually the lower spine and hip) and a formula is used to calculate the overall bone density. Individual bone density is graded by comparing it to the average bone density for a person of similar age, size and gender.

Complications of Orthopaedic Surgery

Infection

Bleeding

Nerve damage (can cause new pain not present before the surgery)

Blood vessel damage

Thrombosis

Bony injury or #

Difference in limb length (with joint replacement/osteotomy)

FB left in the body

Burns (diathermy)

Allergy (to antiseptics etc)

Stiffness of joints
Additional complications after joint replacement operations:
- Failure of the implant (loosening, wear)
- Knocking or clicking sounds (of no concern)
- Dislocation
- Residual pain (artificial joints are seldom completely painfree – they’re not the same as normal joints)

Aseptic Joint Loosening
- Commonest cause of failure of joint replacements
- Pts normally present with renewed pain months or years after initially gaining pain relief after surgery
- X-rays show progressively ↑ radiolucency around the implant
- Risk factors = young patients (under 55), male, obesity

Septic Joint Loosening
- Septic joint loosening (systemic signs) requires removal of joint replacement + ABs (after identifying causative agent)
- Joint replacements in RA is a/w ↑ risk of infection due to altered immune response

Bone Pathology

Bone
- Bone is a dense CT that mineralises
- Provides support, rigidity, attachment and lever for muscles
- Houses haematopoietic stem cells
- 206 bones in total
- Main constituents:
  1. ECM:
     - Osteoid (collagen type 1) provides the scaffold
     - Hard inflexible calcium and phosphorus crystals (calcium hydroxyapatite)
  2. Cells:
     - Osteoblasts: bone forming cells, closely opposed to bone surface in clusters
     - Osteoclasts: large multinucleated cells that resorb bone
     - Osteocytes: when OBs become surrounded by matrix: “mature OBs”, live in lacunae
  3. Ancillary soft tissues:
     - Fatty + haematopoietic marrow
     - Periosteum
     - Tendons, ligaments, joint capsule
     - Cartilage
- Structural types of bone:
  - Compact: forms the outer shell or cortex of all bone including shafts in long bones
  - Trabecular/spongy: found in the expanded heads of long bones and fills most irregular bones
- Woven vs lamellar bone:

<table>
<thead>
<tr>
<th>Sites</th>
<th>Lamellar</th>
<th>Woven</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal bone</td>
<td>Lamellar organisation</td>
<td></td>
</tr>
<tr>
<td>Osteocytes in lacunae</td>
<td>Osteoblasts + osteoclasts (multinucleated)</td>
<td></td>
</tr>
<tr>
<td>Disorganised</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Marrow spaces seen</td>
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Osteogenesis
- 2 modes of bone formation:
  1. Endochondral ossification:
     - Cartilage becomes progressively ossified and is eventually replaced by bone

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Musculo-skeletal, Rheumatology and Plastics

- Occurs in long bones, vertebrae, pelvis, base of skull

- **2. Intramembranous ossification:**
  - Deposition of bone within primitive mesenchymal tissues ie *bone is formed within connective tissue*
  - No intermediate cartilage
  - Occurs in the *vault of the skull, maxilla and mandible*

- Longitudinal bone growth ceases at skeletal maturation, however modelling continues throughout life

**Fracture Healing**

- Fractures are the most common pathological condition of bone
- Recapitulates the embryological development of bone
- Divided into direct (primary) and indirect (secondary):
  - Direct/primary:
    - Occurs with rigid internal fixation
    - Attempts by the cortex to *re-establish Haversian systems*
    - Little or *no periosteal* response and therefore no callous formation
  - Indirect/secondary:
    - *Typical* repair mode, occurs in most fractures
    - Involves a *combination of intramembranous and endochondral ossification*
    - *Enhanced by motion* (within reason) and inhibited by internal fixation
    - See *callous formation*

- Temporal stages of fracture healing:
  - **1. Haematoma** formation:
    - Immediately following injury
    - Pain, swelling, loss of function
    - *Disruption of blood vessels*: cortex, marrow, periosteum, soft tissues
    - Surrounds the # site and *provides a fibrin scaffold*
  - **2. Inflammation:**
    - Required for healing
    - Healing initiated through induction of immune response
    - *Inflammatory cells migrate* to the # site
    - *Cell signalling molecules* are important for *cell migration, differentiation and growth*
  - **3. Soft callus/Granulation tissue:**
    - *Organisation* of the blood clot
    - *Ingrowth of new blood vessels*
  - **4. Hard callus/Reparative stage:**
    - Takes weeks to months
    - Lump may be felt
    - Bone ends anchored together but not stable enough for weight-bearing
    - *Callous grows and bridges # gap*
    - Disorganised large mass of tissue
    - New bone forms by *endochondral ossification*
    - Gradual replacement of cartilage by *woven bone*
  - **5. Remodeling phase:**
    - Several months after #
    - Can now weightbear
    - Still not at normal strength
    - Final stage of healing may continue for month → years
    - Replacement of *woven bone* (*temporary, immature bone where collagen is randomly arranged*) by *lamellar bone* with resorption of callous

- Outcomes:
  - Restoration of original tissue
  - Failure of repair: non-union

- Variables affecting healing:
  - Injury: type, intensity, duration
  - Pt factors: age, metabolic state, disease, medications, smoking
  - Tissues involved: bone, fibrous tissue, cartilage, muscle
  - Treatment: apposition, stabilisation, loading, and motion
Bone Infarction
- AVN
- Femoral head prone to infarction due to blood supply (can also be seen in humeral head post #)
- Appears grossly as subchondral wedge-shaped defects; microscopically as empty lacunae
- Can lead to OA
- #, steroids, vasculitis can predispose to AVN

Osteonecrosis & Osteochondritis
- Osteonecrosis = bone death → due to impaired blood supply or to severe cell damage
- Osteochondritis = poorly named; bone damage + necrosis follow trauma to articular surfaces
- Osteonecrosis stereotype is AVN of femoral head
- ON stages:
  1: bone death without structural change
  2: repair + early structural failure
  3: major structural failure
  4: articular destruction
- ON x-ray: distinctive feature = subarticular segment of ↑ bone density (reactive new bone formation)
- ON underlying conditions = steroid use/Cushings; marrow infiltration (Gaucher’s disease; malignancy); sickle cell disease; perthes; SLE; septic arthritis; post-traumatic etc
- OC conditions include osteochondritis dissecans + Osgood-schlatter’s disease (see Knee section)

Soft Tissue Injury

Prevention of Sport Injuries
- Proper warm up
- Cooling down
- Protective equipment
- Good technique and sensible training schedules

Ligament Injuries
- Sprain: partial tear of ligament or joint capsule but the joint is still stable. Site of tear is tender and there may be bruising. Symptomatic treatment and protection from stress until healing is complete
- Partial Rupture: if rupture is incomplete, treat conservatively (ranging from rest + analgesia to casting for 6/52). Recurrence common
- Complete Rupture: poor healing as scar tissue is not as tough as the ligament. May attempt surgical repair – but it may not help

Tendon Injuries
- Due to sudden, violent contraction
- Most common is Achilles Tendon Rupture. See Lower Leg and Foot Injury, page 402
- Can also rupture long head of biceps and supraspinatus
- Other tendon injuries:
  - Paratendonitis: inflammation due to friction of the paratendon (fatty tissue in the fascial compartment through which a tendon runs). Usually Achilles or wrist tendons. Try good footwear or rest in a splint. Steroid injection (but not into the tendon itself) may be effective. NB steroid injections around the Achilles are controversial – may weaken the tendon
  - Tendonitis: irritation/tearing of fibres due to repeat trauma. Pain worse on contraction. Rest + NSAIDs

Tendonopathies
- Eg Achilles, tennis elbow, patellar tendonopathy
- Tendonosis vs tendonitis – most are non-inflammatory
- Degenerate tendon → injury (acute or repetitive) → disruption of normal collagen array
- Rx with eccentric (load while lengthening) exercises eg Achilles: over edge of a step, up on toes with both legs then slowly down on affected leg only [eccentric movement]

Frost Bite
- Formation of ice-crystals in the skin and soft tissues when temperature < -3 °C
- Presentation: tissue is pale, grey, and doughy – or frozen solid. May develop without person knowing
- Treatment:
  - **Warm slowly** – this will be painful
  - Blisters may form over several days. May develop blackened shell as blisters burst
  - Dry, non-adherent, strictly aseptic dressings and prevention of further trauma (tissues are numb)
  - Recovery takes weeks. Surgery may be required

**Contusion**
- Characterised by **direct trauma** to a muscle group with subsequent **pain and swelling** due to **bleeding within the muscle**
- Management:
  - **RICE**: rest, ice, mild compression and elevation to control swelling, bleeding and pain
  - Intermittent icing **for up to 48 hours**
  - Maybe NSAIDS – but may increase the bleeding
  - Exclude other injuries, including compartment syndrome
  - Once swelling has settled, aim is to restore function, beginning with gentle isometric muscle exercises

**Lacerations**
- Torn, ragged wound
- Treat for bleeding: expose wound to assess for blood loss, cover, direct pressure, elevate, pad and bandage
- If severe then sutures. However, muscle divided transversely will not hold sutures well enough to stop muscular contraction pulling the edges apart

**Enthesitis**
- Inflammation at the site of attachment of bone to a tendon, ligament or joint capsule
- Elbow: See Tennis and Golfer’s Elbow, page 378. Treatment: rest and strapping. Steroid injection if severe
- Plantar Fasciitis:
  - Insertion of the tendon into the calcaneum
  - Pain on standing and walking
  - Is isolated, or with sero-negative arthritis
  - Treatment: **heel pads, reduced walking**, steroid injection

**Chronic Compartment Syndrome**
- Caused by ↑ tissue pressure in a closed fascial space → ↓ circulation to muscles and nerves
- Presentation: **pain or deep ache over compartment**. Usually **after prolonged exercise**. Usually **bilateral**. May have palpable muscle hernias
- Diagnosis: difficult. Elevated pressure within the compartment during/after exercise with slow return to resting pressure
- Treatment: **decrease exercise** (→ ↓ muscle bulk) or elective fasciotomy (can affect muscle strength)
- ‘Shin Splints’: Shin soreness in unfit runner: can be due to a **combination of muscle tears, mild anterior compartment syndrome or stress fracture**

**Causes of Non-Traumatic Limb Pain**
- Muscle disease: polymyositis, polymyalgia rheumatica, tendon inflammation, compartment syndrome
- Bone disease: osteomyelitis, osteomalacia, osteoporosis, tumours
- Vascular disease: arterial or venous (eg DVT)
- Neuropathy: nerve entrapment, neuropathy

**Osteochondritis**
- Osteochondritis: not inflammation
- Aetiology unknown
- Bone centres of children/adolescents become temporarily softened after undergoing osteonecrosis. After variable period of time, bone hardens again in new, deformed shape
- Examples:
  - Perthes: hip
  - Scheuermann’s d: vertebral epiphyses
  - Kohler’s disease: navicular
  - Freiberg’s: head of 2nd or 3rd MT
  - Kienbock’s: lunate (in adults)
- Osgood-Schlatter’s is an osteochondritis-like condition: tibial tuberosity apophysitis and quads tendonitis – repeated traction → microavulsions and inflammation

Osteochondritis Dissecans
- Seen in knee, elbow, hip, ankle, talus
- A loose body results from segment of subchondral bone and cartilage becomes avascular and separates from underlying bone

Nerve Injury
- See Common Peripheral Nerve Lesions, page 182 for common peripheral nerve injuries
- Types:
  - **Neuropraxia**: transient loss due to external pressure. Physiological block to conduction but axon is in anatomical continuity. Funny bone is a common example
  - **Aconotmesis**: damage to axons but Schwann cell remains intact ie due to traction injury. Loss of function for weeks/months due to more severe compression. No loss of neuronal continuity
  - **Neurotmesis**: nerve division. See Wallerian degeneration. No recovery without surgical repair, haphazard matching of motor and sensory fibres leads to inevitable imperfect recovery
- Mechanisms: division, stretching, crushing, ischaemia alone or in combination
- Prognosis depends on age, nerve type, type of lesion, size of gap to be bridged, delay between injury and repair, surgical skill
- Common sites:
  - **Upper Limb**:
    - Axillary nerve:
      - Injured during shoulder dislocation/# of humeral head → cannot abduct + patch of numbness over deltoid
      - Usually recovers spontaneously
    - Median nerve:
      - Hand through window; injured near wrist or high in forearm
      - Low lesions due to cuts in wrist or carpal dislocations → thenar wasting + thumb abduction + opposition weak; sensation lost
      - High lesions due to forearm #/elbow dislocation → same as above but also long flexors to thumb, index, middle fingers are paralysed
  - **Ulnar nerve**:
    - Fracture or pressure near the wrist or elbow
    - Low lesions due to pressure from ganglion or lac → hypothenar wasting + clawing; finger abduction weak + loss of thumb adduction – sensation lost over ulnar ½ fingers
    - High lesions due to elbow # or ulnar nerve entrapment in cubital tunnel → same as above but less noticeable clawing as the ulnar half of FDP is paralysed
  - **Radial nerve**:
    - Cuts around the elbow, or injury in upper arm or axilla
    - Low lesions due to # or dislocation at elbow or open wound → cannot extend MCPJ
    - High lesions occur with humerus # or prolonged tourniquet + Saturday night palsy (arm dangling over back of chair) → wrist drop + sensory loss on dorsum of hand at base of thumb
    - Very high lesions due to axilla pressure (crutch palsy) → triceps wasted
  - **Digital nerve**: finger cuts
  - **Brachial plexus**:
    - Downward pressure at the shoulder damages the upper cord, upward pressure damages lower cord
    - Can be pre-ganglionic (nerve separated from SC) or post-ganglionic (nerve trunk torn apart)
    - Extensive paralysis + loss of sensation – pain is usually severe; 50% have residual function
    - Pre-ganglionic injury suggested by high-energy transfer injury with violent distraction of the arm from the trunk; severe pain; convulsive shoots of lightning like pain; sensory loss above the clavicle; ipsilateral Horner’s syndrome; paralysis of serratus anterior + ipsilateral hemidiaphragm
    - Nerve conduction studies can be useful
    - Repair is urgently needed
  - **Lower Limb**:
    - Common peroneal nerve:
- Damage at the neck of the fibula or LCL injuries
- Foot drop with weak dorsiflexion + eversion; sensation lost over front + outer half of leg + dorsum of foot
- If only superficial peroneal involved → peroneal muscles paralysed + eversion lost + sensory loss
- If deep involved → weak dorsiflexion + sensory loss at 1st web space on dorsum of foot
  - Femoral nerve:
    - Injured by traction during operation/bleeding into thigh
    - Weakness of knee extension + numbness of anterior thigh + medial aspect of leg; ↓ knee jerk
  - Lumbar nerve roots: prolapsed discs
  - Sciatic nerve:
    - Hip dislocation; traction and compression with local trauma
    - Foot drop, numbness + paraesthesia in leg + foot

- Management:
  - Immediate primary repair/suture: if clean cut
  - Secondary repair/suture: clean and debride then suture two weeks later, or when a neuroma has formed + requires excision
  - Cable Grafts: if long area of damage: graft from another nerve

- Nerve entrapment syndromes:
  - Nerves are at risk of entrapment wherever peripheral nerves traverse fibroosseous tunnels
  - Common sites = carpal tunnel, cubital tunnel, Guyon’s tunnel/canal
  - Clinical features = tingling, pain, numbness
  - Treatment = avoidance of compromising postures; surgical decompression

**Back and Neck**

- Spondylosis = degenerative changes
- Spondylolysis = pars interarticularis/neural arch defect
- Spondylitis = inflammatory changes
- Spondylolisthesis = anterior slippage of one vertebra onto another
Background

Spinal Mobility
- Cervical:
  - Most flexibility due to facet joint configuration
  - Rotation, f & e, lateral flexion
- Thoracic:
  - Flexion, Rotation, Lat Flexion
  - Very stable (effect of ribcage)
- Lumbar:
  - Least mobile
  - Limited flexion and no rotation due to facet alignment

Motion Segment
- Anterior - Disc
- Posterior - Facet (Zygoapophyseal Joints)
- Neural Arch (Pedicle, Pars = Lamina)

Disc
- Nucleus pulposus:
  - Shock absorber
  - Resists compression
  - Prone to degeneration + herniation
- Annulus fibrosis:
  - Strong “binder”
  - Dense collagen (type 2) + elastin (less)
  - Thinner posterolaterally therefore herniation occurs here

Vertebral Body
- Increases in size going superior to inferior
- Prone to osteoporosis
- Wedge #s (thoracolumbar region)
- Metastases (adjacent to Pedicles) – see ‘winking owl sign’ (pedicle destruction)
Degeneration

- Tends to start in disc (in our 20s)
- Drop in H2O content → disc narrows
- Discs → stiffer → deform more → less able to recover = creep → secondary effect on facets → OA

Terms

- **Radiculopathy**: disease affecting the nerve roots (characterized by pain which seems to *radiate from the spine to extend outward* to cause symptoms away from the source of the spinal nerve root irritation)

Anatomy

![Anatomy Diagram](image)

History

- **Where** is the pain?
- Where is the pain worst: leg or back [sciatic pain is worse in the leg] (or arm if neck pain)?
- Is it **INTERMITTENT** or **CONSTANT** (to be constant it has to ALWAYS be present; question them more than once about this!)?
- Is it worse with movement or postural in nature (ie mechanical)?
- **SOCRATES**
  - Bladder, bowel, sexual function
  - General health, weight loss, fever
  - Phx: cancer, IVDU
- If musculoskeletal then usually well localised and aggravated by movement
- If progressive and unremitting consider osteoporosis (with crush fractures), osteomalacia, neoplasia (secondaries, leukaemia or myeloma) or infection

Red Flags

- **Constant or progressive pain** which doesn’t change with movement or rest
- **Saddle numbness** (eg on wiping)
- **Fever** (e.g. infection)
- Bowel/bladder involvement (sacral roots): **incontinence** or **retention**
- Also:
  - Young (< 20) or old (> 55)
  - Violent trauma: MVA or fall from a height
  - Bilateral or alternating sciatica
  - Weak legs
  - Weight loss
  - ↑ESR
  - On oral steroids
  - IV Drug use
  - Pain with movement in all directions
  - Localised bony tenderness
  - Past history of cancer
  - CNS deficit at more than one root level or bilateral
- If no red flags then investigations not indicated unless symptoms persist beyond 4 – 6 weeks
**Yellow Flags**
- Barriers to recovery
- *Psychosocial factors* can lead to chronicity
- Problems at home or work/low mood
- Pain sometimes seen as harmful and can lead to avoidance behaviour

**Exam**

**General Inspection**
- Look at **belt line**: is the pelvis horizontal
- Check alignment, scars, lumps, muscles spasms, wasting etc
- **Scoliosis:**
  - If due to a short leg will correct when sitting down
  - If postural, will correct when leaning forward
  - If pathological (structural) will hump to one side (ie won’t correct) when they bend forward
- Dominant hand will usually have a *lower* shoulder

**Neck**
- **GAIT:** while sitting
  - Shape: normal lordosis; scoliosis; torticollis
  - Scars, skin changes, swellings, spasm, muscle wasting
- **Palpate:**
  - *Support the patient’s head* (eg put one hand on their forehead) to encourage relaxation
  - Feel down spinous processes, interspinous ligaments, paraspinal muscles, fascial attachments
  - Palpate thyroid gland, trachea, carotids, lymph nodes
- **Movement:**
  - Test actively
  - Extension, flexion and lateral flexion normally 45°. Left and right rotation normally 70°
  - If you need to measure, then measure from the sternal notch to the chin in each position
- **Neurovascular:**
  - If neck pain, check neurology in arms
  - **Myotomes:**
    - C5: deltoid → abduction
    - C6: biceps → elbow flexion
    - C7: triceps → elbow extension
    - C8: finger flexors
    - T1: finger abduction
  - Dermatomes in hand
  - Reflexes:
    - Biceps: C6
    - Brachioradialis: C6
    - Triceps: C7
    - Finger jerk: C8
- Examine joint above + below

**Thoracolumbar Spine and Sacroiliac Joints**
- **Gait:**
  - Assess heel walking (L5) and toe walking (S1)
  - High stepping → L5
  - Trendelenburg gait
  - Unable to heel push off → S1
  - Myopathic/spastic
- **Inspect:**
  - Muscle wasting in lower limbs
  - For alignment/deformity – inspect from both *back and sides*
  - Look for *scoliosis/kyphosis*, developmental abnormalities, vertebral body disease (eg rickets, Tb) or muscle abnormalities
  - Scars, swellings, skin changes
• Palpate:
  - Down spinous processes, interspinous ligaments, paraspinal muscles, fascial attachments for tenderness and muscle spasm
  - Palpate SJs
  - Gently **percuss spine with closed fist**: severe localised tenderness suggest infection/tumour/trauma → do x-ray
  - Percuss for renal tenderness

• Movement:
  - Flexion (*touch toes*): check for structural scoliosis (will not disappear with movement), extension, lateral bending (slide hand down side of leg as far as possible without bending forward)
  - Rotation: sit on stool (fixes pelvis) and rotate each direction (this is TSp only)
  - **Schober’s Test**: for *lumbar flexion*. Make a midline mark at the level of the posterior iliac spine (about L5). Make another mark 5cm below and 10 cm above the first mark. Ask the patient to touch their toes + measure whilst doing this. An *increase of < 5cm between the upper and lower marks* ⇒ *limitation of flexion*
  - **Lasegue’s Sign** *(straight leg raise; SLR)*
    - For lumbar disc prolapse causing *sciatica*
    - Passive lifting of straight leg is limited by pain as sciatic nerve is stretched (+ passively dorsiflexing the ankle after bringing the leg back down until no pain felt) ⇒ root pain
    - Must lift **BOTH** legs and look at the patient’s FACE
    - Commonly pain/tightness around 40°
    - *A positive test = leg pain, NOT back pain*
    - **Well leg lift** = pain in the *bad* leg when the good leg raised (sign of a big prolapsed disc)
    - **Cross leg lift** = pain in the *good* leg when good leg raised (sign of central disc prolapse; should think of cauda equina syndrome)
  - Palpate sacroiliac joints while prone

• Neurovascular:
  - Dermatomes
  - Myotomes:
    - L2,3,4: hip flexion, knee extension
    - L5, S1: hip extension, knee flexion (do prone)
    - L4,5: ankle dorsiflexion, inversion eversion
    - L5: great toe dorsiflexion
    - S1,2: ankle plantarflexion
  - Power:
    - Knee extension: L2,3,4
    - Knee flexion: L5, S1
    - Toe dorsiflexion (EHL): L5
    - Toe plantarflexion (FHL): S1
  - Reflexes:
    - Knee jerk: L2-4
    - Ankle: S1,2
    - Babinski

• Nerve tension tests:
  - **Straight leg raising/Sciatic stretch/Lasegue test**
  - **Femoral stretch** (for higher lumbar disc prolapses, pain in back + anterior thigh)

• Slump test:
  - The slump test is used for evaluating pts with spinal and lower extremity complaints
  - The test seeks to rule out or ID tension in the neuromeningeal tract
  - The performance of the test places traction on the neuromeningeal tract from head to foot
  - Traction on non-neurological tissues also occurs during testing and thus it is common for tightness (but not the pt’s pain) to be present
  - Pt clasps hands behind back, chin to chest with pressure from examiner. Pt extends one leg at a time, examiner dorsiflexes foot. If pt’s pain is reproduced, release tension by letting head move back to neutral; if this results in resolution of the pt’s symptoms = positive test

• Special tests:
  - Heel/toe walking, squatting may reveal weakness
Measure limb girth for wasting

Other tests:

- Hip examination
- Abdominal exam (Is this a bleeding AAA? Pancreatitis radiating to the upper back?)
- FABER (Flexion, Abduction, External Rotation):
  - Ask the patient to lie supine on the exam table.
  - Place the foot of the effected side on the opposite knee.
  - Pain in the groin area indicates a problem with the hip and not the spine.
  - Press down gently but firmly on the flexed knee and the opposite anterior superior iliac crest.
  - Pain in the sacroiliac area indicates a problem with the sacroiliac joints.

Always test legs:

- Neuro: sciatic pain, sensation, power, reflexes
- Pulses

Examine joint above + below

Xray Interpretation (ABCS)

- Alignment: anterior and posterior lines should be smooth curves
- Bones: assess each vertebrae – trace each round body. Processes and facet joint may be obscured. Look for osteophytes
- Cartilage and joints: discs should be similar and even. Facet joint dislocation only occurs in association with severe injury
- Soft tissue: disruption of shadows
- Non-traumatic injuries very rarely have positive findings on plain X-ray

Cauda Equina Syndrome

- Due to compression from PID (central) or tumour
- Symptoms (“any change in bowel or bladder control?”):
  - 1. Urinary retention → overflow
  - 2. Bowel incontinence
  - 3. Erectile dysfunction
- Signs:
  - Saddle anaesthesia (can check at top of natal cleft)
  - Absent anal sphincter tone/contraction
  - Weakness bilaterally

Neck and Radiating Arm Pain

Neck Pain

- Torticollis (congenital or acquired)
- PID
- Cervical spondylosis (osteoarthrosis)

Cervical Spondylosis

- Spondylosis is the most common disorder of the cervical spine. Universal in patients over the age of 40 but seldom causes symptoms
- Intervertebral discs degenerate and flatten (ie not synovial ⇒ not OA)
- Bony spurs appear at the anterior and posterior margins of the vertebral bodies. Posterily, these may encroach upon the intervertebral foramina, causing pressure on the nerve roots
- Clinical features:
  - Neck pain and stiffness, usually gradual onset and worse on getting up
  - Pain may radiate widely, to occiput, scapular muscles and down one or both arms
  - May be paraesthesia, weakness and clumsiness
  - Weakness of the legs or bladder disturbance suggest cervical cord compression
  - The appearance is normal. Tenderness occurs in the posterior neck muscles and scapular region, all movements are limited and painful
- Differential Diagnosis:
  - Thoracic Outlet Syndrome: pain in the ulnar forearms and hand
  - Carpal Tunnel Syndrome: pain and paraesthesia are worse at night. Nerve conduction is slowed across the wrist
Rotator cuff lesions: pain is like one of a prolapsed cervical disc, but shoulder movements are abnormal and there are no neurological signs

Cervical tumours: symptoms are not intermittent and x-ray may be abnormal

X-ray: cervical disc spaces are narrowed. Corners of vertebrae have osteophytes. Oblique views may show encroachment of the intervertebral foramina

Treatment:
- Heat and massage are soothing
- Neck collar is the most effective treatment during painful attacks
- Physiotherapy
- Surgery is seldom indicated but if necessary then anterior fusion is appropriate

Prolapsed Cervical Disc
- May be precipitated by local strain or injury, esp. sudden flexion and rotation
- May be a predisposition abnormality of the disc with increased nuclear tension
- Prolapsed disc may press on:
  - Posterior longitudinal ligament, causing pain and stiffness
  - Nerve roots, causing pain and paraesthesia in one or both arms
- Usually occurs above or below the 6th cervical vertebra, nerve roots are C6 and C7
- Presentation:
  - Usually acute in onset and more severe than those of neck strain
  - Pain may be referred into the scapula, shoulder or hand and there may be associated paraesthesia
- Differential:
  - Cervical spine infections, pain is unrelenting and local spasm severe, x-ray show erosion of the vertebral end-plates
  - Cervical tumours, neurological signs are progressive and x-rays show bone destruction
- X-rays may show slight narrowing of the disc space. Disc itself is best seen on MRI
- Treatment:
  - Rest: in a collar to prevent unguarded movement
  - Reduce: traction may enlarge the disc space
  - Remove: if symptoms are severe enough the disc may be removed

Injuries of the Cervical Spine
- # of C1: Jefferson’s
- # pedicles of C2: Hangman’s #
- # of odontoid peg
- Wedge/compression #
- Burst #
- #/dislocation
- Avulsion #: Clay shovellers #

Back Pain & Conditions

Background
- Very common (60-80% of the population)
- Most is temporary (90% < 3/12)
- Must be distinguished from serious cause (tumour/infection < 1% of cases) → look for red and yellow flags
- Mechanical back pain is that that is associated with movement or posture

Sources of Pain
- Local: processes compressing or irritating nerve endings, e.g. fractures or tears. If it does not vary with change in position then spinal tumour or infection
- Pain referred to spine: arises from abdominal or pelvic viscera. Often unaffected by position of spine
• Pain of spinal origin: upper lumbar REFERS to groin or anterior thighs. Lower lumbar REFERS to buttocks, posterior thighs or calves/feet (is referred, not due to nerve root compression)
• Radicular back pain: sharp and radiates from spine to leg in territory of nerve root. Coughing, sneezing or voluntary contraction of abdominal muscles often elicits radiating pain. ↑ pain in postures which stretch the nerve root (e.g. sciatic nerve – L5 & S1 - when sitting as it passes posterior to hip, but not femoral nerve – L2 – L3 as it passes in front of the hip)
• Pain associated with muscle spasms: accompanied by abnormal posture, taut para-spinal muscles and dull pain
• Very hard to differentiate lower back pain → cheat and call it lumbar spine dysfunction!

Classification
- Pathological (5%): infection, inflammation, metabolic bone disease, neoplasm
- Referred (5%): abdominal or pelvic organs
- Mechanical (95%):
  - Muscle/ligament injury
  - Intervertebral disc injury
  - Spondylolysis and spondylolisthesis

Age
- Children: congenital or developmental disorders, infection, primary tumours (ie don’t ignore back pain in children)
- Younger adults: disc disease, spondylolisthesis, acute fractures
- Older adults: spinal stenosis, metastatic disease, osteopenic compression

Injuries
- Hyperflexion → wedge/crush fracture around T12 – L2; usually stable
- Shearing → anterior or posterior displacement, intervertebral ligaments torn; maybe #-dislocation with damage to facet joints
- Hyperextension: tears longitudinal ligaments, widens anterior disc space
- Axial compression: squeezes T4 – L5 → disc squeezes out and disrupts longitudinal ligaments
- Spondylolisthesis: defect/fatigue fracture in the pars interarticularis. Most common cause of low back pain in children and adolescents. Defect in the neck of the ‘Scottie dog’ on oblique x-rays
- Stable injuries: vertebral components will not be displaced by normal movements; an undamaged cord is not in danger
- Unstable injuries: further displacement and damage may result from movement
- Complete injuries to lumbar vertebrae:
  - Involving cauda equina + nerve roots
  - Flaccid paralysis + eventual wasting of leg muscles
  - Loss of sensation in lower limbs
  - Variable effects on bowel/bladder function, including loss of reflexes initiating micturition + defecation tone
- Complete lesions in thoracic region:
  - Result in paraplegia (spastic paralysis of the legs)
  - Reflex spasms
  - Loss of sensation distal to the lesion
  - No voluntary control of bladder, bowel + sexual function, although automatic function is ultimately established
- Complete lesions in the cervical regions:
  - Result in quadriplegia
  - Partial or complete involvement of the arms
  - Similar effects on organ function to paraplegia
  - High lesions result in phrenic nerve paralysis + resp failure
- Spinal shock:
  - Immediately after a severe spinal injury, a transient depression of all reflex activity is superimposed on either temporary or permanent local neural damage
  - See flaccid paralysis of all distally supplied muscles + hypotension due to vasodilation below the level of injury
  - Recovery may take days to up to 6/52
Mechanical Back Pain

- Related to movement and posture
- Often no obvious pathology – following trauma or progressive onset. But major cause of people off work etc
- Includes muscle/ligament injury, disc disease, disc protrusion, OA facet joints, spinal stenosis, spondylolisthesis etc
- Spinal movement is complex ⇒ there are many components that could cause pain
- Not related to old age: most common in 25 – 60 year olds
- Patterns:

<table>
<thead>
<tr>
<th>Disc Pain</th>
<th>Facet Joint Pain</th>
<th>Nerve Root Pain</th>
<th>Spinal Stenosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Location of pain</td>
<td>Worst in back. May spread to buttocks or legs</td>
<td>Worst in back. May spread to buttocks or legs</td>
<td>Mainly in legs, may be some in the back</td>
</tr>
<tr>
<td>Pattern</td>
<td>Intermittent or varying intensity</td>
<td>Always intermittent</td>
<td>Usually constant</td>
</tr>
<tr>
<td>Pain worse with</td>
<td>Sitting, bending forward</td>
<td>Bending backwards, standing/walking for long periods</td>
<td>Sitting and bending, and by backwards movement if acute</td>
</tr>
<tr>
<td>Pain better with</td>
<td>Bending backwards, walking better than standing better than sitting</td>
<td>Lying face down, or on back with legs drawn up</td>
<td>Sitting forward, sitting</td>
</tr>
<tr>
<td>Exercises</td>
<td>Face down, push up with hands arching spine</td>
<td>Lie on back, knees to chest. Pelvic tilt (→↑ tilt on walking)</td>
<td>Lie on back on the floor with knees over a chair</td>
</tr>
</tbody>
</table>

- Lumbar Spondylosis:
  - Degeneration of joints and intervertebral discs
  - Gel of nucleus pulposus shrinks and loses compliance causing circumferential bulging of annulus fibrosis
  - Osteophytes may form
  - Most common sites are L5/S1 and L4/L5
  - Facet joint syndrome – secondary osteoarthritis of the facet joints. Pain worse on extension
  - Presentation: midline pain radiating to groin or buttock, worse towards the end of the day, aggravated by coughing or sneezing. Straight leg raising is normal
  - Treatment: analgesics, physio, spinal fusion

- Acute lumbar disc prolapse:
  - Nucleus pulposis extrudes into a fissure in the annulus and bulges beneath the posterior longitudinal ligament:
    - Pressure on ligament → back ache
    - Pressure on dural envelope of the nerve root → pain referred to lower limbs (sciatica)
    - Compression of nerve root → paraesthesia and muscle weakness
  - Symptoms:
    - Back pain (worse on coughing)
    - Buttock pain + sciatica
    - Nerve root paraesthesiae
    - Nerve root weakness
    - Urinary retention (cauda equina compression)
  - Signs:
    - Sciatic scoliosis + flattened lordosis
    - Spasm
    - Tenderness
    - SLR positive + sciatic stretch
    - Neurological signs
  - Posture: stand forwards and sideways tilt
  - Sudden onset lasting for hours/days. Local tenderness and loss of spinal mobility
  - Differential:
    - Inflammation (eg due to Ankylosing Spondylitis or Tb)
    - Vertebral tumours → constant pain
    - Nerve tumours cause sciatic but constant pain
  - X-ray to exclude bone disease. CT/MRI best for localising the lesion
  - Treatment:
Musculo-skeletal, Rheumatology and Plastics

- Rest: most resolve spontaneously
- Reduction: continuous bed rest and pelvic traction for 2 weeks
- Removal: if cauda equina compression, persistent pain after 2 weeks or neurological deterioration
- Rehabilitation: isometric exercises and advice on bending/lifting

- **Spinal stenosis:**
  - Due to progressive loss of disc height, OA of facet joints, posterior osteophytes (ie degenerative) or occasionally congenital
  - Rarely → **neurogenic claudication** (nerve root ischaemia) when walking. Due to ↓ blood flow to the cauda equina (whose metabolic needs ↑ on walking)
  - Differential of vascular and neurogenic claudication:

<table>
<thead>
<tr>
<th>Activity</th>
<th>Vascular Claudication</th>
<th>Neurogenic Claudication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Walking</td>
<td>Distal → proximal pain, calf pain</td>
<td>Proximal → distal pain, thigh pain, symmetrical, tingling nerve pain</td>
</tr>
<tr>
<td>Uphill walking</td>
<td>Symptoms occur</td>
<td>Symptoms don’t occur (leaning forward opens up spinal canal)</td>
</tr>
<tr>
<td>Rest</td>
<td>Relief with standing</td>
<td>Relief when sitting or bending</td>
</tr>
<tr>
<td>Bicycling</td>
<td>Symptoms develop</td>
<td>Symptoms do not develop</td>
</tr>
<tr>
<td>Lying flat</td>
<td>Relief</td>
<td>May exacerbate symptoms</td>
</tr>
<tr>
<td>Treatment</td>
<td>Vascular bypass</td>
<td>Usually have foot pulses (if these are present, not vascular). Rest, decompressive laminectomy</td>
</tr>
</tbody>
</table>

- **Spondylolisthesis:**
  - Anterior or posterior displacement of a vertebrae with or without preceding injury (usually L5 slides forward on S1)
  - Can be congenital (eg defect of articular processes) or acquired (degenerative, trauma, OA of facet joints, pathological, fracture of the neural arch, elongation of the pars interarticularis)
  - Isthmic spondylolisthesis (which includes lytic or stress fracture, an elongated but intact pars or an acute fracture of the pars)
  - Requires bilateral interarticular defect → instability
  - X-ray (AP and lateral) if:
    - < 20 years or > 50 years
    - Suspicious pain
    - Worse at night and in morning (inflammation, infection, tumour)
    - Neurological signs (→ CT/MRI)
  - Management:
    - Conservative: lumbosacral support, exercises to build extensor and abdominal muscles (core strengthening)
    - Surgery: Nerve release and spinal fusion

- **Other non-mechanical back-pain:**
  - Sway Back: pregnancy: altered spinal posture and ligamentous laxity. Conservative treatment
  - Osteoporotic: painless or agonising localised pain that radiates around ribs and abdomen. Caution with spine physio: mechanical lever arm forces on vertebrae are very strong → easy damage
  - Psychogenic pain is a contributing factor in some. Look for signs of secondary gain

**Localisation of Lumbar Root Nerve Entrapment**

<table>
<thead>
<tr>
<th>Nerve Root</th>
<th>Pain felt</th>
<th>Sensory Changes</th>
<th>Reflex Loss</th>
<th>Weakness</th>
</tr>
</thead>
<tbody>
<tr>
<td>L2</td>
<td>Upper thigh</td>
<td>Front of thigh</td>
<td>None</td>
<td>Hip flexor and adductors</td>
</tr>
<tr>
<td>L3</td>
<td>Lower thigh</td>
<td>Inner thigh &amp; knee</td>
<td>Knee</td>
<td>Knee extension</td>
</tr>
<tr>
<td>L4</td>
<td>Knee to med mal</td>
<td>Inner calf</td>
<td>Knee</td>
<td>Knee extension</td>
</tr>
<tr>
<td>L5</td>
<td>Lat shin → dorsum of foot + big toe</td>
<td>Outer calf, upper inner foot</td>
<td>None</td>
<td>Inversion, dorsiflexion of toes</td>
</tr>
<tr>
<td>S1</td>
<td>Post calf → lat foot + little toe</td>
<td>Lateral borders/ sole of foot</td>
<td>Ankle</td>
<td>Plantar flexion</td>
</tr>
</tbody>
</table>

**Spinal Tumours**
- Spine is a common site of mets spread:
  - Breast
  - Prostate
Musculo-skeletal, Rheumatology and Plastics

- Thyroid
- Lung
- RCC
- Almost all give abnormal CRP/ESR
- Suspect if red flags

Spinal Infection
- Starts in the disc (discitis)
- If diagnosed early usually does not need surgery (aspirate suspicious disc for organism prior to Rx of appropriate a/biotics)
- May be primary, secondary or post-operative
- NB. Pott’s disease is extra-pulmonary TB of the spine

Scheuermann’s Disease
- Is a self-limiting skeletal disorder of adolescence
- Pathology: osteochondrosis (osteochondritis) of the secondary ossification centers of the vertebral bodies
- The vertebrae grow unevenly with respect to the sagittal plane; that is, the anterior angle is often greater than the posterior. This uneven growth results the signature "wedging" shape of the vertebrae, causing kyphosis
- Seen in 3 adjacent vertebrae

UMN Lesions
- SC ends at L1, therefore lesions above this level (eg posterior disc prolapsed causing central compression) can cause UMN signs
- Spasticity, clonus, hyperreflexia, Babinski

Investigations
- None in 1st 4-6 wks UNLESS red flags (low yield/ high expense)
- XR/bloods: CRP, ESR/MRI if sx of infection/tumour
- Cauda equina syndrome: urgent ortho referral /MRI

Management of Back Pain
- Mechanical BP:
  - Prevention
  - Rest, warmth, simple analgesia
  - Physio
  - Spinal support or brace
  - Epidural injection
  - Surgery
- Conservative:
  - 80 – 90% of back pain resolves in 4 – 6 weeks
  - Firm bed (eg a board underneath)
  - No slouching, education on how not to stress back
  - Analgesia (→ break cycle of muscle spasm)
  - No bed rest, early return to work
  - Warmth, analgesics
  - Promote self care and responsibility →↓dependence
  - Stay active. Eg swimming. But may need to modify normal activities. Lift carefully, wear low heeled shoes, chair which helps good posture, pillow between knees at night, walking, cycling, swimming
  - Exercises only help with symptoms – don’t affect recovery time
  - Physio – but not while acutely sore
  - Manipulation may help in the first month
  - Advice on prevention
- Check-ups at **1, 4 and 6 weeks** (ACC guidelines)
- If not improved after 2 weeks, consider X-ray, referral, etc
- **Chronic pain:**
  - Maybe weight loss
  - **Avoid sitting for prolonged periods** (discs under ↑ pressure when sitting)
- **Other treatment:**
  - Sciatic pain: epidural steroid injection
  - Surgery: remove disc protrusion, decompression or stabilisation

**Pelvic Injury**

- **Serious**
- Need to check all midline structures: rectum, bladder, urethra, also ureters, iliac vessels
- Immediate risk is bleeding. Usually from **iliac veins – retroperitoneal**
- Signs and symptoms of pelvic bleeding:
  - **Shock** (blood loss, visceral damage)
  - Bruising
  - Abrasions
  - **Ecchymoses** into thigh and perineum
  - Swelling of labia / scrotum, blood at urethral meatus
  - Abdominal tenderness
  - Pain
- **Investigations:**
  - X-rays essential: AP, inlet, outlet, oblique views. **Always look for pairs of fractures**
  - If anterior fracture then must also do x-rays of sacro-iliac joints and lumbar

**Fractures**

- **Structure and stability:**
  - The stability of the pelvic ring depends on both the bony and ligamentous structures
  - The anterior position of the pelvic ring does not participate in normal weight bearing, nor is it essential for maintenance of pelvic stability
  - The posterior arch (sacrum, sacro iliac joint and ilia) all serve as the weight bearing portion of the pelvis
  - The posteriosuperior SI ligaments connecting the iliac tuberosities to the sacrum provide most of the stability to the SI joints
  - Fractures may be unstable or stable (those that don’t involve the pelvic ring or have minimal displacement of the pelvic ring)
- **Types of fractures:**
  - AP compression injury hinges the pelvis open onto the intact posteriosuperior S.I. ligaments. Not grossly unstable
  - Lateral compression. Caused by direct force to iliac crests. May be stable or unstable
  - Vertical shear. Forces through femur directed perpendicularly to the pelvic ring. Causes disruption to the S.I. joint / unimpacted fracture through the sacrum or ilium. Hemipelvis is unstable
  - If >1 fracture then pelvic ring is unstable and up to 25% will have internal injuries
- **Treatment:**
  - **Quick manoeuvre to ↓ bleeding:** internally rotate femurs and tie a towel around the pelvis and pull it tight
  - Most fractures are stable and can be treated conservatively
  - If unstable will require surgical stabilisation
Upper Limb
Shoulder

- Subscapularis attaches to lesser tuberosity, all other RC muscles to GT
- Glenoid labrum deepens the socket
- **Static** stability provided by labrum, capsule + GH ligaments
- **Dynamic** stability provided by RC + biceps
- RC = a cuff that envelopes the humeral head – made up of the 4 tendons of the RC muscles
- Biceps originates from the coracoid + above the glenoid + flexes the elbow, supinates + flexes the shoulder

<table>
<thead>
<tr>
<th>Region</th>
<th>Muscle</th>
<th>Function</th>
<th>Origin</th>
<th>Insertion</th>
<th>Innervation</th>
<th>Blood Supply</th>
</tr>
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<tbody>
<tr>
<td><strong>Anterior Arm</strong></td>
<td>Biceps brachii</td>
<td>Flex shoulder</td>
<td>Long head: supraglenoid tubercle</td>
<td>Bicipital aponeurosis and radial tuberosity</td>
<td>Musculocutaneous</td>
<td>Brachial</td>
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<td></td>
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<td>Flex elbow</td>
<td>Short head: coracoid process</td>
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<td>Supinate when elbow is flexed</td>
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<td>Coracoid process</td>
<td>Upper medial humerus</td>
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<td>Extend elbow</td>
<td>Long head: infraglenoid tubercle</td>
<td>Olecranon process of ulna</td>
<td>Radial</td>
<td>Profunda brachial</td>
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<td>Short and medial head: posterior humerus shaft</td>
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<td>Pronator teres</td>
<td>Pronation</td>
<td>Medial condyle humerus, coronoid process of ulna</td>
<td>Middle lateral radius</td>
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<td>Flex elbow</td>
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<td>Flexor carpi radialis</td>
<td>Flex wrist Abduct wrist</td>
<td>Medial epicondyle humerus</td>
<td>Base metacarpal 2</td>
<td>Median</td>
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<tr>
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<td>Flexor digitorum profundus</td>
<td>Flex entire fingers 2-5</td>
<td>Proximal 3/4 anteromedial ulna</td>
<td>Body middle phalanges 2-5</td>
<td>Median and ulnar * (to medial head)</td>
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<td>Flexor pollicis longus</td>
<td>Flex metacarpophalangeal 1</td>
<td>Anterior radius</td>
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<td>Anterior interosseus (br. of median)</td>
<td>Ulnar interosseus</td>
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<td>Distal anterior radius</td>
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<td>Extensor carpi ulnaris</td>
<td>Extend wrist</td>
<td>Lateral epicondyle humerus Posterior ulna</td>
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<td>Extensor digitorum minimi</td>
<td>Extend entire finger 5</td>
<td>Lateral epicondyle humerus</td>
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<td>Extensor digitorum</td>
<td>Extend entire fingers 2-5 Extend wrist</td>
<td>Lateral epicondyle humerus</td>
<td>Extensor expansion digits 2-5</td>
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<td>Interosseus recurrent</td>
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<td>Posterior interosseus (br. of deep radial)</td>
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<td>Posterior interosseus (br. of deep radial)</td>
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<tr>
<td><strong>Deep extensor forearm</strong></td>
<td>Supinator</td>
<td>Supination</td>
<td>Lateral humerus and elbow ligaments</td>
<td>Wraps around radius shaft</td>
<td>Deep radial</td>
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<td>Abductor pollicis longus</td>
<td>Abduct thumb</td>
<td>Middle posterior radius and ulna</td>
<td>Base metacarpal 1</td>
<td>Deep radial</td>
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<td>Extensor pollicis brevis</td>
<td>Extends thumb carpometacarpal</td>
<td>Posterior radius</td>
<td>Proximal phalanx 1</td>
<td>Posterior interosseus (br. of deep radial)</td>
<td>Posterior interosseus</td>
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<td>Posterior interosseus (br. of deep radial)</td>
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<td>Anconeus</td>
<td>Assist triceps in elbow flexion</td>
<td>Lateral epicondyle humerus</td>
<td>Olecranon</td>
<td>Radial</td>
<td>Middle collateral</td>
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<tr>
<th>Muscle Group</th>
<th>Action 1</th>
<th>Action 2</th>
<th>Action 3</th>
<th>Action 4</th>
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<tr>
<td>Thenar</td>
<td>Abductor pollicis brevis</td>
<td>Abduct thumb</td>
<td>Oppose thumb</td>
<td>Flexor retinaculum</td>
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<td>Flexor pollicis brevis</td>
<td>Flex thumb</td>
<td>Flexor retinaculum</td>
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<td>Recurrent median</td>
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<td>Opponens pollicis</td>
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<td>Recurrent median</td>
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<td>Flex metacarpo-phalangeal 5</td>
<td>Hamate hook</td>
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<td>Oppose digit 5</td>
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<tr>
<td>Hand</td>
<td>Adductor pollicis</td>
<td>Adduct thumb</td>
<td>Metacarpals 2, 3</td>
<td>Capitate</td>
<td>Medial base proximal phalanx 1</td>
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<td>Palmaris brevis</td>
<td>Draw medial skin of palm to center</td>
<td>Hypothenar fascia</td>
<td>Skin of medial palm</td>
<td>Superficial ulnar</td>
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<tr>
<td></td>
<td>Lumbricals</td>
<td>Flex metacarpo-phalangeal, extend interphalangeal</td>
<td>Flexor digitorum profundus tendons</td>
<td>Proximal phalanx, lateral side</td>
<td>Median and ulnar</td>
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<tr>
<td></td>
<td>Dorsal interossei (4)</td>
<td>Abduct fingers</td>
<td>Adjacent metacarpals</td>
<td>Proximal phalanx, on side closer to midline</td>
<td>Ulnar</td>
</tr>
<tr>
<td></td>
<td>Palmar interossei (3)</td>
<td>Adduct fingers</td>
<td>Metacarpals, on side away from midline</td>
<td>Proximal phalanx, on side away from midline</td>
<td>Ulnar</td>
</tr>
</tbody>
</table>

**History**
- Pain
- Stiffness
- Trauma
- Mechanical derangement (eg recurrent dislocation)

**Exam**
- Inspect:
  - Compare both sides, comment on asymmetry/scars/swellings/skin changes/muscle wasting
  - Effusions not seen unless significant
  - Look at each muscle group
  - If shoulder dislocated, there will be a convexity or flattening of the deltoid below the acromion (looks square instead of rounded)
- Palpate:
  - For tenderness and swelling
  - Start at sterno-clavicular joint → AC joint and corocoid process → gleno-humeral joint → spine of scapula
  - Feel along **groove between acromion process and head of the humerus for ligaments of teres minor, infraspinatus and supraspinatus** (supraspinatus most superior + anterior, infraspinatus a little further posterior + teres minor more posteroinferior)
  - Feel along **bicipital groove** (long head of biceps runs here)
  - Feel and look in **axilla: lymph nodes**, check soft tissues for swelling/tenderness
- Move:
  - If active movement is reduced, try passive movement for the remainder of the normal range
  - Do forced adduction with hand over opposite shoulder for AC joint dysfunction (cross-shoulder adduction test)
Abduction: test with elbow flexed. Test passively from behind. Normal is 90°. Hands behind head
Adduction to 50° across the front of the chest. Pain in full adduction if AC joint injury. Hands behind back
External rotation: with elbow flexed to 90°, can externally rotate to ~ 60°. Good test of glenohumeral joint (eg for frozen shoulder). To disable scapular movement and test capsule ROM, lie pt supine and abduct arm to 90° then measure ER (↓ in frozen shoulder)
Internal rotation: test actively: place hand behind back and scratch as high as they can. Compare with good arm. To disable scapular movement and test capsule ROM, lie pt supine and abduct arm to 90° then measure IR (↓ in frozen shoulder)
Flexion: If done actively, possible to 180°. Thumbs facing forwards, arms straight. Look for painful arch from 60 – 120° due to insertion of inflamed rotator tendons catching on the acromion. Is it the same with the arm laterally or medially rotated? Checks for tendon impingement
Extension is possible to 65°

• Special tests: 3, 3, 3 (rotator cuff, impingement, instability)
• Rotator Cuff muscles:
  • Pain worst at 90° abduction
  • Subscapularis: ‘Lift-off test’: Hold hand behind back, with patient pushing out from their back. Try and push them in (Pectoralis Major inactive in this position). Test both individually
  • Supraspinatus: test abduction against resistance, with shoulders abducted to around 30° and thumbs pointing to the ground (turns the glenoid tubercle forward → greater impingement)
  • Infraspinatus + teres minor: externally rotate against resistance

• Impingement tests:
  • Neer’s test: for rotator cuff impingement (flexion of internally rotated arm)
  • Hawkın’s test: for rotator cuff impingement (shoulder + elbow flexed to 90° → now internally rotate)
  • Pain on active abduction

• Instability tests:
  • Sulcus test: pull arm down and look for sulcus deep to the deltoid muscle (distracting the gleno-humeral joint) (actually more of a sign – inspect for this rather than pulling on arm)
  • Anterior drawer test: from the side, hold acromion and corocoid process between your thumb and index finger, hold proximal humerus between the other thumb and forefinger and try and push forward and backwards against each other (see below)
  • Apprehension test for dislocating shoulder: posterior pressure during elevation on an abducted and externally rotated arm

• Other tests:
  • Cross-adduction test for ACJ
  • Push-ups against the wall: look for winging of scapula → serratus anterior dysfunction
  • Apley scratch test

• Examine joint above + below: always examine NECK and ELBOW (joint above and joint below) and distal pulse and SENSATION OVER DELTOID

• X-rays:
  • Do AP and lateral obliquely – as scapular is oblique and don’t want spine and other shoulder in the lateral film
  • Can do an axillary film: abducted 90% and x-rayed from above

• Differentiating:
  • Intra-articular disease → painful limitation of movement in all directions
  • Tendonitis → painful limitation of movement in one plane only
  • Tendon rupture and neurological lesions → painless weakness
  • Referred pain:
    ○ Cervical root lesions (eg due to cervical spine lesions)
    ○ Brachial plexus, thoracic outlet syndromes
    ○ Referred pain from abdominal visera, diaphragm

Injury & Conditions
• Most frequently affected by non-arthritic conditions involving bursa and surrounding tendons: tendonitis, bursitis, frozen shoulder
• RC lesions present as 5 more or less distinct clinical syndromes:
  • 1. Acute tendinitis
  • 2. Chronic tendinitis (impingement syndrome)
  • 3. Tears of the RC
  • 4. Adhesive capsulitis (frozen shoulder)
5. Biceps tendon lesions

**Frozen shoulder:**
- *Adhesive Capsulitis*
- Characterised by pain + immobility/stiffness
- Gradual onset of pain, pain at night, then ↑stiffness as pain gradually subsides
- May follow minor trauma
- ↓Active and passive movement in all directions, following minor trauma. Cause unknown – but ?due to a tendonitis/capsulitis → adhesion of capsule to the humeral head
- Treatment: cautious physio (but not in the inflammatory phase [the painful phase]), mobilisation, NSAIDs, corticosteroid injection into subacromial bursa
- Prognosis: resolution may take years
- Differential:
  - Disuse stiffness
  - Complex Regional Pain Syndrome Type 1

**Rotator Cuff Impingement:**
- *Humeral head is held in place by the rotator cuff muscles forming part of the joint capsule:* infraspinatus posteriorly, supraspinatus superiorly, teres minor and subscapularis anteriorly
- *Impingement of rotator cuff tendons occurs under the coraco-acromial arch.* May be due to osteophytes or narrowing under the coraco-acromial arch. *A painful arc with active abduction occurs*
- With age or injury the tendons of these muscles are prone to hyaline degeneration, fibrosis and calcification → friction, swelling and pain. Prone to rupture
- Tendonitis of more than one tendon ⇒ rotator cuff syndrome
- Presentation:
  - Local tenderness over rotator cuff insertion
  - Supraspinatus tendonitis: the most common: pain on abduction of the arm
  - Subscapularis tendonitis: pain on *internal rotation*
  - Infraspinatus tendonitis: pain on *external rotation*
  - May be accompanied by bicipital tendonitis: pain on resisted *forearm flexion and supination* and on pressure on the tendon of biceps in the bicipital groove
- Treatment:
  - Conservative:
    - NSAIDs
    - Local injection of steroid with local anaesthetic to tendon insertion
    - Rest shoulder initially, in sling if necessary
    - Short-wave diathermy, ultrasound therapy to reduce pain
    - Exercise to lessen the risk of adhesive capsulitis or help restore movement
  - Surgical:
    - ‘Decompress’ the subacromial space by excising the inferior acromion
    - *Excise the coraco-acromial ligament,* anterior acromial process or any obstructive masses
    - Cuff reconstruction for large tears

**Rotator cuff tears:**
- Causes: trauma or degeneration within the cuff
- Hx: chronic pain felt over *deltoid muscle,* especially at one point of abduction
- Exam: look for wasting (especially supraspinatus); *active abduction is ↓* but a full range of passive movement
- Management: partial tears heal with rest + rehab; tears in the elderly should be treated conservatively; should be repaired in the young

**Calcific tendonitis:**
- = deposition of *calcium hydroxyapatite crystals* within the tendon of supraspinatus → local inflammation + muscle spasm
- Presentation: initially pain is dull but pain becomes ↑ *severe* over hours
- Exam: arm held still; *diffuse tenderness* over whole shoulder; ↓ *ROM* due to pain
- Management: rest, NSAIDs, LA injections; surgical = incise the tendon to release the calcific deposit

**Anterior dislocation:**
- Head of humerus anterior to the glenoid fossa:
  - Usually sub-glenoid (ie also inferiorly displaced)
  - Can rarely be subclavicular
- Mechanism: arm abducted and externally rotated then hit from behind (eg tackle injury)
- Clinical: very painful. Patient holds arm at elbow to prevent any movement. Palpate under acromion, is humeral head there?
- Consequential injuries:
  - Check *axillary nerve* (cutaneous sensation from axillary nerve palsy over regimental badge area [over deltoit on upper arm] and action of teres major – medial rotator and adductor - and deltoit – abduction)
  - Hill-Sacks lesion: injury to posterior head of humerus due to repeated trauma: humeral head vs glenoid
  - Bankart lesion: injury to the anterior margin of the glenoid fossa
- Reduction:
  - Kocher
  - Hippocratic manoeuvres
- Management: immobilisation in a sling for 2 to 3 weeks while structures anterior to glenohumeral joint heal (otherwise recurrence), then physio avoiding external rotation
- Posterior dislocation:
  - Mechanism: direct trauma from the front, electric shocks or seizures
  - Head of humerus lies posterior to glenoid
  - Clinical: pain, deformity, local tenderness

**Shoulder Instability**: 2 types:
- Atraumatic, multidirectional (ie generalised laxity), bilateral, treatment: rehab (Physio)
- Traumatic, unidirectional/unilateral, Bankart Lesion (capsule at the front detaches from the glenoid), Treatment: surgery. Progressively less traumatic force required to dislocate it. *External rotation causes apprehension*

**Fracture of Clavicle**:
- Mechanism: *FOOSH*
- Clinical: arm clasped to chest to prevent movement, subcutaneous lump
- Xray: usually middle third
- Treatment: support arm in sling until pain subsides (2-3 weeks)

**A/C joint OA**:
- Often secondary to trauma
- Pain on top of the shoulder is a feature + aggravated by lifting the arm above the head or across the body (passively)

**A/C Joint dislocation/subluxation**:
- Mechanism: usually involves fall in which patient rolls on shoulder
- Clinical: outer end of clavicle prominent, local tenderness present. Confirm subluxation by supporting elbow and detecting movement of clavicle downwards.
- Clavicle is usually attached to the acromion by the ac joint, coroid ligament and trapezoid ligament. In serious injuries all three of these areas can be damaged
- Treatment: *broad arm sling for 4-6 weeks* usually sufficient

**Infantile Torticolis**: Two types:
- Congenital shortening of sterno-mastoid muscle
- Neurological: damage to the spinal accessory nerve from infected lymph nodes in the posterior triangle

**Brachial Plexus injury**:
- *Erb’s Palsy*: C5, C6: *paralysis of deltoid, supraspinatus, teres major, biceps* → waiter’s tip position
  - Klumpke’s Paralysis: C8, T1: arm in adduction, paralysis of small muscles of the hand. May also be Horner’s syndrome

**Biceps/bicipital tendonitis**:
- Inflammation that causes *pain in the front part of the shoulder* or upper arm
- Biceps tendonitis occurs from *overuse* of the arm and shoulder or from an injury to the biceps tendon
- Pain when moving arm and shoulder, especially on forward arm movement over shoulder height
- Tenderness when you touch the front of the shoulder
- Torn **long** head of biceps:
  - Degeneration + disruption are common; usually middle age or elderly
  - Whilst lifting a heavy object, snap is felt → aching + bruising
  - When elbow flexed, muscle contracts into a prominent lump
- Humeral #s: see right

### Upper Arm and Elbow

#### History
- Stiffness
- Pain
- Locking
- Past trauma

#### Exam
- GIPMON
- **Inspect**: in the elbow, look for:
  - Shape, carrying angle (normal = 8-10° valgus)
  - Muscle bulk/wasting
  - Scars, swelling, skin changes
  - Lumps: rheumatoid nodules, gouty tophi, enlarged olecranon bursa
- **Palpate**:
  - Temperature
  - Tenderness over the *lateral epicondyle* (tennis elbow) or *medial epicondyle* (golfer’s elbow)
  - Tenderness over **radial nerve** (feel over radial tunnel – arcade of Frohse) + pain on resisted supination
  - Tenderness over radial collateral ligament and radial head
  - Tenderness over olecranon fossa and *olecranon bursa* and triceps insertion
  - Tenderness over *biceps tendon* + *aponeurosis* (lacertus fibrosus)
• Move:
  ➢ F & E: normal range is from 0° – 150°. Limitation of extension →
  early synovitis
  ➢ Pain on resisted extension = tennis elbow
  ➢ Pronation & supination (with shoulders adducted)
  ➢ Ligament stability

• Neurovascular:
  ➢ Depending on indications, test ulnar/radial nerves

• Examine joint above + below

• Radiology of elbow:
  ➢ If looking for effusion on an x-ray (eg blood in joint following fracture
  of the head of the radius) look for protrusion of the Haversian fat
  pads in the coronoid and olecranon fossa → radiolucent triangles
  ➢ Avulsion of the medial epicondyle in children: ‘Little leaguers’ injury from pitching in baseball
  ➢ Medial = trochlear articulates with the ulnar (literally = ‘pulley’)
  ➢ Lateral = capitulum articulates with the radius (TUCR)

Injury

• Fracture of proximal humerus:
  ➢ Mechanism: fall on outstretched arm, most common in post menopausal women
  ➢ Clinical: appearance of large bruise on upper arm. Signs of axillary nerve or brachial plexus injury should
  be sought. Exclude dislocation of the shoulder
  ➢ Treatment: sling. Begin mobilising early as pain permits: gentle arm swinging, climbing fingers up the wall.
  If > 2 parts fractured, then surgery
  ➢ Major complication: shoulder stiffness

• Humeral shaft fractures:
  ➢ Most treated conservatively – u-slab, collar and cuff, sling, brace, etc.
  ➢ Complication: risk of radial nerve injury in spiral groove

• Supracondylar fracture of the humerus:
  ➢ Eg child falling onto outstretched hand
  ➢ Radial pulse may not return for 24 hours
  ➢ Can lead to Volkmann’s Ischaemic Contracture due to disruption to the brachial artery. Muscle necrosis
    (especially FPL and FDP) → flexion deformity at elbow and wrist. Arm is blue, there is no radial pulse and
    passive finger extension is painful (the key sign)
  ➢ Cast in < 90° flexion

• Fractured Head of Radius:
  ➢ Mechanism: FOOSH forces elbow into valgus. Common in adults
  ➢ Clinical: Painful rotation of forearm, tender
  ➢ Treatment: Sling

• Fractures of Olecranon:
  ➢ Mechanism: direct # due to blow or fall on elbow causes a comminuted fracture. Indirect # = clean
    transverse break is due to traction when patient falls on hand whilst triceps contracted (attaches to
    olecranon)
  ➢ Clinical: graze or bruise over elbow. With a transverse fracture there may be a palpable gap and they are
    unable to extend elbow against resistance
  ➢ Treatment: undisplaced transverse needs immobilisation in cast at 60 degrees flexion for 2-3 weeks then
    exercises begun

• Pulled Elbow:
  ➢ Mechanism: radial head stretching annular ligament and slipping out from under its cover. Usually kids 2 –
    6 years old when parents have pulled on child’s arm (esp when crossing road)
  ➢ Clinical: tenderness over radial aspect, supination limited
  ➢ Treatment: sling, usually results in spontaneous reduction

Other Elbow Conditions

• OA:
  ➢ Secondary to trauma
  ➢ Pain + stiffness common, sometimes locking
  ➢ Management: analgesia, strapping, physio; surgery (fusion/elbow replacement/removal of loose bodies)

• RA:
- Often involved in RA
- Pain, swelling, stiffness
- Management: control RA; surgical (synovectomy, radial head excision, fusion, replacement)

**Tennis elbow:**
- *Enthesitis* (enthesis = sites of tendon or ligament attachment to bone) of the **common extensor origin on the lateral epicondyle of the humerus** → pain on contraction/stretching of the **forearm extensors**
- Assessment:
  - Loathe to move elbow
  - Localised tenderness over CEO
  - Pain on passive stretching of CEO
  - Pain on resisted extension of wrist
- Management: rest, physio, NSAIDs in the early stages, steroid injections, surgery later on

**Golfer’s elbow (or any throwing sport):**
- *Enthesitis* of the common flexor origin on the **medial epicondyle**
- Same treatment as tennis elbow

**Olecranon bursitis:**
- Due to superficial nature, is prone to inflammation due to acute or repetitive trauma
- Can be painful or painless

**Radial tunnel syndrome:** pain on resisted supination +/- sensory change in radial nerve

**Ulnar nerve entrapment:**
- Fracture at elbow causing valgus deformity + subsequent attenuation of the nerve or prolonged or recurrent pressure on the ulnar nerve → compression of the nerve in the **cubital tunnel**
- Can also see compression at the wrist in the ulnar (*Guyon*) canal **between the pisiform + hook of hamate** but this is less common
- Presentation: weakness/clumsiness of the hand. **Wasting** of the ulnar innervated muscles (hypothenar eminence and the interossei) with sensory loss in the little and ulnar side of 4th fingers
- Exam: *Froment’s sign*: specifically tests adductor pollicis: grip paper between thumb + a flat palm
- Treatment: surgical decompression
- NB: Deep motor branch of the ulnar in the hand can be damaged by recurrent pressure from tools (screwdrivers, handlebars, crutches, etc)

**Forearm, Hand, Wrist**
* ulnar nerve also supplies adductor pollicis *

- Naming:
- Don’t number fingers, **name them**: thumb, index, middle, ring and little
- Don’t describe structures as medial or lateral, use **radial and ulnar**
- Palmar surface of hand = **volar**
- **Carpal tunnel:**
  - Transverse carpal ligament/flexor retinaculum attaches to pisiform, hamulus of hamate, tubercle of scaphoid and trapezium
  - FDS + FDP + FPL run through here (9 tendons) + median nerve
- FDS + FDP are connected to each other by slender tendinous bands called vincula

**History**
- Pain
- Swelling
- Stiffness
- Paraesthesia
- Weakness

**Exam**
- Always examine whole hand and **compare** with other hand
- GIPMON (gait, inspection, palpation, movement, operation, neurovascular)
- **Inspection:**
  - Work from wrist to finger tips, both volar and dorsal aspects of hand. Can do this while patient sitting with hands on pillow
  - Colour, swelling, skin, deformity, wounds, scars, muscle wasting
  - To assess **muscle wasting**, **assess the radial border** (thenar eminence) and the **ulnar border** (hypothenar eminence) ie hands laterally
  - **Fingers:** ulnar deviation, palmar subluxation, joint swelling, Heberden’s, Bouchards nodes, Boutonniere, Swan-neck, Z deformity
  - **Nails:**
    - **Psoriasis:** pitting (small depressions in the nails), onycholysis (white across distal, lateral or proximal portion), hyperkeratosis (thickening of the nail), transverse nail ridges (‘tide marks’ – signs of previous inflammation)
    - **Splinter haemorrhages** in rheumatoid arthritis and SLE
    - **Rheumatoid vasculitis:** small, periungual brown spots
    - Periungual telangiectases in SLE, erythematous and scleroderma
- **Palpation:**
  - And passive movement together: temperature, tenderness, swelling, osteophytes, laxity
  - If complaining of nerve type symptoms → feel over carpal tunnel, also cubital tunnel and arcade of Frohse
- **Move:**
  - **ROM:**
    - **Fingers, wrists:**
      - Do **prayer sign** – if cannot get hand flat, then unable to extend fully
      - Then dorsum of hands together (Phalen’s test)
      - Make a fist to test finger flexion
    - **Forearms:**
      - With shoulders adducted so that when pronating/supinating the shoulders are taken out of play
  - **Neuro:** **duck-hand** – do it here or will forget!
- **Function/Operation:**
  - **Grip strength:** squeeze two fingers
  - Pincer grip
  - Key grip: try and pull thumb and forefinger apart
  - **Opposition:** try and pull thumb and little finger apart
  - Functional test: undo a button, write with a pen
- **Neurovascular:**
  - If carpal tunnel syndrome or injury to hand → do thorough – ie every finger
  - If carpal tunnel → do **straight arm raise** test → straight arms above head for 1 min → if symptoms appear = positive. Also do Phalen’s (active flexion) + Durkan’s (pressure over CT)
  - Quick sensory:
    - “Can you feel me touching you?” “Does it feel normal?” “Does it feel the same on both hands?”
    - Ulnar: pulp of little finger
• Median: pulp of index finger
• Radial: web of dorsum of hand between thumb + index finger

Quick motor:
• Ulnar: abduct fingers (intrinsic muscles) + Froment’s test (hold paper between thumb and palm of hand)
• Median: thumb abduction

Principles of motor testing:
• For individual movements e.g. thumb abduction, move the body part into the required position (e.g. thumb abduction) and ask them to hold it there whilst you try and overcome them
• Want to test intrinsic muscles that have no extrinsic help
• Look for wasting, test power and sensation

Ulnar Nerve (Medial cord, C8, T1)
• Abductor of little finger
• Adductor pollicis: grip paper between thumb and side of index finger and try and pull it away. If they bend the thumb, they’re trying to use flexors to help (ie fail the test)
• Lumbricals: flex MCP and extend IP joints. Ulnar does ring and little finger
• Ulnar claw hand: hyperextend the fingers and the ring and little fingers curve forward due to lack of lumbricals

Median Nerve (Lateral and Medial Cords, C6,7,8,T1):
• Opposition of thumb to little finger: requires median eminence
• NB opposition of the thumb requires flexion, abduction and rotation
• Abduction of thumb: Abductor pollicis brevis and longus (other two muscles of thenar eminence can be ulnar)
• Anterior Interosseous Nerve Compression: compressed under the fibrous origin of flexor digitorum → weakness of FPL, pronator quadratus and flexor profundus to the index and middle fingers → 'Benediction Hand' when they try and make a fist.

Radial Nerve (posterior cord, C5,6,7,8):
• Check back of first web space (between thumb and index finger). Only sensory area reliably supplied by radial nerve
• Motor distribution:
  • Upper arm: triceps
  • Proximal to supinator, this branch innervates ECRL, ECRB, brachioradialis, supinator
  • Distal to supinator tunnel: EI, ECU, APL, EPL, EPB
  • Posterior Interosseous nerve compression: passing through supinator muscle. Weakness of the long finger extensors, short and long thumb extensors but no sensory loss.
• Sensory distribution: Terminal part supplies the dorsum of the hand. Posterior Cutaneous branch supplies a variable area on the back of the arm and forearm
• Common sites affected: axilla (eg pressure from crutches), midhumeral fracture, at and below the elbow (dislocations and Monteggia fractures)

Feel pulses

- Tendons:
  - Inspect for swelling, tendon ruptures
  - Palpate for tendons/sheaths for thickening/nodules/tenderness
- Move:
  • FDP – flexes DIPJ; hold middle phalanx and flex distal phalanx
  • FDS – flexes PIPJ, defunction FDP by holding other fingers in extension, hold proximal phalanx of middle finger, flex finger and distal phalanx should be floppy
  • FPL – flexes IPJ of thumb
  • Extensor tendons – by holding hand out flat with fingers extended
  • Flexor pollicis longus: hold proximal phalanx of thumb and flex the end
  • Extensor pollicis longus: can rupture after a Colles fracture → can’t straighten distal thumb (Mallet Thumb)

- Mallet finger = ruptured extensor tendon
- Boutonniere deformity = disruption of the central slip → FDS dominates, fixed flexion deformity
- Vaughan-Jackson lesion = extensor digitorum communis (EDC) rupture
- Dupuytren’s contracture = thickening of palmar aponeurosis (not tendons)
- Trigger finger = lump forms in tendon disallowing tendon to move through fibrous flexor tunnel/sheath

Testing ligaments:

Musculo-skeletal, Rheumatology and Plastics
- Look for deformity/swelling
- Feel for tenderness
- Move for instability
- Ligaments: test like knee. Opening to the sides, forward and posterior displacement when fully flexed and then when not quite fully flexed
- Napier’s ligament: anterior over the 1st CMC joint

- Test vasculature:
  - Look for colour
  - Feel for temperature/capillary refill/pulses
  - Do Allen’s test: squeeze fist, compress radial and ulnar arteries, open fist, release one artery at a time and time return of colour

**Injuries**

- Fractures of the forearm and wrist:
  - Mechanism: FOOSH; occur commonly in road accidents, direct blow causes transverse at same level. Twisting may cause spiral or oblique fractures at different levels
  - Clinical: Fracture usually obvious. Pulse must be felt and hand examined for circulatory or nerve defects
  - Treatment: Kids only need cast for 6-8 weeks. Adults often require internal fixation.
  - Fractures of either the radius or ulna alone, with shortening (ie angulation or displacement) are associated with dislocation of the other:
    - **Monteggia Fracture:**
      - (MUF! = monteggia ulna fracture)
      - Fracture to proximal ulna and dislocation of radial head
      - Mechanism: fall on hand, body twisting at time of impact
      - Clinical: ulnar deformity obvious, but dislocation may be masked by swelling. Look for pain and swelling on lateral side of elbow. Wrist and hand must be examined for signs of injury to radial nerve
      - Treatment: Restore length to ulna then reduce. Above elbow cast, arm at 90 degrees flexion 6 weeks
    - **Galeazzi Fracture:**
      - Fractured radius and subluxation or dislocation of distal radio-ulnar joint (DRUJ)
      - Clinical: more common than Monteggia, important to check for ulnar nerve injury
      - Treatment: As for Monteggia
  - **Colles’ Fracture:**
    - Fracture of the radius within 2.5cm of the wrist with dorsal angulation/displacement. If displacement occurs the classic dinner fork deformity occurs
    - Mechanism: Most common fracture resulting from a FOOSH. Sometimes the TFCC (Triangular Fibrocartilage Complex) is torn therefore disrupting the DRUJ and causing ulnar angulation also
    - Clinical: Pain and tenderness over distal end of radius after a fall. Deformity and radiology also often definitive
    - Treatment: If displaced then reduce, plaster cast in ulnar deviation and slight flexion for 5-6 weeks with finger and wrist exercises
    - Complications: Radial drift or ulna prominence in mal union. Delayed rupture of tendon of extensor pollicis longus due to roughness at site of injury or decreased blood supply (→Mallet thumb). Carpal tunnel syndrome also possible
  - **Smith’s Fracture:** Due to fall on the back of hand. Reverse of Colles fracture (ie volar displacement rather than dorsal)
  - **Barton’s Fracture:** Intra-articular fracture of the distal radius. Unstable

- Distal radio-ulnar joint:
  - Triangular ligament (TFCC): holds radius in place while it rotates around the ulnar
  - Test for dislocation: grip around the proximal wrist and squeeze or supinate → pain

- **Scaphoid fractures:**
  - Rare in skeletally immature children
  - 2nd in occurrence to radial fracture – usually young adult males
  - Waist of scaphoid the most common site
  - Caused by fall on radial side of outstretched hand → land on tubercle of the scaphoid with wrist hyper-extension
- Blood supply is distal to proximal pole ⇒ prone to avascular necrosis or poor healing
- If suspected treat as a fracture, immobilise joints above and below (i.e. Colles’ cast, with thumb free, up to 10 weeks to healing) – may not see it on first Xray and prone to non-union. Can see on bone scan after about 1 day. However, over diagnosed

- Carpal dislocations:
  - Perilunate dislocation: associated with distal radius fracture. Lunate stays attached to radius, all other carpals dislocated dorsally
  - Trans-scaphoid perilunate dislocation: as for perilunate dislocation, but fracture through the waist of the scaphoid leaves the proximal fragment in place. Treatment: reduction/surgery

- Metacarpal Fractures:
  - 5th most common. Treatment: Buddy strapping, or strapping + slab
  - 1st metacarpal: Bennett’s Fracture – through base of the metacarpal and intra-articular into the 1st CMC joint. Following a fall or blow on a clenched fist or forced abduction of the thumb (skiers). Ligament of Napier can commonly be injured as well. Unstable as oblique and proximal fragment is attached to trapezium and distal fragment has strong muscles attached to it that pull it proximally. Reduce and plaster with thumb held abducted and extended. Transverse fracture is straightforward: Scaphoid cast
  - Multiple metacarpal fractures: twisting and crush injuries. Realignment with Kirschner wires or small bone plate

- Triangular fibrocartilage tears: see chronic pain often related to old sprain – may also be loss of grip strength + clicking on supination. Dx confirmed by arthroscopy

- MCP dislocation: Uncommon. May require open reduction

- Finger injuries:
  - Mallet Finger: can’t extend DIP: rupture or avulsion of extensor tendon, eg by ball hitting outstretched finger. If < one month since injury then splint in extension otherwise surgery (but may not get full flexion back)
  - Button Hole (Boutonniere) Deformity: can’t extendPIP joint of finger and hyperextension of DIP: Rupture/detachment of central slip of extensor tendon with lateral bands slipping down the side of the finger
  - Skiers/Gamekeeper’s Thumb: rupture of the ulnar collateral ligament of the MCP joint of the thumb, caused by forced abduction. If stable then splint. If unstable (can’t oppose fingers) then repair (adductor tendon may get in the way and prevent reattachment)
  - Dislocation of the phalanges: usually always ligament injury as well. Swelling may take up to 2 years to reduce. Reduction can be spontaneous or via longitudinal traction. Buddy strapping + early mobilisation
  - Phalangeal fractures: Buddy taping: encourage flexion, deny rotation, allow for swelling (ie not too tight)

**Other Hand Conditions**

- Dupuytren’s Contracture:
  - Painless fibrosis (thickening + contraction) of the palmar aponeurosis (can also occur on the foot)
  - Usually familial (associations with alcoholism and manual work over-rated), anti-epileptics (phenytoin)
  - Bilateral in 45%, can see plantar aponeurosis (plantar fibromatosis) or penile fascia (peyronie’s disease) involvement
  - Causes puckering of the skin over the distal palmar crease and gradual flexion of the fingers (usually starts at base of ring and little fingers) ⇒ fixed flexion deformities
  - Treatment conservative. If they can’t push their palmar MCP joints into the table then consider surgical release
  - Prognosis worse if younger

- Ganglia:
  - Painless, jelly filled, tense swelling caused by a partial tear or bulging of a joint capsule, a/w joints or tendon sheaths
  - Commonly in the dorsal wrist + foot, can be seen on long bones after trauma
  - May resolve or cause little trouble
  - Signs: tense, fluctuant, globular swelling deep to skin + incompletely mobile on the deep aspect as attached to neighbouring joint or tendon sheath
  - Don’t respond to injection. Surgical excision if symptomatic/cosmetic

- Trigger Finger (Stenosing Tenosynovitis):
  - Flexor tendon inflames and then jams going through entrance to the synovial sheath at the base of the finger (under the palmar crease)
  - May find crepitus, swelling, triggering and tenderness
➢ See triggering when trying to extend; can see fixed flexion deformity late in disease
➢ The affected finger catches in flexion + then straightens suddenly when extending with assistance + a snap (often reproducible)
➢ Common in RA
➢ Treatment: incise the tendon sheath

• de Quervain’s Syndrome:
  ➢ = de Quervain’s stenosing tenovaginitis
  ➢ Stenosing tenosynovitis/inflamed tendon sheath of EPB and APL
  ➢ Pain over the styloid process of the radius (dorsal wrist)
  ➢ Finckelstein’s sign: pain on forcible adduction and flexion of the thumb into the palm
  ➢ Management: Rest, NSAIDs, cortisone injection, surgery (tendon sheath is incised up the middle)

• OA: primary OA is uncommon. Secondary most common after ununited scaphoid # +/- AVN

• Kienbock’s disease: rare; osteochondrosis/osteonecrosis/AVN of the lunate

Carpal Tunnel Syndrome

• Compression of the median nerve as it passes through the carpal tunnel in the wrist
• Epidemiology: Common. Usually women 30 - 50 years
• Causes: due to thickened tendons or synovitis in the carpal tunnel (or post wrist # or ganglion within carpal tunnel)
  ➢ Rheumatoid arthritis
  ➢ Hypothyroidism
  ➢ Acromegaly
  ➢ Pregnancy (2nd ary to oedema)
  ➢ Obesity
  ➢ Amyloid
  ➢ Diabetes Mellitus
  ➢ Idiopathic

• Symptoms: pain/tingling in the hand and wrist classically in the median nerve distribution (palm and thumb, index and middle fingers). Worse at night/wakes at night, shakes hand, can’t get it comfortable. Loss of grip/clumsiness

• Signs:
  ➢ Wasting of thenar eminence, weak thumb abduction (due to APB NOT APL – as this is in the forearm) and opposition (late signs)
  ➢ Tinel’s test: pain is reproduced by tapping a tendon hammer over the carpal tunnel (bit of a crap test)
  ➢ Phalen’s test: flex both wrists for 30 or 60 seconds – may precipitate paraesthesia if carpal tunnel syndrome
  ➢ Durken’s test: pressure over CT for 1 min
  ➢ Straight arm raise: above head for 1 min → may reproduce pain

• Investigations: median nerve conduction velocity test
• Treatment:
  ➢ Light splint to hold wrist in slight dorsiflexion, NSAIDs and vitamin B6
  ➢ Diuretics
  ➢ Corticosteroid injection
  ➢ Surgical decompression – often see recovery of thenar eminence wasting

Lower Limb

<table>
<thead>
<tr>
<th>Region</th>
<th>Muscle</th>
<th>Function</th>
<th>Origin</th>
<th>Insertion</th>
<th>Innervation</th>
<th>Blood Supply</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gluteal</td>
<td>Gluteus medius</td>
<td>Hip abductor</td>
<td>Dorsal iliac crest</td>
<td>Greater trochanter</td>
<td>Superior gluteal</td>
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<td>Hip medial rotator</td>
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<td>Gluteus minimus</td>
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<td>Tensor fascia lata</td>
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<td>Iliotibial tract</td>
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<td>Lat. circum. fem.</td>
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<td>Stabilizes hip, knee</td>
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All three gluteal muscles act as hip abductors and medial rotators and receive the superior gluteal nerve and artery. Gluteus medius covers gluteus minimus.

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<td>Inf &amp; sup gluteal</td>
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<td></td>
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<td>Obturator internus</td>
<td>Hip lateral rotator</td>
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<td>Inf. gluteal</td>
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<td>Inferior gemellus</td>
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<td></td>
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<td>Quadratus femoris</td>
<td>Hip lateral rotator</td>
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<td>Med. circum. fem.</td>
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<td></td>
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<td>Obturator externus</td>
<td>Hip lateral rotator</td>
<td></td>
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<td>Med. circum. fem.</td>
</tr>
</tbody>
</table>

Hold hands to mimic chicken tail to understand direction of gluteus maximus fibers (inferolaterally) and why it is a hip extensor.

Last 6 muscles are the classic lateral rotators.

All classic lateral rotators insert into greater trochanter, receive sacral plexus and inferior gluteal a. EXCEPT
- Piriformis also gets sup gluteal a. due to position (inf. and sup. gluteal aa. emerge around piriformis)
- Quadratus femoris is lower (no more room on trochanter) and receives med. circum. fem. a.
- Obturator externus must receive obturator n. and a. through obturator canal

Piriformis through quadratus femoris listed in superior-to-inferior order.

Region | Muscle          | Function            | Origin                          | Insertion                  | Innervation      | Blood Supply       |
<table>
<thead>
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<tr>
<td>Anterior Thigh</td>
<td></td>
<td>Sartorius</td>
<td>Hip flexor</td>
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<td>Upper medial tibia</td>
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<td>Hip abductor</td>
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<td></td>
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<td>Knee flexor</td>
<td>Ventral ilium</td>
<td>L1-LS</td>
<td>Lesser trochanter</td>
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<td></td>
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<td>Iliacus</td>
<td>Psoas</td>
<td>Ventral ilium</td>
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<td>Hip adductor</td>
<td>Pubic ramus</td>
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<td>Ant. inf. iliac spine</td>
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<td>Patellar ligament</td>
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<tr>
<td>Vastus medialis</td>
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<td>Knee extensor</td>
<td>Upper femur</td>
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<td>Vastus intermedialis</td>
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<td>Upper shaft femur</td>
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<td>Vastus lateralis</td>
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<td>Hip adductor</td>
<td>Pubis</td>
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<td>Obturator</td>
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<tr>
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<td>Hip adductor</td>
<td>Pubis</td>
<td>Post. shaft femur</td>
<td>Obturator</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Adductor brevis</td>
<td>Hip adductor</td>
<td>Pubis</td>
<td>Post. shaft femur</td>
<td>Obturator</td>
</tr>
</tbody>
</table>

All muscles above EXCEPT iliopsoas basically receive femoral n. and a.
The 3-and-1 quadriceps femoris are knee extensors, go from femur into patellar ligament, and receive femoral n. and a. EXCEPT
- Rectus femoris spans two joints
Sartorius also spans two joints and runs inferomedially.
Rectus femoris is most anterior muscle of thigh and covers vastus intermedialis
As expected, medial to lateral: medialis, intermediate, lateralis.

Musculo-skeletal, Rheumatology and Plastics
The 3-and-1 medial thigh muscles are all hip adductors, go from pubis to femur, and receive obturator n. and a. EXCEPT
- Gracilis spans two joints and thereby flexes knee
Hamstring part of adductor magnus receives sciatic n.
Gracilis is most medial muscle and covers adductor magnus
From anterior to posterior: longus, brevis, magnus

<table>
<thead>
<tr>
<th>Posterior Thigh</th>
<th>Muscle Types</th>
<th>Function</th>
<th>Origin</th>
<th>Insertion</th>
<th>Innervation</th>
<th>Blood Supply</th>
</tr>
</thead>
<tbody>
<tr>
<td>Biceps femoris, long head</td>
<td>Hip extensor</td>
<td>Knee flexor</td>
<td>Ischial tuberosity</td>
<td>Fibula head</td>
<td>Tibial</td>
<td>Perforating branch of profunda femoris</td>
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<tr>
<td>Biceps femoris, short head</td>
<td>Knee flexor</td>
<td>Lateral shaft femur</td>
<td>Fibula head</td>
<td>Fibular</td>
<td>Perforating branch of profunda femoris</td>
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<tr>
<td>Semitendinosus</td>
<td>Hip extensor</td>
<td>Knee flexor</td>
<td>Ischial tuberosity</td>
<td>Upper medial shaft tibia</td>
<td>Tibial</td>
<td>Perforating branch of profunda femoris</td>
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<tr>
<td>Semimembranosus</td>
<td>Hip extensor</td>
<td>Knee flexor</td>
<td>Ischial tuberosity</td>
<td>Medial condyle tibia</td>
<td>Tibial</td>
<td>Perforating branch of profunda femoris</td>
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<tr>
<td>Hamstring part of adductor magnus</td>
<td>Hip extensor</td>
<td>Ischial tuberosity</td>
<td>Adductor tubercle</td>
<td>Tibial</td>
<td>Perforating branch of profunda femoris</td>
<td></td>
</tr>
</tbody>
</table>

The 3-and-1 hamstring muscles are all hip extensors and knee flexors, come from ischial tuberosity, receive tibial n. & perf. br. EXCEPT
- Hamstring part of adductor magnus only spans hip, and is not a knee flexor
Short head of biceps femoris also is a major exception
From medial to lateral: semimembranosus, semitendinosus, biceps femoris

Region | Muscle | Function | Origin | Insertion | Innervation | Blood Supply |
<table>
<thead>
<tr>
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</thead>
<tbody>
<tr>
<td>Anterior Leg</td>
<td>Tibialis anterior</td>
<td>Dorsiflexion Inversion (DI)</td>
<td>Shaft tibia</td>
<td>Medial cuneiform Dorso base 1st metatarsal</td>
<td>Deep fibular</td>
<td>Anterior tibial</td>
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<tr>
<td>Extensor hallucis longus</td>
<td>Dorsiflexion Inversion (DI)</td>
<td>Lower shaft fibula</td>
<td>Distal phalanx of big toe</td>
<td>Deep fibular</td>
<td>Anterior tibial</td>
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<tr>
<td>Extensor digitorum longus</td>
<td>Dorsiflexion Eversion (DE)</td>
<td>Shaft fibula</td>
<td>Phalanges toes 2-5</td>
<td>Deep fibular</td>
<td>Anterior tibial</td>
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<tr>
<td>Fibularis tertius</td>
<td>Dorsiflexion Eversion (DE)</td>
<td>Lower shaft fibula</td>
<td>Base 5th metatarsal</td>
<td>Deep fibular</td>
<td>Anterior tibial</td>
<td></td>
</tr>
</tbody>
</table>

All dorsiflexors; inversion/eversion dependent on insertion point relative to 2nd toe.
All receive deep fibular n. (so called as viewed from posterior) and anterior tibial a.

Lateral Leg | Fibularis longus | Plantarflexion Eversion (PE) | Shaft fibula | Plantar base 1st metatarsal | Superficial fibular | Perforating branch of fibular artery |
| Fibularis brevis | Plantarflexion Eversion (PE) | Lower shaft fibula | Lateral base 5th metatarsal | Superficial fibular | Perforating branch of fibular artery |

Tendons of muscles run under lateral malleolus.
Easy to feel lateral muscles tense with plantarflexion and eversion.

Posterior Leg | Gastrocnemius (P) | Plantarflexion Knee flexor | Condyles tibia | Calcaneum | Tibial | Sural (br. of popliteal) |
| Soleus (P) | Knee flexor | Shafts tibia and fibula | Calcaneum | Tibial | Posterior tibial | Fibular Sural |
| Plantaris (P) | Knee flexor | Lateral femur | Calcaneum | Tibial | Sural |
| Popliteus (P) | Unlocks knee | Lateral femur | Shaft tibia | Tibial | Posterior tibial |

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<thead>
<tr>
<th>Region</th>
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<tbody>
<tr>
<td>Dorsal foot</td>
<td>Extensor hallucis brevis</td>
<td>Extend hallux</td>
<td>Calcaneum</td>
<td>1 phalanx</td>
<td>Deep fibular</td>
<td>Dorsalis pedis Arcuate</td>
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<tr>
<td></td>
<td>Extensor digitorum brevis</td>
<td>Extend toes</td>
<td>Calcaneum</td>
<td>2-4 phalanx</td>
<td>Deep fibular</td>
<td>Dorsalis pedis Arcuate</td>
</tr>
<tr>
<td>Plantar foot, 1st layer</td>
<td>Abductor hallucis</td>
<td>Abduct hallux</td>
<td>Medial calcaneum</td>
<td>Medial 1 phalanx</td>
<td>Medial plantar</td>
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<tr>
<td></td>
<td>Abductor digiti minimi</td>
<td>Abduct toe 5</td>
<td>Calcaneum</td>
<td>Proximal 5 phalanx</td>
<td>Lateral plantar</td>
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<tr>
<td></td>
<td>Flexor digitorum brevis</td>
<td>Flex toes 2-4</td>
<td>Medial calcaneum</td>
<td>Middle 2-4 phalanx</td>
<td>Medial plantar</td>
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</tr>
<tr>
<td>Plantar foot, 2nd layer</td>
<td>Quadratus plantae</td>
<td>Laterally pull flexor digitorum longus tendon</td>
<td>Calcaneum</td>
<td>Flexor digitorum longus tendon</td>
<td>Lateral plantar</td>
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<tr>
<td></td>
<td>Lumbricals</td>
<td>Extend toes</td>
<td>Flexor digitorum longus tendon</td>
<td></td>
<td>Lateral plantar except #1 (med. pl.)</td>
<td></td>
</tr>
<tr>
<td>Plantar foot, 3rd layer</td>
<td>Flexor hallucis brevis</td>
<td>Flex hallux</td>
<td>Cuboid, cuneiform</td>
<td>Proximal 1 phalanx</td>
<td>Medial plantar</td>
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<tr>
<td></td>
<td>Adductor hallucis</td>
<td>Adduct hallux</td>
<td>Base 2-4 metatarsal</td>
<td>Proximal 1 phalanx</td>
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</tr>
<tr>
<td></td>
<td>Flexor digiti minimi</td>
<td>Flex toe 5</td>
<td>Base 5 metatarsal</td>
<td>Proximal 1 phalanx</td>
<td>Lateral plantar</td>
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<tr>
<td>Plantar foot, 4th layer</td>
<td>Dorsal interossei (4)</td>
<td>Abduct toe</td>
<td>Metatarsals</td>
<td>Phalanges</td>
<td>Lateral plantar</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Plantar interossei (4)</td>
<td>Adduct toes</td>
<td>Metatarsals</td>
<td>Phalanges</td>
<td>Lateral plantar</td>
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</tr>
</tbody>
</table>

All lateral plantar innervation except medial plantars as marked in italics. Interossei mnemonic PAD/DAB: plantar adduction, dorsal abduction. Anterior tibial gives rise to dorsalis pedis and arcuate aa. Posterior tibial gives rise to medial and lateral plantar aa. Best way to remember is what you saw in dissection! Know location and function (more important than origin/insertion).

**Gait**

Components of Gait

- Aim of gait is to keep the body’s centre of gravity travelling in smooth line → ↓energy
- Gait simplified: heel strike → stance → toe off → swing through
- Gait consists of a:
  - **Stance** phase (60% of the cycle):
    - **Heel strike**: Forefoot not yet in contact. Knee in full extension. Quads contract to prevent buckling of the knee.
    - **Foot Flat**: Dorsiflexors slowly relax to bring foot to ground, and hip extensors propel body forward
    - **Mid stand**: body directly over ankle
    - **Heel off**: Triceps surae contract
    - **Toe off**: Hallucis and flexor digitorum longus contract
  - **Swing** phase (40% of the cycle):
- Acceleration: iliopsoas contracts (flexes hip), passive knee extension, dorsiflexors contract so foot clears the ground
- Mid swing
- Deceleration: hamstrings stop hyper-extension of the knee and gluteus maximus slows hip flexion
  - **Double** stance: both feet on ground for 20% of the cycle when walking. When running this % reduces to 0% (ie swing > 50% of cycle so both feet off the ground at some point)

**Abnormalities of Gait**

- Causes a limp
- The main causes of abnormal gait are:
  - Pain → **Antalgic gait** (non-specific). Pain → **shortened stance phase** on affected leg, shortened swing of opposite leg
  - Weakness
  - Joint abnormality
- Usually noticed during stance phase when one leg is bearing the body’s weight

<table>
<thead>
<tr>
<th>Gait</th>
<th>Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antalgic</td>
<td>Short stance phase</td>
</tr>
<tr>
<td>Stiff leg</td>
<td>Fused hip/knee causing abnormal swing-through</td>
</tr>
<tr>
<td>Trendelenburg</td>
<td>Proximal abductor muscle weakness → pelvis on opposite side sags during stance</td>
</tr>
<tr>
<td>Short leg</td>
<td>During stance, short leg results in pelvis + shoulder on affected side to sag</td>
</tr>
<tr>
<td>Shuffling</td>
<td>Short swing-through</td>
</tr>
<tr>
<td>Stamping</td>
<td>Swing-through is abnormal with broad base + high stepping → <strong>peripheral neuropathy</strong></td>
</tr>
<tr>
<td>Ataxic</td>
<td>Broad-based with unsteadiness on turning → cerebellar disease etc</td>
</tr>
<tr>
<td>Foot drop</td>
<td>During swing-through, foot scuffs/slaps on ground → <strong>L5 root lesion, common peroneal nerve palsy or polio</strong></td>
</tr>
<tr>
<td>Scissor</td>
<td>Cerebral palsy with <strong>adductor spasm</strong> → swing-through of one leg blocked by the other</td>
</tr>
</tbody>
</table>

**Observing Gait**

- Once you’ve identified the gait, think of causes from top down:
  - Stroke
  - Spinal cord lesion
  - Nerve root
  - Peripheral nerve
  - Muscle (either weakness or pathology)
  - Joint
  - Bone (eg fracture)

**Hip and Femur**
Overview

- Primary concerns:
  - Range of motion
  - Gait
- Also need to examine:
  - The lower back and sacro-iliac joints
  - Vasculature of the leg: pulses, temperature, capillary refill
  - Peripheral nerves: eg sensory, motor, reflexes
- Problems arising with the hip:
  - Fracture
  - Arthritis
  - Dislocation: trauma, also in congenital abnormalities, infection, Cerebral Palsy
  - Epiphyseal dislocation (typically a chubby 11 year old boy with a slipped femoral epiphysis)
  - Infection: septic arthritis

History

- Pain
- Past trauma
- Impact on daily activities
- Walking distance
- Climbing stairs
- Getting out of low chairs
- Location:
  - Anterior/groin pain: ?hip
  - Lateral: ?trochanteric bursitis, referred from spine
  - Posterior: referred from spine, gluteus medius tendonitis

Hip Exam

- Gait:
  - Walking: on toes - plantarflexion (tests S1), on heels - dorsiflexion (test L5)
- Inspection:
  - While standing:
    - Alignment of pelvis and shoulders, muscle wasting, swellings (eg herniae, lymphadenopathy), scars
    - Observe from front and do TRENDELENBURG TEST: get pt to put fingers in your upturned hands + alternate standing on one leg. Sagging to contra-lateral side is Trendelenburg positive (ie weak hip abductors)
    - Observe from back: wasting of gluteals, posterior surgical scars, etc
    - Test the joint above (sacro-iliac joints and lumbar spine): Bend over (measure how far they do down – eg fingers to floor, toes, mid-calf, etc). Extend back
    - Test the joint below: crouch down to test knees
    - Palpate sacro-iliac joints and lumbar spine for tenderness
  - On bed, look especially for:
    - Scars, hernia, bruising, inflammation, muscle wasting: gluteals, quads, biceps and adductors
    - Lie pt prone or assess whilst standing
    - Leg length (check they’re lying straight and pelvis is straight):
      - Real leg length discrepancy: measure ASIS to medial malleolus on each side. If there is a discrepancy then flex both knees to isolate the discrepancy to above or below the knee (look at knee height)
      - Apparent leg length discrepancy: measure umbilicus to medial malleolus. If discrepancy but no real leg length discrepancy then postural cause
- Palpation:
  - Bony tenderness over ASIS, and over greater trochanter for bursitis
  - Groin: lumps: hernias, lymph nodes, femoral artery aneurysm ⇒ pain is not hip pain
  - Check for ili-tibial band pain over the greater trochanter ⇒ pain is not hip pain
- Move:
  - ROM: always state start and end: from X to Y degrees (eg adduction from 0 to 30 degrees)
  - Compare sides
  - Test flexion (and do Thomas’ test here – see below)
To test adduction (0 - 20°) and abduction (0 - 50°), **stabilise hip by holding hand across pelvis or abduction the opposite leg**

- Internal (0 - 45°) and external rotation (0 - 45°): flex hip and knee and lever hip using lower leg
- Don’t test extension (but do it prone if you’re going to)

**Neurovascular:**
- **Leg pulses** → relevant to operative risks

**Special tests:**
- **Thomas test** for **fixed flexion deformity** (ie not full extension): Bring up good leg with hand under the spine. When pelvis starts to flex the bad leg won’t be able to remain straight if there is fixed flexion deformity. Quantify by measuring the degrees that the bad leg has risen from lying flat
- **FABER (Flexion, Abduction, External Rotation):**
  - Ask the patient to lie supine on the exam table.
  - Place the foot of the effected side on the opposite knee.
  - Pain in the groin area indicates a problem with the hip and not the spine.
  - Press down gently but firmly on the flexed knee and the opposite anterior superior iliac crest.
  - Pain in the sacroiliac area indicates a problem with the sacroiliac joints.
- **Quadrant test:**
  - To assess structures in the inner and outer quadrant of the hip
  - Pt supine with their hip flexed and the clinician places one hand over the top of the patients knee. The patients hip is flexed to 90 degrees and the hip is adducted until the pelvis begins to raise off of the table. This exam tests the inner quadrant and compresses the intraarticular structures, insertion of the TFL, the ilioasaes, ilioasa bursae, insertion of pectineus, adductor longus and femoral neck.
  - The second portion of the test can be done by flexing the hip to end range with adduction and adding a compression force at the knee joint along the axis of the femur. The examiner then abducts the femur and assesses symptoms through the ROM. Pain with this may be due to capsular problems or loss of joint congruency

- **Finally check:**
  - **Joint above:** ie spine (did this while standing)
  - **Joint below:** check knee

- **X-ray**

**Diagnostic Calendar**
- 0 - 5 = DDH/infection/transient synovitis
- 5 - 10 = Perthes
- 10 - 20 = SUFE
- Adults = arthritides, AVN, impingement

**Hip OA**
- Primary (idiopathic) or secondary (acetabular dysplasia, perthes, SUFE etc)
- See soft + fibrillated cartilage, bone cysts + sclerosis + capsular fibrosis
- 80-90% of 80 year olds’ hips show radiographic evidence of OA; >10% of unilateral hip OA become bilateral over the next 5-8 yrs
- **Symptoms:** activity pain (can be referred to knee) → rest pain; stiffness; limp
- **Signs:**
  - Antalgic or Trendelenburg gait
  - Apparent shortening with adduction of the hip
  - Leg externally rotated + adducted
  - Fixed flexion deformity (positive Thomas test)
  - Mild muscle wasting
  - ↓ROM (especially internal rotation)
- **Standard x-ray signs**
- **Management:**
  - Non-operative: ↓** weight** (1kg weight loss = ↓ force across the hip of 3kgf), physio, walking stick, NSAIDs
  - Surgical: THR, arthrodesis/osteotomy possible in younger pts
    - Anterior/anterolateral approach = ↓risk of dislocation + sciatic nerve not at risk but femoral nerve is
    - Posterior approach = faster + easier, less muscle splitting, fem nerve not at risk but sciatic nerve is +
      ↑ infection risk
**Injury & Conditions**

- **Fracture of femoral neck:**
  - Commonest site in elderly, associated with osteoporosis
  - Types: subcapital, transcervical, basicervical, intertrochanteric, subtrochanteric

  - **Clinical:** History of fall, pain in hip. Patient lies with *limb in external rotation and leg looks short*
  - **Location:** Key issue is disruption of blood flow to the femoral head. Most blood flow is via the attachment of the capsule. If disrupted (via a fracture at or above a basicervical fracture) → avascular necrosis
  - **Treatment:** Operative mostly. Displaced fractures will not unite without internal fixation. Richardson’s screw often used, otherwise hip replacement
  - **Complications include:** dementia, pressure sores, pneumonia, urinary infection, *not* liver failure
  - **Clinical difference between a dislocated femur and a fractured neck of femur:** both are shortened. Neck of femur: leg *externally* rotated; dislocation: leg *internally* rotated (*in points out and out point in*)

- **Femoral shaft fracture:**
  - **Clinical:** Mostly young adults. *Shock is severe and with closed fracture fat embolism common.* Leg is rotated externally may be short and deformed. *Thigh swollen and bruised.* Shock MUST be treated, ABG should also be done
  - **Risk of fat embolism:** do CXR (?pleural effusion, congested pulmonary veins etc)
  - **Treatment:** Intramedullary nailing

- **Comminuted fractures of the femur:**
  - **Mechanism:** Violent trauma (eg motor bike accident)
  - **Traction or external fixation +/- grafting to fill the gaps**

- **Supracondylar fracture of the distal femur:**
  - **Mechanism:** Forceful flexion/hyperextension in osteoporotic bone
  - **Gastrocnemius then pulls the femur forward**
  - **Internally fixate with long blade plate**

- **Condylar fracture of the femur:**
  - **Mechanism:** Fractures entering the intercondylar notch can divide a condyle from the femur (eg knee hitting dashboard)
  - **Management:**
    - Undisplaced: aspirate + traction for 4 weeks then cast
    - Displaced: open reduction and internal fixation
  - **Complications:** avascular necrosis, collapse, varus or valgus deformity

- **Osteonecrosis of the femoral head:**
  - AVN
  - Ischaemia → infarction → structural weakness + collapse of bone
  - Aetiology unclear (arterial insufficiency post #/dislocation; venous occlusion in Perthes)
  - **Management:** treat cause, NSAIDs, surgery (core decompression - ↓intraosseous pressure + ↑venous drainage; arthroplasty)

- **Hip TB:** see x-ray changes of osteoporosis + joint destruction

**Knee**

**Anatomy**

- **Active stabilisers:** muscles & tendons
- **Passive stabilisers:** ligaments & menisci
- **MCL:**
  - Proximal attachment: medial epicondyle
  - Distal attachment: 3 finger breadths below knee joint on the tibia
- **LCL:**
  - Proximal attachment: lateral epicondyle
- Distal attachment: fibular head

- ACL:
  - Proximal attachment: lateral femur (AL)
  - Distal attachment: anterior tibial plateau

- PCL:
  - Proximal attachment: medial femur (PM)
  - Distal attachment: posterior tibial plateau

**History**

- Pain
- Locking, clicking, giving way
- Injury
- About the injury (HIS):  
  - **How did you do it:**
    - Direct blow or indirect (eg twisting → consider meniscus lesion)
    - Which way did tibia move in relation to femur
  - Immediate disability:
    - Inability to walk, knee collapsing (?ACL injury), locking (?meniscus), catching, clicking.
    - For days or weeks, hamstring spasm protects the painful knee. As pain and effusion settle, the knee gradually straightens
    - NB neither cartilage or inner two thirds of menisci are innervated – pain from these injuries is caused by consequential tension/damage to other structures
  - **Sensations:** hearing or feeling a pop, snap or tearing
  - Swelling:
Musculo-skeletal, Rheumatology and Plastics

- Want to know about onset and size of swelling
- If the knee swells straight after an injury → ?ACL injury causing bleeding into the joint or other haemarthrosis (eg # or synovial injury). Soft tissue swelling/effusion takes up to a day

- **Symptoms** since the injury:
  - Locking: question carefully to distinguish from pain-induced hamstring spasm
  - Giving way
  - Swelling

- **Function:**
  - Difficulty with stairs (going up or down? Often worse going down)
  - Trouble getting out of low chairs
  - Waking with pain at night after having leg bent

- **Red flags:**
  - Neurovascular damage
  - Extensor mechanism rupture
  - Infection
  - Bleeding disorders
  - Possibility of cancer

**Exam**

- **Quick run through:**
  - **Gait**
  - **Inspect**
  - **Palpate**
    - Bones
    - Ligaments
    - Effusions
  - **Move**
    - F & E
    - Stress ligaments
    - Straight leg raise
  - **Other**
    - Menisci
    - Patella apprehension
  - Neurovascular

- **Adequately expose** the leg

- **Gait and squats:**
  - **Valgus** deviation (deviation away from midline, eg knock knee – Genu valgus)
  - **Varus** deviation (deviation towards midline, eg bow leg – Genu varum)
  - **Lateral thrust:** posterolateral insufficiency, knee goes posterolaterally, a result of Medial Compartment OA.
  - **Squat** on their haunches and on each leg and **duck walk**:
    - Pain in the front then it is an anterior problem (ie patello-femoral joint)
    - In the popliteal fossa → could be a *medial meniscal tear*
  - **Hop** on each leg: tests strength (motor) for the gastrocnemius and soleus muscles
  - View from the side: any fixed flexion deformity or genu recurvatum

- **Inspect:**
  - From the front, side and behind
  - **Inspect the popliteal fossa** (then you don’t have to get them to roll over on the bed). Look for Baker’s cyst – protrusion of the synovium into the popliteal fossa
  - **Swelling, scars, skin changes, muscle wasting**: measure thigh circumference
  - Get them to push their knee down into the bed to test:
    - Extension (fixed flexion deformity)
    - For muscle wasting in vastus medialis
  - Can measure angles with a goniometer

- **Palpate:**
  - Feel for **temperature** compared with rest of leg and with other knee
  - Feel for **effusion** (meniscal pathology often produces an effusion)
Stroke/swipe/bulge test: for pt’s left knee, stand on left side of bed (+ vice versa for other knee); with radial side of right hand, stroke up medial side of left knee → let go and with back of right hand stroke up lateral side of left knee → if effusion, will see fluid move from lateral → medial

O Patellar tap: push down from superior → inferior + hold just above patella → press down on patella whilst holding

O Cross fluctuation test: tap one side of suprapatellar pouch while holding fingers on other side, feeling for fluid moving to strike the other fingers

- Palpate joint line along tibial plateau (watch their face): start along the bases of the ‘soft triangles’; tenderness here may indicate a meniscal tear, above or below the joint line the meniscus won’t be causing it
- Palpate medial and lateral collateral ligaments (LCL can be felt easily when crossing one leg over the other [FABER])
- Palpate tibial tuberosity and infra-patellar ligament
- Palpate popliteal fossa and feel pulse

• Move:
  - Straight leg raise: checks extensor mechanism – quads, patella ligament, etc. If damaged traumatically then urgent surgery (the key knee injury where you wouldn’t wait for the swelling to go down before operating). If patella or quad tendon disruption or patella #, will not be able to straight leg raise
  - Whilst straight leg raising, check for hyperextensibility by holding both legs straight + asking pt to push their knee down
  - Flex their knee. Bring the other leg up with the knee in flexion to compare. Have one hand on the patella to feel for crepitus. Measure distance from heel to buttock. Whilst flexing knee, can do patellar apprehension test

- Anterior Cruciate Ligament:
  - Lachman’s Test: with leg in slight flexion on the bed (eg rolled up towel or your knee underneath it) push down on distal femur while pulling up on proximal tibia (push + pull). Tests both ACL + PCL
  - Pivot Test (hard to elicit unless relaxed or under GA): Flex the knee, put it in valgus, then extend it. If ACL is ruptured, the knee jumps smartly forward
  - Anterior drawer to test the ACL. Compare with the other side. Sit on foot and pull tibia towards you

- Posterior Cruciate Ligament:
  - Lachman’s Test also tests PCL to an extent
  - Feet flat on the bed leaving both knees in 90° flexion
  - Look across the two knees for posterior sag, which could indicate a PCL rupture
  - Stabilise the tibia (sit on their foot), relax hamstrings and push tibia towards body (posterior drawer test)

- McMurray’s Test for meniscal tears (not particularly reliable): Feel and listen for a click as meniscal tag snaps free
  - Start with leg in almost full flexion with one hand on foot and the other over the meniscus, apply rotating force using the foot as a lever
  - Medial meniscus: externally rotate the tibia on the femur, apply valgus pressure. Extending the leg will cause pain/clicking
  - Lateral meniscus: externally rotate the tibia on the femur, apply varus pressure. Further flexing the leg will cause pain/clicking

- Collateral Ligaments:
  - With leg under your arm + tucked on your iliac creast do the Valgus stress test and Varus stress test by rocking your pelvis side to side:
    - With the knee still in 10-15° steady it as you pull the leg into valgus, this tests the medial collateral ligament and the ACL. Now Push it into Varus, this tests the lateral collateral ligament
    - Lay the leg flat and repeat with the knee in full extension: tests all structures – not just the collateral ligaments. If laxity in full extension, then ACL or PCL damage as well
- **Patellofemoral joint:**
  - Ask about pain going up and down stairs
  - Palpate
    - Border
    - Anterior surface: Push it in – ‘any pain?’
    - Tendon and ligament insertions (especially tibial tuberosity)
    - Posterior surface (by pushing it to one side and then the other)
    - Solomon’s test: With leg in full extension, try and lift patella and get fingers underneath. If can’t then effusion/synovitis
  - Site on edge of bed with legs handing over: Look at the direction that the patellar points in. Have the patient flex and extend at the knee → should follow an inverted J course
  - **Patella apprehension test:** press the patella laterally and hold it slightly subluxed → watch the person’s face and ask them to flex their knee → If they grimace or show signs of pain then the test is positive and is diagnostic of recurrent patellar subluxation or dislocation

- **Joint Above and Below. Check the HIP (pain is referred to the knee from there)**
- Check the ankle and the foot pulses, and distal neurology
- **Link back to Examinations**

**Knee Injury**

- Immediate onset of knee swelling is due to bleeding into the joint, so called **haemarthrosis**. Causes for this would be:
  - ACL (most common) or PCL tear (+/- avulsion # associated with it)
  - Patella dislocation
  - Osteochondral #
  - **Medial meniscal tear** (peripheral - as they are more vascular)
  - Collateral ligament injury
  - Capsule tear
  - Bleeding diathesis

- General principles of ligament injury:
  - Pain + slight joint opening ⇒ good (strain/partial rupture)
  - No pain + big joint opening ⇒ bad (complete rupture)

- Always x-ray adequately. Small bony fragments on x-ray ⇒ soft tissue injury until proven otherwise

- In kids, bone and growth plates are weaker than ligaments

**Meniscal Tears**:

- Variety of types: fragments causing locking, tears on internal or external margins:
  - Bucket-handle/longitudinal split
  - Degenerate meniscus
  - Flap tear

*Musculo-skeletal, Rheumatology and Plastics*
- Radial split
- Horizontal split
- Meniscal tears frequently overdiagnosed
- Medial most common
- May develop secondary to chronic ACL injury
- Clinical tests unreliable individually
- Painful block to knee extension more likely ACL tear than displaced meniscus
- Clinical: twisting injury or squatting, unable to straighten knee, locking (typically bucket handle tears), pain, maybe associated pop, crack or tearing sensation
- Investigations: arthroscopy or MRI
- In absence of mechanical symptoms a trial of rehabilitation is appropriate
- Most tears are in avascular area & therefore won’t heal - peripheral longitudinal tears in young patients may be suitable for repair (have some blood supply)
- Management: excise tears or reattach. Aim is to preserve as much of the meniscus as possible

- MCL injury:
  - Usually contact injury eg tackling injury
  - Focal tenderness
  - Severity graded by laxity testing
  - Exclude associated ACL injury
  - Isolated MCL injuries can be managed non-operatively
  - Bracing is appropriate for Grade III injuries

- Lateral/Medial Collateral Ligament:
  - Most common knee ligament injury (MCL)
  - Medial is attached to the medial meniscus. Lateral isn’t → less injury. But if it is, consider check for fibular head fracture and common peroneal nerve damage
  - Mechanical: Blow to medial/lateral side of knee pushing the joint into varus/valgus
  - Presentation: Tenderness over ligament (unless complete rupture → no pain), pain worse under varus/valgus stress, effusion
  - Management: Isolated tears heal well without operating. Immobilisation in scott brace/leg plaster at 10º flexion (6 weeks) then mobilise cautiously. May have ongoing instability

- ACL injury:
  - Prevents posterior displacement of the femur on the tibia and hyperextension. Is the weaker of the 2 cruciates. Anterior-medial bundle is taut throughout flexion → anterior drawer test +ive if AMB affected
  - ACL injuries frequently overlooked
  - Very common in NZ + in netball injuries
  - 5 times higher in women than in men participating in the same sports
  - Most patients with ACL damage complain of immediate and profound pain that is exacerbated with motion and an inability to weightbear
  - Most patients report a snapping or popping sensation or sound at the time of injury
  - An acute knee injury heralded by a pop or snap, followed by a rapidly evolving effusion, almost always affirms a rupture of the ACL
  - Disruption of the ACL may occur alone or with other knee injuries, especially a lateral meniscal injury or tear of the MCL
  - ACL tears are associated with anterior blows (to the thigh with stationary tibia) that hyperextend the knee, excessive noncontact hyperextension of the knee, and extreme deceleration forces to the knee
  - Usually non-contact wrenching injuries
  - Early swelling indicating haemarthrosis
  - Unable to continue playing
  - 75% of haemarthroses
  - Mechanism: indirect; sharp twisting movement with valgus strain or tackle that pushes the tibia forward of femur; hyperextension on its on can also produce an isolated ACL rupture
  - Can occasionally avulse a fragment of bone at the tibial plateau (requires surgery)
  - Presentation: may hear a snap, swelling, pain, effusion (very rapid if due to haemarthrosis). If delayed then knee gives way, can run in a straight line but can’t turn corners
  - Often tear medial meniscus (→ OA and instability)
  - Tests:
    - Painful block to knee extension common
    - Classical anterior drawer test at 90º may be equivocal
- **Lachman test:** Modified anterior drawer test at 20° most clinically accurate test for ACL injury
- **Pivot shift test is a complex test which is not performed in an acute knee injury**

- **X-ray for avulsion fracture** of tibial insertion seen in young patients

- **Management:**
  - Analgesia
  - Cast brace
  - Conservative: aspirate and physio to strengthen hamstrings; bracing during activity
  - Surgical: reconstruction of ligament (repair impossible as ligaments devitalise rapidly after injury; use intraarticular patellar tendon or hamstring tendon graft)
  - Surgical reconstruction is appropriate for patients with disabling functional instability

- **PCL injury:**
  - PCL prevents anterior displacement of femur on tibia and hyper-flexion
  - PCL injuries more common in sport than previously recognised
  - Mechanism: blow to anterior tibia when knee flexed (“dashboard injury”) or hyperextension and hyperflexion may also cause PCL injury
  - BEWARE hyperextension varus mechanism causing NEUROVASCULAR injury
  - Presentation: swelling, pain, effusion, posterior sag at 90º flexion
  - Tests:
    - Posterior tibial sag at 90° flexion
    - Posterior drawer test +ve
    - Beware false +ve anterior drawer
    - X-ray for an avulsion fracture (→ requires surgery)
  - Most do well with conservative treatment. Can often manage without a PCL. Quads exercises decrease backwards tibial sag

- **Disruption of extensor mechanism:**
  - Rupture of Rectus Femoris: sudden violent contraction → transverse tear. Feel defect in muscle.
    - Conservative treatment: ice, elevation, analgesia, mobilisation within limits of comfort. Functional deficit negligible
  - Ruptured Quadriceps tendon: sudden violent contraction. Need to reattach
  - Ruptured patella tendon: Forced flexion injury. Repair if weakness or extensor lag

- **Dislocation of the patella:**
  - History = usually one of direct trauma to the medial side – pt sees + feels the bone displace + knee locks to 30-40º flexion
  - Sharp twisting motion on flexed knee or blow to side of leg → haemarthrosis and medial tenderness (medial structures torn)
  - To reduce: gently extend the knee, then gentle traction. Primary concern is distal circulation → reduce at scene of injury if possible
  - Aspirate and irrigate if necessary, splint for 4 weeks
  - Test for reproducibility by applying firm pressure on the lateral side + extending the knee – the bone may reduce with a snap
  - Physio to strengthen quads (necessary for patella stability)
  - If recurrent then ?underdevelopment of lateral femoral condyle

- **Osteochondral Fractures:**
  - In young person, twisting or direct blow can → detachment of sliver of bone and cartilage. Most common with patellar dislocation
  - Haemarthrosis and fat from cancellous bone causing a fat-fluid line on lateral radiograph
  - If small then remove, if large then reattach

- **Chondral separations or flaps:** Fragments of articular cartilage. Need arthroscopy or MRI. Flaps are usually ground away. Separations are removed
• Chondromalacia Patellae: young women. Patellar aching after prolonged sitting due to softening or fibrillation of the patellar articular cartilage. Conservative treatment: vastus medialis strengthening

• Osteochondritis Dissecans:
  - = shearing osteochondritis (small segment of articular cartilage + bone may separate as an avascular fragment)
  - Almost certainly due to repeated minor trauma producing an osteochondral # of a convex joint surface
  - ↓Blood to subchondral bone (cause unknown) → focal necrosis of cartilage and bone → loose fragment
  - Presentation: pain in young adulthood, worse on walking and hyperextension, M>F, intermittent swelling, maybe locking
  - X-ray: small irregularities on medial condyle +/- fragments
  - Treatment: wait, or surgery if no radiological signs of union

• Osgood Schlatter’s Disease:
  - Is a traction apophysitis (apophysis = bony outgrowth; “pulling osteochondritis”) of the proximal tibial tubercle at the insertion of the patellar tendon
  - Can be seen at calcaneal tendon (= Sever’s disease)
  - Painful + tender
  - Settles with rest

• Bursitis: 16 bursae around the knee. Most commonly affected are:
  - Prepatellar bursa: ‘housemaid’s’ knee
  - Infrapatellar bursa: ‘Vicar’s knee’ – they kneel more upright
  - Anserine bursae: on medial side of the head of the tibia, under the ligaments of semi-tendonosis, gracilis and sartorius
  - Aspiration distinguishes friction bursitis from infective or inflammatory bursitis

• Knee OA:
  - Pain is most common complaint → initially after walking → later at rest
  - Stiffness + swelling + locking (loose bodies) also can feature
  - Management: weight loss, NSAIDs, physio, walking stick

• Haemarthrosis of the knee is the most common presenting complaint of a 0% FVIII haemophilia

Ottawa Knee Rules
• X-ray if any of:
  - Age 55+
  - Any bony tenderness
  - Inability to flex 90 degrees
  - Inability to weightbear
• Haemarthrosis is also indication for x-ray

Management of Knee Injury
• ↓Weight
• MRI has largely replaced diagnostic arthroscopy
• Exercises to strengthen hamstrings and quads (eg straight leg raise while seated)
• Check for flattened arches → exercises
• Aquajogging
• Analgesics (NSAIDs, consider COX2)
• If tense haemarthrosis then aspiration will give immediate relief and aid diagnosis (ie send it to the lab: ?blood, infection or gout)

Urgent Specialist Referral
• Red flags:
  - Neurovascular injury
  - Extensor mechanism rupture
  - Infection
  - Bleeding disorders
  - Possibility of cancer
• Severe knee injuries
• Significant fractures
Lower Leg and Foot

- Foot stabilisers (maintain the arch of the foot):
  - Active: tibialis posterior + peroneus longus
  - Passive: plantar fascia
- Forefoot = navicular/cuboid distally
- Hindfoot = os calcis + talus
- Peroneal nerve: supplies sensation to the 1st dorsal workspace + motor to ?EHL
- Syndesmosis is a slightly movable articulation where the contiguous bony surfaces are united by an interosseous ligament, as in the inferior tibiofibular articulation (also radiocarpal joint)

History

- Pain
- Instability (usually side to side)
- Swelling
- Trauma

Exam

- Gait
- Inspect: shape, skin changes, swelling, deformity, muscle wasting, callosities, colour. Up on toes. Inspect shoes
- Hop on each leg: tests strength (motor) of the gastrocnemius and soleus muscles and will give pain if stress #
- Deformities include:
  - Hallux valgus:
    - Lateral deviation of the MTP joint of the big toe (bunion)
    - Causes: biomechanical, pointed shoes or wearing heels, flat foot (flattening of the longitudinal arch)
    - Management: shoe fitting to foot; surgery (arthroplasty or osteotomy)
  - Hallux rigidus:
    - Stiff, painful big toe → OA at 1st MTPJ; during walking, big toe is unable to extend during toe-off
    - Management: rocker-bottom sole on shoe allows foot to roll forward more easily or surgery
  - Intoeing: three components: metatarsus adductus + tibial torsion + femoral neck anteversion
  - Claw toes:
    - Fixed flexion deformity: extended at MTP joints, and flexed at PIP and DIP joints
    - Due to imbalance of extensors and flexors (eg previous polio or spina bifida, ie neuromuscular disorder)
    - Can develop metatarsalgia
    - Management: pads in shoes; surgery (fusion at PIPJ)
  - Crowding of the toes: rheumatoid arthritis
  - Hammer toe: Extended at the MTP joint, hyperflexed at the PIP joint, extended at the DIP joint (cf boutonniere deformity of the finger)
  - Mallet toe
  - Club foot: talipes equinovarus
  - Sausage deformity of the toes: psoriasis, ankylosing spondylitis and Reiter’s disease
  - Winter heels (Haglund’s deformity): Achilles bursitis
  - Inspect transverse and longitudinal arch:
    - Pes planus: Flat feet. May be valgus and eversion deformity. Normal when a child is learning to walk. If the arch forms when walking on toes then OK
    - Pes cavus: Accentuated longitudinal arches: idiopathic, spina bifida or previous polio (ie neuromuscular) → weight on head of metatarsals → pain.
  - Calluses over the metatarsal heads on the plantar surface occur with subluxation of these joints
- Palpate:
  - Temperature, swelling, lumps
  - Metatarsal squeeze (tenderness common in early rheumatoid arthritis + Morton’s neuroma + bursitis)
  - Medial + lateral ligaments
  - Swelling around the lateral and medial malleoli (don’t confuse with pitting oedema)
  - Feel over 5th metatarsal base + head + tuber of os calcis (where plantar fasciitis tender)
  - IP joints typically affected in sero-negative arthritis
  - Palpate Achilles tendon for nodules and Achilles tendinitis
Palpate inferior heel for plantar fasciitis (can occur with seronegative-arthropathies)

**Move:**
- Hold midfoot and test dorsiflexion (normal ~ 20°) and plantar flexion (~ 50°)
- **Subtalar joint:** test inversion and eversion. Look for tenderness more than range of movement
- **Midtarsal (midfoot) joints** allow rotation when hindfoot fixed (place hand on heel and invert + evert the forefoot)
- Stress varus + valgus for stability
- **Ankle drawer test:** for instability due to anterior talofibular ligament rupture
- SIMMONDS/Thompson’s test: calf squeeze for disruption of Achilles

**Neurovascular:**
- Pulses, CR
- Sensation, **power**, reflexes

**X-ray:** stress x-rays (valgus + varus) can be done and can show talar shift in the mortice

**Lower Leg and Foot Injury**

**Ankle anatomy:**
- Lateral malleolus of the fibula is firmly attached to tibia by the anterior and posterior inferior tibio-fibular ligaments
- Talus is held in place by deltoid ligament on medial side and calcaneo-fibular ligament on lateral side
- Commonest ankle injury occurs when the talus is rotated, fracturing one or both malleoli and rupturing the ligaments
- Most common injury is varus (inversion) + injury to anterior talofibular ligament (one of the 3 lateral collateral ligaments)

**Fracture of the tibia:**
- Most common site of open fractures
- Clinical: Skin may be undamaged or obviously divided. Foot rolled outwards, leg bruised and swollen. Need to assess *circulation and sensation* in toes
- Treatment:
  - Closed fractures need to be observed for *compartment syndrome* and soft tissue damage. Obtain fracture alignment and start weight bearing early
  - Open fractures require immediate antibiotics, debridement, then stabilization and rehab

**Distal fibial fracture:**
- Check even, clear joint space around the ankle (should be = space between sides of the mortice)
- Check ankle joint is not subluxed
- **Check ligaments on the other side (eg Deltoid). If damaged → unstable** (if talus has shifted during injury ligament will be injured on opposite side + therefore tender + therefore unstable)
- Classified as Weber A (below the tibiofibular joint), B (involving the tibiofibular jt), C1 or C2 (above the tibiofibular jt); Weber C is bad, Weber A benign
- If stable, cast for symptomatic relief for 6 weeks

**Diastasis:**
- Dislocation where no true joint exists
- Separation of the distal tibia and fibula. Talus goes with the fibula. Leads to incongruity of the tibial-talus joint

**Ruptured deltoid ligament:** always exclude *proximal fibular fracture* (Maisoneuve Fracture)

**Dislocation of the ankle:** *reduce urgently* (ie before lengthy transport) otherwise ischaemia of overlying skin

**Varus ankle aprain:** can *avulse the base of the 5th MT* (where peroneus brevis inserts)

**Achilles tendon rupture:**
- Mechanism: *forced dorsiflexion against resistance* (eg jumping, due to a forward lunge in squash) – an *eccentric* injury
- Presentation:
  - Lie prone with foot over end of the bed. Foot normally slightly plantarflexed. If rupture → neutral/dorsiflexed position
  - Swelling plus defect felt in tendon. Squeezing is positive (Simmond’s test). Foot doesn’t move when calf is squeezed
- Management: Hold the ends together until healed – either surgical or conservative.
Conservative: 4 weeks in full plantarflexion below the knee cast then a further 3 weeks with foot half way to neutral. Walking with heeled shoe for a further 8 weeks but not bare-foot. Physio + ultrasound to reduce swelling. Rerupture rate 20%

Operative:
- Makes the tendon heal at the right length, doesn’t heal any faster
- Indicated if: a re-rupture, late presentation (> 48 hours), open wound, or if strong healing necessary (eg athlete)
- Risk: poor skin healing

Nothing vigorous for 6 months post injury

- Ruptured plantaris: severe pain, unable to bear weight
- March Fractures: in the shaft of the 2nd and 3rd metatarsals (2nd most commonly), following excessive walking. X-rays may be normal. Conservative treatment unless severe, in which case cast
- Lisfranc Dislocation:
  - #/dislocation of the midfoot (TMTJ)
  - Of the 1st TMT joint – may impair blood supply to the medial foot

Foot and Ankle Conditions

- Charcot’s Joint = neuropathic joint:
  - Causes: diabetic neuropathy, tabes dorsalis, cauda equina, leprosy
  - Gross disorganisation of the joints (even dislocation) following repeated minor trauma → recurrent stress fractures that aren’t felt due to neuropathy

- Metatarsalgia:
  - Pain in distal foot due to high pressure on the MT heads during walking
  - Can be a/w claw toes
  - Caused by:
    - Freiberg’s infarction: collapse and reformation of the epiphyses of the 2nd and 3rd metatarsal heads
    - Morton’s neuroma of the digital nerve
    - Synovitis + bursitis
    - Sesamoid fracture
    - Injury
    - Pes cavus
  - Management: padded MT bar fitted into the shoes helps to spread the load; surgery (osteotomy)

- Chronic instability:
  - Better prevented than cured
  - Caused by inversion or eversion injury, tearing the collateral ligament
  - Stress x-rays will demonstrate talar tilt → maybe painful
  - Management: non-operative = alter lifestyle, supportive footwear; surgical

- Arthritis:
  - Less commonly affected than hip or knee but can be seen post trauma; RA involvement is to a similar extent as the hip + knee
  - Management: non-operative = walking stick, firm boots, NSAIDs; surgical = fusion or arthroplasty

- Plantar fasciitis:
  - Painful heel condition due to inflammation of plantar fascia at its origin from the os calcis
  - Can be precipitated by trauma/excessive weightbearing
  - Tender over most prominent point of os calcis on sole of foot
  - X-ray can show spur on plantar aspect of os calcis
  - Management: foam heel wedge or steroid injection; surgery to release plantar fascia

- Achilles tendinitis:
  - Local inflammation at insertion of TA (tendo-achilles)
  - May be precipitated by trauma/new footwear
  - Management: heel wedge, steroid injection; surgery to incise the inflamed sheath

Facial Fractures

Nasal Fracture

- Fracture of the nasal cartilages and nasal bone are common and leave a deformity if not correctly treated
- If a nasal fracture is suspected, hold the patient’s nose gently and move it slightly. Pain or abnormal movement indicates a fracture
• Treatment: Dislocated or displaced fractures of the nasal bones need to be repositioned accurately. Refer to ENT

Zygoma
• Fractured by a direct blow to the face
• If there is bruise over the cheekbone, check zygoma fracture
• On inspection and palpation, the zygoma bone should be depressed
• If untreated, depression zygoma will cause diplopia and damage to the infraorbital nerve
• Treatment: fragments need repositioning. May require fixation with wires or external fixation

Orbital Fractures
• If direct trauma to the orbit or eye, look for orbital fracture
• Diplopia and the abnormal position of the eye should lead to the diagnosis
• Treatment: Surgery

Maxilla
• Le Fort classification of maxillary fractures:
  ➢ 1: through the maxilla, leaving nose and orbits intact
  ➢ 2: through the maxilla, into the orbit and across the nose leaving the lateral side of the face mobile
  ➢ 3: same as 2 but fracture extends through the lateral wall of the orbit and across the nose
• All maxillary fractures are an emergency because the lateral wall of the face may be unstable & can fall backwards to obstruct the airway
• Treatment: Secure airway. External fixation to the skull

Mandible
• Dislocation of the TMJ can follow direct or indirect trauma, or even a wide yawn
• Dislocation can usually be reduced easily if the mandible is intact
• Can recognise a fracture by tenderness when the mandible is palpated or squeezed gently, and by a deranged dental occlusion
• X – ray if in doubt
• Soft tissue swelling round a fractured mandible can obstruct the airway
• Treatment: Surgery. May require internal fixation, interdental wiring and dental treatment

Joint and Bone Infections

Septic Arthritis
• Presentation: systemic illness with fever, usually one joint (knee most common), swelling, effusion, warmth, markedly reduced movement of the affected joint, and very painful to move (cf adjacent osteomyelitis → some pain only). Hip and shoulder have less swelling
• In neonates, may overlap with acute haematogenous osteomyelitis
• Risk factors: diabetes, recurrent steroid injections, systemic steroids, alcoholic liver disease, immunosuppression
• Differential:
  ➢ Gout and pseudogout
  ➢ Haemarthrosis
  ➢ Acute osteomyelitis
  ➢ Acute traumatic arthritis
• Pathogenesis:
  ➢ From haematogenous spread or extension of osteomyelitis, often following distant infection. Also following penetrating injury
  ➢ WBC enzymes rapidly erode hyaline articular cartilage → surgical emergency: empiric antibiotics and rapid drainage. Urgent – can destroy a joint in 24 hours. In neonates/kids can damage growth plate → growth disturbance
  ➢ S. Aureus, also S pneumoniae and S pyogenes. In high-risk groups, M Tb and Candida. Neonates consider S agalactiae, Haemophilus and N gonorrhoea (did they have bacterial conjunctivitis soon after birth?). Pseudomonas from foot wound
  ➢ Tb arthritis: usually haematogenous spread from lungs to hips (kids), knees (adults) or spine. X-ray shows marginal erosions and destruction of sub-chondral bone (like Rheumatoid – but different distribution).
Have granulomas (except in AIDS). Histology: Granulomas are pink, cf lymphoid aggregates in Rheumatoid that are blue

- **Investigations:**
  - *Joint aspiration* BEFORE ABs (arthrocentesis: opaque fluid with WBC > 50,000/ml)
  - FBC, ESR, CRP, **blood cultures**, plain Xray, US (for detection effusion)
  - Xray delays rather than establishes the diagnosis

- **Management:**
  - Flucloxacillin: for staph aureus, but also covers S pneumonia, S pyogenes, S agalactiae
  - If neonate:
    - And unimmunised consider H. Influenzae: cefuroxime or cefotaxime
    - Consider G–ive: gentamycin
  - Arthroscopic or open washout (URGENTLY)
  - Initial splinting for pain relief, but then encourage mobility
  - If there is a joint prosthesis, revision may be necessary

- **Complications due to delayed diagnosis:**
  - Joint degeneration, joint dislocation, ankylosis
  - Damage to the growth plate → growth arrest (epiphysis can be destroyed → unstable pseudoarthrosis = Tom Smith’s dislocation)

**Osteomyelitis**

- Common in *low socio-economic* and warmer weather
- May follow *minor trauma* with or without infection elsewhere in body
- **Physical findings:**
  - Look: redness + oedema, limb held still
  - Feel: warmth, focal bony tenderness, fluctuant swelling over bone
  - Move: pain on movement

- **Acute haematogenous osteomyelitis (= primary OM):**
  - **Presentation:**
    - Early: short, febrile illness, bone pain, metaphyseal tenderness (point tenderness)
    - Late: swelling/erythema (suggest abscess). Cellulitis. Adjacent joints sore but some movement still possible
    - Vascular supply to bone is compromised and infection spreads to surrounding soft tissue
  - **Differential diagnosis:**
    - Septic arthritis
    - Cellulitis
    - Trauma (#)
    - Tumour
  - **Aetiology:**
    - 1. Trauma/surgery → **direct introduction** of bacteria (= secondary OM)
    - 2. **Direct extension from infective site**: eg dental infection → jaw, diabetic foot → bones of foot
    - 3. **Haematogenous** seeding:
      - Commonest site in children is **metaphysis of the long bones**. Femur and tibia account for > ½ all cases (especially around knee joint). Epiphyseal growth plate acts as a barrier to the spread of infection to the joint. May spread through Haversian and Volkmann’s canal system to form a subperiosteal abscess (requires drainage)
      - In adults, haematological spread less common. Tends to affect subperiosteal cortices of long bones. Also cancellous bone of vertebral bodies, may → compression fracture
      - Eg: sluggish blood flow → easy thrombosis following trauma → predisposes to infection (esp staph aureus)
  - **Pathology:** Inflammatory response → oedema → compromised vascular supply → necrosis → spread of infection through cortices → pus under periosteum → shearing of periosteum → further disruption to blood vessels
  - **Causative organisms:**
    - Under one year: staph aureus, strep agalactiae, E coli. May be non-specific illness
    - Children: staph aureus, strep pyogenes, H influenzae
    - Adults: staph aureus, staph epidermis and G negatives (E coli, salmonella and pseudomonas from foot wounds)
    - M. Tb and Candida in high risk groups
  - **Complications:**
Spread of infection → septicaemia, septic arthritis
- Fracture, abscess formation
- Chronic osteomyelitis in 5 – 20% of cases

**Subacute osteomyelitis**: Focal rather than systemic response to infection. Xray shows bone destruction.
Differential includes bone tumour and stress fracture

**Chronic osteomyelitis**:
- Usually delayed or inadequate treatment
- Pain, swelling +/- discharging sinuses
- Xray: destruction, with **sequestrum (areas of necrotic bone which can’t be resorbed)** harbouring bacteria and **involucrum (periosteum surrounding necrotic bone/abscess)**. Brodie’s abscess: abscess surrounded by sclerotic bone due to organisms of low virulence
- Treatment: **sequestrum must be removed**, may require repeated surgery. Poor penetration of antibiotics
- Complications:
  - Persistently discharging sinus
  - Chronic ill health
  - Pathological fractures/deformities
  - Malignant change → SCC

**Investigations**:
- **Blood**: FBC, ESR, CRP, *Blood cultures (+ive in 50%)*
- **Imaging**:
  - Plain films: no changes until **day 10-14** (then periosteal reaction/involucrum)
  - US: subperiosteal abscesses
  - Bone scan: very sensitive but not specific (can show ↑activity after a few days)
  - MRI: very sensitive but expensive
  - CT: good for detecting degree of bone destruction

**Treatment**:
- High dose IV antibiotics for at least 2 – 4 days (for children, Flucloxacinill 50 mg/kg/6 hourly, max 2 g), followed by 3 – 4 weeks of oral therapy. Should **continue until ESR has returned to normal**
- Non-operative (only an option for acute osteomyelitis): splinting + elevation + ABs
- Surgery to decompress and remove necrotic bone if chronic or failed medical treatment (acute), or subperiosteal abscess drainage

**Specific presentations**:
- Osteomyelitis of the calcaneum: infection 5 – 10 days after puncture wound. *P aeruginosa*
- Discitis: inflammation of the lumbar disc, usually < 8 years
- Pelvic osteomyelitis: pain referred to the abdomen, buttock or leg. *S aureus*. Bone scan diagnostic
- Tub Osteomyelitis: rare in developed world. Occurs in 1-3% of patients with pulmonary Tb. Insidious. After months: pain on movement, fever, night sweats, weight loss. Destructive. If lumber or thoracic vertebrae may → hunchback deformity

**Osteomyelitis Pathology**
- Inflammation of bone and marrow due to infection
- Most commonly a **primary** focus of disease, also maybe part of a systemic infection
- Clinical presentation: varied, long bones/vertebrae of healthy pts, x-ray = lytic lesion and zone of sclerosis, bx and bone culture
- Mechanism of infection:
  - Haematogenous spread
  - Extension from contiguous site
  - Direct implantation
- **Staph aureus** responsible in 90% of cases
- Can be a hx of minor trauma
- Location of lesion influenced by vascular circulation and changes with age
- Pathogenesis:
  - Essentially: infection → inflammation → ischaemia → necrosis → periosteal reaction
  - Infection localises in bone, bacteria proliferate and cause an inflammatory response leading to cell death and ↓ blood supply
  - Tissues become ischaemic
  - Area of bone undergoes necrosis and infection spreads through shaft
  - Inflammation reaches and disrupts the periosteum which further impairs blood supply
  - Suppurative and ischaemic injury causes large areas of necrosis = **sequestrum** ("sequestered")
Musculo-skeletal, Rheumatology and Plastics

- Rupture of periosteum forms a draining sinus into soft tissue
- With time a host response develops with formation of a sleeve of reactive bone = involucrum ("involved")

**Microscopy:**
- Inflammation and fibrosis of the marrow space: acute = neuts; chronic = plasma cells
- Necrotic bone: lacunae which are empty

**Clinical consequences:**
- Systemic illness
- Pain, pathological #, chronic draining sinus
- Endocarditis, sepsis
- SCC in sinus tract

**Pyogenic Infections of the Hand & Other Locations**
- Usually history of trauma
- **Paronychia:** common infection of periungual tissues, usually by Staph Aureus
- **Felon:** deep infection of the pad of the finger. Usually Staph aureus following puncture wound
- **Cellulitis:** Strep Pyogenes infection
- Suppurative flexor tenosynovitis:
  - Infection of flexor tendon sheaths
  - Presentation: swollen finger with painful motion. Symmetrical swelling, tenderness, erythema along tendon sheath. Semi-flexed posture and severe pain on passive extension of DIP joint
  - Signs: crepitus, erythema, vesicle formation, colour, pain, pus
  - Tests:
    - Culture of pus, blood culture, FBC
    - X-ray to rule out foreign body, air in tissue or joint, associated fracture
  - Treatment: irrigate, leave wound open and dress after swelling has decreased, antibiotics, splint

**Atypical infections:**
- Herpes infections of the thumb and fingers (eg Whitlow's lesions)
- Fungal infections: more indolent. Sporotrichosis common

**Bites:**
- Animal bites often become infected with staph + strep and other unusual organisms
- Human bites are even more prone to infection – staph most common
- All wounds should be presumed infected – x-ray to exclude # or FB
- Treat aggressively – debridement + washout + IVABs; splint post-op

**Metabolic Bone Disease**
- **Osteoporosis:** bone matrix reduced in amount but normally mineralised (ie ↓bone mass due to loss of both protein matrix and Ca in equal proportions)
- **Osteomalacia:** normal amount of bone matrix but deficient mineralisation (ie ↓Ca)
- Both will appear on x-ray as osteopenia (poverty of bone)

**Bone Metabolism**
- **Osteoblasts:**
  - Synthesise osteoid: normally this is a thin layer as the time between matrix deposition and mineralisation is short. If either ↑osteoid or delayed mineralisation → thick layer (hyperostoidosis), eg:
    - ↑Bone formation: fracture callus, Paget’s disease, hyperparathyroidism
    - ↓Calcium, phosphorus, or vitamin D
    - Blocked mineralisation due to inhibitory/toxic substances (eg aluminium, iron, fluoride)
  - Mediate osteoclast activity
  - Flat when inactive, plump when active. Become buried in cortex (then called osteocytes)
  - ↑Activity due to: physical activity, ↑PTH, growth factors, fluoride
  - ↓Activity due to: inactivity and steroid hormones
- **Osteoclasts:**
  - Regulated by PTH and osteoblasts
  - Large cells containing 2 – 4 nuclei
  - Adhere to bone and are seen in depressions referred to as Howship’s lacunae or resorption bays → scalloped appearance of resorbed bone
- **Woven bone:** immature bone laid down by osteoblasts in a callus (eg healing of a fracture)
- **Lamellar bone:** parallel and organised
**Tetracycline:**
- Give pulses before bone biopsy
- Binds to **actively mineralising surfaces** and fluoresces in UV light under the microscope
- **Shows the extent of mineralisation** and amount of bone formed over a given time

**Osteoporosis**

- Normal bone composition – just less of it. Either primary or secondary
- Epidemiology:
  - Often presents with a hip fracture. 3 per 1000 in men and 6 per 1000 in women over 65 per year. Number of vertebral fractures and resulting disability unknown
  - ¼ of those > 80 going to hospital with a fracture don’t return to their previous residential status
- Pathogenesis:
  - Bone is constantly turning over. From the 3rd decade, **resorption exceeds bone formation** – the two become uncoupled. In women, this accelerates post menopause (oestrogen is protective). Around menopause will lose 6 – 10% of bone mass, then returns to gradual decline
  - Trabecular bone (20% of skeleton) turnover 8 times that of cortical bone (80% of skeleton). Femoral head has lots of trabecular bone ⇒ good place to measure loss. Use Singh Index of number of trabecular groups present (6 = good, 1 = bad)
  - Also thinning and attenuation of the cortices
  - Fracture risk a combination of density (which we can measure) and structure (which we can’t)
  - By the time they present with a fracture, osteoporosis is usually advanced
- Severity depends on:
  - Peak bone mass. Peaks around age 30. Largely determined by type of inherited vitamin D receptor. Also Ca intake in teens, etc
  - Sex: peak bone mass of males > females
  - Age: men affected later than women
  - Also **physical activity positive** (disuse → localised osteoporosis), smoking **negative**, calcium intake
- Distribution:
  - Osteoporotic vertebra (most common fracture):
    - Lose secondary trabeculae 1st (leaves vertical lines of primary trabeculae) → clear glass appearance
    - Changes in shape: wedge, biconcave, planar (ie flat)
    - Anterior part of vertebrae reduced
    - May occur with trivial trauma or lifting
    - Small fractures don’t cause immediate pain – comes on after several days. If no scoliosis then can heal
  - Fractures affecting proximal femur, proximal humerus, distal radius resulting from falls
  - Look for insufficiency factors in the sacrum, pubis, and supra acetabular
- Differential of osteoporosis:
  - Male: hypogonadism (⇒↓testosterone), excess alcohol
  - Female: ↓Ca and Vit D post menopause
- Scanning for osteoporosis:
  - Plain x-ray insensitive: don’t show changes until 30 – 40% of bone mass lost. Radiodensity varies due to exposure, developing, and patient’s build
  - Dual Energy X-ray Absorbiometry = DEXA:
    - Measures bone density (ie Ca density) by firing X-rays of 2 different wave lengths – one maximally absorbed, the other absorbed as much as carbon, and subtract the two
    - Number of standard deviations from the mean (of 30 year old women) more important than actual density. T < -2.5 standard deviations = Osteoporosis. Osteopenia: -1 < T < -2.5 (Z score is cf peers)
- Management:
  - Prevention:
    - Physical exercise (⇒bone laid down)
    - Adequate Ca (prevents bone resorption)
    - Vitamin D if house bound (a small amount of sun is sufficient)
    - Rocaltol: 1,25(OH)2D3 (activated vit D)
    - HRT: most stop before 5 years – compliance problem. Can start at any age – but if elderly need to build up gradually
  - Treatment: **alendronate** (or Fosamax) → osteoclast action → turnover → gain bone
**Pathology**

- **Macro:**
  - Entire skeleton affected
  - Post-menopausal OP affects bones with ↑ SA ie vertebral bodies
  - May see complications: collapse, #
- **Micro:**
  - Trabeculae: thin, ↓ in number → microfractures

**Osteomalacia**

- = normal amount of bone matrix but deficient mineralisation (ie ↓ Ca)
- Osteomalacia in adults = Rickets in kids
- Present with bone pain, fractures (eg neck of femur) or waddling gait (proximal myopathy)
- Aetiology:
  - Deficiency or abnormal metabolism of vitamin D
  - Calcium deficiency
  - Renal failure
- Pathology:
  - Intracortical tunnelling (due to secondary hyperPTH)
  - Coarsened indistinct trabecular pattern (due to seams of osteoid) → frosted glass appearance
  - Looser's zones: the hallmark of osteomalacia: lateral margin of scapula, ribs, pubic rami, proximal femur, proximal ulna
    - This is a pseudofracture seen in osteomalacia
    - On x-ray, it appears as a thin, translucent band, about 2 mm in width, which runs perpendicular to the surface of the bone extending from the cortex inwards
    - Looser's zones are incomplete stress fractures which heal with callus lacking in calcium, and are most readily seen in the pubic rami, the necks of the humeri and femora and at the axillary edge of the scapulae
  - Micro: ↑↑ in unmineralised bone (up to 40 – 50%) + disorganisation of trabecular architecture
- In children:
  - Changes around metaphyses of most rapidly growing bones (knee and wrist)
  - See irregular and broadened epiphyseal growth plates + metaphyseal cupping
- Investigations:
  - X-rays: generalised osteopenia + multiple, bilateral, symmetrical partial linear fractures (stress fractures)
  - Maybe ↑ALP, ↓vitamin D
  - PTH assay not very helpful: normal range is too wide (0.5 – 5) so can mask an increase. Mild increase → ↑ osteoclastic activity, but serum Ca normal so remineralising normally → osteopenia and not osteomalacia

**Increased Bone Resorption**

**Hyperparathyroidism**

- See also Parathyroid, page 145
- Old term: osteitis fibrosa cystica
- ↑PTH (either primary of secondary) → ↑Ca and ↓ PO4
- Presentation: kidney stones, peptic ulcer, bone pain, nausea, vomiting, weakness, headaches, depression (bones, stones, groans). Now rare – usually picked up as an incidental finding of hypercalcaemia
- Affects cortical bone more than cancellous/trabecular bone
- ↑ Osteoclast and osteoblast activity
- May → reactive fibrosis tissue (eg following microfractures and secondary haemorrhages) → mass called a ‘Brown tumour’
  - Brown tumour occurs in severe hyperparathyroidism
  - Due to micro# + secondary haemorrhage with influx of multinucleated macrophages → reactive fibrous tissue
  - Appears as lytic lesions of the bone
  - Brown macroscopically
- X-ray: generalised osteopenia and tufts on end of distal phalanges
- Differential:
Blood sample with dehydration or tourniquet $\rightarrow$ ↑Ca
Malignant disease and/or neoplastic syndrome with PTHrH secretion
Sarcoidosis
Vit D intoxication
Diuretic therapy

- Treatment: neck exploration for parathyroid adenoma

Pathology:
- Macro:
  - Cortical bone affected more severely than cancellous
  - Thinned cortices
  - Radial aspect of middle phalanges
- Micro:
  - Osteoclasts that bore into the haversian canals and trabeculae
  - ↑OB activity

Renal Osteodystrophy

- = All skeletal changes resulting from chronic renal disease, including:
  - ↑Osteoclast resorption (mimicking hyperPTH)
  - Delayed matrix mineralisation (osteomalacia)
  - Osteosclerosis
  - Growth retardation
  - Osteoporosis
- Due to:
  - PO4 retention $\rightarrow$ Secondary HyperPTH $\rightarrow$ ↑Osteoclast activity
  - Metabolic acidosis $\rightarrow$ bone resorption
  - ↓ Conversion of 1,25(OH)2D3 in kidneys $\rightarrow$ hypocalcaemia
  - Aluminium deposition (from antacids, dialysis fluid) at the site of mineralisation $\rightarrow$ ↓mineralisation
- Similar impact to osteomalacia: ↑PTH $\rightarrow$ osteoclastic bone resorption
- Investigations:
  - X-ray and bone densitometry
  - Bloods: Ca, albumin, phosphate, PTH, ALP, Vitamin D3 levels
  - Urine Ca usually low and faecal Ca high

Paget’s Disease

- Common (5-11%) in northern Europeans, rare in Blacks/Asians, M = F, usually old
- = ↑osteoclastic activity $\rightarrow$ ↑osteoblastic activity $\rightarrow$ quiescent phase (no resorption/reformation) $\rightarrow$ weaker + thicker bone
- Presentation:
  - Monostotic (affecting a single bone), asymptomatic and incidental finding on x-ray (doesn’t spread)
  - In a small number, widespread, polyostotic lesions with bone pain (worse at night), fracture, arthritis or development of a sarcoma
  - Usually axial skeleton (spine, skull, pelvis) and femur or tibia (can see bowing)
- Pathogenesis: viral infection (paramyxovirus) of osteoclasts $\rightarrow$ ↑↑ osteoclast activity $\rightarrow$ ↑↑ osteoblast activity $\rightarrow$ disorganised, WOVEN bone. Normal bone mineralisation. Also genetic and geographic predisposition
- Gross: enlarged bone with thick cortices
- Micro: irregular trabeculae with numerous osteoclasts and plump osteoblasts, jigsaw pattern
- Prognosis:
  - Progressive bone deformity and micro fractures, anterior bowing of the femur. Arthritis due to deformed joints
  - Osteosarcoma in 5 – 10% of those with severe disease
- Investigations:
  - X-ray: early radiolucency. Late: loss of distinction between cortical and cancellous bone (may be confused with primary bone tumour)
  - ↑Bone formation $\rightarrow$ ↑↑ALP but Ca and PO4 normal.
  - ↑Urinary hydroxyproline
- Treatment:
  - Mild: NSAIDs – indicated if pain
  - Severe: bisphosphonates (alendronate), calcitonin
• Complications:
  ➢ Fractures
  ➢ *Spinal stenosis* → nerve compression
  ➢ Osteosarcoma
  ➢ OA
  ➢ Enlargement of the skull, femur, clavicle, tibia (‘Sabre Tibia’)
  ➢ Neural deafness due to bone overgrowth
  ➢ *High* output heart failure (due to ↑ blood flow to bone)

• Pathology:
  ➢ Macro:
    o Mono or polyostotic
    o *Axial skeleton/femur*
    o X-ray findings: enlarged bone with thick cortex
  ➢ Micro:
    o Mosaic pattern (abnormal mosaic cement lines)
    o +/- osteoclastic activity

**Bone Tumours**

• Primary bone tumours are rare (secondaries more common)

• **Myeloma accounts for half** of malignant bone neoplasms:
  ➢ Old, M > F, pathogenic fractures, pepper-pot skull, normocytic anaemia with *Rouleaux*
  ➢ Gross: red currant jelly lesions
  ➢ See Multiple Myeloma, page 486

• NB. **Sarcomas** are malignant neoplasms arising from or differentiating towards mesenchymal tissue eg bone, cartilage, fat, muscle, nerve, blood vessels, fibrous connective tissue

• Classification based on histology of tumour cell – cell of origin is unknown/debated. Diagnosis difficult. Requires clinician, radiologist, pathologist

• Pain is common + localised at site of tumour – unrelenting + worse at night (benign tumours are often asymptomatic unless a pathological # occurs)

• Classification:

<table>
<thead>
<tr>
<th>Histologic Type</th>
<th>Benign</th>
<th>Malignant</th>
</tr>
</thead>
<tbody>
<tr>
<td>Haematopoietic</td>
<td></td>
<td>Myeloma</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Lymphoma</td>
</tr>
<tr>
<td>Chondrogenic</td>
<td>Chondroma/enchondroma</td>
<td>Chondrosarcoma</td>
</tr>
<tr>
<td></td>
<td>Chondroblastoma</td>
<td></td>
</tr>
<tr>
<td>Osteogenic</td>
<td>Osteochondroma</td>
<td>Osteosarcoma</td>
</tr>
<tr>
<td></td>
<td>Osteoid osteoma</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Osteoblastoma</td>
<td></td>
</tr>
<tr>
<td>Fibro-histiocytic</td>
<td>Fibrous dysplasia</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Non-ossifying fibroma</td>
<td></td>
</tr>
<tr>
<td>Unknown</td>
<td>Giant Cell Tumour</td>
<td>Malignancy in giant cell tumour</td>
</tr>
<tr>
<td></td>
<td></td>
<td><em>Ewing’s sarcoma</em></td>
</tr>
</tbody>
</table>

• Investigations:
  ➢ X-ray: benign tumours have a sharp margin + cortex is intact; malignant tumours are expansive with indistinct margins + cortical destruction
  ➢ Isotope scan: differentiates secondary deposits
## General Malignancy Classification

### Secondary Bone Tumours
- Most common bone cancer \( \Rightarrow \) always ask about previous primaries
- Source: breast > prostate > kidney > lung > thyroid
- Sites: vertebrae, ribs, pelvis, proximal femur, humerus
- Multifocal sites often
- Spread: usually haematogenous. Occasionally local extension
- Usually osteolytic (except prostate ca + 10% of breast cancers (or most according to Nowitz) which are osteosclerotic) \( \Rightarrow \) pathological #
- Two age distributions: adults > 40 (carcinomas), children < 10 (neuroblastoma, retinoblastoma, rhabdomyosarcoma)
- Presentation:
  - Pain + history of cancer in 50 – 70 year old
  - In children < 6 years: from neuroblastoma
  - Symptoms of hypercalcaemia: anorexia, nausea, weakness, depression, polyuria
- Investigations:
  - Xray: usually osteolytic lesions (if osteoblastic probably carcinoma)
  - Bone scan, FBC, ALP, Electrophoresis (myeloma)
  - FNA: determining cell of origin helps guide management
- Treatment: usually palliative, control pain, prophylactic fixation, spinal stabilisation, radiotherapy (↓pain). Pathological #s do not unite spontaneously + should therefore be internally fixed

### Example of Benign Versus Malignant Bone Tumour

<table>
<thead>
<tr>
<th>Chondroma</th>
<th>Chondrosarcoma</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical (age + site)</td>
<td></td>
</tr>
<tr>
<td>Younger</td>
<td>Older</td>
</tr>
<tr>
<td>Extremities (hand/feet)</td>
<td>Flat bones of pelvis + ribs + large bones</td>
</tr>
<tr>
<td></td>
<td>eg shoulder</td>
</tr>
<tr>
<td>Radiology</td>
<td></td>
</tr>
<tr>
<td>Well circumscribed</td>
<td>Destructive</td>
</tr>
<tr>
<td>Oval</td>
<td>Expansile</td>
</tr>
<tr>
<td>Radiolucent</td>
<td>Popcorn calcifications</td>
</tr>
<tr>
<td>Pathology</td>
<td></td>
</tr>
<tr>
<td>- Macro</td>
<td></td>
</tr>
<tr>
<td>Smooth, well circumscribed</td>
<td>Irregular, a/w #, large</td>
</tr>
<tr>
<td>- Micro</td>
<td>Cytological features of malignancy</td>
</tr>
<tr>
<td>Orderly cartilage formation with no cellular atypia</td>
<td>Myxoid stroma (‘Loose’ pale-to-lightly basophilic, as stained by H&amp;E; cells present include fibroblasts)</td>
</tr>
</tbody>
</table>

### Primary Bone Tumours
- Mostly first 3 decades (greatest skeletal growth activity)
- Predominantly distal femur/prox tibia (highest growth rate)
- Benign > malignant
- Diagnosis:
  - Age:
    - Children < 20
      - Osteochondroma
      - Osteoid osteoma
      - Osteoblastoma
    - Osteosarcoma
    - Ewing’s sarcoma

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<table>
<thead>
<tr>
<th>NOF</th>
<th>Young adults &lt; 40</th>
<th>Giant cell tumour</th>
<th>Enchondroma</th>
<th>Osteosarcoma</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Older adults &gt; 40</td>
<td>Osteoma</td>
<td>Myeloma</td>
<td>Chondrosarcoma</td>
</tr>
</tbody>
</table>

- Anatomic location: ie metaphyseal, epiphyseal, diaphyseal

- Nature of pain (ie osteoid osteoma)
- Multiple vs solitary
- Radiology
- Histology (H & E + immunohistochemistry to determine cell lineage)

**Benign Osteogenic Tumours**

- **Osteochondroma (exostosis):**
  - Most common benign tumour of bone
  - Results from displacement of a lateral portion of the growth plate → growth of an aberrant focus of cartilage on the surface of the bone (?adherent growth plate)
  - Very small chance of malignant progression
  - Cartilage-capped lateral bony projection from the metaphysis, usually long bones. Also know as an **exostosis**
  - Can be hereditary (→ multiple, present in early adulthood → diaphyseal aclasis)
  - Symptoms due to size, impingement or fracture
  - Macro:
    - Cartilage capped outgrowth
    - Metaphysis of long bones
    - Mushroom shaped
  - Micro:
    - Hyaline cartilage overlying bone
  - X-ray: mushroom like growth from metaphysis
  - Regular shape. If irregular then ?malignant

- **Osteogenic tumours:** produce osteoid:
  - **Osteoid osteomas + osteoblastomas** look exactly the same but differ in size, site, and clinical features:

<table>
<thead>
<tr>
<th>Osteoid osteoma</th>
<th>Osteoblastoma</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Size</strong></td>
<td></td>
</tr>
<tr>
<td>&lt;2cm</td>
<td>&gt;2cm</td>
</tr>
<tr>
<td><strong>Site</strong></td>
<td></td>
</tr>
<tr>
<td>Cortex of femur/tibia</td>
<td>Spine</td>
</tr>
<tr>
<td><strong>Clinical</strong></td>
<td></td>
</tr>
<tr>
<td>Severe nocturnal pain relieved by ASA</td>
<td>Dull achy pain not relieved by ASA</td>
</tr>
</tbody>
</table>

- Macro:
  - Circumscribed masses of gritty haemorrhagic tissue
- Micro:
  - Interconnecting trabeculae of woven bone
  - Prominent osteoblasts
  - Stroma contains capillaries
- Treat conservatively

**Malignant Osteogenic Tumours – Osteosarcoma**

- Proliferating malignant tumour producing osteoid
After multiple myeloma, it is the most common primary malignant bone tumour but still very uncommon

50 – 60% of cases are near the knee (either distal femur or proximal tibia); metaphyseal (area of greatest bone growth)

Bimodal age distribution:
- Adolescent growth (age 10 – 30; 75% < 20). M:F = 2:1
- 25% of osteosarcoma in 60 – 70s, secondary to existing disease (e.g. in < 1% of Paget’s), previous irradiation, etc

Presentation: painful, enlarging mass, pathological #

Very aggressive: assumed to have metastasised at diagnosis – usually to lung (haematologically; in preference to lymph nodes)

Risk factors:
- High risk: Ollier’s disease (multiple chondromas)
- Moderate: Paget’s, radiation
- Low: bone infarct, chronic osteomyelitis

X-ray:
- Geographic destruction, dense or lytic
- Raised periosteum
- See spiculated periosteal reaction (sunray lesion)

Macro: haemorrhagic

Micro: osteoid formation, malignant spindle cells (often see spindle cells in mesenchymal tumours)

Investigations: X-ray, serum ALP (markedly ↑), and biopsy

Treatment: chemotherapy → resection → prosthesis → post-op adjuvant chemo (high dose methotrexate)

5 year survival 60%

Benign Chondroid Tumours

Chondroma/Enchondroma:
- Collections of cartilage in or on bone
- Enchondroma = within the medullary cavity of tubular bones of the hand and feet
- Chondroma = on the surface of bone
- Asymptomatic or pain a/w pathological #
- Ollier’s disease: multiple chondromas, may undergo malignant transformation to osteosarcoma
- Differential is chondrosarcoma – suspect if large bone in an older patient, erosion of the cortex or suspicious histology

Chondroblastoma: benign chondroid neoplasm at the end of long bones during teens

Malignant Chondroid Tumours – Chondrosarcoma

Malignant tumour of cartilage, with no tumour osteoid or bone being formed

Pain becomes severe and persistent, swelling

Typically age 30-70 (average 45 years), second most common malignant matrix (chondroid matrix) producing tumour of bone; M > F

Most common in the medullary cavity of the flat bones of the central skeleton: pelvis, shoulders and ribs. Rare to involve the extremities

Macro:
- Large bulky tumours
- Nodules of grey/white translucent glistening tissue

Musculo-skeletal, Rheumatology and Plastics
- Calcification
- Infiltrates bone marrow

- Micro:
  - Neoplastic cartilage (hypercellular, multinucleate cells, mitoses, pleiomorphism etc)
  - Conventional chondrosarcoma: *diaphysis or metaphysis of long bones*. Margins poorly defined. Eroded or thickened cortex.

- X-ray: fluffy *calcification*
- Treatment: tend to *metastasise late* (to lung and other bones) → attempt *local excision and replacement* with prosthesis (RT ineffective)
- Prognosis (depends on grade + size): Grade 1 and 2 80 – 90% 5-year survival, Grade 3 (rare) 40% 5-year survival. Local or distant metastasis may occur up to 20 years later

**Benign Fibrohistiocytic Tumours**

- Fibrous cortical defect and non-ossifying fibroma: look identical but vary in size
- Developmental defects, seen in the *metaphysis* of distal femur/proximal tibia
- Most common (up to 50%) benign bone tumor in children. M > F
- Fibrous cortical defect: <3cm
- Non-ossifying fibroma: >3cm
- In most cases, no treatment is necessary because these tumours typically ossify after a few years
- Asymptomatic but can see pathological #
- **Macro**: sharply demarcated lucencies, thin zone of sclerosis
- **Micro**: cellular lesions, fibroblasts + histiocytes
- **No rx necessary**

**Malignant Fibrohistiocytic Tumours**

- Small print
- **Fibrosarcoma**:
  - Malignant tumour of fibroblasts (ie collagen producing cells)
  - Occurs in any connective tissue but more common in the extremities and middle aged
  - Fibrosarcoma of the bone is *rare*. Swelling, pain, pathological fracture
- **Synoviosarcoma**:
  - Rare malignant tumour of the synovium, usually sharply circumscribed
  - Rapid enlargement of the joint with pain. Usually knee, hip or shoulder
  - May extend along fascial lines and invade bone
  - Treatment: if small then excise, if high grade: resection + radiotherapy + chemotherapy

**Unknown Histiogenesis**

- **Ewing’s Tumour**:
  - 2nd most common bone tumour in children
  - Rare. t(11;22)(q24;q12) usual → fusion product acts as an oncogene
  - Usually age 5 – 10, 80% < 20yrs
  - Usually *diaphysis of long bones* or *iliac wing*, presenting with localised pain or swelling
  - Painful enlarging mass
  - **X-ray**:
    - Destructive lytic lesion
    - Permeates soft tissues
    - Often associated with a lamellated or "onion skin" periosteal reaction
  - **Macro**: arises in medullary cavity, tan white colour
  - **Micro**:
    - Sheets of uniform small round blue cell
    - Little stroma
    - Necrosis
  - Treatment: chemo + surgery +/- radiation
  - 75% 5-year survival
  - Can mimic osteomyelitis
- **Giant Cell Tumour**:
  - Uncommon, usually *benign* but locally aggressive
  - F > M, age 20 – 40

*Musculo-skeletal, Rheumatology and Plastics*
- Ends of long bones or anywhere, lytic lesions
- Macro: large red/brown lesions
- Micro: contains multineutelated giant cells + uniform oval mononuclear cells
- High local recurrence (50%), rarely metastasises
- Treatment: conservative surgery

**Lesions That Simulate Bone Neoplasms**

- **Fibrous dysplasia:**
  - Components of normal bone present but **do not mature normally**
  - **Monostotic** (70%): adolescents, ribs/femur/tibia/jaw/skull
  - **Polyostotic** (27%): earlier age, craniofacial involvement, crippling deformities, #
  - McCune-Albright syndrome (3%): polyostotic FD + skin pigmentation abnormalities
  - Macro: well circumscribed, intramedullary, ground glass appearance on x-ray, tan/white
  - Micro: curvilinear trabeculae of woven bone, cellular fibroblastic stroma
  - Complications: #, polyostotic \(\rightarrow\) malignant transformation

**Paediatric Orthopaedics**

**Congenital Abnormalities**

**Cleft Lip and Palate**

- Failure of fusion of maxillary and premaxillary processes during week 5. With cleft lip, the lesion runs from the lip to the nostril, can be bilateral
- Incidence: 0.8 – 1.7 per 1000
- Cause: genes, drugs (benzodiazepine, antiepileptics), rubella
- Treatment:
  - Feeding with special teats
  - Surgery: repair lip at 3 months old, palate at 1 year old
- Prognosis: Unilateral or incomplete \(\rightarrow\) good results. Bilateral lesions \(\rightarrow\) some residual deformity
- Complications: otitis media, aspiration pneumonia, speech problems (refer to SLT)

**Developmental Dysplasia of the Hip**

- Old term = Congenital Dislocation of the Hip
- Occurs after birth. Covers a spectrum from instability through subluxation to dislocation
- NB. The stimulus for a concave acetabulum is the presence of a femoral head (and vice versa) therefore is key to maintain the femoral head and acetabulum in contact for appropriate development of both
- More common on the **left**. 25% bilateral
- Incidence: 1 – 1.5 in 1000, more common in **girls**
- Natural history: 1:60 born with instability \(\rightarrow\) 60% of these become stable after the first 1/52 of life
- Often packaged with spina bifida, foot deformities and torticollis
- Risk factors:
  - Extended breech, females, positive family history, first child, post-maturity, oligohydramnios
  - Five f’s: female, FHx, first-born, foot first, foot deformity
- Clinical: from 12 months shortening of the limb, external rotation and asymmetrical skin creases. Delayed walking, Trendelenburg gait and OA in early 30s
- Diagnosis:
  - Asymmetric skin folds
  - Barlow’s test: test for instability. **Down and adduct**. Fix the pelvis with one hand and try press the head and neck of the femur backwards in adduction out of the acetabulum
  - Ortolani’s test: flex hips to 90º then abduct them \(\rightarrow\) click/clunk as femoral head slips back into the acetabulum
  - Galeazzi test: flex hips + knees and place feet flat on the floor. A difference in knee height = positive test = likely dislocated hip
  - Hip abduction: will be ↓ in dislocated hip
  - Examine neck (torticollis), spine (signs of spina bifida), feet (metatarsus adductus, calcaneovalgus) also
- Investigations:
  - Neonatal = ultrasound to assess acetabular shape + dynamic imaging (whilst doing ortolani’s/barlow’s)
  - > 4/12 = x-ray (no point before this as femoral head is not ossified)
X-ray:
- Draw horizontal line (Hilgenreiner's line) through triradiate cartilage + a vertical line (Perkins line) at most lateral edge of superior acetabulum → femoral head should be in the lower inner quadrant
- Acetabular index: angle between horizontal line through triradiate cartilage + superior border of acetabulum should be < 27.5° (↓ as child ages, ie should be < 24° at 24/12)

Treatment:
- Obtain reduction, maintain reduction (to allow acetabulum to grow), monitor acetabular development
- 0-6/12: constant bracing (Pavlik harness) to maintain or achieve reduction
- 6-8/12: closed or open reduction (with tendon/ligament release) of hip joint + Pavlik harness
- >18/12: ie post walking: open reduction + femoral osteotomy +/- pelvic osteotomy

Prognosis:
- The earlier the treatment the better the outcome. Otherwise degenerative changes in the femoral head (eg anteversion), acetabulum, capsule, altered alignment
- Poor prognosis: boy, late detection, Ortolani's negative (ie doesn’t reduce easily)
- Clicking: a common finding and rarely associated with CCH

Club Foot
- = Congenital Talipes Equinovarus (CTEV)
- Can be:
  - Positional (ie held in a club foot position but correct themselves)
  - Idiopathic, or
  - Teratologic (syndromic eg spina bifida)
- Incidence: 1 in 1000. M:F 2:1. 50% bilateral. ↑ incidence in MAP. Associated with other abnormalities (eg myelomeningocele)
- Natural history: walks on dorsolateral aspect of foot
- Pathogenesis: unclear, genes vs envt
- Twisting of calcaneum, navicular, + cuboid around the talus (talus is generally in the normal position)
- Small foot at birth, plantar flexed (equinus), heel in varus, forefoot displaced towards midline, forefoot inverted and lateral border convex, ankle is fixed, calf is wasted
- Diagnosis:
  - Usually clinical
  - Can be seen antenatally on US but 0-35% false positive rate
- Examination:
  - Equinus + varus position of foot
  - Leg length
  - Calf circumference (wasting on affected leg)
  - Skin creases (see medial crease on plantar aspect; in positional club foot, will see 2-3 creases over Achilles, idiopathic, only 1)
  - Spine + neuro exam
  - Neonatal hip exam
- Treatment:
  - Early diagnosis
  - Ponseti technique:
    - Avoids open surgery in 89%
    - Manipulation, casting + limited surgery
    - Weekly above knee cases for 6/52 with derotation of the forefoot a little more each week
    - Achilles tendon tenotomy at 6/12 to correct equinus deformity
    - Long-term splinting
  - Open surgery if Ponseti technique fails
Descriptive Terms

- Calcaneo-Valgus Foot: Dorsiflexed and heel in valgus

Tarsal Conditions

- Peroneal Spastic Flat Foot (old term)
- An abnormal union between one or other of the bones of the hind foot
- Autosomal dominant failure of segmentation or maturation of the mesenchyme
- Incidence 1%
- Diagnosis: flat foot as child with ↑ stiffness of the hind foot. Progressive onset of pain in adolescence
- Diagnosis: lateral and oblique x-rays. MRI
- Treatment: 6 weeks casting, rigid orthosis, resection of the bar if found early, otherwise fusion

In-Toeing

- Caused by torsional deformity of either the tibia or the femur

Internal Tibial Torsion:
- Internal bowing of the tibia caused by intrauterine positioning
- Exclude other problems of hip, knee and foot
- Usually self corrects by age 5

Femoral Anteversion:
- ↑ Angle between femoral shaft and neck – normal is 15 degrees
- Exam: intoed gait and excess internal rotation of the hip. Egg-beater running style
- Treatment: tend to correct up to 5 years of age. Avoid sitting with legs in internal rotation. Osteotomy to derotate if deformity is severe and does not correct

Genu Valgum and Varum

- Knock knee + bow leg
- In babies + toddlers, there is physiological bowing that corrects at 2-3 years of age
- Later, at 4 or 5 there may be knock-knee of unknown cause – all but 2% of these correct spontaneously
- Can be seen in rickets

Scoliosis

- Lateral spine curvature
- Types:
  - Non-structural or postural curves:
    - Curve disappears on bending forward
    - If due to limb length inequality, will disappear on sitting
  - Structural curves: has lateral deviation and rotation of the vertebra. When child bends forward there is a hump to one side and curve is still present/exaggerated eg congenital, neuromuscular, miscellaneous
- Idiopathic types often present during adolescent growth phase
- Causes pain, deformity and impaired lung function
- Usually progressive. Follow carefully or active management (casts or surgery)
**Other Congenital Skeletal abnormalities**

- **Neurofibromatosis:**
  - Commonest single gene disorders – autosomal dominant
  - NF1, 1:3,500
  - NF2, 1:50,000
  - Neurofibromatoma, Café au lait, scoliosis, skeletal overgrowth, tibial bowing (pseudoarthrosis), thinning, fracture
  - See Neurofibromatosis, page 535

- **Osteochondritis juvenilis (osteochondrosis):** bony centres in children/adolescents become temporarily softened →deformity due to pressure →harden again in 2 – 3 years in deformed shape

- **Skeletal dysplasia:** achondroplasia, osteogenesis imperfecta, plus numerous others

- **Soft tissue disorders:** Marfan’s, plus numerous others

- **Chromosomal disorders:** Trisomy 21, 13, 18

- **Metabolic:** Numerous, including Wilson’s, haemophilia

- **Neuromuscular:** Charcot Mari Tooth, Duchenne, Cerebral palsy

- **Spinal dysraphism**

**Joint Injury and Infection**

- **See Joint and Bone Infections, page 404, for Infection**

- **Differential of joint swelling:**
  - Acute rheumatic fever
  - Septic arthritis
  - Reactive arthritis
  - Henoch-Scholein Purpura
  - Juvenile chronic arthritis
  - Sero-negative arthritis
  - Rickets and vitamin deficiencies: A, folate, B12, C
  - Transient synovitis
  - Trauma
  - Haemophilia
  - Osteomyelitis

**Salter-Harris Classification**

- Epiphyseal #s may result in arrest of growth + subsequent deformity – accurate reduction is necessary

**Legg-Calve-Perthes Disease**

- = Perthes disease
- AVN (osteonecrosis) of the femoral head
- **Osteochondritis and osteonecrosis** of the femoral epiphysis. Softens bone then gradually reforms in a deformed shape
- Poorly understood. Typically affects boys aged 3-12 (5-7 most commonly), bilateral in 10-15%
- Often presents with intermittent hip pain but **knee pain** is also common (**knee pain is hip pain until proven otherwise**) + limp
- Relationship with smoking + children are often skeletally delayed (ie small)
- DDx: transient synovitis (irritable hip) – US may show effusion – bed rest
- X-ray:
  - Epiphyseal changes progressively over 2 years
  - Four stages:
1. Initial stage (often see sclerosis)
2. Fragmentation
3. Healing
4. Remodeling

- Treatment:
  - Younger the patient the better the prognosis. Usually benign. Maintain motion
  - Principles: acetabulum acts as a mould for the soft femoral head + helps to form a spherical femoral head, therefore need to maintain femoral head in acetabulum
  - Aim to ↓ irritability (i.e., hip pain) to maintain ROM
  - Contain the femoral head in the acetabulum with either a brace or osteotomy to tilt the femoral head into the acetabulum

- Prognostic factors: younger at presentation (= good) + amount of femoral head involvement
- Natural history: relatively benign in 60-70%; OA in the rest in their 50s → THJR

**Slipped Upper Femoral Epiphysis**
- = displacement of the femoral neck from the upper femoral epiphysis ie SH I
- Femoral shaft rotates externally + displaces anteriorly from the epiphysis
- Most common disorder of the hip in early adolescence, especially overweight and boys

- Clinical:
  - Groin, thigh, knee pain
  - Limp
  - External rotation of leg + shortening + loss of flexion (when flexing hip, it will externally rotate)
  - Classically obese + hypogonadal

- Epidemiology:
  - 2/100,000 in US
  - 10-13 yrs girls, 12-16 boys
  - 60-70% are boys
  - Bilateral in up to 50%

- Stable = 90% are chronic and stable (can bear weight) with limp for several months; 0% → AVN
- Unstable = acute + unable to walk; 50% can → AVN due to disrupted blood supply
- X-ray – can look at Trethowans line (on AP), more easily seen on lateral x-ray however
- Treatment: in situ pinning with single screw (pinning ↓ risk of AVN); rarely proximal femoral osteotomy required for excessive external rotation + loss of flexion
- Prognosis: onset of OA accelerated

**Supracondylar Humeral Fracture**
- Most common fracture above the elbow, typically extension injury by fall on outstretched hand
- Type 1: undisplaced. Type 2: displaced but some cortical contact. Type 3: Completely displaced
- Complications: nerve palsy (usually resolves after 6 - 8 weeks), vascular injury (esp brachial artery), compartment syndrome
- Treatment: closed reduction and percutaneous pin fixation. Non-displaced fractures without collapse of the medial or lateral columns can be treated by immobilisation. Open reduction if unsatisfactory closed reduction, open fracture or if vascular compromise

**Medial Epicondyle Fractures**
- Often accompanied by dislocation. Bony fragment may be trapped in the joint preventing reduction
- Usually treated non-surgically

**Fractures of the Forearm**
- 75% are fractures of the distal radial metaphases. Loss of reduction in 1/3 of cases

**Wrist and Hand Fractures**
- Radius and ulnar fractures account for 45% of childhood fractures
• Scaphoid fractures account for only 0.45% of paediatric upper extremity fractures
• 75% of finger injuries are stable and can be treated with simple immobilisation (often little finger)
• In toddlers and young children, most common pattern of injury is a crush injury of the finger, leading to distal phalangeal fracture, nail bed laceration and/or distal tip amputation
• In teenagers, diaphyseal level phalangeal fractures are common, with malrotation most apparent with digital flexion
• In teenagers, fractures of the metacarpal neck are common (“Boxer’s Fractures”)
• Fingertip trauma may lead to complete or incomplete amputation. Various treatment approaches. For more proximal amputations, replantation is now standard over 1 year. Best prognosis with sharp injuries (more common in adolescents, crush more common when younger)
• See also Forearm, Hand, page 379

Transient Synovitis of the Hip
• Transient synovitis is common and self-limiting, often following URTI
• Hip or knee pain, limp, decreased motion but normal xray
• Main differential: septic joint. If in doubt, aspirate

Femoral Shaft Fractures
• Common, generally solid healing
• Various treatment options including spica casting and traction
• Subsequent limb overgrowth is common but not predictable

Limb Length Inequality
• Various causes: check for soft-tissue hypertrophy, vascular anomalies, etc etc
• Often idiopathic. If mild (< 1.5 cm) then monitor with serial exam and x-rays
• Treatment depends on severity – involves surgical, gait, etc

Other
• Knee injury:
  ➢ Osteochondral fractures of the knee: associated with patellar dislocations
  ➢ Osteochondritis Dissecans: Fragmentation or separation of a portion of the articular surface of the knee. Symptoms include vague pain, clicking, popping or effusion. Initial treatment is immobilisation
  ➢ See also Knee Injury, page 397
• Physseal fractures of the distal tibia

Rheumatology
• A mix of systemic inflammatory disease, clinical immunology, and musculoskeletal medicine

<table>
<thead>
<tr>
<th>Systemic inflammatory disease</th>
<th>Clinical Immunology</th>
<th>Musculoskeletal medicine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rheumatoid arthritis</td>
<td>Systemic lupus erythematosus</td>
<td>Osteoarthritis</td>
</tr>
<tr>
<td>Psoriatic arthritis</td>
<td>Scleroderma</td>
<td>Septic arthritis</td>
</tr>
<tr>
<td>Ankylosing spondylitis</td>
<td>Polymyositis</td>
<td>Gout</td>
</tr>
<tr>
<td>Reactive arthritis</td>
<td>Sjogren’s syndrome</td>
<td>Regional pain disorders</td>
</tr>
<tr>
<td>Systemic vasculitis</td>
<td></td>
<td>Fibromyalgia</td>
</tr>
<tr>
<td>Polymyalgia rheumatica</td>
<td></td>
<td>Metabolic bone disease</td>
</tr>
</tbody>
</table>

GALS
• Gait:
  ➢ Observe gait
  ➢ Observe patient in anatomical position
• Arms:
  ➢ Active movement – arms behind head, behind back, supination, pronation
  ➢ Observe backs of hands and wrists
  ➢ Observe palms
  ➢ Assess power grip and grip strength
  ➢ Assess fine precision pinch
  ➢ Squeeze MCPJs
• Legs:
  ➢ Assess full f & e
  ➢ Assess internal rotation of hips
- Perform patellar tap
- Inspect feet
- Squeeze MTPJs
- Spine:
  - Inspect spine
  - Assess lateral flexion of the neck
  - Assess lumbar spine movement

**Overview**

<table>
<thead>
<tr>
<th>Disease</th>
<th>Epidemiology</th>
<th>Tests</th>
<th>Treatment</th>
<th>Select Features</th>
</tr>
</thead>
<tbody>
<tr>
<td>RA</td>
<td>1% F:M 2:1 Peak onset: 45-65</td>
<td>Anti-CCP in 98% RhF in 70% HLA DR4/DR1 ANA in 30%</td>
<td>Early DMARDs</td>
<td>Episcleritis, scleritis</td>
</tr>
<tr>
<td>OA</td>
<td>Common F:M 3:1</td>
<td>CRP↑ + x-ray</td>
<td>Paracetamol + codeine NSAIDs maybe Weight loss if BMI &gt;28</td>
<td></td>
</tr>
<tr>
<td>Gout</td>
<td>1% M:F 5:1</td>
<td>Aspirate Neg birefringent Uric acid (&gt; 0.41 mmol/L → crystals)</td>
<td>Allopurinol NSAIDs Colchicine</td>
<td>Acute gout normally monoarticular A/w trauma, surgery, starvation, infection + diuretics</td>
</tr>
<tr>
<td>Pseudogout</td>
<td>?</td>
<td>Aspirate Pos birefringent rhomboid crystals Chondrocalcinosis</td>
<td>NSAIDs Steroids Hydroxychloroquine</td>
<td>A/w OA, old age, haemochromatosis, hyperparathyroidism</td>
</tr>
<tr>
<td>AS</td>
<td>0.25 – 1% M:F 6:1 at 16y/o, 2:1 at 30 y/o</td>
<td>HLA B27 in &gt; 95% Clinical (Schober’s + sacroiliitis + costochondriasis) Seronegative (RhF)</td>
<td>Exercise NSAIDs Maybe steroid inj Biological agents</td>
<td>Sacroiliitis Enthesitis Costochondritis Uveitis&lt;br&gt;1.5 - 4 x mortality than expected (amyloidosis, heart disease)</td>
</tr>
<tr>
<td>Enteropathic arthritis</td>
<td>10-30% of Crohn’s and UC get arthritis; Crohn’s &gt; UC</td>
<td>HLA B27</td>
<td>Sacroiliitis in only 5% Associated with intestinal bypass surgery and Whipple’s Disease</td>
<td></td>
</tr>
<tr>
<td>Psoriatic arthritis</td>
<td>10-40% of those w psoriasis</td>
<td>HLA B27 X-ray: Pencil in cup deformity</td>
<td>NSAIDs Sulfasalazine Methotrexate Biological agents</td>
<td>Polyrthritis (RA-like) DIPJ involved Psoriatic mutilans in 3% Lateral onycholysis/other nail changes</td>
</tr>
<tr>
<td>Reactive arthritis</td>
<td>?</td>
<td>HLA B27</td>
<td>Rest Splint NSAIDs Steroid injection DMARDs if severe</td>
<td>Sterile, non-erosive asymmetric polyarthritis of LL GI + urethritis causing bugs (Reiter’s = urethritis + conjunctivitis + arthritis) Can see keratoderma blenhorrhaga + circinate balanitis + iritis</td>
</tr>
<tr>
<td>Juvenile RA</td>
<td>&lt;16 ys</td>
<td>RhF pos or neg (pos = worse prognosis)</td>
<td>Specialist NSAIDs, steroids, DMARDs (incl bio agents)</td>
<td>Still’s disease = fever, rash, arthritis Many different patterns Uveitis Lasts &gt; 6/52</td>
</tr>
<tr>
<td>Systemic sclerosis</td>
<td>F:M 3:1</td>
<td>Anti-centromere in 70-80% of CREST (ie limited SS)&lt;br&gt;Anti-RNA polymerase in 20% of diffuse</td>
<td>Immunosuppressive eg cyclophos Raynauds: hand warmers, CCBs, ACEi</td>
<td>SS features scleroderma + vasculitis Limited (eg CREST) + diffuse types</td>
</tr>
<tr>
<td><strong>Musculo-skeletal, Rheumatology and Plastics</strong></td>
<td></td>
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<thead>
<tr>
<th><strong>Anti-topoisomerase</strong></th>
<th>in 40% of diffuse Anti-Sc170 in diffuse</th>
</tr>
</thead>
<tbody>
<tr>
<td>o ANA in 64% (Nucleolar pattern but centromere pattern in limited)</td>
<td></td>
</tr>
<tr>
<td>RhF in 30%</td>
<td>(regular ACE↓ risk of renal crisis)</td>
</tr>
<tr>
<td><strong>Limited disease has 70% 10-year survival; diffuse has 55% 10-year survival. Death from lung/renal effects</strong></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>MCTD</strong></th>
<th>o Speckled ANA pattern</th>
</tr>
</thead>
<tbody>
<tr>
<td>o Anti-RNP</td>
<td>Features of SS, SLE + polymyositis</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Polymyositis + Dermatomyositis</strong></th>
<th>ALT + CK ↑</th>
</tr>
</thead>
<tbody>
<tr>
<td>EMG + muscle bx confirms dx Anti-Mi2, Anti-Jo1 positive</td>
<td>Prednisolone Immunosuppressant s</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>SLE</strong></th>
<th>0.2% F:M 9:1</th>
</tr>
</thead>
<tbody>
<tr>
<td>10% of relatives may be affected</td>
<td>ANA +ve in &gt;95% Ds-DNA in 60% (95% specific, 30% sensitive in all pts, 60% sens in active d)</td>
</tr>
<tr>
<td>RhF 40% +ve syphilis (VRDL) due to anti-cardiolipin Anti-Sm Antiphospholipid antibody HLA BB, DR2/3 pos Drug-induced + active SLE = anti-DNAhistone Homogenous = SLE</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Vasculitis</strong></th>
<th>Histology</th>
</tr>
</thead>
<tbody>
<tr>
<td>ANCA</td>
<td>Steroids</td>
</tr>
<tr>
<td>ESR/CRP</td>
<td>Medium/small vessel d = steroids + cyclophos</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Wegener’s</strong></th>
<th>cANCA</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>URTI, lungs, and kidneys</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Microscopic polyangiitis</strong></th>
<th>pANCA positive</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>NB. Churg Strauss also ANCA pos</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>GCA</strong></th>
<th>25% of PMR Elderly (rare &lt;55)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ESR</td>
<td>40-60mg prednisone STAT then for 2yrs</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>PMR</strong></th>
<th>Common &gt; 70, rare &lt; 60</th>
</tr>
</thead>
<tbody>
<tr>
<td>CRP/ESR</td>
<td>Pred 15mg/24h ~ dramatic response within 4 days ↓ dose slowly by 1mg/month Continue for ≥2yrs</td>
</tr>
<tr>
<td>CK normal</td>
<td>Symmetrical aching morning stiffness proximally Systemic features = fatigue/wt loss/fever etc 10% carpal tunnel</td>
</tr>
<tr>
<td>ALP ↑ maybe</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Polyarteritis nodosa</strong></th>
<th>M:F 2:1</th>
</tr>
</thead>
<tbody>
<tr>
<td>↑WCC</td>
<td>Rx HTN</td>
</tr>
<tr>
<td>Eosinophilia</td>
<td>Steroids</td>
</tr>
<tr>
<td>ANCA negative</td>
<td>Cyclophos</td>
</tr>
<tr>
<td>Do bx</td>
<td>Refer</td>
</tr>
<tr>
<td></td>
<td>Necrotising vasculitis medium vessels → infarcts/aneurysm/thrombosis A/w Hep B</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Sjogren’s</strong></th>
<th>15 – 65 yrs F:M 9:1</th>
</tr>
</thead>
<tbody>
<tr>
<td>ANA in 60-70% (68%) Anti-Ro/La (SSA/SSB) RhF in 100% Schirmer’s test (&lt;5mm in 5min)</td>
<td>Treat dryness (eye drops, drink etc) NSAIDs + hydroxychloroquine</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Anti-phospholipid syndrome</strong></th>
<th>Secondary to SLE in 20-30%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anticardiolipin antibody Lupus anticoagulants</td>
<td>ASA</td>
</tr>
</tbody>
</table>

| **CLOT**: coagulation defect, livedo reticularis, obstetric (recurrent miscarriage), TCP | **Risk** |

| **Limited disease has 70% 10-year survival; diffuse has 55% 10-year survival. Death from lung/renal effects** | **Features of SS, SLE + polymyositis** |

---

**Note:** The above table summarizes information from various sources on musculoskeletal, rheumatology, and plastic conditions, focusing on key diagnostic markers, treatments, and associated conditions. For more detailed information, consult specialized medical resources.
History

- Joints:
  - Pain
  - Swelling
  - Morning stiffness (often = inflammatory)
  - Loss of function
  - Deformity
  - Weakness
  - Instability
  - Changes in sensation
- Eyes:
  - Dry eyes and mouth
  - Red eyes
- Systemic:
  - Raynaud’s phenomenon
  - Rash, nail changes, fever, fatigue, weight loss, diarrhoea, mucosal ulcers

Screening Questions

- Do you have any pain or stiffness in your muscles, joints or back?
- Can you dress yourself completely without any difficulty?
- Can you walk up and down stairs without any difficulty?

History Taking

- Evolution:
  - Acute or chronic?
  - Associated events
  - Response to treatment?
- Current symptoms:
  - Pain
  - Stiffness
  - Swelling
  - Pattern of joint involvement
- Involvement of other systems:
  - Skin, eye, lung or kidney symptoms?
  - Malaise, weight loss, fevers, night sweats?
- Impact on lifestyle:
  - Needs/aspirations
  - Ability to adapt to functional loss

Arthritis Overview

- Monoarthritis (or oligo if 2-4 joints) vs polyarthritis (>4 joints)
- Osteoarthritis vs systemic/inflammatory
- Symmetrical vs asymmetrical
- Proximal vs distal
- Upper limb vs lower limb
- Large jt vs small jt

Examination

- Screening exam (OHCS, p 666):
  - Observe from behind: muscle bulk (shoulders, buttocks), straight spine, swellings, deformities
  - Observe from the side: cervical and lumbar lordosis, thoracic kyphosis
  - Touch your toes: spine and hip flexion
  - Observe from in front
  - Ear to shoulder: lateral cervical flexion, flexion, extension and rotation
  - Open and close the mouth: TMJ, orofacial pain
  - Hands behind head: shoulder and sternoclavicular movement, then straight above
  - Arms straight: elbow extension
  - Examine hands: nails, pray sign, press dorsum of both hands together
- Observe legs: bulk, swelling, deformity
- Knee effusion
- Observe feet
- Observe walking

Patterns of Polyarthropathy

- Rheumatoid arthritis:
  - Usually symmetrical
  - Hands: PIPJ, MCPJ, wrist jts
  - Elbows
  - Small joints of upper CSp
  - Knees
  - Feet: tarsal and MTPJ

- Seronegative spondyloarthritides:
  - Commonly asymmetrical and lower limb
  - AS:
    - SIJ + spine
    - Hips, knees, and shoulders
  - Psoriatic arthritis:
    - DIPJ
    - SIJ
    - Rheumatoid pattern
  - Reiter’s syndrome:
    - SIJ + spine
    - Hips, knees, ankles + most joints of the feet

- Primary OA:
  - Usually symmetrical + can affect many joints
  - Fingers: distal (Heberden’s nodes) + proximal (Bouchard’s nodes) IPJ + MCPJ of the thumbs
  - ACJs
  - Small joint of the spine (lower CSp + Lsp)
  - Knees
  - MTPJ of the great toe (hallux rigidus)

- Secondary OA:
  - Asymmetrical + affects previously injured, inflamed or infected weightbearing joints
  - Hip, knee, intervertebral disc

Differentials for Arthritis

Causes of Monoarthritis

- Acute monoarthritis:
  - Septic arthritis: either haematogenous (staph or gonococcal) or following penetrating injury
    - Emergency: needs microbial diagnosis (gram stain/culture) before ABs started
    - Needs washout/removal of metalware
  - Traumatic
  - Gout, pseudogout
  - Haemarthrosis (eg haemophilia)
  - Sometimes seronegative spondyloarthritides

- Chronic monoarthritis:
  - Chronic infection (eg Tb)
  - Osteoarthritis
  - Seronegative spondyloarthritides
  - Metastasis

Causes of Polyarthritis

- Acute polyarthritis:
  - Infection: viral (mumps, rubella, EBV, etc), bacterial
  - Rheumatic fever
  - Onset of chronic polyarthritis
  - Drug allergies

- Chronic polyarthritis:
- Rheumatoid arthritis
- Seronegative spondyloarthritis
- Primary osteoarthritis
- Gout, pseudogout or hydroxyapatite arthropathy
- Connective tissue disease (eg SLE)
- Infection (eg Tb)

Differential by Distribution

- **Inflammatory:**
  - Peripheral, symmetrical, small joint polyarthritis:
    - RA
    - Lupus and Connective Tissue Diseases (non-deforming and non-nodular)
  - Asymmetrical, large joint, oligoarthritis, possibly with spinal disease: sero-negative spondyloarthropathies:
    - Ankylosing Spondylitis
    - Reactive Arthritis and Reiter’s Disease
    - Psoriatic Arthritis
    - Arthritis of IBD
  - Acute inflammatory mono or oligo arthritis: septic arthritis or gout

- **Non-inflammatory:**
  - Osteoarthritis: weight bearing joints or hands
  - Soft tissue or locomotor pain syndromes

- **Sacro-ilits:** occurs in Ankylosing Spondylitis, Reiter’s Syndrome, Crohn’s Disease, Chronic Polyarthritis

Causes of Arthritis and Nodules

- Rheumatoid arthritis
- SLE (rare)
- Rheumatic fever (rare)
- Granulomas, eg sarcoid (very rare)

Raynaud’s Phenomenon/Disease

- **Episodic digital ischaemia,** precipitated by cold or emotion
- Fingers ache and go pale → blue → red/purple (pain most severe in this stage, during reperfusion)
- May be:
  - Idiopathic: Raynaud's disease
  - Associated with underlying cause (Raynaud's phenomenon): Scleroderma, SLE, RA, arteriosclerosis, leukaemia, drugs, etc. Not polyarteritis nodosa
- Keep warm, stop smoking, try Ca channel blockers (eg diltiazem)

Synovial Fluid

<table>
<thead>
<tr>
<th>Type</th>
<th>Appearance</th>
<th>Viscosity</th>
<th>WBC/mm³</th>
<th>Neutrophils</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>Clear, colourless</td>
<td>↑</td>
<td>≤200</td>
<td>None</td>
</tr>
<tr>
<td>OA</td>
<td>Clear, straw</td>
<td>↑</td>
<td>≤1000</td>
<td>≤50%</td>
</tr>
<tr>
<td>Haemorrhagic</td>
<td>Bloody, xanthochromic</td>
<td>Varies</td>
<td>≤10000</td>
<td>≤50%</td>
</tr>
<tr>
<td>Acutely inflamed eg RA/gout</td>
<td>Turbid, yellow</td>
<td>↓</td>
<td>1-50000</td>
<td>Varies</td>
</tr>
<tr>
<td>Septic</td>
<td>Turbid, yellow</td>
<td>↓</td>
<td>10-100000</td>
<td>&gt;90%</td>
</tr>
</tbody>
</table>

Radiology

- **Principles:** Looking for:
  - Morphologic change in an individual joint
  - The skeletal distribution

- **Features:**
  - Joint space narrowing, either localised or uniform
  - Erosions (if at the margin then periarticular erosions)
  - Osteophytes: bony lip at edge of joint
  - Subchondral cysts: formed by synovium getting through fissures in the cartilage
  - Subchondral sclerosis: micro-fractures in the subchondral bone → attempted repair → dense white band
  - Periarticular osteopenia: cytokine mediated thinning of the surrounding bone (check other joints)
  - Periarticular soft tissue swelling:
    - Fusiform: in inflammatory
Features of different arthropathies:

<table>
<thead>
<tr>
<th>Signs</th>
<th>Rheumatoid</th>
<th>Primary Osteoarthritis</th>
<th>Gout</th>
<th>Psoriatic Arthritis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Uniform joint space narrowing</td>
<td>Localised joint space narrowing (ie not whole joint space)</td>
<td>Erosions (often para-articular or long way from the joint, may have cave like opening with overhanging margins)</td>
<td>Pencil in cup deformity</td>
</tr>
<tr>
<td></td>
<td>Erosions</td>
<td>Subchondral cysts</td>
<td>Relative preservation of joint space and bone density until late in the disease</td>
<td>Erosions</td>
</tr>
<tr>
<td></td>
<td>Periarticular osteopenia</td>
<td>Marginal osteophytes</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Fusiform soft tissue swelling</td>
<td>Subchondral sclerosis</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Can get cysts (called geods in RA)</td>
<td>Joint incongruity</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Distribution

<table>
<thead>
<tr>
<th>Signs</th>
<th>Rheumatoid</th>
<th>Primary Osteoarthritis</th>
<th>Gout</th>
<th>Psoriatic Arthritis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Hand: proximal joints</td>
<td>Weight bearing joints: hip, knee, C5-C6 (fulcrum for flexing the neck)</td>
<td>Any small joints of hands and feet</td>
<td>DIPJ</td>
</tr>
<tr>
<td></td>
<td>Small and large joints</td>
<td>Distal Hand: DIP, PIP and 1st CMCI</td>
<td>Elbows and knees Asymmetric</td>
<td>S1J</td>
</tr>
<tr>
<td></td>
<td>Symmetric</td>
<td>Asymmetric</td>
<td>Asymmetric</td>
<td>Asymmetric</td>
</tr>
</tbody>
</table>

Other arthropathies are variations on this:
- Secondary OA (eg due to previous trauma or infection). Looks like OA but not standard (eg uniform joint space)
- If inflammatory but wrong distribution → ?sero-negative

Idiot’s rule of thumb for hand arthritis:
- Rheumatoid: MCP and MTP joints
- Psoriasis: DIP joints
- Osteoarthritis: DIP + IPJ

Osteoarthritis

- Loss of articular cartilage in a synovial joint, and associated changes in underlying bone and other joint tissues
- Is degenerative not inflammatory
- Very common, although prevalence unknown due to variations in diagnosis
- Risk factors:
  - Age: 75% of over 70 year olds and 90% of 80 year olds
  - Previous injury
  - Female (3:1) and obesity (especially hip and knee)
  - Paget’s/AVN/DDH/SUFE
- Non-specific symptoms:
  - Pain: initially with/after exercise or at the end of the day, later also at rest and related to other factors. Pain with sleeping on hip at night
  - Stiffness: not as prominent as in inflammatory arthritis, ↓ towards end of the day
  - Swelling: due to ↑synovial fluid (may contain a few mononucleocytes) and bony thickening
  - Loss of function (common to all arthritis)
  - Signs: joint instability, crepitus, joint tenderness, derangement, ↓ range of movement, effusion, fixed deformity

Distribution

- Primary osteoarthritis:
  - Idiopathic
  - Often – but not always - symmetrical
  - Fingers: DIP and PIP, MCP joint of thumb but not of fingers. Can lead to:
- **Heberden’s Nodes**: marginal osteophytes at the base of the distal phalanx
- **Bouchard’s Nodes on proximal** IP joints
- **Weight bearing joints**: Hips, knees
- **Less Common**:
  - Acromioclavicular joints
  - Lower cervical and lumbar spine
  - MTP joints of big toes

- **Secondary Osteoarthritis** (secondary to *joint disease or injury* – consider especially if it doesn’t fit the joint distribution of primary):
  - Asymmetrical
  - Trauma (eg intra-articular fracture, dislocation, etc)
  - Infection
  - Metabolic: haemophilia, gout (or pseudogout if bigger joints), haemochromatosis
  - Avascular necrosis: see Complications of Fractures, page 349
  - Congenital (eg DDH)
  - Inflammatory (reactive or primary)
  - Neoplasia (eg prostate → femoral head)

**Investigations**

- **X-ray**:
  - 1. ↓ joint space
  - 2. Osteophytic lipping
  - 3. Sclerosis
  - 4. Subchondral cysts
  - 5. Joint incongruity
- Lab tests usually normal (check for normal ESR, CRP (*CRP can be mildly elevated*), RF, ANAs, joint aspirate)

**Management**

- **Conservative**:
  - Inform, education
  - Do nothing, or
  - Pharmacology (analgesics, **NSAIDs**): Paracetamol and codeine if necessary. NSAIDs work reasonably well but can cause GI bleeds; use only if paracetamol not working. Potential for COX-2 inhibitors. Also glucosamine (from health food shop, 1500 mg/day)
  - **Steroid injection** if secondary inflammatory component
  - Weight loss if BMI >28
  - Physiotherapy:
    - Obtain and maintain full range of motion (↓ range of motion → ↑ loading on a smaller area of cartilage → wears out faster)
    - Exercise: eg **quad exercises** for osteoarthritis of the knee
  - Orthotics and other devices:
    - Devices to reduce weight bearing across affected joints
    - Raising bed and chairs to reduce strain, walking sticks, handrails, etc
  - Aspiration of joint fluid
- **Surgery**, especially for knee and hip (determined on functional/pain criteria):
  - Arthroscopic debridement (buys time)
  - Osteotomy: take out a wedge of bone above or below the joint – realigns stress through the joint → more even wear
  - **Arthroplasty**: a prosthesis (considerable variety). Main indication is pain. **Best way to treat severe OA**. Surgery to correct fixed flexion deformity is less successful. NB don’t forget DVT prophylaxis
  - Arthrodesis: joint fusion

**Pathology**

- Most common joint disorder (80% of those over 55)
- Related to wear and tear of ageing; ↓ synthesis + ↑ breakdown of articular cartilage
- Integrity of joint requires even load distribution, abnormalities predisposing to degenerative joint disease (DJD) = misalignment due to trauma, subchondral bone changes (eg paget’s), crystal deposition (gout)
- -itis is a misnomer – minimal inflammation
- Cartilage = collagen proteoglycans + water (70%). Made by chondrocytes

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Musculo-skeletal, Rheumatology and Plastics
Musculo-skeletal, Rheumatology and Plastics

Articular cartilage tissue changes:
- **Fibrillation** or fraying of the surface
- Thinning with fissures and clefts
- Eventually denuded = eburnation

Subchondral bone changes:
- Bone under degenerating cartilage shows ↑ remodelling with sclerosis and bone cysts
- New articular bone growth seen at margins in non-pressure zones = osteophytes


- Micro: villus fronds in cartilage

- Gross: Shiny, subchondral bone (eburnisation), subchondral cysts, osteophytes (extra-articular overgrowth of bone → attempt to ↑ weight bearing area)

**Inflammatory Arthritis**

**Management of Inflammatory Arthritis**

- The different arthropathies overlap
- The issue is less which arthritis it is, but whether there are risk factors for serious disease (of which the type of arthritis is but one factor). This risk assessment will determine whether treatment is aimed at:
  - Aggressive treatment: use of immunosuppressives and DMARDs to induce/maintain remission
  - Symptomatic treatment

- Non-operative management:
  - Conservative: **NSAIDs** etc
  - **Intra-articular steroid** injections: controversial (2 or 3 max at any one site → may ↑ joint degeneration)
  - Weight reduction
  - **Aids** to daily living: crutches etc
  - Activity modification

- Operative management:
  - Arthroscopy: washout (removes inflammatory mediators + fragments of cartilage)
  - Synovectomy: excision of the synovium or tendon sheath in RA can be beneficial
  - Joint surgery

- Risk factors for any inflammatory disease:
  - Evidence of active inflammation: eg morning stiffness, ↓function, biochemical markers
  - Extra-articular involvement: eg lung, vasculitis, etc
  - Gradual onset (this is worse than sudden onset)
  - Large joint involvement
  - Genetic markers: HLA DR1 and DR4, etc (HLA DR is a MHC II cell surface receptor – various types of this are involved in several AI conditions)
  - Presence of rheumatoid factor (-ive prognostic factor for erosions in rheumatoid arthritis)
  - Radiographic abnormalities

**Blood Tests in Inflammatory Arthritis**

- **Gout and seronegative arthritis** are not normally positive for **rheumatoid factor and auto-antibodies**
- **Rheumatoid Factor**: IgM against Fc portion of IgG. Can be tested with the Rose-Waaler titre. Positive in:
  - 70-80% of RA
  - 40% of SLE
  - 100% of Sjogren’s
  - 30% of PSS

- **ANA**: Autonuclear Antigens
  - Screening test for SLE: present in > 95% at titre > 1:200 – but not specific
  - Present in RA (30%), Sjogren’s (68%), PSS (64%), and normal (0 – 2%)
  - Expressed in titres (dilutions at which antibodies can be detected). 1:40 (ie serum has been diluted 40 times) or 1:80 may not be significant (~1:160 and less are deemed significant)
  - Also ↑ with age, other autoimmune diseases, drugs, infections
  - Patterns:
    - Homogenous = SLE
    - Speckled = MCTD
- Nucleolar = systemic sclerosis
- Centromere = limited systemic sclerosis
- Diffuse ANA suggests dsDNA may be +ive
- Speckled ANA suggests ENA may be +ive
- Anti-DNA histone: suggests active SLE. Also in 95% of drug SLE
- Anti-dsDNA = SLE
- Anti-centromere: suggests systemic sclerosis

- dsDNA: 70% of SLE. Specific (ssDNA is not). Titres correspond to clinical activity and risk of nephritis
- HLA B27: ~7% of the population have this but highly associated with spondyloarthropathies
- ENA: Extractable Nuclear Antigens (not all speckled ANA results are due to ENAs):
  - Anti-Ro (SSA): Sjogren’s, SLE (30%)
  - Anti-La (SSB): Sjogren’s. Always associated with SSA. Found in only 10% of SLE
  - Anti-Sm: 30% of SLE. Specific
  - Anti-RNP: SLE (40%), polymyositis, scleroderma, mixed disorders
  - Anti Jo-1; anti-Mi2: polymyositis and dermatomyositis
  - Anti-Scl70: diffuse systemic sclerosis

- Anti-phospholipid antibodies (attacks phospholipid on platelets)
  - Occurs in 50% of SLE. Do Lupus anti-coagulopathy test
- 3 types:
  - Lupus anticoagulant: Causes ↑APTT, but causes thrombosis in vivo
  - Anti-cardiolipin
  - False positive VRDL test (syphilis)
  - 1 and 2 associated with fetal loss, clotting, thrombocytopenia, valvular heart disease
  - Antiphospholipid Syndrome: recurrent miscarriages, thrombocytopenia and recurrent arterial or venous thrombosis

- ANCA: Associated with some small vessel vasculitis. Can divide arteritis into ANCA +ive and –ive (although pANCA may also be found in 20% of polyarteritis nodosa):
  - Cytoplasmic anti-neutrophil cytoplasmic antibody (cANCA): Specific but not sensitive for Wegener’s disease > 90% +ive
  - Perinuclear anti-neutrophil cytoplasmic antibody (pANCA): Microscopic polyangitis ~ 75% (vasculitis in kidney and lung) and PAN
  - ANCA negative small vessel vasculitides include Henoch-Schonlein Purpura

- CD4+:CD8+ ratio (normally ~3) ↑ in Polymyalgia Rheumatica

**Pharmacology**

**NSAIDS**

- Action: Many! Inhibit PG synthesis by inhibiting cyclo-oxygenase (converts arachidonic acid to PGG2 and PGH2):
  - COX-1: present in blood vessels, stomach, kidney (eg might actually help in heart disease – eg aspirin)
  - COX-2: induced during inflammation → PGs (eg Celecoxib/Celebrix and rofecoxib/Vioxx)

- Effects:
  - Analgesic: Effective against pain where PGs sensitise nociceptors
  - Anti-inflammatory: Reduce vasodilation, oedema, pain. Effect may not be clinically obvious for 2 – 3 weeks
  - Antipyretic: acts in hypothalamus

- Pharmacokinetics: well absorbed, no first pass metabolism (except aspirin), highly protein bound

- Side effects:
  - ↑ Risk in elderly
  - GI: dyspepsia, mucosal irritation, ulceration (relative risk 5 times, ↑↑ if on warfarin, etc)
  - Renal: Little effect on renal function in normal people. If chronic renal impairment, CHF, gout, or longer T½ NSAIDs then Na retention and oedema in 3 – 5%
  - Skin: rashes, urticaria, photosensitivity and erythema multiform
  - Other: headache, ↓platelet function → ↑ bleeding time, blood dyscrasias (aplastic anaemia with indometacin and phenylbutazone)

- Interactions:
  - ↓Antihypertensive effect of ACE inhibitors
  - ↓Diuretic action of frusemide and thiazide diuretics
  - ↑Methotrexate levels
Musculo-skeletal, Rheumatology and Plastics

- Not if on anti-coagulants → GI bleed
- Patient instructions: Only take them PRN to avoid risk of bleed – so don’t take them on good days. Watch for abdominal pain, black stools. Smoking and alcohol ↑ the risk. Don’t supplement them with OTC NSAIDs
- Commonly used NSAIDs:
  - Salicylates: Aspirin (not in kids) and Diflunisal
  - Propionic Acids (better tolerated and more sensitive for COX-2): Ibuprofen, Naproxen
  - Pyrazoles: Phenylbutazone
  - Acetic Acids: Indometacin (potent, CNS side effects), sulindac
  - Paracetamol (no anti-inflammatory or GI effects)
  - Only use COX-2 when long-term use is essential and past history of ulcer

Other Pain Relief
- Amitriptyline: a TCA which in low dose has pain modifying effects
- Tramadol: opioid analgesic with less respiratory depression, ↓ constipation and ↓ addiction

Immune Suppressive Drugs
- For acute inflammatory problem (arthritis, connective tissue, etc)
- Prednisone: 60 mg/day starting dose
- Methylprednisolone (iv)

Disease Modifying Anti-Rheumatic Drugs (DMARDs)
- Aim: to suppress inflammatory activity → ↓ destructive changes (NSAIDs reduce inflammation but don’t act on the pathway that leads to joint destruction)
- Indicated for patients at an early stage with high markers of disease activity ⇒ don’t wait for RF, nodules or erosions
- Effect:
  - Suppress inflammatory activity
  - Reduce the need for NSAIDS and corticosteroids which have greater potential toxicity
- First line agents (high efficacy especially in combination, low toxicity):
  - Methotrexate: takes several months to work. Action: ↓ IL-1, ↑ IL-10, ↓ neutrophil chemotaxis. SE: nausea, bone marrow suppression, GI ulceration, teratogenic. Inhibits folate metabolism → give folic acid 5 – 10 mg/wkly, rare: irreversible liver toxin. Monitor FBC, LFTs, Cr if renal impairment
  - Sulphasalazine/salicyprin: start low, increase to 2-3g per day. Best tolerated. Effect after 3 – 6 months. SE: nausea, rashes, ↓ sperm count, hepatitis, oral ulcers, rarely: blood dyscrasia, Stevens-Johnson, neutropenia, monitor FBC and LFTs
  - Leflunamide
- Others:
  - Cyclosporin A: SE nephrotoxicity
- Beneficial but don’t alter progression of radiological changes:
  - Azathioprine
  - D-Penicillamine. SE: ↓ marrow, proteinuria, ↓ taste, oral ulcers, myasthenia, Goodpasture’s
- Biological agents: anticytokine therapy: eg against TNF
  - Infliximab
  - Etanercept
  - Adalimumab

Rheumatoid Arthritis
- Chronic systemic inflammatory disorder
- Symmetrical, erosive, deforming arthropathy
- Epidemiology:
  - Peak onset: 45-65
  - Prevalence: 1%
Female: male = 2:1

Pathogenesis

- ?Microbial agent initiates the disease: current suspect is EBV, plus others
- Presentation of (unknown) antigen to CD4+ T-helper cells + plasma cells and macrophages → cytokine-mediated (TNF-α) synovial neutrophilic exudate + ↑vascularity → cartilage-degrading enzymes + fibrosis + pannus formation + ↑osteoclastic activity + ligament and tendon damage
- → Painful, unstable, disrupted joint (eg subluxed, deformed, etc)
- 65 – 80% are HLA DR4 or DR1 +ve, plus further specific DR alleles (eg Q(k)/RA motif in the DRB1-HV3 region of the T-cell antigen receptor)
- Autoimmunity to type 2 collagen can be demonstrated in most patients with RA
- 70% have Rheumatoid Factors: autoantibodies (IgM) to the Fc portion of autologous IgG
- Implicated mediators are cytokines: TNF, IL-1, IL-6, IL-15, interferon-α, growth factors, proteases, elastases

Presentation

- Small (and large) joint symmetric polyarthritis, see synovitis + tenosynovitis
- Common: swollen, painful, stiff hands and feet, especially in the morning. Progresses to larger joints
- Less common:
  - Palindromic: relapsing and remitting monoarthritis of different large joints
  - Persistent monoarthritis (especially the knee)
  - Systemic illness: ↓weight, pericarditis, pleurisy
  - Vague limb girdle aches
  - Sudden-onset widespread arthritis
- Greatest damage occurs in first 4 – 5 years
- Active RA is characterised by inflammation of the synovial tissue which if untreated leads to permanent structural damage and eventual long term disability
- Pattern of involvement:
  - Usually symmetrical
  - Most RA involves:
    - PIP and MCP joints and wrists (DIP spared, cf OA) in the hands
    - Tarsal and MTP joints in the foot (IPJ spared)
  - Also can involve:
    - Elbows
    - Shoulders (eg Pencilling – erosion of distal end of the clavicle)
    - Small joints of upper cervical spine: Atlanto-Axial instability: anterior subluxation of C1 on C2 with cervical flexion due to erosion of the transverse atlantal ligament → threatens spinal cord
    - Lumbo-sacral region usually spared
    - Hips
    - Knees

Deformities

- Initially sausage-shaped fingers and MCP joint swelling
- Ulnar deviation and volar subluxation (partial dislocation) of the fingers
- Fingers: Swan Neck and Boutonniere (buttonhole)
- Z deformity of the thumb: hyperextension of the IP joint and fixed flexion and subluxation of the MCP joint
- Subluxation of the wrist, with prominent radial head

Extra-Articular Involvement

- Nodules: subcutaneous central zone of fibrinoid necrosis surrounded by palisading histiocytes and fibroblasts. May occur in viscera, including heart, lung and GI
- Anaemia
- Lymphadenopathy
- Vasculitis
- Carpel Tunnel Syndrome (early manifestation)
- Multifocal neuropathies (= Mononeuritis Multiplex): Sequential, multifocal, random involvement of non-contiguous peripheral nerve trunks (there are other causes besides RA)
- Splenomegaly
- Eyes: *episcleritis, scleritis*, keratoconjunctivitis sicca
- Pericarditis
- Pulmonary fibrosis
- Amyloidosis
- *Not* glomerulonephritis

**Diagnostic Criteria**
- For research
- 4 out of 7 of: morning stiffness >1hr, arthritis of ≥ 3 joints, arthritis of hand joints, symmetrical arthritis, rheumatoid nodules, RhF +ve, radiographic changes

**Investigations**
- X-ray
- Bloods:
  - Rheumatoid factor +ve in ~ 70% (See Blood Tests in Inflammatory Arthritis, page 429)
  - Anti-cyclic citrullinated peptide antibodies (anti-CCP) are highly specific (~98%) for RA
  - HLA DR1/DR4 linked (not actually part of routine bloods but is a/w ↑ severity)

**Treatment**
- Early use of DMARDs improves symptoms + long term outcomes
- Regular exercise
- Physiotherapy
- Occupational therapy
- Household and personal aids (eg wrist splints)
- Intraleisional steroids
- Surgery
- Drugs:
  - NSAIDs (eg ibuprofen): Least likely to cause a bleed. Contraindicated if asthma or peptic ulcer. To control inflammation/pain
  - Steroids: oral, parenteral, intra-articular to control flare-ups. Can reduce erosions if given in early disease. Need to keep dose low (ie 7.5 mg/day) – but due to symptomatic improvement patients often want more. SE: ↓bony density, cataract, fluid retention, peptic ulcers
  - DMARDs: See Disease Modifying Anti-Rheumatic Drugs (DMARDs), page 431. All have side effects, monitoring essential. All can cause rash

**Pathology**
- Chronic systemic inflammatory disorder
- Principally affects joints with progressive damage over years
- F > M
- Immune mediated evidence:
  - Association with MHC genes (HLA DR4 or DR1)
  - Activation of T cells by as yet unknown antigens in the immunogenetically susceptible host is most probably the event that initiates the rheumatoid process
  - Large numbers of APC and T helper cells found in synovial pannus
  - Activated B cells present in the joint → produce rheumatoid factor that leads to formation of immune complexes → perpetuate inflammation and destruction

**Features:**
- Small joints > large joints
- Swelling and stiffness
- Warm and painful
- Destruction of the tendons and joint capsule leads to characteristic deformities
  - Radial deviation at wrist
  - Ulnar deviation of fingers
  - Finger abnormalities: swan neck, boutonniere

**Histology:**
- Pannus = synovium expanded by chronic inflammatory cells, fibrosis and proliferation of synovial lining, expanding into joint space and covers cartilage
- *Destroys cartilage*, impairs nutrition, damages ligaments and tendons

*Musculo-skeletal, Rheumatology and Plastics*
- May penetrate bone
- Leads to painful, unstable, disrupted joints

**Juvenile Rheumatoid/Idiopathic Arthritis**

- Arthritis beginning at or before 16 years of age (usually early childhood)
- Signs: high, swinging, early evening fever, pink maculo-papular rash, arthralgia, arthritis, myalgia, generalised lymphadenopathy
- Number of different types:
  - Oligoarthritis/pauciarthritis (persistent): asymmetrical, affecting 4 or fewer joints, especially wrist, knees, ankles. Usually remission in 4 – 5 years
  - Oligoarthritis (extended): Oligoarticular onset progressing to > 4 joints
  - Polyarticular JCA: Usually in teenagers progressing to widespread joint destruction, especially hands (less so the DIPs)
  - Extra-articular involvement can include: pericarditis, myocarditis, pulmonary fibrosis, glomerulonephritis, uveitis and growth retardation
  - Still’s disease = swinging fevers, rash, arthritis
- Differences from Adult RA:
  - Oligoarthritis is more common
  - Systemic onset is more frequent
  - Large joints affected more than small joints
  - Rheumatoid nodules and rheumatoid factor are usually absent but if RhF positive this is a –ve prognostic factor
  - ANAs often positive
- Treatment:
  - Referral to specialist
  - Low dose NSAIDs/paracetamol (Aspirin: beware of Reye’s Syndrome: acute noninflammatory encephalopathy and hepatic failure in 4-12 yr olds; typically occurs after a viral illness, particularly an URTI; associated with the use of aspirin during the illness)
  - Corticosteroids
  - DMARDs
- Prognosis: variable: up to 50% have long term disability
- Completely different disease entity to Juvenile Spondyloarthropathies – although clinically may overlap.
  - Enthesitis common

**Spondyloarthropathies (Seronegative Arthritis)**

- Rheumatoid factor is negative – but exclude seronegative RA
- Clinical overlap between the conditions
- Acronym: PEAR: Psoriasis, Enteropathic (IBD-related), Ankylosing Spondolytis, Reactive/Reiter’s
- Have in common:
  1. Seronegativity (rheumatoid factor –ve)
  2. HLA B27 association (inherited gene marker associated with a number of related rheumatic diseases)
  3. Involvement of spine (spondylo-) and sacroiliac joints (= axial arthritis)
  4. Usually asymmetrical large joint mono or oligoarthritis (<5 joints)
  5. Enthesitis: inflammation then calcification of tendon/ligament insertion into bone (enthesopathy; eg plantar fasciitis, achilles tendonitis, costochondritis)
  6. Dactylitis: inflammation of an entire digit (sausage digit) due to soft tissue oedema + tenosynovial + jt inflammation
  7. Extra-articular manifestations: uveitis, aortic regurgitation, upper zone pulmonary fibrosis
- Characteristic features:
  - Lower limb, asymmetric oligoarthritis
  - Sacroiliitis → inflammatory back pain
  - Association with HLA-B27
- Involvement of the SI in spondyloarthropathies:
  - Involved in 95% of AS
  - Symptoms of inflammatory back pain
  - X-ray: erosions + sclerosis ↓ joint space
- If type not clear then classified as ‘Undifferentiated spondyloarthropathy’:

<table>
<thead>
<tr>
<th>Sex</th>
<th>Reiter’s</th>
<th>Reactive</th>
<th>Psoriatic</th>
<th>Enteropathic</th>
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_Musculo-skeletal, Rheumatology and Plastics_ 434
Ankylosing Spondylitis

- Chronic systemic inflammatory disorder of the axial skeleton, affecting SI joints and spine, of unknown aetiology
- Ankylosing = fibrous replacement of the joint → bony fusion

Features:
- Spinal inflammation + ankylosis, also SI
- Peripheral joint involvement → large joints in lower limb
- Extra-articular features → uveitis (ask: have you ever had a painful, red eye?), aortic regurgitation
- NB. Uveitis = inflammation of the uvea (middle chamber = iris, ciliary body, choroid)

Epidemiology:
- Prevalence: 2 – 5 per 1,000 males. Men have more progressive disease
- Men more common and present earlier (2:3:1)
- Onset usually between 15 – 40 years (often in 20s)
- 1.5 - 4 x mortality than expected (amyloidosis, heart disease)
- >95% HLA-B27 +ve:
  o 5 – 20% risk for positive individual
  o 11 HLA subtypes identified with different disease susceptibilities
  o Strong ethnic variances in HLA prevalence: present in Caucasians, absent in indigenous people of South America and Australia, high prevalence in Eskimos....

Clinical presentation:
- 75% first present with insidious/gradual onset of dull back ache, worse at night, improved by exercise
- Morning stiffness, backache, pain radiating from sacroiliac joints → hips/buttocks, loss of spinal movement (spinal ankylosis, distraction of < 5cm on flexion with Schober’s test)
- Pain generally improves towards the end of the day
- Progressive loss of spinal movement
- Can lead to flattening of lumbar spine, thoracic kyphosis, neck hyperextension
- Fatigue common

Distribution:
- Sacroiliac joints and spine (lumbar to start with, C-spine later):
  o Bilateral sacro-iliac joint tenderness
  o Tenderness of the lumbar vertebrae
  o Loss of thoracic kyphosis and lumbar lordosis
  o Early restriction in lateral flexion of the spine – test by seeing how far they can slide their hand down the side of their leg without bending forward. Later loss of movement in all directions
- Hips (30%), also knees and shoulders
- Peripheral arthritis infrequent

Other features:
- Commonly:
  o Enthesitis, especially Achilles tendonitis, plantar fasciitis + at tibial, ischial tuberosities + iliac crests
  o Iritis/Anterior Uveitis (25 – 30%): unilateral, acute, painful, with photophobia and blurred vision. Can → blindness. To test: shining light in opposite eye causes pain in the affected eye
  o Costochondriasis + chest pain referred from thoracic vertebrae
  o Chest wall rigidity → ↓VC
  o Osteoporosis (up to 60%)
- Rare:
  o Neurological involvement: secondary to spinal fracture (eg C-spine), atlanto-axial subluxation, cauda equina syndrome
  o Amyloidosis
  o Carditis and aortic regurgitation due to fibrosis of the aortic valve (can also affect AV bundle → arrhythmias)
  o Apical lung fibrosis (rare)
Musculo-skeletal, Rheumatology and Plastics

- **Pathogenesis:**
  - Cross reactivity between Klebsiella pneumoniae antigens and HLA B27
  - *Antibody complexes cause synovitis, enthesopathy* (including tendon attachment calcification) → *capsular ossification, ankylosis (bony fusion)* of the sacroiliac joint, inflammatory arthritis of the synovial joints in the spine and ossification of spinal ligaments

- **Diagnosis is clinical:** history of inflammatory spine disease + SI tenderness, ↓L-spine mobility, ↓chest expansion

- **Differential from RA:**
  - Spine rarely affect in RA
  - Small peripheral joints rarely affected in AS
  - In AS there are no subcutaneous nodules and no RhF (but there may not be in RA either)

- **Investigations:**
  - *X-rays:* ‘bamboo’ or ‘railroad’ spine, squaring of vertebrae, syndesmophytes (bony proliferation due to enthesitis between ligaments and vertebrae; these fuse with the above vertebral body causing ankylosis, eventually causing calcifications of ligaments), erosions of the apophyseal joints (between rib tuberosities and spinal processes), eventually bony ankylosis of the SI joints (also seen in Reiter’s and Crohn’s diseases)
  - **Bloods:**
    - FBC (mild normochromic anaemia in 15%)
    - ↑ESR and CRP

- **Treatment:**
  - Physiotherapy/Exercise (not rest) to maintain posture and mobility
  - NSAIDs to relieve pain and stiffness (especially phenylbutazone). If ineffective try sulphasalazine
  - Local corticosteroids for uveitis, enthesitis, peripheral synovitis
  - Disease modifying drugs if severe

### Psoriatic Arthritis

- **Epidemiology:** occurs in 10 – 40% of psoriasis patients, age 20-40, male = female
- **Arthritis may predate onset psoriasis**
- **May only be family history of psoriasis**

- **Pathology:**
  - Can have a reactive type presentation due to a host of possible infective/inflammatory agents
  - Primary lesion = synovitis (similar to RA): hypertrophic villi, T-cell infiltration, aggregates of T cells. But usually only minimal joint impairment
  - **Arthritis/Psoriatic Mutilans** = Articular destruction in a subset (25%) with pannus formation, cartilage erosion, etc

- **Clinical presentation:**
  - *Usually psoriasis develops first,* then arthritis, but 15% go the other way
  - Usually insidious but can present acutely
  - Check for *nail pitting,* transverse ridging, *onycholysis*
  - Extra-articular manifestations are uncommon (except for *conjunctivitis and iritis*)

- **Distribution:**
  - Monoarthritis (1) or Oligoarthritis (2-4) or Polyarthritis (>4)
  - Small or large joints
  - Spinal involvement
  - Often asymmetric, *mainly oligo* but can be polyarthritis
  - Often *upper* limb
  - DIP joints in hands and feet especially affected – unique to PA
  - Sacroiliac joints and spine (20 – 40%) – asymmetric involvement common
  - Rheumatoid pattern
  - Inflammation of *digital tendon sheaths* → sausage finger (*dactylitis*)
  - Enthesitis: Achilles tendonitis and plantar fasciitis

- **Diagnosis:** *Psoriasis* (exclude seborrhoeic dermatitis and fungal infections) or *psoriatic nail involvement* + seronegative arthritis. Increased likelihood in B27 +ive
- **Investigations:** X-ray of hands → **DIP involvement + resorption of the terminal phalanges** (see “pencil in cup” deformity)
- **Treatment:**
  - NSAIDs for pain – but may worsen skin lesions
  - Corticosteroid injections for local synovitis, but less use as can flare skin

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Musculo-skeletal, Rheumatology and Plastics

- If severe: methotrexate – can also help skin disease
- Differentiating from RA:
  - Presence of skin rash
  - Asymmetric
  - DIP and PIP involvement
  - Can overlap with RA and present as a symmetrical, destructive arthritis. Look for psoriasis and nail changes

**Reiter’s Syndrome**
- A form of reactive arthritis
- Classic triad: *urethritis, conjunctivitis* and *seronegative arthritis*. Recurrence in 50%, attacks can last several months
- Caused by sterile synovitis following chlamydia/non specific urethritis/shigella infection
- Distribution of arthritis usually lower limb (may be chronic or relapsing):
  - Sacroiliac joints and spine
  - Hips
  - Knees
  - Ankles and most of the joints of the feet
- Other features:
  - Iritis
  - Keratoderma blenorrhagica (brown, aseptic abscesses on soles and palms)
  - Mouth ulcers
  - Circinate balanitis (painless serpiginous penile rash)
  - *Enthesopathy* (plantar fasciitis, Achilles tendonitis)
  - *Not* onycholysis (differentiates from psoriasis)
- Investigations:
  - *Chlamydia*: First of 2 glass urine test shows more debris in the first glass in urethritis (cf prostatitis where there is more in the 2nd)
  - Anti-chlamydial antibodies
  - *Neutrophils* in synovial fluid
  - X-rays: periosteitis at ligamentous insertions. Rheumatoid like changes if chronic
- Pathogenesis: following non-specific urethritis, *Chlamydia or Shigella infection* in those genetically pre-disposed (ie HLA B27). Hyperaemic synovial membrane, but no pannus or cartilage erosion (except if progressive). Profuse osteolysis and formation of new periosteal bone
- Management: treat causal agent, rest, splint, NSAIDs, steroid injections, recovery may be slow

**Other Reactive Arthritis**
- Onset after gastro-intestinal infection or urethritis
- Variable course
- Infective causes: Yersinia, Chlamydia, Campylobacter, Salmonella, Shigella, Clostridium difficile... (all have lipopolysaccharide in their outer cell membrane)
  - Sterile immunological reaction in joints due to cross reactivity of antigens
- Usually B27+
- Presentation:
  - Acute asymmetrical polyarthritis (esp of lower limb) 1-2 weeks post infection lasting for 3 – 6 months
  - Can become chronic with relapsing and remitting course
  - *Enthesitis* is common (eg → plantar fasciitis or Achilles tendonitis)
  - Can also get:
    - Skin lesions resembling psoriasis: *circinate balanitis* (penile lesions), *keratoderma blenorrhagica* and nail dystrophy
    - Iritis
- Investigations:
  - Causative agent: Blood culture/serology for antibodies/stool culture
  - HLA-B27, X-ray, ESR, joint aspiration for septic arthritis
- Diagnosis is clinical
- Management:
  - Treating persisting infection has little impact on course
  - NSAIDs/corticosteroids
Methotrexate etc if necessary

- Also in leukaemia, endocarditis, acne, acromegaly, Wilson’s disease, sarcoid, sickle cell, haemochromatosis

**Enteropathic Arthropathies**

- Associations:
  - Inflammatory bowel disease (10-30% of Crohn’s and UC get arthritis; Crohn’s > UC)
  - Also associated with intestinal bypass surgery and Whipple’s Disease
- Variable course: IBD activity associated with peripheral arthritis but not with spinal inflammation
- Asymmetrical lower large joint mono- or oligo arthropathy
- No joint destruction
- Sacroilitis or Spondylitis in 5% (70% of these have HLA-B27)
- Manage underlying condition:
  - Sulphasalazine for both bowel disease and arthritis (treat IBD then treat arthritis as you would for RA)
  - NSAIDs and steroid injections for monoarthritis

**Crystal Arthropathy**

- Deposition of crystals in and around joints
- Sudden onset, extremely painful, monoarticular (or polyarticular)
- Diagnosis – joint aspirate

**Gouty Arthritis**

- An disorder of purine metabolism characterised by hyperuricaemia, deposition of monosodium urate crystals in joints + periarticular tissues + recurrent attacks of acute synovitis
- Prevalence: 1%, male:female = 5:1. Common in Maori and Polynesian populations. Most people with hyperuricaemia don’t have gout
- Family history common
- Types:
  - Acute Gout:
    - Severe pain, redness and swelling, may be febrile
    - Differential of acute gout: septic arthritis or haemarthrosis
  - Chronic Recurrent Gout:
    - Urate deposits with inflammatory cells surrounding them (tophi) in avascular areas: pinna, infrapatella and Achilles tendons, joints, eye, etc ⇒ chronic tophaceous gout = gouty tophi
    - Bone erosion and loss of cartilage
- Distribution:
  - Acute gouty arthritis is usually monoarticular
  - Affects MTP joint of the great toe in 75% of cases
  - Ankle and knees involved after recurrent attacks
  - Fingers, wrists and elbows affected late
- Pathogenesis:
  - Uric acid is the last step in the breakdown of purines
  - Hyperuricaemia (uric acid > 0.41 mmol/L) ⇒ precipitation + deposition of monosodium urate crystals (MSU) in joints (and visera, especially the kidney) ⇒ chemotactic to leukocytes and activate complement (ie inflammation) ⇒ accumulation of neutrophils and macrophages ⇒ erosion, synovitis, secondary OA
  - Acute arthritis: neutrophilic infiltrate with needle shaped crystals
  - Chronic arthritis: granulomatous inflammation surrounds aggregates of crystal
  - May be precipitated by trauma, surgery, starvation, infection and diuretics
  - Hyperuricaemia results from ↑ turnover or ↓ excretion
- Causes of ↓ excretion:
  - Primary gout
  - Renal failure ⇒ hyperuricaemia which rarely ⇒ gout
  - Hypertension
  - Primary hypoparathyroidism
  - Hypothyroidism
  - ↑ Lactic acid production (eg from ETOH)
- ↑ Cell turnover (↑ turnover of purines) due to:
  - Lymphoma, leukaemia, severe psoriasis, haemolysis, muscle necrosis
  - Disorders of purine synthesis (eg Lesch-Nyhan syndrome)
• An ↑ risk of gout with high meat and seafood consumption but not with consumption of purine rich vegetables/protein. A lower risk with high consumption of low fat dairy
• Hyperuricaemia can also cause renal failure eg cytotoxic treatment
• Diagnosis:
   **Aspiration:** needle shaped, negatively birefringent (no double refraction) urate crystals in tissues and synovial fluid (serum urate not always ↑) – also neutrophils (+ ingested crystals)
   ↑ESR
   Check renal function and BP
   X-rays: in early stages may only show soft tissue swelling; chronic changes = asymmetrical, punched-out cysts in juxtaarticular bone, joint space narrowing + secondary arthritis
• **Acute** treatment:
   1. NSAIDs (eg ibuprofen, Naproxen, indomethacin, not aspirin) – but problematic in renal failure and heart failure (→ fluid retention). Also contra-indicated if on anticoagulants (→ GI bleed)
   2. **Colchicine** (concentrates in neuts, inhibits microtubule formation, preventing their migration + activity)
   3. Prednisone
• Prevention:
   Avoid prolonged fasts
   Avoid purine-rich foods (offal, oily fish, beer), ↓obesity and excess alcohol (used to be called the ‘disease of kings’)
   No aspirin: salicylates competes with uric acid for excretion →↑serum urate
   Long term (‘interval’) treatment: **Allopurinol**:
    o Xanthine-oxidase inhibitor →↓serum urate
    o But not during an acute attack – wait three weeks. Mobilises gouty tophi →↑systemic urate → precipitates acute gout. Use with colchicine cover
    o SE: rash, fever, ↓WCC
    o Allopurinol can also be used during chemotherapy for leukaemia/lymphoma/myeloma to prevent gout from ↑purines
    o Also uricosuric drugs (→↑excretion): probenecid or sulfinpyrazone

**Pseudogout**
• = Calcium Pyrophosphate Deposition (CPPD)
• Onset in 30s
• Sporadic, hereditary, and secondary forms (OA, old age, haemochromatosis, hyperparathyroidism, haemochromatosis)
• Deposition of chalky white crystalline material – usually calcium pyrophosphate
• Produces an acute, subacute or chronic arthritis, mimics other disorders
• → **Chondrocalcinosis**: deposition in articular cartilage → calcification on x-ray
• Predominantly large joints (especially the knees)
• Aspirate: weakly positively birefringent (double refraction; = blue when parallel to axis of red compensator) rhomboid shaped crystals and chalky white material
• Treat with NSAIDs, or steroids or hydroxychloroquine

**Gout Versus Pseudogout**

<table>
<thead>
<tr>
<th>Gout</th>
<th>Pseudogout</th>
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<tbody>
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<td>Smaller joints</td>
<td>Larger joints</td>
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<tr>
<td>Pain intense</td>
<td>Pain moderate</td>
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<tr>
<td>Joint inflamed</td>
<td>Joint swollen</td>
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<td>Gouty tophi</td>
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<td>Hyperuricaemia</td>
<td>Uric acid normal</td>
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<tr>
<td>Urate crystals</td>
<td>Calcium pyrophosphate crystals</td>
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</tbody>
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**Connective Tissue Diseases**
• = Collagen vascular diseases
• Affect many organ systems, associated with systemic fever and malaise, run a chronic course, respond to steroids, associated with anaemia of chronic disease and a raised ESR

**Systemic Lupus Erythematosus**
• Non-organ specific autoimmune vasculitis with positive ANAs
• The classic autoimmune disease
Diverse clinical manifestations with multiple autoantibodies. Severity + clinical features very variable, from minimal rash to severe multi-organ life-threatening disease. Discoid lupus = skin involvement only. See Discoid Lupus Erythematosus (DLE), page 529.

**Essentials**

- Multi-system auto-immune disease
- Women, onset <50yrs
- Very variable:
  - Mild – rash, arthralgia, fatigue
  - Severe – nephritis, cerebral lupus, serositis
- Diagnosis:
  - Symptoms
  - Serology – positive ANA
- Treatment:
  - Mild – NSAIDs, hydroxychloroquine
  - Severe – Immunosuppression, azathioprine, cyclophosphamide

**Epidemiology**

- Prevalence = 20-150 cases/100,000
- Incidence = 1-10 per 100,000/yr; has ↑
- 65% cases between 16-55 yrs, rest above and below those ages; peak age of diagnosis: 30 - 40
- F:M = 9:1
- Tends to affect women of reproductive age, OCP a/w 50%↑ risk
- Commoner in pregnancy, Afro-Caribbeans, Asians

**Genetics and Environment**

- Genetics:
  - 14-57% concordance b/w monozygotic twins, 5-12% have relatives w SLE
  - HLA-DR2/3, complement C2, C4, other genes implicated – need 4-8 predisposing genes to get SLE
- Environment:
  - Infectious agents eg EBV
  - Vit D deficiency, UV light
  - ?silica dust, ?drug allergies
  - ?ETOH protective

**Pathophysiology**

- Appears to involve defect in apoptosis
- See multiple autoAb against multiple tissues (blood vessels, nuclear Ags, haematopoietic cells)
- Results in direct damage mediated by autoAb:
  - Gell-Coomb’s type 2 (eg cytopenias)
  - Immune complex disease – Gell-Coomb’s type 3 (eg GN)

**Clinical Features**

- Fatigue is often the most debilitating feature but not included in the diagnostic criteria
- Skin involvement (malar + photosensitive rash)
- Joint involvement (inflammatory arthralgia)
- Serositis (pleuritis)
- Fever
- Mouth ulcers + hair loss
- Libman-Sacks endocarditis (non-infective)
- Renal (haematuria, proteinuria, renal failure): requires intensive immunosuppression
- More severe = cerebral involvement, bowel haemorrhage/infarction, pancreatitis, PE, myocardial involvement + coronary vasculitis

**Lab Features**

- ANA positive >95% cases, but not specific
- Patterns – usually homogenous but can see other patterns (speckled and diffuse)
- Anti-ds-DNA antibody positive (Farr RIA) – 95% specific, 30% sensitive in all pts, 60% sens in active d
- NB. ANA is seen in many inflammatory, infectious, and neoplastic conditions + 5-15% of normal people
- Raised ESR (CRP much lower + can be normal)
- Low C3, C4 + CH100 (ie consumption of complement)
Diagnostic Criteria

- **S** Serositis (inflammation of serous linings of organs eg pleuritis, pericarditis, peritonitis)
- **O** Oral ulcers
- **A** Arthralgias (not arthritis; non-erosive)
- **P** Photosensitivity
- **B** Blood – Haemolytic anaemia, leucopaenia, lymphopaenia, thrombocytopaenia
- **R** Renal – persistent proteinuria, cellular casts, RPGN
- **A** ANA positive
- **I** Immunological markers – anti-dsDNA, anti-Sm, antiphospholipid antibody
- **N** Neurological – Seizures, Psychosis
- **M** Malar rash
- **D** Discoid rash

- If meets many criteria = classical SLE
- If 4 or more criteria = definite SLE
- <4 criteria = undifferentiated connective tissue disease – at 10 yrs, some have symptoms that have resolved, some stable, some progress

**Treatment**

- Mild = observe, topical corticosteroids for rash, avoid sunlight, **hydroxychloroquine** – good for skin + joint disease
- Moderate = PO corticosteroids, methotrexate, azathioprine
- Severe = IV corticosteroids, IV cyclophosphamide, mycophenolate mofetil, SC transplant, etc
- Other = if associated anti-phospholipid syndrome, give anti-coags

**Monitoring**

- Clinical (hair loss, rash, arthralgia, lethargy etc etc)
- Lab (FBC, ESR, Cr/urine, anti-DS-DNA, complement)
- Activity/damage scores/indexes
- Drugs
- Corticosteroids (SEs, bone dens)
- Methotrexate (respiratory – baseline CXR, FBC/LFTs)
- Hydroxychloroquine (retinal damage)
- Azathioprine (FBC, LFTs)
- Cyclophosphamide (FBC, urinalysis + cytology)

**Prognosis**

- Unpredictable + needs close monitoring
- ~ 5-10% **mortality** at 10yrs
- Death from active disease, SE of drugs (infection, malignancy), cardiovascular
- Poorer prog: renal d, HTN, male, etc

**Antiphospholipid Syndrome**

- Secondary to SLE in 20-30% of cases or as a primary disease
- Antiphospholipid antibodies are present: anticardiolipin antibody + lupus anticoagulants
- Produce features of **CLOT**: coagulation defect, livedo reticularis, obstetric (recurrent miscarriage), TCP
- Treat with low dose ASA or warfarin if recurrent thromboses

**Drug Lupus**

- Caused by isoniazid, hydralazine, procainamide, chlorpromazine, anticonvulsants
- Lung and skin effects greater than renal and CNS
- **ENA anti-histone** more likely to be positive
- Remits if drug stopped
- Sulfonamides and the Pill may exacerbate idiopathic SLE

**Sjogren’s Syndrome**

- = Dry eyes, dry mouth and associated with rheumatoid arthritis
- Epidemiology: onset 15 – 65 years, more common in women
- Types:
  - Primary (ie no other connective tissue disease)
Secondary: associated with other connective tissue diseases: Rheumatoid (50% of Sjogren’s have RA), SLE, Scleroderma, Polymyositis, Primary biliary cirrhosis (ie autoimmune disorders), graft-versus-host disease, AIDS

- Presentation:
  - Gritty, sore eyes: keratoconjunctivitis sicca (↓lacrimation → dry eyes)
  - Dry mouth: xerostomia (↓salivation) – can’t swallow, need sips of water at night, enlarged tender parotids
  - Also dry nose, vagina
  - Tiredness/depression
  - Arthritis as in SLE
  - Raynaud’s
  - Pulmonary fibrosis, pleurisy
  - Also peripheral neuropathy, renal involvement, hepatosplenomegaly, pancreatitis, etc

- Compared to RA:
  - ANA is more strongly positive in Sjogren’s
  - Arthritis is not destructive

- Investigations:
  - Schirmer test: < 5 mm of filter paper under the lower eye lid is wet after 5 minutes
  - ↑ESR & CRP. May have normal CRP (can get this in most CTDs, but not RA)
  - 100% have RhF
  - ANA positive in 60 – 70%
  - Anti-Ro (SSA) and Anti-La (SSB) present in 70% of primary, and 10% of secondary. NB Ro and La antibodies cross the placenta causing congenital heart block

- Pathology:
  - Connective tissue disease
  - Lymphocytes and plasma cells infiltrate exocrine/secretory glands (also skin, lungs and liver) causing fibrosis
  - Inflammation and destruction of exocrine glands: especially saliva and tears, with CD4+ lymphocytes
  - HLA DR3 association

- Treatment
  - Artificial tears and saliva
  - Hydroxychloroquine and methotrexate

Progressive Systemic Sclerosis (PSS)

- Connective tissue disease with inflammation, vasculitis and fibrotic changes in skin and viscera
- Epidemiology: female = 3 * male. Any age, but peak is 30 – 50 years
- Pathology:
  - Small vessel damage + oedema → collagen laid down → fibrosis and contraction
  - Dilation of other vessels → telangiectasia

- Presentation:
  - Raynaud’s (90%) may precede other signs by years
  - Then swelling of fingers and hands
  - Then skin gets tight, waxy and tethered (eg fingers – pointy fingers, forearms, face – no wrinkles, pointy nose)
  - Other: telangiectasia, nail bed spots, symmetrical polyarthritis

- Types:
  - Diffuse systemic sclerosis: widespread skin involvement with early visceral involvement → kidney (proteinuria, sediment, maybe crisis ↑BP), polyarthritis, myopathy, lung fibrosis (↓expansion + ↓gas transfer → SOB) and GI fibrosis
  - Limited systemic sclerosis: includes CREST syndrome (probably very different disease entity to Diffuse): Calcinosis (subcutaneous calcium deposits on hands) + Raynaud’s phenomenon + disordered oesophageal motility (heart burn and dysphagia) + sclerodactyly (Scleroderma of the hands) + telangiectasia.
  - Centromeric ANA * (anticientromere antibody)
  - Limited scleroderm/Morpheoa:
    - Tightening and fibrosis of the skin: proximal skin scleroderma (eg face – can they open their mouth wide, any wrinkles – if so then no involvement. Limited mouth opening = microstomia) or any 2 of sclerodactyly (can they make a fist, Prayer sign: can they oppose palmar MCP joints), digital pitting scars, pulp loss, bibasilar lung fibrosis. Late visceral involvement
- Scleroderma limited to the hands and maybe face (‘Limited Scleroderma’) is probably a presenting symptom of CREST syndrome even if the other features aren’t present
- Morphea (localised skin sclerosis) rarely, if ever, progresses to PSS

- **Investigations:**
  - FBC: normocytic anaemia, haemolytic anaemia
  - ↑ESR
  - **ANA positive in 75%.** May have autonuclear autoantibodies in any of these three forms to: topoisomerase (Scl-70), RNA polymerases and centromeres. Anticentromere (ACA) in Limited and CREST. Anti-Scl-70 in diffuse.
  - RF +ive in 30%
  - 24 hour urine
  - Hand x-ray. Can get distal phalange resorption
  - Barium swallow and CT of lung

- **Treatment:**
  - No cure but can use immunosuppressants eg cyclophosphamide
  - Education, support groups, etc
  - Raynaud’s: warmth and vasodilators (Ca blocker)
  - Oesophageal mobility: omeprazole, cisapride, reflux prevention
  - Renal & Raynaud’s: ACE inhibitors
  - Scleroderma: D-penicillamine (antifibrotic) or immunosuppressants (little efficacy from steroids)

- **Prognosis:** Limited disease has 70% 10-year survival; diffuse has 55% 10-year survival. Death from lung/renal effects

**Mixed Connective Tissue Disease**
- Features of SLE, PSS and polymyositis
- **Anti-RNP** (ribonuclear protein) +ive without other types of ANA

**Relapsing Polychondritis**
- Attacks cartilage, affecting the pinna, nasal septum + larynx (hence, stridor)
- Associated with aortic valve disease, polyarthritis + vasculitis
- Rx with steroids + immunosuppressants

**Polymyositis and Dermatomyositis**
- Myositis includes polymyositis + dermatomyositis → progressive muscle weakness due to striated (voluntary) muscle inflammation
- Peaks age 10-14 (mainly dermatomyositis) and 45 – 60 years (mainly polymyositis). Rare

**Presentation**
- **Voluntary muscle inflammation → insidious, symmetrical, proximal** muscle weakness (shoulders, hips, trunk, neck – compared to polymyalgia rheumatica which just has stiffness). May → atrophy and contractures
- Skin (only Dermatomyositis): *Gottron’s lesions/papules:* erythematous plaques or macules over MCP joints, extensor knees, wrist and elbows (pathognomic if ↑CK + weakness). Rash over upper chest, neck, etc.
- Other symptoms: fatigue, malaise, weight loss, fever, etc
- Causes **dysphagia, dysphonia,** facial oedema, respiratory weakness
- Also Raynaud’s, lung involvement (interstitial fibrosis), polyarthritis, retinitis, myocardial involvement, purple rash on cheeks and light exposed areas

**Differential Diagnosis**
- Infection
- Muscular dystrophy
- Endocrine: thyroid, PTH, ↑Ca, ↓K
- Neurology: motor neuron, Guillain Barre, Myasthenia Gravis
- Drugs
- Diagnosis of exclusion

**Investigations:**
- ↑ESR, CRP, CK, maybe ↑AST and LD
- RF positive in 50%
- ANA may be +ive, as well as myositis specific antibodies (eg anti-Mi2 + anti-Jo-1 – linked to HLA DR3)
- EMG → denervation and myopathy (not usually done)
- Biopsy: inflammatory muscle infiltrate + fibrosis

**Associations:**
- Other autoimmune rheumatological diseases
- Malignancy in 10%
- Coxsackie virus, rubella & influenzae

**Treatment:**
- Rest
- Steroids, methotrexate, Ig
- Active graded exercise between attacks

**Polymyalgia Rheumatica**
- Old ladies with *morning stiffness and PAIN* in proximal muscles (shoulders + pelvis) +/- mild polyarthritis, *depression, weight loss, anaemia, malaise, fever, anorexia*, maybe jaw claudication, angina, hypopituitarism, *not* weakness
- Common in >70 year olds (rare <60)
- May be features related to underlying CTDs (arthritis if superimposed RA, headache in GCA ⇒ ask about headaches, visual disturbance etc)
- ?Syndrome with many underlying causes (eg variety of connective tissue diseases)
- Differential:
  - RA with onset of central joints
  - Frozen shoulder
  - Carcinomas: breast, thyroid, prostate
  - Myeloma
  - Polymyositis
  - Bacterial endocarditis
- Investigations: ↑ESR, anaemia, no abnormality on X-ray, *usually RF + ANA negative* (but RF can be positive), CK not usually raised, liver involvement →↑ALP
- Treatment: dramatic response to low dose steroids (eg 15 mg/day)

**Vasculitis**
- = Inflammation of the blood vessels
- Systemic symptoms due to end-organ damage due to blocked blood vessels

<table>
<thead>
<tr>
<th>ARTERITIS – inflammation of artery walls – oedema + fibrin + neuts + MO seen IN vessel wall</th>
<th>Path</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infectious arteritis</td>
<td>Syph macro = asc aorta aneurysm, intima tree-bark appearance</td>
</tr>
<tr>
<td>Many types of MO, either septic emboli or direct extension</td>
<td></td>
</tr>
<tr>
<td>Myotic aneurysm seen at bifurcation where septic emboli lodged, weakening the wall</td>
<td></td>
</tr>
<tr>
<td>Non-specific histology (oedema, neuts, MOs)</td>
<td></td>
</tr>
<tr>
<td>Syphilitic arteritis = causes ischaemic damage by occluding vasa vasora and results in prox aortic aneurysms</td>
<td></td>
</tr>
<tr>
<td>Giant cell arteritis – medium and small arteries</td>
<td>Syph micro = perivasc inflamm cell infiltrate</td>
</tr>
<tr>
<td>AKA temporal arteritis – affects esp head + neck art</td>
<td></td>
</tr>
<tr>
<td>P/W pain + tenderness over temporal art, raised ESR/CRP</td>
<td></td>
</tr>
<tr>
<td>Immune reaction to IEL</td>
<td></td>
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<tr>
<td>Can cause blindness – treat prophylactically with steroids</td>
<td></td>
</tr>
<tr>
<td>Polyarteritis nodosa – medium sized muscular arteries</td>
<td>Positive bx show acute and chronic infl cells within walls of vessel, incl giant cells engulfing IEL</td>
</tr>
<tr>
<td>Immune complex (Type III) mediated arteritis</td>
<td></td>
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<tr>
<td>Associated with Hep B, not ass. w ANCA</td>
<td></td>
</tr>
<tr>
<td>Focal, random and episodic appearance in young adults</td>
<td></td>
</tr>
<tr>
<td>P/W non-specific symptoms (fever, malaise, wt loss or infarction of organ e.g. bowel, kidney, testis); <em>does not involve lungs</em> (cf. Wegener’s); ESR always raised</td>
<td></td>
</tr>
<tr>
<td>Treat with steroids</td>
<td></td>
</tr>
<tr>
<td>Macro = aneurysmal dilatation, nodularity, obstruction of med art</td>
<td></td>
</tr>
<tr>
<td>Micro = transmural acute and chronic infl, fibrinoid necrosis</td>
<td></td>
</tr>
</tbody>
</table>
Leucocytoclastic vasculitis – small vessels (arterioles + venules)
- Henoch-Scholein purpura included in this category
- Hypersensitivity angiitis occurring in the skin – immune attack against vessels triggered by meds and other things

Neut invasion of walls of small vessels

Takayasu’s arteritis
- Aortic arch + great branches thicken and ostia become stenotic; granulomatous vasculitis

Kawasaki’s disease
- Fever, conjunctivae, cervical LNs, rash, red swollen hands – ~20% coronary artery involvement

Wegener’s granulomatosis
- Lungs and kidneys; c-ANCA positive; granulomatous vasculitis

Wegener’s granulomatosis
- ANCA +ve: microscopic polyangiitis, Wegener’s, Churg-Strauss syndrome
- ANCA –ve: HSP, Goodpasture’s

Disease (not necessarily vasculitis) by vessel size

Large vessels
- Atherosclerosis, GCA, Takayasu’s

Medium vessels
- Polyarteritis nodosa, Kawasaki

Small vessels
- ANCA +ve: microscopic polyangiitis, Wegener’s, Churg-Strauss syndrome
- ANCA –ve: HSP, Goodpasture’s

Small arteries and arterioles
- Hypertension + DM

• Associations:
  ➢ Occurs in non-organ specific autoimmune diseases (e.g., RA, SLE)
  ➢ Principal feature of other connective tissue diseases that may or may not be autoimmune
  ➢ Also occurs in conditions not usually included in connective tissue diseases (e.g., drug reactions)

• Defined by size of blood vessels involved:
  ➢ Large vessel vasculitis: Giant cell arteritis, Takayasu’s arteritis
  ➢ Medium sized vessels: Polyarteritis Nodosa (PAN), Kawasaki’s disease
  ➢ Small vessel vasculitis: Wegener’s Granulomatosis, Microscopic Polyarteritis, Henoch-Schonlein purpura

• Consider vasculitis in any unidentified multisystem disorder

• Clinical features suggesting vasculitis:
  ➢ Multisystem inflammatory disease
  ➢ Rapidly progressive major organ dysfunction
  ➢ Constitutional symptoms (fever, weight loss)
  ➢ High ESR, severe anaemia, thrombocytosis
  ➢ Evidence of small-vessel inflammation:
    o In the kidneys = active urinary sediment
    o In the lungs = haemoptysis, dyspnoea
    o In the skin = palpable purpura/hemorrhage
  ➢ Acute neurologic changes:
    o Foot drop
    o Altered mental status

Giant Cell Arteritis/Temporal Arteritis
• Large/medium arteries (especially temporal arteries → medical emergency – affects ciliary/retinal arteries)
• Overlaps with Polymyalgia Rheumatica in 25% of cases (→ stiff proximal muscles in the morning). See Polymyalgia Rheumatica, page 444
• From 55 years, peaking at 75
• Clinical:
  ➢ Initially persistent headache + fatigue, then superficial pain and tenderness over temporal arteries
  ➢ Can → unilateral visual disturbance
  ➢ Can also see arthritic pain, jaw claudication, fever, malaise
  ➢ ↑ESR/CRP (Age and ESR both over 60 in 3/4 cases)
• Immune reaction to internal elastic lamina
  ➢ Diagnosed by biopsy showing giant cells engulfing the IEL and inflamed media. Biopsy is critical as treatment should continue for 2 years and therefore want to be sure of diagnosis
  ➢ Presumptive treatment with steroids (40-60mg/24hr PO IMMEDIATELY). Immediate risk is blindness, but longer-term morbidity is due to steroid treatment!

Polyarteritis Nodosa
• = necrotising vasculitis causing aneurysms + thrombosis in medium sized arteries leading to infarction in affected organs
• Presents with non-specific symptoms – fever, malaise, abdominal pain, renal failure, purpura
• Immune complex mediated arteritis (type 3 hypersensitivity)
• 40% associated with Hep B
Necrotising vasculitis of medium sized arteries (not arterioles). Involves smaller arteries – kidney, heart, liver, GI. Often patchy distribution. Macroscopic: small nodules. Microscopic: fibrinoid necrosis, intimal proliferation, media destruction, inflammation of adventitia, scarring if chronic

Investigations: FBC, biopsy of affected organ, ECG, ANCA may be +ive

Treatment: steroids/immunosuppressives (azathioprine/cyclophosphamide). Treat HTN

Kawasaki Disease

= Mucocutaneous Lymph Node Syndrome ~ Childhood Polyarteritis Nodosa

Immune mediated injury to vascular endothelium, including coronary arteritis

?post viral

Fever in kids (usually < 5) for > 5 days with bilateral, non-purulent conjunctivitis, oral mucosal changes, cervical lymphadenopathy, changes in the extremities (eg swelling of hands and feet), & generalised rash

Investigations: Echo for coronary aneurysm, FBC (↑WBC, ↑platelets), ↑CRP

Differential: Scarlet fever, EBV

Complications: pancarditis, aneurysms or dilatation

Treatment: none, or high dose IgG/steroids

Wegener’s Granulomatosis

Generalised necrotising arteritis of small arteries of the respiratory tract and kidney with non-caseating granuloma formation

Wegener’s triad:
1. Aseptic necrosis of the lower and upper respiratory tract
2. Generalised necrotising vasculitis of arteries + veins
3. Focal necrotising glomerulonephritis of the kidney

Presentation:
- Upper airways disease (chronic rhinitis/epistaxis/sinusitis/mouth ulcers) unresponsive to therapy. CXR shows spots. May have haemoptysis. Progresses to ulceration of nasal mucosa, perforation of the septum, heavy nose bleeds, granulomatous invasion of large bronchi → bronchial stenosis
- Glomerulonephritis. If untreated then slow progression to end stage renal failure
- Systemic: fever, night sweats, weight loss, etc
- Non-deforming arthritis and arthralgia

Progression highly variable

Investigations:
- ↑ESR, c-ANCA positive, CXR (nodular masses, cavitation)
- Renal biopsy: necrotising glomerulonephritis: may be focal and crescentic. Immunoflouresence is –ive ⇒ pauci-immune

Treatment: steroids +/- cyclophosphamide → 90% remission but frequent relapse. Continue for a year then taper off

Microscopic Polyarteritis

Vasculitis of small-medium sized vessels

Multisystem involvement including glomerulonephritis

Kidney involvement: crescentic rapidly progressive GN common, no immune deposits on immunoflouresence (ie pauci immune)

Biopsy: fibrinoid necrosis and cellular proliferation within capillaries

Frequently positive for p-ANCA

Treatment: similar to Wegener’s

Henoch-Schonlein Purpura

Leukocytoclastic vasculitis of small vessels with deposition of IgA immune complexes in the skin, gut and kidney

A form of secondary vasculitis in response to hypersensitivity

Usually in young children, associated with URTIs

HSP affects the capillaries in the skin and frequently the kidneys.

Symptoms:
- HSP results in palpable purpuric rash over the buttocks and lower limbs
- Associated with arthritis
- Cramping abdominal pain.
Occasionally patients may suffer intussusception or chronic renal impairment but these sequelae are rare, only 5% of patients developing renal impairment.

- Renal involvement: macroscopic or microscopic vasculitis, mesangial proliferative glomerulonephritis, maybe crescentic, IF +ive for mesangial IgA deposition
- The prognosis for patients with HSP is generally excellent.
- Usually self-limiting, otherwise steroids

**Others**

- Hypersensitivity angiitis (Leukocytoclastic vasculitis): Type 3 immune injury. Associated with medicines, lupus, HBV. Microscopically: neutrophils, fibrinoid necrosis
- Takayasu’s arteritis: Aortic thickening with autoimmune granulomas = Pulseless Disease. Rare, in young females, hypertension, pain of affected artery
- Thromboangitis obliterans = Buerger’s disease. Neurovascular bundles – mainly in legs and arms of young/middle aged smokers – become inflamed and thrombosed
- Behcet’s disease: Systemic vasculitis, commoner in Turkey and Japan, oral and genital ulcers, eye lesions (iritis), arthritis of knee, ankles, wrists and elbows. Can see thromboembolic disease

**Pain Syndromes**

**Chronic/Complex Regional Pain Syndrome (Type 1)**

- = Reflex Sympathetic Dystrophy
- = Algodystrophy
- Can develop as a consequence of trauma affecting the limbs with or without obvious nerve lesion
- Cause: ?peripheral sympathetic over-activity, pathological interaction of sympathetic and afferent systems
- Presentation:
  - Pain
  - Abnormal blood flow (cold or hot) and sweating (including distal to the trauma)
  - Structural changes eg muscle wasting (over months to years can → contractures)
- Treatment: difficult: pain relief, rehabilitation, physio, early refer to pain management clinic

**Fibromyalgia**

- Aetiology: unknown
- Presentation:
  - Diffuse musculoskeletal pain (over all 4 quadrants and axial) but normal muscle power
  - Morning stiffness
  - Paraesthesia
  - Tender points over the body
  - Skin fold tenderness
  - Sleep disturbance, fatigue and vertigo
- ESR usually normal
- Associations: Raynaud’s phenomenon, anxiety/depression, IBS
- Diagnosis: based on finding a number of separate, defined tender points
- Treatment: analgesics and exercise

**Plastic and Reconstructive Surgery**

- Restoration of function and correction of deformity
- Resulting from trauma, neoplasia, etc
- Largely about transferring tissue
- Techniques:
  - Direct closure
  - Graft: gets blood supply from wound site
  - Flaps: brings blood supply with it (especially over bony prominences, and if further surgery will go through it again)
  - Tissue expansion
- Always:
  - Repair in layers
  - External layers everted (if inverted then retraction → depression)
- Burns: See Burns, page 799
See Mr Tan’s very interesting but non-examinable hand-outs

**Skin Cancer**

- **Basal Cell Carcinoma (BCC)**
  - Most common skin cancer in NZ
  - Fair skin, age, sun exposure
  - Seen with Gorlin’s syndrome, Xeroderma pigmentosa and sebaceous naevus
  - Types:
    - 1. Nodular-ulcerative. Most common. Pearly border, telangiectatic vessels, central ulceration
    - 2. Superficial. Erythemoid, scaly
    - 3. Morphoeic. Indistinct margins, plaque like, high recurrence
    - 4. Pigmented. Differential MM
  - Slow steady growth, locally destructive
  - May be fatal if left
  - Metastasis very very rare
  - Treatment options:
    - Surgery. Can evaluate diagnosis and margins. Simple
    - Cryotherapy. Only for shallow lesions, Scars
    - Dermatologic Curretage
    - Radiotherapy Beware “danger areas”. Detection and Rx of late recurrence difficult

- **Squamous Cell Carcinoma (SCC)**
  - Seen in/associated with:
    - Sun exposure, fair skin, smokers
    - Chemicals; arsenic, bitumen, chimney sweeps
    - Chronic scars; sinuses, ulcers, burns, osteomyelitis, radiation
    - Immunosuppresion; transplants, HIV
  - Sun exposed areas
  - SCC in-situ (no BM invasion) = Bowen’s disease (trunk and limbs), Erythroplasia of Queyrat (glans)
  - 20% of solar keratoses may transform to SCC eventually
  - Can see keratin horns
  - Keratoacanthoma (KA) clinically and histologically similar. Resolves over about 6 weeks
  - Metastasizes via lymph nodes (therefore check lymph node drainage region)
  - Late spread is systemic
  - Danger areas hand, scalp and lower lip
  - Treatment (local, nodal and systemic):
    - Surgical Wider margins than for BCC. 0.5 -1cm
    - Chemo Topical SFU (efudex) for in-situ lesions ie Bowen’s
    - Radiotherapy
    - Regional lymph node dissection for high risk lesions
    - Systemic chemo for palliation only

- **Melanoma**
  - Neoplasia of melanocytes
  - Increasing incidence and mortality in White populations world wide
  - Most common fatal skin cancer
  - Incidence varies widely between populations: Scotland 5 per 100,000. QLD 30 per 100,000
  - NZ incidence 1:50 in lifetime
  - Sun exposure important but not only factor
  - High risk: red hair, fair, positive family history, higher social status, atypical mole syndrome, various syndromes
  - Lower incidence: Mediterraneans and Asians. Rare in Blacks. Palms, soles, ungual more common in “blacks”
  - Precursors
    - Pigmented naevi precursor in 50%. Change important. Size, shape, contour, pigmentation, itching, bleeding
    - Congenital melanocytic naevi. 2.5% of infants. Only giant naevi statistically increased risk of melanoma
    - Atypical mole syndrome. Usually familial. Large 5-10mm, irregular shape and pigmentation, flat, crops. Only group to benefit from mole mapping
    - Xeroderma pigmentosa. DNA repair defect. MM in sunexposed areas. Incidence 3% by teenage years
Musculo-skeletal, Rheumatology and Plastics

- **Hutchinson’s melanotic freckle**, Lentigo maligna. Usually on face of elderly people. 5% develop MM.

- **Types of melanoma:**
  - Superficial spreading: 70%. Radial growth before vertical growth phase
  - Nodular melanoma: 14%. Early vertical growth phase
  - Acral lentiginous: Soles, palms, ungual
  - Lentigo maligna MM: Arise in HMF
  - Amelanotic melanoma

- **Prognostic factors:**
  - **Depth** most important. Breslow’s depth (from granular layer). Clark’s level/thickness more subjective.
    - Level I-V
  - **Lymph node involvement** is next most important after depth
  - Ulceration, microscopic satellites, acral subtype worsens prognosis

- **Survival:**
  - <0.76mm: 95% 10 YS
  - 0.76-1.5: 80% 10 YS
  - 1.5-2.5: 60% 10 YS
  - >8: 10% 10 YS
  - 1 node: 40% 10 YS
  - >2 nodes: 13% 10 YS

- **Treatment:**
  - Primary excision bx with 1-2mm margins – when depth known, do wide excision depending on depth (ie ~ 5-10mm)
  - Surgical excision. Margin tailored to depth and local conditions. Wide excision to underlying fascia
  - Removal of involved or high risk lymphatic basin
  - Radiotherapy for close margins lymph nodes or palliation
  - Prophylactic lymph node dissection and sentinel node (first node it will drain to – use dye to determine) biopsy is highly controversial. It improves prognostic accuracy but no proven survival advantage

- **Site**
  - Female – more common extremities
  - Male – more common axial
  - Other – mucosal, uveal tract

**Initial Management of Burns**

- **Burn Mortality:**
  - Proportional to:
    - 1 Extent: TBSA and depth
    - 2 Age
    - 3 Inhalation
    - 4 Comorbid conditions

- **Aetiology:**
  - Thermal
  - Electrical (has an entry and exit burn)
  - Chemical
  - Friction
  - Cold

- Depth of tissue destruction proportional to 1. **duration** of exposure and 2. **temperature**

- **Burn First Aid:**
  - **Stop** burning process
  - **Cool** burn wound (cold/lukewarm running water, not ice – can cool the pt too quickly)

- **Burn Assessment:**
  - ABCDE
  - Fluid resuscitation
  - Xrays - trauma series
  - Analgesia – IV morphine
  - NGT (burns stop stomach emptying)
  - Secondary survey
  - History - mechanism of injury
  - Comprehensive head to toe examination
Any sign of **inhalation** injury?
Need for escharotomy?

- **Escarotomy**: for **circumferential deep burns**. Is not a fasciotomy rather an incision that *extends into unburnt skin and down to unburnt tissue*.

- Estimation of burn depth:
  - Colour
  - Blisters
  - Capillary refill
  - Sensation
  - Healing
  - **Partial** thickness ie superficial if red, and has CR, and is **painful**
  - **Full** thickness if darker colour, has no sensation, no CR

- Lund and Browder Charts:
  - Differences in Children
  - Rule of nines (unreliable in children)

- Re-evaluate:
  - *Tetanus* prophylaxis
  - Haemochromogens (coloured breakdown pigments from Hb)
  - Hb/ Hct & U&Es
  - CXR
  - ABG, CO
  - ECG
  - Blood glucose

- Burns Unit referral criteria:
  - **10%** TBSA
  - **Full thickness >5%** TBSA (ie because these will likely require grafting)
  - *Special areas* (face, hands, feet, genitalia, joints)
  - Inhalation injury
  - Chemical or electrical burn
  - Extremes of age

- Fluid resuscitation:
  - 2 large bore IV lines
  - (FBC, U&Es, Coags, Amylase, CO, Ca)
  - Estimate burn area
  - IDC if > 15% TBSA
  - Urine output – Adult 0.5ml/kg/hr - Child 1 ml/kg/hr

- Parkland Formula:
  - 3-4 mls/kg/% burn over 24 hours
  - Give **half in first 8 hours** *(from burn time)*
  - Hartmanns
  - Add maintenance in children (Dextrose)

- Increased fluid requirements:
  - Children
  - Inhalation injury
  - Electrical injury
  - Delayed resuscitation
  - Dehydration - firefighters, intoxicated

- Inhalation injury signs:
  - Burns - nose, mouth, pharynx
  - Carbonaceous sputum
  - Change of voice, hoarse cough
  - Inspiratory *stridor*
  - Singed nasal hairs
  - Accessory muscle use
  - Systemic intoxication (eg CO etc)

- Inhalation injury classification:
  - 1 Airway injury *above* larynx
  - 2 Airway injury *below* larynx
  - 3 Systemic intoxication
• Inhalation injury treatment:
  ➢ **Humidified oxygen** via rebreathing mask
  ➢ 8/ minute
  ➢ Respiratory support as needed

• Electrical burns are different:
  ➢ Entry and exit wounds
  ➢ Specific patterns according to voltage
  ➢ Size of wound often underestimated
  ➢ High fluid requirement
  ➢ Consider cardiac monitoring if across chest
  ➢ **Haemochromogens** (RBCs breakdown pigments) seen in urine - UO >100mls/ hr
  ➢ Need for fasciotomy?

• Influence of acute management:
  ➢ Early wound closure
  ➢ Early wound treatment - hypertrophic scars and contractures
  ➢ Pressure areas - alar cartilages
  ➢ Placement of SSG (split skin graft) donor
  ➢ Preserve precious donor sites
  ➢ Education
  ➢ Psychological support

• Burns Unit Transfer
  ➢ Airway
  ➢ Fluid resuscitation
  ➢ IDC
  ➢ Gladwrap wounds

**Bat Ears & Ear Deformation**

• Aetiology:
  ➢ Absent antihelical fold
  ➢ Deep conchal bowl

![Diagram of ear anatomy showing normal ear and prominent ear]
**Scope & History of Plastics in NZ**

- Specialized branch of surgery dedicated to the *restoration of function* and *correction of deformities* resulting from *birth defects, cancer and trauma* including *burns*
- Plastic Surgery is about the *Quality of Life*
- “Plastic” is derived from a Greek word meaning “to mould”
- History of Modern Plastic Surgery
  - The need for Plastic Surgery arose with widespread casualties in WWI and WWII
  - WWI – Trench warfare with severe maxillofacial injuries
  - WWII – Including facial burns to fighter pilots – Guinea Pig Club
  - Need to introduce new tissue from elsewhere and reconstruct complicated defects
  - New Zealander *Harold Gillies* is the Modern father of Plastic Surgery
  - His cousin Archie McIndoe started the Guinea Pig Club
- Scope of New Zealand Plastic Surgery
  - 4 regional units in New Zealand
  - Each unit has peripheral clinics and OT sessions
  - Eg for Wellington: Napier/ Hastings, Palmerston North, Nelson
- Regional Services provided at each unit
  - Breast Reconstruction, Burns Surgery, Cleft Lip/Palate Surgery, Facial Palsy Surgery, Hand Surgery, Oculoplastic Surgery, Maxillofacial Surgery, Skin Cancer Surgery
- Supra – Regional services provided by some units:
- Multidisciplinary clinics with other specialties
  - Skin cancer clinic, Cleft, Maxillofacial, Craniofacial, Hand, Head and Neck, Microtia
- **SCOPE**
  - **SKIN**
    - a) Burns
      - Acute management and secondary reconstruction
    - b) Trauma
      - Especially tissue loss
    - c) Neoplasia
      - Benign – Naevi and vascular anomalies
      - Malignant – BCC, SCC, melanoma etc
    - d) Lymph node
      - Parotid, neck, axilla, groin
    - e) Radiotherapy complications
  - **HEAD & NECK SURGERY**
    - Salivary gland tumours
    - Parotid, submandibular, intraoral
    - Facial palsy and facial nerve surgery
    - Intraoral cancers
    - Resection and reconstruction
    - Neck nodes
    - Neck dissection
    - Craniofacial
    - Tumours of the skull base
    - Trauma
    - Parotid duct, lacrimal apparatus, facial nerve, eyelids, nose etc
    - Cosmetic
    - Brow, eyelids, face, neck, nose
  - **CONGENITAL FACIAL SURGERY**
    - Clefts of lip and palate
    - Ear reconstruction
  - **CRANIOFACIAL SURGERY**
    - Congenital: Craniosynostosis
    - Facial clefts
MAXILLOFACIAL SURGERY
- Orthognathic surgery
- Fractures of maxilla, zygoma and mandible
- Jaw tumours
- TMJ reconstruction

BREAST SURGERY
- Reconstruction after cancer
- Congenital deformity
- Asymmetries
- Augmentation
- Reduction
- Mastopexy (breast uplifting)

TRUNK SURGERY
- Spine: Myelomeningocoele
- Post cardiac surgery complications
- Pressure sores
- Large hernias
- Cosmetic: Abdominoplasty, Body lift, Liposuction

UPPER LIMB
- Congenital: a) syndactyly (digital fusion) b) polydactyly (digital duplication) c) hypoplasia/absence d) other
- Trauma: skin, nerve, tendon, bone, joints, Replantation, Secondary reconstruction – tendon transfers, nerve grafts, digit recon
- Degenerative: Dupuytrens, Tenosynovitis, (arthritis Ortho in WGTN region)
- Nerve: Compressions esp median and ulnar
- Neoplasia: Skin, soft tissue, bony tumours

LOWER LIMB
- Coverage in mutilating injuries
- Coverage of bone and fractures
- Coverage of exposed joint replacements
- Osteomyelitis
- Lipodystrophy and lymphoedema

GENITAL
- Hypospadias
- Vaginal agenesis
- Vaginal reconstruction

TRAINING IN PLASTIC AND RECONSTRUCTIVE SURGERY
- Year 1-6 MBChB: Consider elective in Plastic Surgery
- Year 7, 8 House Surgeon
- Year 9, 10 Registrar, Basic surgical training (RACS)
- Year 11-14 Advanced trainee in Plastic Surgery
- Year 15 Overseas fellowship

Craniosynostosis
- Early suture closure
- Incidence 1: 2000
- Brain growth 80% adult age 1, 90% adult age 2

Unicoronal synostosis    Metopic synostosis
Types - single suture - multisuture (Apert, Crouzon, Pfieffer etc)

Shapes
- Sagittal synostosis → Scaphocephaly
- Metopic synostosis → Trigonocephaly
- Bicoronal synostosis → Brachycephaly
- Unicoronal synostosis → Plagiocephaly

X-ray unnecessary

Problems
- ICP raised 25%
- Developmental delay 33%
- Blindness rare
- Cortical perfusion 95%
- Psychological distress common

Treatment  
If not operating
- <6 months  
  Springs suitable for most types  
  ICP monitoring
- >6 months  
  Traditional craniofacial remodelling  
  (SPECT scan)

Deformational Plagiocephaly
- Back to sleep campaign has caused epidemic
- Confused with lambdoid synostosis

Assessment:
- Exclude torticollis
- Exclude craniosynostosis
- X-ray not necessary

Signs:
- Flat occiput: Ipsilateral frontal bossing
- Parallelogram head (vs trapezoid): Skull base sheared
- Ipsilateral ear pushed forward

Treatment:
- Intervene ASAP during rapid brain growth phase
- Keep pressure off flat spot
- Helmets no longer used
- Turn cot around
- Toys to one side
- Sleep alternate sides
- Cuddly “sausage” behind back
- Safe-T wrap (velcro binder)
- Mattress wedge
- Tummy time

Flaps & Grafts
- A graft must get its blood supply from the bed it is placed on ie vascularised tissue
- A graft cannot therefore be placed onto avascular tissue. Eg cortical bone, cartilage, bare tendon, infected wound
A flap contains its own **blood supply**

A flap may be placed onto avascular tissue (or used to support a graft)

A graft or a flap **may contain any tissue type**. Eg just skin, just fat, just bone or just cartilage. Or it may contain a **combination of tissue types** = a so called **compound graft** or **compound flap**

Skin grafts:
- A skin graft may be **split thickness** (SSG) or **full thickness** (FTSG)
  - **SSG**:
    - A SSG leaves behind **deep** dermis (ie SSG does take **some** dermis) from which the donor site can epithelialise
    - The deeper the graft, the longer the tissue donor site will take to heal (SSG will heal by itself as epidermal appendages eg sweat glands, hair follicles burrow deep into the dermis and contain some epidermis/basal layer so will allow regeneration of epidermis)
    - A further graft may be taken from the donor site when it has healed. Eg in large burns
    - **Advantages** of SSG include high take and large source of skin
    - **Disadvantages** include high contraction, no sweat/sebaceous gland transfer (shiny), less durable, poor colour match and no hair
  - **FTSG**:
    - A FTSG graft **donor site must be directly closed**. This **limits the size of the graft**.
    - The thicker the graft, the more the tissue is like the area from which it was harvested
    - **Advantages** of FTSG include **less contraction**, the ability to transfer hair follicles (eg eyebrow reconstruction), skin sweats, colour of donor site, more durable, better cosmesis
    - **Disadvantages** include higher failure rate, limited size
  - Can also take bone, cartilage etc grafts

Flaps:
- Flaps can be **local** in that they are moved from an adjacent site OR
- A flap may be **completely separated from its blood supply then reconnected using microsurgical techniques**. This is a **microvascular flap** or **free flap**
- Other common types include muscle, osseous, osseocutaneous, musculocutaneous, fasciocutaneous

**Accident Compensation Corporation (ACC)**
- Provides economic support for injured people and aims to reduce the physical impact of injury
- Is a no fault, compulsory scheme
- NZers gave up right to sue in return for specified support
- Resources available:
  - Costs of retrieval from accident scene
  - Costs of diagnosis and physical rehabilitation
  - Compensation for loss of earnings (80% of pre-injury income after 1 week off work)
  - Vocational support: retraining if necessary to return to work
  - Range of personal support to help make living with an injury more comfortable
Haematology and Immunology

Haematology Examination

General Inspection
- General: appears well/ill, in no distress, breathing RA, pale/flushed, clues at the bedside

Hands
- Signs of anaemia: pallor, koilonychia
- Others: splinter haemorrhage etc
- Pulse

Arms
- Inspection: bruising, jaundice
- BP

Axilla
- Lymph nodes (rolling motion, press firmly, four corners of the axilla)

Face
- Eyes: blue sclerae, jaundice, conjunctival pallor
- Nose: bleeding
- Mouth: ulcers, angular cheilitis (Fe def anaemia), atrophic glossitis (smooth; severe Fe def/B12 def)
- Neck: lymph nodes (from behind)

Chest
- Examine for signs of infection if suspected/neutropenic

Abdomen
- Inspect: bruising, jaundice
- Liver
- Spleen: use “vice grip” = left hand curled around side of patient’s rib cage with anterior forearm squeezing in on anterior rib cage during inspiration (to prevent chest wall expanding during inspiration and thus facilitating spleen’s downward descent)
- Feel for masses (ie intra-abdominal LNs)
- Inguinal lymph nodes

Haematology Overview

<table>
<thead>
<tr>
<th>Cell/System</th>
<th>Disorders</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anaemia</td>
<td>Microcytic: Iron Deficiency, Thalassemia, Chronic Disease (can be normocytic)</td>
</tr>
<tr>
<td></td>
<td>Macrocytic: Alcoholism, ↓B12/folate (Megaloblastic), Newborn. Also liver disease, marrow disorders, drugs, malaria, idiopathic</td>
</tr>
<tr>
<td>Pancytopenia</td>
<td>Aplastic Anaemia</td>
</tr>
<tr>
<td></td>
<td>Also alcohol, bone marrow infiltration, megaloblastic anaemia, hypersplenism</td>
</tr>
<tr>
<td>Other Red cell</td>
<td>Spherocytosis, Hb abnormalities</td>
</tr>
<tr>
<td>Hypocoagulation</td>
<td>Haemophilia A &amp; B, Von Willebrands, DIC</td>
</tr>
<tr>
<td></td>
<td>Also liver disease, ↓Vit K, Renal failure, iatrogenic (aspirin, heparin)</td>
</tr>
<tr>
<td>Hypercoagulation</td>
<td>Primary: Factor V Leiden, ↓Antithrombin 3, ↓Protein C &amp; S</td>
</tr>
<tr>
<td></td>
<td>Secondary: Malignancy, pregnancy, stasis, age, myeloproliferative diseases</td>
</tr>
<tr>
<td>Thrombocytosis</td>
<td>Reactive: Infection, inflammation, bleeding, malignancy, splenectomy</td>
</tr>
<tr>
<td>Thrombocytopenia</td>
<td>Primary: Essential thrombocytopenia</td>
</tr>
<tr>
<td>Platelet function disorders</td>
<td>Immune thrombocytopenia, Heparin induced, artefact, dilutional, marrow production failure, peripheral consumption (drugs, DIC, etc)</td>
</tr>
<tr>
<td>Myeloproliferative</td>
<td>Mainly acquired: aspirin, uraemia, paraproteinaemias</td>
</tr>
<tr>
<td>Myelodysplasia</td>
<td>Chronic Myelocytic Leukaemia, Acute Myelocytic Leukaemia, Polycythaemia Rubra Vera, Essential thrombocythaemia, Myelofibrosis</td>
</tr>
<tr>
<td>Lymphoproliferative</td>
<td>Chronic lymphocytic leukaemia, acute lymphocytic leukaemia, multiple myeloma</td>
</tr>
</tbody>
</table>
- BM: 1 trillion cells, produces daily 200 billion RBCs (T1/2 **120d**), 10 billion WCC (T1/2 **hrs**), 400 billion platelets (T1/2 **10d**)
- Also see Blood Tests, page 16
- Also see Blood Products, page 877 (including transfusion)

**Pathology**
- Haematopoietic cytokines:
  - Stimulate differentiation of SC into specific mature cells
    - EPO
    - TPO – thrombopoietin
    - G-CSF
    - GM-CSF
    - SCF (stem cell factor)
    - IL3
- **Massive splenomegaly:**
  - Lymphoma
  - Myeloproliferative disorders
  - Malaria

**Signs and Symptoms**

<table>
<thead>
<tr>
<th>Haematology S + S</th>
<th>Cause</th>
<th>Symptom</th>
<th>Sign</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anaemia</td>
<td>Tiredness</td>
<td>Pallor</td>
<td>PRBC + EPO</td>
<td></td>
</tr>
<tr>
<td>Thrombocytopenia</td>
<td>Nose bleeds</td>
<td>Bruising, petechiae , bleeding</td>
<td>Platelets + thrombopoietin</td>
<td></td>
</tr>
<tr>
<td>Neutropenia</td>
<td>Mouth ulcers</td>
<td>Mouth ulcers, fever, infections</td>
<td>G-CSF (GM-CSF for monocytes) + ABs</td>
<td></td>
</tr>
</tbody>
</table>

**Acute Phase Proteins**

<table>
<thead>
<tr>
<th>Acute phase</th>
<th>Clinical events</th>
<th>Reactants ↑</th>
<th>Reactants ↓</th>
<th>Tests</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tissue injury</td>
<td>Fibrinogen</td>
<td>Albumin</td>
<td>ESR:</td>
<td></td>
</tr>
<tr>
<td>Inflammatory states eg autoimmune conditions</td>
<td>Factor VIII</td>
<td>Prealbumin</td>
<td>Gravity sedimentation</td>
<td></td>
</tr>
<tr>
<td>Malignancy</td>
<td>vWF</td>
<td>Transferrin (Fe carrying protein – decreased transferrin enhances ability to fight infection)</td>
<td>Storm: bacteria or tissue damage leading to macrophage activation – IL6 release – liver production of CRP</td>
<td></td>
</tr>
<tr>
<td>Infection</td>
<td>Complement</td>
<td>CRP</td>
<td>Haptoglobin</td>
<td>Levels rise within 6hrs of stim</td>
</tr>
<tr>
<td></td>
<td>CRP</td>
<td>Haptoglobin</td>
<td></td>
<td>Binds to phosphocholine (on surface of dying cells + bact)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Activates complement</td>
</tr>
</tbody>
</table>
Microscopy of Abnormal Cells

Red Blood Cells

- Oval macrocytes + hypersegmented neutrophils ⇒ megaloblastic anaemia (B12/folate)
- Target cell RBCs (haemoglobin in the middle – non-specific): most commonly seen in patients with liver disease (eg too much alcohol)
- Small pale RBCs, target cells + pencil poikilocytes (elongated RBCs) ⇒ iron deficiency
- Rouleaux: red cells stack like coins, fall fast if high ESR. Stick together due to ↑immunoglobulin or fibrinogen). Causes: inflammation, myeloma
- No lighter patch in middle ⇒ spherocytes
- Spherocytosis: if only some RBCs, then spleen has taken out a bit of membrane ⇒ autoimmune haemolytic anaemia. If all RBCs are spherocytes then hereditary spherocytosis. If spherocytes + reticulocytes then spherocytic anaemia
- Cygnet shape (ring form with blue circumference) inside cell ⇒ malaria parasite
- Tear drop red cells ⇒ myelofibrosis or polycythaemia
- ↑ Polychromasia ⇒ some red cells a bit blue due to stain – still contain some RNA
- Reticulocytes: normal is 0.2 – 2%. Look big and blue. Will be high in anaemia (except ?anaemia of chronic disease)
- Howell-Jolly Bodies: Little purple/black dots (like a ball bearing) in RBC = remnant DNA that hasn’t been removed by the spleen. Seen in splenectomy patients
- Fragmented cell: red cell sliced in circulation (DIC, artificial heart valve)

**White Blood Cells**
- Normal lymphocyte: small, little/no cytoplasm
- Neutrophils have multilobed nuclei, ≥ 6 lobes is hypersegmented (megaloblastic anaemia: B12, folate. Also drugs, chemotherapy, renal failure)
- Plasma cell: eccentric nuclei, clock-face chromatin. If eccentric nucleus (clear area next to nucleus) in bone marrow ⇒ multiple myeloma
- Neutrophil maturation:

<table>
<thead>
<tr>
<th>Stage</th>
<th>Granules</th>
<th>Chromatin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blast</td>
<td>No</td>
<td>Large</td>
</tr>
<tr>
<td>Myelocytes</td>
<td>Large</td>
<td>Large</td>
</tr>
<tr>
<td>Metamyelocytes</td>
<td>Large</td>
<td>Large</td>
</tr>
<tr>
<td>Band</td>
<td>Horse-shoe shaped</td>
<td>Smaller</td>
</tr>
<tr>
<td>Neutrophil</td>
<td>Segmented neutrophil, dense</td>
<td>Smaller</td>
</tr>
</tbody>
</table>

- Normal differentiation: Neutrophils 80%, Lymphocytes 20%
- **Toxic changes** (i.e. ‘switched on’): ↑ granules, vacuoles, Dohle bodies (blue clumps in cytoplasm), nuclear clumping. Strong indicator of bacterial infection
- If high lymphocytes and lots of ‘atypical lymphocytes/mononuclear cells’ then viral infection: EBV, HIV, CMV
- Eosinophil: normal is reddish cytoplasmic granules. ↑ In toxoplasmosis, allergy (asthma, drugs, etc), gut parasites
- Bone marrow biopsy: normal is about ½ fat, ½ cellular

**Leukaemias**
- **Smudge cells** ⇒ CLL. Middle aged, significant lymphadenopathy
- ↑ WCC, enlarged lymph nodes, splenomegaly, lots of white cells, majority are mature neutrophils ⇒ CGL (= CML)
- Acute leukaemias: cells immature
- Auer rods in a blast ⇒ **acute myeloblastic leukaemia**

**Anaemias**
- = Hb level below normal for age and sex
- Normal Hb levels:
  - Male 130 – 180 g/l
  - Female 120 – 155 g/l
- Mild is > 100
- Moderate is 80 – 100
- Severe is < 80
- Symptoms:
  - SOB/CP on exertion
  - Tiredness/fatigue
  - Headache
  - Palpitations
  - Lack of concentration
  - ↓O2 delivery ⇒ bring on underlying angina or pain/claudication in legs
- Signs:
  - Blue sclerae
  - Pale conjunctiva, palmar creases, nail beds: but insensitive test
  - Tachycardia
  - ↑RR
<table>
<thead>
<tr>
<th>MCV</th>
<th>Causes</th>
<th>Specific symptoms</th>
<th>Specific signs</th>
<th>Blood film</th>
<th>Other lab tests</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 78fl</td>
<td>Fe deficiency</td>
<td>1. Anaemia</td>
<td>1. Glossitis</td>
<td>1. Microcytic</td>
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<td></td>
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<td>2. Food cravings (pica)</td>
<td>2. Hypochromic</td>
<td>2. Target cells</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>4. ↑ Infection</td>
<td>4. Koilonychia</td>
<td>poikilocytes</td>
<td>Increased</td>
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<tr>
<td></td>
<td></td>
<td>5. Impaired growth</td>
<td>5. Blue</td>
<td>platelets</td>
<td>platelets(5)</td>
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<td></td>
<td></td>
<td></td>
<td>Ferritin</td>
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<td>Serum Fe</td>
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<td>↑ TIBC</td>
<td>(liver produces</td>
<td>more transferrin</td>
<td>to</td>
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<td>use little Fe</td>
<td>available)</td>
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<td>↓ % saturation (of</td>
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<td>transferrin)</td>
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<tr>
<td></td>
<td>Causes:</td>
<td>1. Diet</td>
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<td></td>
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<td>2. Malabsorption</td>
<td></td>
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<td>3. Increased demand</td>
<td></td>
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<td></td>
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<td>4. Increased loss (eg GIT/ menstrual bleeding)</td>
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</tbody>
</table>

**Thalassemia**

Mostly auto recessive; defective α or β chain production

**Chronic d**

Hb < 80g/L or MCV < ~70fL doesn’t really fit the chronic d picture

### Microcytic Anaemia

- **MCV** = MCV < 80 fl (normal is 80 – 100)

**Causes**

- Iron deficiency anaemia
- Thalassemia
- Chronic disease (see Anaemia of Chronic Disease, page 465)
- Other Causes: Sideroblastic anaemia, lead poisoning

### Iron Deficiency Anaemia

- See also Iron Deficiency, page 985 for Iron Deficiency Anaemia in Children
- Commonest cause of anaemia
- 15-25% of healthy pre-menopausal women have low ferritin
- 2 mls of blood = 1 mg of iron. Easy to get anaemia from a small trickle bleed
- Average menstrual loss = 60 ml
- Iron absorption:
  - Western diet contains 10 – 30 mg iron (mostly red meat)
  - 10 % normally absorbed (in duodenum) therefore need 1-3mg/d
  - 20 – 30% absorbed in Fe deficiency and pregnancy
  - Absorbed in duodenum, proximal jejunum
- Iron transport and storage:
  - Fe carried by Transferrin (MW 80,000): made in liver, T½ 8 – 10 days
  - Ferritin: Water-soluble protein – MW 465,000. Stores iron in cells. Is proportional to body iron stores
  - Also stored in haemosiderin
- TIBC (total iron binding capacity):
  - Tests the blood’s capacity to bind transferrin w Fe
Measures the max amount of Fe that it can carry, which *indirectly measures transferrin*

- **Clinical features of iron deficiency:**
  - Anaemia
  - Glossitis: swollen tongue, sore, lost papilla
  - Koilonychia: spoon shaped nails
  - Dietary cravings *(pica)*: eating strange stuff – kids eat dirt, pregnant women eat ice
  - Blue sclera: highly specific
  - Pharyngeal webs → dysphagia

- **Diagnosis:**
  - *Microcytic hypochromic anaemia*: use MCV (not MCH – but highly correlated)
  - On film may see: target cells (haemoglobin in middle – non-specific), pencil poikilocytes, ↑ platelets
  - Lab findings: ↓ serum ferritin (sufficient on it’s own) – will also see ↓ serum Fe (but Serum Iron useless) and ↑ transferrin/ICP (Iron combining protein). Mean cell volume in normal range may disguise a combination of small Fe deficient cells plus lots of large reticulocytes

**Macrocytic Anaemia**

- = MCV > 100 fl

**Causes**

- Newborn
- ↓ B12/folate
- Alcoholism (most common cause but usually mild)
- Liver disease
- Primary marrow disorders
- Hypothyroidism
- Drugs
- Malaria
- Idiopathic/others

**Megaloblastic Anaemia**

- Is NOT the same as macrocytic anaemia

**Causes:**

- ↓ Folate (comes from leafy green veges)
- ↓ B12 (comes from meat)
- Drugs that interfere with B12 metabolism
- Leads to defective DNA synthesis and delayed maturation of the nucleus cf. cytoplasm
- Big red cells and hypersegmented neutrophils (≥ 6 segments)

**Clinical features:**

- Anaemia
- Infection (↓ neutrophil function)
- Jaundice (↑ bilirubin)
- Purpura
- Malabsorption (↓ gut lining)

**Lab features:**

- MCV > 100 fl
- Oval macrocytes
- ↓ WBC and ↓ platelets

**Investigations:** *blood film* and *B12/folate* levels. Serum folate is useless – stored in RBCs

**Vitamin B12**

- Deficiency can lead to:
  - Peripheral neuropathy
  - Subacute combined degeneration of the cord (dorsal column)
  - Psychosis
- Found in animal foods
- Binds to IF + absorbed in TI
- Stores last for 2-3 years
• Could be diet: if ↓↓animal products, gastric surgery
• Could be malabsorption (IBD/CD) or pernicious anaemia: check IF antibodies against gastric parietal cells
• Investigations: FBC, serum B12, IF Abs

Folate

• From foliage – leafy veg
• Stores = 5-10mg; 2-4/12; intake 50-100ug/d; prox SI absorption
• In coeliac can see poor absorption of Fe in duodenum therefore microcytic, but also poor absorption of folate therefore macrocytic – can balance each other and see a normocytic anaemia; normocytic can also be seen in conjunction with chronic disease (tend towards microcytic)
• Causes of deficiency: ↓intake, ETOH, pregnancy, drugs, malabsorption
• ↓intake: chronic illness; ETOH; cooking (intolerant to heat)
• Drugs: anticonvulsants, ABs, OCP, methotrexate

Pancytopenia

Stem Cells

• Blood stem cells detected by CD34+
• Live in bone marrow: biochemical environment there necessary for survival – from fat, fibroblasts, endothelial & macrophage cells

Pancytopenia

• Confirmed ↓RBC, ↓WBC and ↓platelets
• Causes:
  ➢ ↓Production:
    o Bone marrow infiltration (eg cancer)/failure
    o Megaloblastic anaemia (Vit B12, folate deficiency → PCP as they are needed for DNA replication)
    o Miscellaneous (e.g. alcohol)
    o Aplastic anaemia
    o Myelodysplasia
  ➢ ↑Margination: Hypersplenism
• Bone marrow bx indicated

Aplastic Anaemia

• Rare
• Defect in supportive environment: dysfunctional stem cells, autoimmune damage
• Diagnostic criteria:
  ➢ Neutrophils <0.5x10⁹/L
  ➢ Platelets <20x10⁹/L
  ➢ Reticulocytes <10x10⁹/L
  ➢ Hypocellular marrow <20% normal
• Causes:
  ➢ Intrinsic defect in stem cells – reduced numbers + dysfunctional – idiopathic ~ 50%
  ➢ Extrinsic damage to stem cells – immune or toxins (eg chloramphenicol + anticonvulsants)
• Treatment:
  ➢ Supportive care eg transfusion
  ➢ Immunosuppressive treatment (cyclosporin, prednisolone)
  ➢ Stem cell transplantation

Hereditary Spherocytosis

• Autosomal dominant
• Normal RBC has surplus membrane → floppy
• Spherocytes have less membrane → tight
• Could take out spleen if symptomatic (destruction occurs here)

Haemolytic Anaemia

• Can be seen in leukaemias (especially CLL) as these are malignant disease of the immune system → immune system a bit confused
• Evidence of RBC destruction (eg jaundice) + evidence of increased RBC production (eg reticulocytosis)
Tests for destruction:
- 1. FBC (anaemia)
- 2. ↑bilirubin
- 3. ↓haptoglobin (haptoglobin is a plasma protein that binds Hb and free Fe → used up in haemolysis therefore ↓)
- 4. ↑LDH

Tests for ↑ production:
- 1. Reticulocyte count
- 2. BM aspirate (hyperplasia)

Causes:
- Intravascular (eg broken down within BVs): eg crappy heart valves
  - Urinary haemosiderin positive test indicates intravascular HA [haemosiderin is an Fe-storage complex; is released in haemolysis]
- Extravascular (broken down in spleen – which really still is IV!):
  - Familial or autoimmune (AI will be Coomb’s/DAT test positive)
  - Round + dense RBCs seen (ie no pale central area)
  - Non-spherocytic (congenital: G6PD, PK deficiency, SCA)
- Non-immune acquired HA: infectious (malaria, dengue), mechanical (heart valves), microangiopathic (DIC, HUS, ca, vasculitis)

Haemoglobin Abnormalities

<table>
<thead>
<tr>
<th>Syndrome</th>
<th>Abnormality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Haemolysis</td>
<td>Crystalline Hbs (S, C, D, E) → unstable Hb</td>
</tr>
<tr>
<td>Thalassemia</td>
<td>α or β, due to ↓globin chain synthesis:</td>
</tr>
<tr>
<td></td>
<td>Thalassemia major – transfusion dependent, homozygous β0, Mediterranean,</td>
</tr>
<tr>
<td></td>
<td>splenomegaly, frontal bossing of forehead, bad teeth</td>
</tr>
<tr>
<td></td>
<td>Thalassaemia intermedia</td>
</tr>
<tr>
<td></td>
<td>Thalassaemia minor - β0 trait - ↓MCV. α0 trait - ↓MCV, Hb H bodies, target</td>
</tr>
<tr>
<td></td>
<td>cells</td>
</tr>
<tr>
<td>Familial Polycythaemia</td>
<td>AH1, measure P 50 for O2</td>
</tr>
<tr>
<td>Methaemoglobinocaemia</td>
<td>Failure of reduction</td>
</tr>
</tbody>
</table>

Data Interpretation

- Pregnancy →↑Fe requirements and ↑fibrinogen (→↑ESR)
- If mild microcytic anaemia and normal ferritin it’s not iron: check either thalassaemia or anaemia of chronic disease
- Ferritin is an acute phase protein. It will be raised in chronic disease. So if there is chronic inflammation and a low-normal ferritin, the underlying ferritin is likely to be below normal
- Mildly ↑MCV could be because of ↑reticulocytes → check haemolysis

Haemolysis tests:
- ↑Production: reticulocytes, blood film
- ↑Breakdown: Hb and Haptoglobins (binding protein for haem – used up in haemolysis → would fall)
- Coombs test: is there antibody on the RBC
- If Fe in urine (Urine haemosiderin) then intravascular haemolysis (not spleen – which is extravascular). E.g. aortic value replacement →haemodynamic/shear stress from turbulent flow

Defects in Haemoglobin Synthesis

- Four major problems can manifest during this delicate process:
  - Qualitative defects of globin chain synthesis result in hemoglobinopathies such as sickle cell disease
  - Quantitative defects of globin chain synthesis result in hemoglobinopathies such as thalassemia
  - Defects in synthesis of the heme portion result in porphyrias
  - Defects involving incorporation of iron into the heme molecule result in sideroblastic anemias

Porphyria

- Disorder of haem synthesis → toxic metabolites
- Many types, all due to genetic deficiency. Homozygous not viable. Heterozygotes can produce enough haem, but when the system is challenged →↑ toxic metabolites
- Symptoms:
Uncommon, but differential in intermittent abdominal pain
- Can be intermittent or constant
- Can acutely cause psychotic symptoms
- Sun sensitivity (accumulation of metabolites in skin)
- Neuro-visceral symptoms (pain but no organ pathology)
- Rare types can cause sideroblastic anaemia

Investigations:
- Urine test for metabolites (porphyrins)
- Then specific test for which porphyrina
- ALA synthase controls the rate limiting step at the beginning of the pathway:
  - Induced by: BZDs, alcohol, oestrogen and progesterone (→ onset at puberty or on starting the OCP), sulphonamides, tetracycline, theophylline
  - Inhibited by haem, glucose

Blood Transfusion
- Pretransfusion compatibility testing prior to transfusion involves the following;
  - Group and Screen (also called Group and Hold and Group and Save):
    - Involves:
      - Determining the patient’s ABO and Rh D group.
      - Performing an antibody screen, and identifying any atypical antibodies which may be present.
      - Checking the results against any historical data that might be available for the patient
  - Crossmatching:
    - Involves a serological test to ensure compatibility between a unit of blood and the patient
- Can group and hold first and then crossmatch later when actually needed

Haematology of Systemic Disease
- Also see Hypercoagulable States, page 470
- E.g. Cancer →↑ESR, ↑Neutrophils, ↑coagulation, anaemia

Erythrocyte Sedimentation Rate (ESR)
- Normal varies by age and sex (increases with age)
- Rouleaux: red cells stack like coins, fall fast
- Due to:
  - Acute phase reactants: esp. fibrinogen
  - Gamma globulins
  - Anaemia
- Clinical uses: collaborative test, monitor course of disease
- ↑ESR in pregnancy, infection, tumours, connective tissue disorders, multiple myeloma

Leucocytosis

<table>
<thead>
<tr>
<th>Leucocytosis – neutrophilia</th>
<th>Toxic changes</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Causes</strong></td>
<td><strong>Left shift</strong></td>
</tr>
<tr>
<td>1. Physiological eg exercise</td>
<td>Shift to immaturity (early release from BM)</td>
</tr>
<tr>
<td>2. Infection</td>
<td>Blasts → promyelocytes → myelocytes → metamyelocytes → bands → neuts</td>
</tr>
<tr>
<td>3. Inflammation</td>
<td>See increased bands + metamyelocytes in peripheral blood</td>
</tr>
<tr>
<td>4. Cancer</td>
<td>Indicates bacterial infection</td>
</tr>
<tr>
<td>5. Acute bleeding</td>
<td></td>
</tr>
<tr>
<td>6. Acute haemolysis</td>
<td></td>
</tr>
<tr>
<td>7. Blood disorders</td>
<td></td>
</tr>
<tr>
<td>8. Steroids</td>
<td></td>
</tr>
</tbody>
</table>

- Normal range varies with age (esp. kids)
- Neutrophils:
  - In adults: 2 – 7.5 x 10^9
Lobed nucleus, lots of granules in cytoplasm
Made in marrow, transported via blood
Neutrophilia in many states, not just infection, and including stress. Physiological neutrophilia e.g. exercise → ↓margination

**Lymphocytosis**
- In acute infections: pertussis, infectious lymphocytosis, EBV, viral hepatitis
- In chronic infections: brucellosis, Tb, Syphilis
- In haemopoietic disorders

### Anaemia of Chronic Disease

<table>
<thead>
<tr>
<th>Anaemia of disease</th>
<th>Features</th>
<th>Causes</th>
<th>Pathogenesis</th>
<th>Fe lab studies</th>
<th>Things to exclude</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anaemia of chronic disease</td>
<td>• Common&lt;br&gt;• Normocytic to microcytic&lt;br&gt;• Mild-moderate severity (Hb 80-100g/L)</td>
<td>1. Malignancy&lt;br&gt;2. Infection eg TB, SBE, osteomyelitis, HIV&lt;br&gt;3. Chronic inflammation eg RA, SLE</td>
<td>1. Decreased RBC survival&lt;br&gt;2. Low EPO secretion&lt;br&gt;3. Low BM response to EPO&lt;br&gt;4. Iron-limited erythropoiesis&lt;br&gt;5. Immune system activation due to release of macrophage cytokines (TNF, IL-1, IL-6) eg bacteria → kuppfer cells (liver macrophages) → IL6 → hepatocyte production of hepcidin&lt;br&gt;• Hepcidin: &lt;br&gt;○ ↓ Fe GIT absorption&lt;br&gt;○ ↓ Fe release from macrophages + therefore decreases serum Fe levels&lt;br&gt;Low Fe inhibits proliferation of bacteria</td>
<td>Serum ferritin = normal&lt;br&gt;Serum iron = low (as Fe not being released from macrophages and ↓ Fe GIT absorption therefore decreased serum Fe)&lt;br&gt;Transferrin (TIBC) = low (as Fe not being released from macrophages and ↓ Fe GIT absorption)&lt;br&gt;% Sats = low (as Fe not being released from macrophages and ↓ Fe GIT absorption)</td>
<td>1. Fe deficiency&lt;br&gt;2. Renal failure&lt;br&gt;3. BM infiltration&lt;br&gt;4. Haemolysis</td>
</tr>
</tbody>
</table>

### Causes:
- Chronic infections e.g. TB, SBE, AIDS
- Chronic inflammatory states e.g. RA, ulcerative colitis
- Recognise it so patient is not over-investigated

### Features:
- Mild to moderate anaemia: 70 – 100 g/L (usually 90 – 100)
- Normocytic to mild microcytosis

### Differential diagnosis:
- Fe deficiency
- Renal impairment
- Marrow infiltration
- Haemolysis

### Iron Studies (highly examinable):

<table>
<thead>
<tr>
<th>Fe deficiency</th>
<th>Chronic Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum Iron</td>
<td>↓</td>
</tr>
<tr>
<td>TIBC</td>
<td>↑</td>
</tr>
<tr>
<td>%Saturation</td>
<td>↓</td>
</tr>
<tr>
<td>Marrow Iron</td>
<td>↓</td>
</tr>
<tr>
<td>Serum Ferritin</td>
<td>↓</td>
</tr>
</tbody>
</table>

### Blood results in chronic disease:
- ↑Ferritin
- ↓Protein (especially albumin)
- ↑Globulins

---

**Haematology and Immunology**  465
• Pathogenesis
  ➢ ↑RBC destruction → ↓survival
  ➢ ↓Iron metabolism
  ➢ Impaired erythropoietin response
  ➢ Cytokines (TNF-α, IL-1, interferons)

• Treatment
  ➢ Won’t respond to iron, etc
  ➢ Treat underlying cause
  ➢ Erythropoietin (but very expensive)

**Haemostasis**

• Necessary factors for haemostasis (stopping bleeding):
  ➢ Vasoconstriction
  ➢ Platelets
  ➢ Coagulation (= fibrin production)

---

**Haemostasis**

- Conversion of soluble fibrinogen into insoluble fibrin
- Stopping bleeding; requires:
  1. Vasoconstriction
  2. Platelets
  3. Coagulation

**APTT** – measures intrinsic pathway (and therefore is the pathway that is upset in haemophilia, i.e., don’t measure INR for haemophilia!)

**Prothrombin time/INR** – measures extrinsic pathway

  ➢ Measured by adding an anticoagulant (citrate – chelates Ca so it won’t clot) to plasma → sent to lab → TF and Ca added and time to clot measured

**Extrinsic pathway:**
  ➢ Extrinsic to the blood vessel
  ➢ Tissue thromboplastin (TF) triggers this pathway

**Intrinsic pathway** – from within the BV eg endothelial damage

---

**Coagulation**

- Key reaction: fibrinogen → fibrin

---

**Contact activation (intrinsic) pathway**

- Damaged surface

**Tissue factor** (extrinsic) pathway

- Trauma

**Common pathway**

- Fibrinogen (I) → Fibrin (I)

**Intrinsic pathway:**

  ➢ XII → II via IX and VIII
  ➢ Triggered by damage to endothelium
  ➢ Measured by Partial thromboplastin Time (PTT) = Activated PTT (APTT). Also called PTTK
Reduced by heparin treatment

Extrinsic Pathway:
- VII → II
- Triggered by chemicals extrinsic to blood stream (TF)
- Measured by **Prothrombin time or INR** (International Normalised Ratio): ratio of Patient PT to Control. Normal < 1.3. INR mainly measures top end of the extrinsic pathway – so INR may not be affected by heparin even though it affects the common pathway. APTT more sensitive to ↓common pathway
- ↑ by warfarin treatment

Disorders of Coagulation

<table>
<thead>
<tr>
<th>Disorders of coagulation</th>
<th>Acquired</th>
<th>Features</th>
</tr>
</thead>
<tbody>
<tr>
<td>Liver disease</td>
<td>Liver plays a central role in coag → synthesis of:</td>
<td>Coag factors</td>
</tr>
<tr>
<td>DIC</td>
<td>Will see:</td>
<td>Ischaemia (due to fibrin deposition in microcirculation)</td>
</tr>
<tr>
<td>Vitamin K deficiency/ Warfarin</td>
<td>Causes by:</td>
<td>1. Release of thromboplastin (TF):</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2. Activation of XII (endothelium):</td>
</tr>
<tr>
<td></td>
<td></td>
<td>3. Activation of II, X:</td>
</tr>
<tr>
<td>Uraemia/RF</td>
<td>Complex mechanisms</td>
<td>platelet function</td>
</tr>
<tr>
<td>Massive blood transfusion</td>
<td>Dilutional effects – coag factors and platelets</td>
<td>Can see DIC</td>
</tr>
<tr>
<td>Factor inhibitors</td>
<td>Autoantibodies</td>
<td>Usually against FVIII – haemophilia</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Congenital</th>
<th>Features</th>
<th>Lab</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Von Willebrand’s disease</td>
<td>Autosomal dominant Bleeding symptoms:</td>
<td>INR</td>
<td>Normal</td>
</tr>
<tr>
<td></td>
<td>Mucocutaneous – platelet bleeding (eg menorrhagia, nose bleeds, bruising etc)</td>
<td>APTT</td>
<td>Normal</td>
</tr>
<tr>
<td></td>
<td>Made by megakaryocytes + endothelium (also stored here)</td>
<td>Fibrinogen</td>
<td>Normal</td>
</tr>
<tr>
<td>vWF:</td>
<td>Needed for <strong>platelet adhesion</strong></td>
<td>Platelets</td>
<td>Normal</td>
</tr>
<tr>
<td></td>
<td>PI function (PFA100)</td>
<td>Factor VIII</td>
<td>↓</td>
</tr>
<tr>
<td></td>
<td></td>
<td>vWF antigen</td>
<td>↓</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Ristocetin assay</td>
<td>↓</td>
</tr>
</tbody>
</table>

1. Treat underlying cause
2. Platelet transfusion
3. FFP
4. Cryoprecipitate (fibrinogen)
**Haemophilia A (VIII)**

**Bleeding symptoms:**
- Deeper than pl bleeding – joints and soft tissues (muscles), cuts, dental, ICH, surgery

**Severity (VIII):**
- Mild >5%; moderate 1-5%; severe <1%

**Sequelae:**
- Synovitis
- Arthropathy (pain, deformity)
- Fatal bleeds
- Infection

<table>
<thead>
<tr>
<th>INR</th>
<th>Normal</th>
</tr>
</thead>
<tbody>
<tr>
<td>APTT</td>
<td>Prolonged</td>
</tr>
<tr>
<td>Fibrinogen</td>
<td>Normal</td>
</tr>
<tr>
<td>Platelets</td>
<td>Normal</td>
</tr>
<tr>
<td>PI function</td>
<td>Normal</td>
</tr>
<tr>
<td>Factor assay (VIII/IX)</td>
<td>↓</td>
</tr>
</tbody>
</table>

**Haemophilia B (IX)**

<table>
<thead>
<tr>
<th>INR</th>
<th>Normal</th>
</tr>
</thead>
<tbody>
<tr>
<td>APTT</td>
<td>Prolonged</td>
</tr>
<tr>
<td>Fibrinogen</td>
<td>Normal</td>
</tr>
<tr>
<td>Platelets</td>
<td>Normal</td>
</tr>
<tr>
<td>PI function</td>
<td>Normal</td>
</tr>
<tr>
<td>Factor assay (VIII/IX)</td>
<td>↓</td>
</tr>
</tbody>
</table>

**Other factor deficiencies**
- Eg FXI

---

**Hypo-Coagulation Diseases**

- **Congenital:**
  - Haemophilia A
  - Haemophilia B
  - Von Willebrand’s Disease
  - Rare factor deficiencies (eg FXI)

- **Acquired:**
  - Liver diseases →↓coagulation factors
  - DIC
  - Vitamin K deficiency: needed for factors 2, 7, 9 and 10
  - Uraemia: renal failure →↓platelets and coagulation function
  - Massive blood transfusions → dilution of clotting factors
  - Factor inhibitors (autoimmune)

**Von Willebrand’s Disease**

- ↑Bleeding time, ↑APTT due to ↓VIII (VW factor is a binding protein for VIII)
- Symptoms: Superficial bleeds (purpura) – mouth, nose, gut, bruising, heavy menstrual bleeding
- Autosomal dominant
- Comes in mild, moderate and severe forms

**Haemophilia**

- Ratio of 4:1 of A (↓factor VIII) to B (Christmas disease) (↓factor IX)
- Prevalence of 13 – 18 per 100,000 males in Wellington (high)
- Symptoms: bleeding into soft tissues, joints, dental extraction. Deep bleeds → major orthopaedic implications. NOT superficial or gut

- **Classification:**
  - Severe: < 1% - joint bleeds, e.g. once a fortnight or month
  - Moderate: 1 – 4 % - some joint bleeds, main problem with trauma, not spontaneous bleeds
  - Mild: 5 – 25% - main problem is with trauma

- **Lab diagnosis:**
  - INR: normal
  - APTT: prolonged
  - Fibrinogen: normal
  - Platelets: normal
  - Bleeding time: normal
  - Factor assay reduced (do VIII first then IX)

- **Symptoms of a joint bleed:**
  - Strange sensation: not really a pain – treat at this point, they will know despite no signs yet
  - Swelling

- **Treatment:**

---

**NB.** For those w FVIII inhibitors, can give FVII (which bypasses intrinsic system + activates coag cascade – expensive!)
- Factor replacement: either prophylactic or on demand
- Choice of factor product: blood derived or recombinant
- Management of inhibitors

**Disseminated Intravascular Coagulation (DIC)**

- Laying down of fibrin inappropriately within vasculature

**Causes:**
1. *Activation of extrinsic system by thromboplastin* (triggers VII). Thromboplastin is a lipoprotein substance from cell membranes. Due to: **massive injury** (↑↑release of thromboplastin), **septicaemia** (damage to endothelium), **tumour cells breaking down**
2. *Activation of intrinsic system:* **anoxia, acidosis, sepsis, burns**
3. *Direct activation of II & X:* **amniotic fluid embolism,** pancreatitis (→ release of toxic enzymes into blood)

**Lab screen:**
- ↑PT (Prothrombin time)
- ↑APTT
- ↓Fibrinogen
- ↓Platelets
- ↑Fibrin degradation products

**Treatment:**
- Correct cause
- Platelet transfusion
- Fresh Frozen plasma
- Cryoprecipitate (good source of fibrinogen)

**Case Examples**

<table>
<thead>
<tr>
<th>Case</th>
<th>Tests</th>
<th>Diagnosis</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>30 y/o male with oozing post tooth extraction, leading to significant bleeding + hypotension</td>
<td>Hb → 70 Platelets → normal Coags → normal Factor assay → FVIII 18%</td>
<td>Mild haemophilia A If bleeding but all tests normal → do factor assays (sensitivity of coag screen is not 100%)</td>
<td>DDAVP (only for haem A/VWD) FVII Tranexamic acid (blocks fibrinolysis)</td>
</tr>
<tr>
<td>50 y/o male post prostate surgery → bleeding unabated → transfusion</td>
<td>→ As above (Hb 92, normal pl + coags) → factor assays: FIX 23%</td>
<td>Mild haemophilia B Lupus anticoagulant → IgG auto-Ab (inhibitor) to a factor (eg VIII or IX)</td>
<td>FIX Tranexamic acid</td>
</tr>
<tr>
<td>42 y/o female with SLE on steroids → UGI bleed requiring transfusion</td>
<td>→ As above (Hb 89, pl normal, APTT 84s, INR normal) → Do 1:1 (normal + pt plasma) → if APTT normalises = haemophilia, if not = inhibitor (auto-Ab)</td>
<td>Lupus anticoagulant to a factor (eg VIII or IX)</td>
<td>FVIIa to switch on extrinsic system Immunosuppression (cyclophosphamide, prednisone)</td>
</tr>
<tr>
<td>28 y/o female, menorrhagia, 2 uneventful pregnancies</td>
<td>→ Hb 82 and microcytic, pl 520 - increased due to Fe def → Coags normal but FVIII 22% → vWF 24%, vWF (ag) 30% → PFA100 = 180 (&lt;150)</td>
<td>Von Willebrand disease</td>
<td>Tranexamic acid (take when period starts) DDAVP FVIII</td>
</tr>
<tr>
<td>19 y/o in labour, needs C-section. PHx bleeding with sutures but no previous surgery or teeth extraction</td>
<td>→ Hb 110, pl normal → APTT 72s → 1:1 mix, showed correction → FXI 5%</td>
<td>FXI deficiency (3rd most common factor deficiency)</td>
<td>FFP Recombinant FXI</td>
</tr>
<tr>
<td>23 y/o female, heavy periods, excess bruising</td>
<td>All tests normal</td>
<td>Simple easy bruisability</td>
<td>No treatment and no risk during surgery</td>
</tr>
<tr>
<td>65 y/o female with black stools. In AF</td>
<td></td>
<td>Warfarin toxicity</td>
<td>Stop warfarin IV vit K FFP Prothrombinex: contains FII, VII, XI, X</td>
</tr>
</tbody>
</table>
54 y/o female with mets, oozing following venepuncture + bruising → INR + APTT normal → ↓ fibrinogen + platelets Chronic DIC (with compensated coag system) Platelets + FFP (but will be consumed) Low dose heparin (can switch off DIC)

Hypercoagulable States

<table>
<thead>
<tr>
<th>Hypercoagulability</th>
<th>Changes to blood (hypercoagulability)</th>
<th>Changes to flow (stasis)</th>
<th>Changes to vessel wall (endothelial damage)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. High fibrinogen (eg tissue damage)</td>
<td>1. Immobilisation</td>
<td>1. Direct trauma</td>
<td></td>
</tr>
<tr>
<td>2. High factor VIIIc (eg inflammatory states)</td>
<td>2. Surgery</td>
<td>2. Hypoxia</td>
<td></td>
</tr>
<tr>
<td>3. High vWF (eg malignancy)</td>
<td>3. Anaesthesia</td>
<td>3. Endotoxin</td>
<td></td>
</tr>
<tr>
<td>4. Decreased fibrinolysis</td>
<td>4. Local pressure</td>
<td>4. Burns</td>
<td></td>
</tr>
<tr>
<td>→ ie these happen as part of an acute phase response</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- **Primary Causes:**
  - 1. Factor V Leiden:
    - Most common primary cause
    - Point mutation on factor V prevents breakdown → ↑ levels of Va → hypercoagulable
    - Heterozygous have lifetime risk of 30 – 40% of thrombotic event, Homozygous then 50 – 60%
    - In thrombotic patients, 20 – 40% have factor V Leiden, mainly in Caucasians
  - 2. Prothrombin gene mutation
  - 3. Antithrombin 3 deficiency:
    - Reduced breakdown of thrombin
    - Heparin co-factor, α2 globulin
    - Autosomal dominant, 1:2-5000 in Caucasian
    - Found in 2 – 3 % of DVTs
    - Can also cause mesenteric or brachial thrombosis. These are rare so → ↑ index of suspicion
  - 4. Protein C or S deficiency
  - 5. Homocysteinaemia
  - NB. Inherited prothrombotic conditions have NORMAL coagulation screens (INR, fibrinogen etc)

- **Secondary Causes:**
  - Malignancy
  - Pregnancy and for 6 weeks afterwards: hypercoagulable, stasis, venous compression. If concurrent primary disorder then prophylaxis with sc heparin (warfarin contra-indicated)
  - Stasis: immobilisation, surgery, local pressure
  - Age
  - Myeloproliferative disorders
  - Antiphospholipid Syndrome (acquired, aggressive)
  - Infection
  - Trauma

**Data Interpretation**

- Serum = plasma that’s clotted: i.e. no clotting factors
- Citrated plasma: *citrate chelates calcium* – so can’t act as a co-factor in clotting. Add Ca to reverse
- Aspirin for Coronary Heart Disease mimics VWD. (i.e. ↑ bleeding time, everything else normal). T½ of platelets = 3 – 4 days. Need to stop aspirin 10 days before surgery. ½ an aspirin enough to increase bleeding time. 45 minutes to have an effect after oral dose
- Heparin → ↑ APTT
- Fractionated Heparin → ↑ TT (APTT may be normal)
- Warfarin → ↑ INR
- Try to determine deficiency (e.g. FVIII or Warfarin → ↓ 2,7,9,10) or Inhibition (e.g. aspirin, heparin)

### Platelets and Platelet Disorders

**Platelets**

- No nucleus: contain granular cytoplasm
Normal count: $150 - 450 \times 10^9$/L
Normal size: 2 – 3 um
From megakaryocyte in bone marrow (from pluripotential stem cell under the influence of thrombopoietin)
$10^{11}$ produced per day; 1 megakaryocyte makes 1-3000 platelets
Lifespan 10 days – destroyed mainly in spleen. 20 – 30% of total body platelets are pooled in spleen
Regulation of production by either receptor mediated catabolism or induced TPO production
Function – form haemostatic plug:
- Adherence: via Ia, indirectly via lb & vWF
- Shape change
- Release reaction
- Aggregation: glycoprotein IIb/IIIa via fibrinogen

Bleeding time: time taken for a standardised skin incision to stop bleeding at venous pressure of 40 mmHg. Normal is 1 – 7 minutes. Depends on platelet numbers, platelet function, vascular factors (e.g. connective tissue disorders)

Disorders:
- Thrombocytosis: too many
- Thrombocytopenia: too few
- Functional disorders

Thrombocytosis
- $\geq 450 \times 10^9$/l

Primary:
- Less common
- Myeloproliferative disorders: essential thrombocythemia + others
- JAK2 (a tyrosine kinase) implicated – results in a proliferative + survival advantage of haematopoietic progenitor cells; used in dx + rx with specific blocking drugs

Management:
- Observation
- Aspirin
- Hydroxyurea (blocks folate metabolism)
- Anagralide
- Low risk = <40 yrs: treat with aspirin
- Intermediate risk = 40-60 yrs: treat with aspirin + ?hydroxyurea
- High risk = > 60 yrs/platelets > 1500/previous thrombosis or risk factors for: treat with aspirin + hydroxyurea

Reactive/Secondary:
- Far more common
- Doesn’t necessarily confer increased risk of thrombosis therefore generally doesn’t require treatment
- Mostly transient (except post splenectomy)
- Transient:
  - Acute haemorrhage/trauma (surgery)
  - Acute infection or inflammation
  - Response to infection
- Sustained:
  - Fe deficiency
  - Haemolytic anaemia
  - Post splenectomy
  - Cancer
  - Chronic inflammation or infection (connective tissue disease, IBD, Tb etc)

Increased risk of venous and arterial thromboses

Venous Thromboembolism

<table>
<thead>
<tr>
<th>Venous thromboembolism (VTE)</th>
</tr>
</thead>
<tbody>
<tr>
<td>VTE = fibrin + RBC clot as cf. arterial clots (platelet based)</td>
</tr>
<tr>
<td>Virchow's triad (changes to flow, changes to blood, changes to vessel)</td>
</tr>
<tr>
<td>Air travel VTE is a real phenomenon and multifactorial (changes to flow [sitting], changes to blood [stasis, dehydration], changes to vessel [hypoxia])</td>
</tr>
</tbody>
</table>
Pathogenesis is multifactorial and complex (see below)

- At risk pts should be IDed
- Prophylaxis /preventive options (eg air travel) can be initiated (eg LMWH for those with significant RF; stockings etc) but should be tailored to individual risk
- Only at risk pts (RF described below) have been shown to develop VTE on long haul flights, therefore if no RF = sweet!
- Trouseau’s syndrome: malignancy presenting as DVT/PE → therefore need to take a GOOD ROS!!

Changes to flow
- Standing reduces blood velocity by 50%
- Sitting reduces BV by 66%

Changes to blood
The hypercoagulable state:
1. Primary:
   - Inherited thrombophilias, mostly autosomal dominant
   - 2-4 X risk of DVT
   - Factor V Leiden
   - Prothrombin gene mutation
   - Pro C + S def, ATIII deficiency etc
2. Secondary:
   - More common than primary
   - Malignancy
   - Pregnancy
   - Surgery/trauma
   - Stasis
   - Myeloproliferative disorders
   - Antiphospholipid disorder
   - Dehydration (leads to haemoconcentration, seen in flying)

Changes to vessel
1. Direct trauma (eg during THJR – need to dislocate hip, direct damage)
2. Hypoxia:
   - Leads to decreased endothelial cell fibrinolysis
   - At high altitude (flying), O₂ sats ↓
   - Factor VIIa ↑

Risk factors
1. Hx of VTE (OR 16)
2. Malignancy
3. Surgery
4. Obesity
5. Venous insufficiency
6. CHF
7. Hx of >3 pregnancies

Management for air travel
1. Hydration
2. Activity
3. LMWH – works; ASA does not
4. Stockings
5. Defer flying for those whom risk deemed too great

Warfarin Anticoagulation & VTE Treatment
- VTE treated with:
  - 1. LMWH, 1.5mg/kg od SC (until INR in therapeutic range for 5 days)
  - 2. Warfarin
- Warfarin:
  - Acts on FII, VII, IX, X → these have T1/2 ranging from 6hr → 60hr therefore need to use LMWH when initiating warfarin therapy
  - Key principles:
    o 1. Use only when clinically appropriate
    o 2. Use appropriate target INRs
    o 3. Monitor
    o 4. Don’t use longer than is necessary
- Warfarin risks:
  - Major bleeding: clinically overt with Hb ↓ >20g/L
  - Minor bleeding
  - RF for bleeding: old, female, HTN, arterial disease, alcoholism, liver disease, labile INRs, drugs (eg NSAIDs)
- Warfarin in pregnancy:
  - Teratogenic in all 3 trimesters: can see skeletal, nose & eye abnormalities, mental retardation
  - Switch to LMWH
  - 6/52 post pregnancy is a high risk period for VTE/PE
- New anticoagulants:
Dabigatran: oral direct thrombin inhibitor:
- Peak concentration in 1.5hr, predictable pharmokinetics (→ no monitoring needed)
- 80% renally excreted therefore need to check renal function (if CrCl <30 → bleed)
- No reversal drug

Rivaroxaban: oral factor Xa inhibitor

Thrombocytopenia
- ≤150 x 10^9/L
- Symptoms: mucocutaneous bleeding:
  - In skin & mucosal surfaces
  - Petechiae (<1 mm), purpura (1-5 mm), ecchymoses (>5mm), menorrhagia
  - Bad bleeding (e.g. in stools) usually only becomes significant below platelet count of 10
- Pathophysiological mechanisms causing low platelets:
  1. ↓ Production:
     - Marrow production failure (low platelet count & reduced/absent megakaryocytes):
       - Component of pancytopenia
       - Isolated thrombocytopenia: alcohol, chlorthiazides, rare megakaryocytic hypoplasias
  2. ↑ Destruction:
     - Peripheral consumption (more common – low platelet count, but normal/increased megakaryocytes):
       - Immune:
         - ITP
       - Secondary to drugs (e.g. quinine, heparin), autoimmune disease (SLE), CLL, virus (e.g. HIV)
     - Non-immune:
       - DIC
       - Haemolytic uraemic syndrome
       - Dilutional thrombocytopenia: bleeding, splenomegaly, massive blood transfusion
  3. Sequestration
  4. Artefact (e.g. clot in sample – usually due to using EDTA tube not citrate)

Immune-Mediated Thrombocytopenia (ITP)
- Autoantibodies or immune complexes bind to platelets and cause premature destruction in spleen – lifespan reduced to 1 – 2 days
- BM aspirate shows megakaryocyte hyperplasia
- ITP does not cause splenomegaly
- Acute ITP:
  - Immune complex mediated (although Ab sometimes hard to detect in many assays)
  - Majority of childhood ITPs
  - Often follows viral infection
  - 90% resolve spontaneously within one month
  - Rarely requires treatment
- Chronic ITP:
  - Autoantibody to platelet glycoprotein
  - Majority of adult ITP
  - Usually no preceding illness
  - 10% resolve spontaneously: need to treat, although if platelets at around 30 – 50 may not need treatment – may dip during a viral illness. Need to review pre-surgery
- Treatment (if any needed):
  1. Steroids (1 mg/kg prednisone per day). 30% don’t respond
  2. IV immunoglobulins (swamp Fc receptors in spleen so platelets not destroyed – temporary). 30% don’t respond. Not plasmapheresis as auto-Abs are IgG
  3. Platelet transfusion: will get eaten up but still useful when severely TCP
  4. Splenectomy (see Splenectomy, page 495 for risks)
  5. Rituximab (monoclonal anti CD20)
  6. Review if ever pregnant: antiplatelet IgG may cross the placenta
- Consider testing for H.pylori, HIV, HCV as can be related to ITP

Heparin-Induced Thrombocytopenia
- 1% of patients develop a drug-dependent antiplatelet antibody
- 3% of these immune complexes bind platelet Fc receptors & induce aggregation
- Presentation is thrombocytopenia followed by thrombosis
- Can be fatal
- Management: *stop heparin*

**Thrombotic Thrombocytopenic Purpura**
- Thrombotic thrombocytopenic purpura is an uncommon syndrome characterised by:
  - fever
  - microangiopathic haemolytic anaemia
  - thrombocytopenia
  - neurologic and renal abnormalities
- The cause is unknown but it often follows infection or in women, oral contraception or pregnancy. Young adults from 20 to 50 years are predominantly affected, with a slight female preponderance.
- See fragmented RBCs (schistocytes – see right), anaemia, TCP, negative Coomb’s
- Treat with plasmapheresis + maybe steroids/other cytotoxics, maybe splenectomy

**Platelet Function Disorders**
- Congenital: rare
- **Acquired**: common:
  - *Aspirin* (inhibits cyclo-oxygenase → ↓TXA2 → ↓aggregation)
  - *Uraemia* (i.e. renal failure)
  - Cardiac bypass
  - Myelodysplasia
  - Paraproteinaemias

**Myeloproliferative Disorders (MPD)**

<table>
<thead>
<tr>
<th>Myeloproliferative disorders</th>
<th>Chronic granulocytic (myeloid) leukaemia</th>
<th>Chronic idiopathic myelofibrosis</th>
<th>Essential thrombocythemia</th>
<th>Polycythemia vera (PV)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical features</td>
<td>1. Fatigue</td>
<td>1. Older age</td>
<td>1. Sustained (2° thrombo is transient) pl &gt;450</td>
<td>1. Symptoms: HA, weakness, pruritis (only seen in 1° PCT), dizziness, sweating</td>
</tr>
<tr>
<td></td>
<td></td>
<td>5. Wt loss</td>
<td>5. Bleeding (due to defective pl)</td>
<td></td>
</tr>
<tr>
<td>Lab findings</td>
<td>1. ↑WCC</td>
<td>1. Anaemia</td>
<td>1. ↑platelets (&gt;600)</td>
<td>1. ↑Hb</td>
</tr>
<tr>
<td></td>
<td>2. ↑platelets</td>
<td>2. ↑WCC initially then ↓</td>
<td>2. Abnormal pl morphology</td>
<td>2. ↑platelets</td>
</tr>
<tr>
<td></td>
<td>3. Mild anaemia</td>
<td>3. ↑pl initially then ↓</td>
<td>3. PI function studies abnormal</td>
<td>3. ↑neut</td>
</tr>
<tr>
<td></td>
<td>4. Hyperplastic BM w granulocytic proliferation</td>
<td>4. Tear drop RBCs</td>
<td>4. BM – many megakaryocytes</td>
<td>4. ↑RBC mass</td>
</tr>
<tr>
<td></td>
<td>5. ↑uric acid (high cell turnover)</td>
<td>5. BM shows collagen fibrosis</td>
<td>5. Hb normal or mild Fe def anaemia (due to bleeding)</td>
<td>5. ↓EPO (neg FB)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>6. Leukoerythroblastosis due to extramedullary haematopoiesis</td>
<td>6. WCC normal/mild ↑</td>
<td>6. BM hypercellular</td>
</tr>
</tbody>
</table>

**Blood film**
Most cells are mature, therefore = chronic + will see leukoerythroblastosis

| Cytogenetcs | Philadelphia chromosome = 9:22 translocation | JAK2 chromosome mutation positive in 50% | JAK2 association | Gain of function mutation of JAK2
| --- | --- | --- | --- | --- |
| Known as: BCR-ABL fusion oncogene | Philadelphia mutation negative | JAK2 association | Encodes tyrosine kinase which ↑ EPO | 97% of pts w PV have this mutation therefore if neg 2nd PCT much more likely
| Encodes active tyrosine kinase → doesn’t allow apoptosis to take place | Is an acquired translocation in pluripotent SC in BM |

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Karyotype</th>
<th>BM bx</th>
<th>JAK2</th>
<th>HCT</th>
<th>Dilutional RBC studies</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Imatinib mesylate – blocks tyrosine kinase</th>
<th>Observation (rarely)</th>
<th>Observation</th>
<th>JAK2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hydroxyurea (chemo)</td>
<td>Chemo (not overly useful)</td>
<td>Aspirin</td>
<td>HCT</td>
<td></td>
</tr>
<tr>
<td>IFN</td>
<td>Splenectomy (massive spleen causes stomach compression + anorexia)</td>
<td>Chemo – hydroxyurea (blocks folate metabolism) + anagralide</td>
<td></td>
<td></td>
</tr>
<tr>
<td>BM transplant if refractory or mutation so that resistant to imatinib</td>
<td>SC transplant</td>
<td>IFN in pregnancy instead of the above</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Natural hx</th>
<th>Chronic phase → accelerated phase → blast transformation → death</th>
<th>Mean survival 3-4yrs 10% develop acute leukaemia</th>
<th>Can progress to acute leukaemia</th>
</tr>
</thead>
</table>

**Introduction**

- Primary clonal proliferation (ie low-grade cancers) of myeloid (ie marrow) cells
- Essentially 4 conditions
  - Polycythaemia rubra vera
  - Essential thrombocythaemia
  - Myelofibrosis
  - Chronic granulocytic leukaemia (=chronic myeloid leukaemia)
- Arises at pluripotent stem cell level
- Leads to mixed picture as diseases merge
- Variation is based on degree and type of proliferation:

**Leukoerythroblastosis**

- In peripheral blood, see:
  - Nucleated RBC +

**Haematology and Immunology**
- Immature neutrophils
- Implies **disturbance of the blood/marrow barrier** (normally nucleated RBCs + immature cells cannot cross this barrier) or blood cell making outside the BM
- Seen in:
  - Myelofibrosis
  - Immaturity → normal in newborns
  - Toxic → septicaemia
  - Hypoxic → eg resp failure
  - Maximal function → eg haemolysis (many RBC produced causing them to be pushed out early into peripheral bl)
  - Mechanical damage → mets from prostate, breast, lung
  - Extramedullary haematopoiesis:
    - Blood cell making outside the BM – in the **spleen or liver**
    - These organs do not have a B/M barrier + thus immature cells can be pushed out into peripheral blood
    - Common in **myelofibrosis**

**Polycythaemia Vera**

**Overview**

- = Erythrocytosis

<table>
<thead>
<tr>
<th></th>
<th>Males</th>
<th>Females</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hb</td>
<td>&gt; 175</td>
<td>&gt; 155</td>
</tr>
<tr>
<td>Red Cells</td>
<td>&gt; 6.0 *10^11/l</td>
<td>&gt; 5.5</td>
</tr>
<tr>
<td>PCV (packed cell volume)</td>
<td>&gt;58%</td>
<td>&gt; 48%</td>
</tr>
</tbody>
</table>

- Investigation: total red cell volume by 51Cr. Also erythropoietin assay
- Classification (given Raised PCV):
  - ↑RCM (Red cell mass) = absolute
  - Normal RCM = apparent
- Types:
  - **Relative (spurious)** – can be seen in some normal males
  - Primary
    - Less common
    - **Polycythemia vera** = polycythemia rubra vera
  - Secondary
    - More common
    - Seen in:
      - Hypoxic conditions (**cyanotic heart d, lung d, obesity hypoventilation**, high altitude, abnormal Hb)
      - Normoxic conditions (**renal disorders, liver d**, tumours – eg RCC – secreting more EPO)

**Primary Proliferative Polycythaemia**

- **Clonal (ie malignant) stem cell disorder**: dysregulation → **EPO independent, autonomous RBC proliferation**
- **JAK2** mutation (chromosome 9p; acquired mutation → cancer) → abnormal tyrosine kinase → EPO independent RBC colonies
- Generally, see ↑Hct, ↑Hb, ↑platelets, ↑neutrophils
- Predominant age 55 – 60 years, 2-10/100,000/yr
- Median untreated survival = 18/12
- Can → acute leukaemia (10%) or myelofibrosis (30%)
- Diagnosis:
  - RCM > 36 ml/kg (i.e. absolute polycythaemia)
  - No secondary cause: e.g. O2 saturation > 92% (e.g. COPD)
- Symptoms:
  - HA, weakness, dizziness, visual disturbance etc
  - Pruritis
- Signs:
  - Splenomegaly
  - Hepatomegaly
  - Plethora
- Complications:
Vascular complications: TIA, cerebral thrombosis, microvascular (e.g. toes, heart ie MI), headaches, DVTs (but usually arterial problems due to ↑viscosity e.g. stroke)

Haemorrhage

- Lab findings:
  - JAK2 mutation positive
  - Hb & PCV ↑
  - ↑WBC in 2/3 (↑WCC and platelets as marrow is hyperactive)
  - ↑Serum B12
  - Low erythropoietin
  - Platelets 400 – 800 in 50%
  - Hypercellular marrow: little fat, ↑in megakaryocytes
  - ‘Hot’ looking bone scan: lots of activity
  - Tear drop red cells (if myelofibrosis or can be seen in any cause of massive splenomegaly → squeezing through tight spaces)

- Treatment:
  - Venesection: take off a unit of blood every 3 or 4 months (if old do it slow), aim for Hct/PCV 0.45
  - Aspirin
  - BM suppression with hydroxyurea
  - α-interferon

- Course:
  - 30% progress to myelofibrosis
  - AML transition
  - ?Splenectomy if massive
  - Median survival if treated = 8 – 15 years

Secondary Causes of Polycythaemia

- More common than PV/PRV
- EPO driven: ↑Hb/Hct, not neuts/platelets as cf PRV
- Seen in:
  - Hypoxic conditions (cyanotic heart disease, lung disease, obesity hypoventilation/OSA, high altitude, abnormal Hb)
  - Normoxic conditions (renal disorders eg renal artery stenosis, liver d, tumours – eg RCC – secreting more EPO)

Apparent Polycythaemia

- ↑Packed cell volume (=PCV = Haematocrit) but normal RCM (ie RBCs a greater proportion of a unit of blood, but normal volume of RBCs in the body):
  - Diuretics
  - Alcohol
  - Hypertension
  - Early primary polycythaemia
- High altitude: initially ↓plasma volume then absolute polycythaemia (and O2 curve shifts left)

Essential Thrombocythaemia

Thrombocytosis

- Thrombocytosis = a platelet count greater than normal (150-400 x 10⁹/L)
- Seen most commonly in trauma/surgery + Fe def
- Causes:
  - Primary
    - Less common
    - Seen in essential thrombocythemia + other myeloproliferative disorders
  - Secondary
    - Far more common
    - Doesn’t necessarily confer increased risk of thrombosis
    - Mostly transient (except post splenectomy)
    - Seen in haemorrhage, trauma (surgery), malignancy, inflammation, post splenectomy

Essential Thrombocythaemia

- Clinical presentation:
Any age, usually older
Often asymptomatic
Bleeding (defective platelets) OR thrombosis (e.g. digital arteries → necrotic toes)
Splenomegaly (2 – 3 cm) in 70%

- Lab results:
  - ↑ Platelets, often > 1000 x 10^9/L
  - Morphology abnormal, normal plus large platelets
  - Platelet function studies abnormal
  - HB normal or mild anaemia
  - WBC normal or mild ↑
  - Bone marrow: many megakaryocytes

- Treatment:
  - Chemotherapy: hydroxyurea
  - Radioactive phosphorous: P32 – stored in bone so zaps marrow
  - Interferon
  - Prognosis: if platelet s down then good, if not then bad

Myelofibrosis

- Clinical presentation:
  - Old age
  - Preceding polycythaemia in 30%
  - Anaemia
  - Slow onset, weight loss, night sweats – insidious
  - Massive hepatosplenomegaly. Large spleen → pressure on splenic blood supply → infarction → pain

- Lab results:
  - Hb low
  - WBC high early, low late
  - Platelets high early, low late
  - Leucoerythroblastosis
  - Tear drop red cells
  - LAP (leucocyte alkaline phosphatase)
  - Philadelphia chromosome –ive
  - Fibrosis of bone marrow

- Treatment is mainly supportive: observation, low dose chemotherapy, splenectomy (symptomatic effect only)

- Prognosis:
  - Mean survival 3 – 4 years, may become transfusion dependent
  - 10% develop AML

Chronic Granulocytic Leukaemia

= Chronic Myeloid Leukaemia

- Clinical presentation:
  - Any age
  - Tired, off colour, sweats
  - Slow onset
  - Large spleen (also liver)

- Lab results:
  - ↑↑ WBCs (30 – 300). In chronic there will be mature and immature blasts (myelocytes, promyelocytes and lymphocytes as well. Just a general left shift). In acute there will be immature only
  - Bone marrow has ↑↑ neutrophils
  - Philadelphia chromosome +ive
  - Low leucocyte alkaline phosphatase (LAP)
  - ↑ Uric acids

- Course:
  - Chronic phase: median duration 3 – 4 years
  - Transformation (either to myeloblastic/AML or lymphoblastic) aggressive/acute – end stage

- Treatment:
  - Hydroxyurea: controls proliferation but won’t stop transformation
  - Interferon: suppresses marrow, in 15% Philadelphia goes away (→ no transformation)
  - Autotransplant: use patient’s stem cells
- Allotransplant (use sibling): 60% cure, 20% death, 20% remission
- MUD (Matched unrelated donor)
- ‘Mini-transplant’: new stem cell technique with no high dose chemo/radiotherapy. Transplant mops up weakened immune system without you needing to kill it
- New drug: Glevac (STI571) – targets Philadelphia Chromosome:
  - Acquired genetic defect – 9:22 translocation → BCR-ABL oncogene (functional oncogene) → P210-BCR-ABL oncoprotein
  - Leads to cell proliferation, ↓ adhesions and ↓ apoptosis without regulation

**Myelodysplasia/Myelodysplastic Syndromes**

*Description*
- = Clonal (ie malignant) abnormality of haematopoietic stem cells
- *Heterogeneous* group of disorders
- Abnormal, ineffective haematopoiesis
- Involves 1 or more lineages (RBC, platelets, neuts)
- Irreversible quantitative (↓) and qualitative defects (ie cells don’t work properly)
- Manifests as marrow failure with risk of life-threatening infection + bleeding
- Tendency to evolve to acute leukaemia (30%)

*Clinical*
- Usually elderly
- Features of bone marrow failure: tired (anaemia), bleeding (thrombocytopenia), infection (neutropenia)
- Mild splenomegaly in 10 – 20%
- Incidental finding on blood film in 20%
- 4 – 12 per 100,000 per year (definitional problems)
- Tests:
  - Pancytopenia with ↓ reticulocytes
  - Marrow cellularity ↑ due to ineffective haematopoiesis
  - Ring sideroblasts (abnormal blasts with excessive accumulation of iron in the mitochondria) may be seen

*Variants*
- Refractory anaemia +/- further features (eg excess blasts) [Refractory anemia with excess blasts (RAEB) is a myelodysplastic syndrome characterized by ↑ myeloblasts in the bone marrow and/or blood or the presence of Auer rods]
- Chronic myelomonocytic leukaemia

*Differential Diagnosis*
- Megaloblastic anaemia
- Acute leukaemia
- Heavy metal toxicity (lead, arsenic)
- Chronic infection
- Immune deficiency (esp HIV)
- Anticancer chemo/radio therapy
- Myeloproliferative disorders
- Bone marrow hypoplasia

*Progression*
- 70 – 80% die of marrow failure
- 20 – 30% die of progression to leukaemia
- Median survival varies with subtype from 6 – 50 months
- Prognosis depends on the classification of myelodysplastic disorder

*Treatment*
- Response rates to treatment poor
- Supportive care (eg transfusion – RBC/platelets, EPO/G-CSF, antibiotic treatment of infection/prophylaxis)
- Maybe cytotoxic chemotherapy (eg lenalidamide)
- Bone marrow transplant can offer cure in some patients
- Anaemia management (biggest morbidity comes from anaemia): erythropoietin (although this is not available for MDS in NZ), transfusion

**Secondary Myelodysplasia**

- ↑Incidence
- Complication of former treatment: alkylating agents (including cyclophosphamide, widely used as an immunosuppressive, eg in Rheumatoid arthritis) and topoisomerase II agents
- Risk related to cumulative dose and duration of exposure
- Peak 5 years post treatment; 3-4% of those on alkylating agents will develop this
- Poor prognosis

**Leukaemia**

- Leuk: Greek for white
- = Cancer dominantly of white cells arising in MARROW. Lymphoma primarily arises in lymph nodes
- Acute or chronic
  - Based on time course i.e. hx of s & s (acute = days to weeks; chronic = longer!)
  - Based on cell maturation i.e. differentiated or undifferentiated (acute = undifferentiated blast cells; chronic = mature, well diff cells)
- Granulocytic (myeloid) or lymphocytic
- Summary:

<table>
<thead>
<tr>
<th></th>
<th>Acute</th>
<th>Chronic</th>
</tr>
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<tbody>
<tr>
<td>Myeloblastic/Granulocytic</td>
<td>Neutrophil precursors, Sudan black for peroxidase, Auer rod in cell</td>
<td>Mature neutrophils and blasts, Philadelphia +ive, Converts to AML after 3 years, Proliferation of mature B cells, Doesn’t convert to ALL, Longer mean survival</td>
</tr>
<tr>
<td>Lymphoblastic</td>
<td>T/B Cell precursors, PAS stain for glycogen</td>
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</tbody>
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**Chronic Leukaemia**

- NB. Do see some blasts in chronic leukaemia but many more in acute leukaemia
- Chronic Myeloblastic Leukaemia (CML): Converts to AML/AGL. See Chronic Granulocytic Leukaemia, page 478
- Chronic Lymphoblastic Leukaemia (CLL): see Chronic Lymphocytic Leukaemia, page 488. Doesn’t convert to ALL

**Acute Leukaemia**

<table>
<thead>
<tr>
<th>Acute leukaemia</th>
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<tbody>
<tr>
<td><strong>Definition</strong></td>
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<td><strong>Features</strong></td>
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<td><strong>Lab tests</strong></td>
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</table>
1. Supportive care:
   - **Venous access** – hickman’s (tunnelling ↓ chance of infection; can take blood; high flows ↓ local toxicity effects)
   - **RBC** if anaemia
   - **Platelets** if TCP
   - **ABs/G-CSF** if infection/neutropenia

2. Cytotoxic treatment:
   - **Remission induction** (DEFINITION: blasts <5% of BM + pt well + normal peripheral blood count)
   - **Consolidation** (to prevent relapse)
   - **CNS prophylaxis** (cancer cells can cross BBB but most drugs do not)
   - **SC transplant** (SCT; for those at high risk of relapse)

**Tumour cell mass**
- $S + S = 10^{12}$ tumour cells
- Remission = $10^6$ tumour cells
- Post remission = $10^3$ tumour cells (pt’s own immune system takes over and holds these at bay)

**Rx results**
1. AML CR (cure rate – i.e. remission) = 80%; survival rate = 40%
2. ALL CR = 90%; survival rate = 70% (children – this is the most common childhood leukaemia)

**BM aspirates**
- Subtype of AML
- Acute promyelocytic leukaemia
- Can see DIC
- PMI/RAR-α fusion gene
- Can treat with all trans retinoic acid (ATRA) – is a vit A analogue → signals to cells to diff into neuts and therefore allows cells to go through normal apoptosis pathways

- Rapid onset, 100% mortality within 3 months if untreated
- Very undifferentiated (anaplastic) cells: blasts, no normal cells in blood
- Types:
  - Acute Myeloblastic Leukaemia (AML). Chance of cure with chemo alone = 20 – 40%. With transplant = 60%. Has Auer rod in blast
  - Acute Lymphoblastic Leukaemia (ALL) – most common childhood cancer
- Signs and symptoms are due to:
  - Tissue infiltration (hepatosplenomegaly, lymphadenopathy, bone pain)
  - Marrow failure (infection, bleeding, anaemia)
- Presentation:
  - Tired due to **anaemia**, breathless
  - **Bleeding** due to ↓platelets, nose bleeds
  - **Bacterial infection**
  - Hepatosplenomegaly, ↑lymph nodes, bone pain (push on sternum)
- Investigations:
  - FBC: ↓Hb, ↓platelets, white count: high, normal or low (sometimes leukaemia cells stay in marrow)
  - Bone marrow: > 20% of nucleated cells in the marrow are leukaemic blasts
- Classification:
  - Cytochemistry:
    - Staining. PAS - +ive stain for glycogen ⬇ lymphoblastic
    - Sudan black +ive for peroxidase ⚫ myeloblastic
  - Immunology: flow cytometry
  - Cytogenetics

**Treatment**
- Supportive Care:
- Antibiotics, platelet + RBC transfusion. NB. Can see alloimmunisation (immune reaction to different HLA) in platelet transfusion \(\rightarrow\) will see no \(\uparrow\) in platelets post transfusion (need to HLA type these patients and match platelets to them)
- Venous catheter: Hickman catheter

**Cytotoxic** Treatment:
- Complex multi-drug protocols
- **Remission induction**: 1-4 weeks depending on protocol. FBC normal and < 5% blasts in marrow (that’s normal). AML – achieved in 70 – 80%. ALL – achieved in 70 – 80% of adults, 95% of kids
- **Consolidation**: more drugs to mop up residual blasts, including CNS prophylaxis (some drugs don’t penetrate CNS well)
- But 60 – 80% chance of relapse over next 2 – 4 years
- Dose-limiting level is marrow toxicity i.e. aplasia
- Conditioning regime – wipe out BM and IS (eg with cyclophosphamide + total body radiation) – then SCT

**Bone Marrow Transplantation**
- = Haematopoietic stem cell transplantation
- Stem cells + BM:
  - Normal BM has \(\sim 1\%\) SC; SC differentiate into other cell lines and also self-renew
  - SC will die outside of the BM but can transit in and out briefly; they are taken back up by specific receptors in the BM (therefore SCT can be given IV)
  - **Cyclophosphamide** forces SC out of BM so they can be harvested in the peripheral blood
- SC sources:
  - Sources of stem cells: self (autologous), twin (syngenic), HLA matched sibling (allogenic), HLA partial matched sibling, matched unrelated donor (MUD)
  - From cord blood, BM, peripheral blood
- SC dose:
  - Specific amounts required of either nucleated SC or CD34 positive cells (both are the same thing but measure different parts of the SC)
- HLA:
  - Differentiate self from non-self; HLA-A, HLA-B, HLA-C, many different alleles
  - Can see:
    - Graft rejection
    - GVHD – skin, gut reactions etc; happens in SCT, as entire BM + immune system is wiped out prior to transplant
    - Graft vs tumour effect – SCT acting on any residual tumour cells
- Process: patient and donor preparation, conditioning (chemo & high dose radiation to eradicate tumour cells + also immunosuppress to allow transplant of foreign cells), stem cell infusion, neutropenic phase, post neutropenic phase
- Peritransplant mortality = 20%

**Fever in a Neutropenic Patient**
- Contributes to 50 percent of deaths associated with leukemia, lymphomas, and solid tumors
- **Bacterial** infections are common in patients with febrile neutropenia, but **fungal** sources are increasingly prevalent
- Symptoms include a temperature of 38.5° C or more and an absolute neutrophil count (ANC) less than 0.5 \(\times\) 10\(^9\) per L
- Neutrophil survival time = \(\sim\) 6 hrs
- Eg in patients undergoing chemotherapy
- Neutropenia:
  - Neutrophils \(< 0.5 \times 10^9/L\) (less than 0.2 \(\Rightarrow\) serious concern)
  - Neutrophils falling
  - Prolonged neutropenia (> 7 days)
- Indicators of serious infection:
  - Signs and symptoms of infection will be reduced – can’t mount an inflammatory response
  - Temperature:
    - \(> 38.5\) C
    - \(> 38\) for 4 hours
    - Patient feels unwell but no temperature

---

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The elderly and those on steroids don’t mount a fever very well, so may need to have a lower threshold.

Types of Infection
- Drives focused history:
  - Respiratory: SOB, cough
  - Skin infection
  - Mouth and teeth
  - Perianal (pain on moving bowels and wiping)
  - Pain around central line
  - Less often: bowel & UTI

Focused Exam
- Signs of septic shock: pulse, BP and peripheral circulation
- Chest: percussion and auscultation (but ↓ neuts so signs are often hard to come by)
- Mouth: a good look around – mucositis: ulcers etc
- Skin infections, especially lines
- Quick abdominal – for tenderness only
- Exam perianal area – test for sensitivity to touch. Don’t do PR (risk of minor trauma → bacteraemia)

Investigations
- FBC
- Blood culture (debate about whether to take it from the central line or not)
- CXR
- Swabs from anything that looks infected, including central line and do appropriate cultures
- CRP: ↑ in bacteraemia
- Urinalysis
- Normally don’t find anything. Over half infections are low grade line infections – but can kill very fast in neutropenic pts
- If in doubt, treat empirically NOW. If infected will deteriorate quickly
- Empiric antibiotics:
  - Tazocin monotherapy (= piperacillin + tazobactam)
  - +/- Vancomycin (for staph line sepsis)

Causes of Infection

<table>
<thead>
<tr>
<th></th>
<th>Frequency</th>
<th>Risk</th>
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<tbody>
<tr>
<td><strong>First Fever</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Staph</td>
<td>+++</td>
<td>+</td>
</tr>
<tr>
<td>Staph haemolytic strep</td>
<td>+</td>
<td>++</td>
</tr>
<tr>
<td>G -ive bacilli</td>
<td>+</td>
<td>+++</td>
</tr>
<tr>
<td><strong>Subsequent infections</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Staph</td>
<td>+++</td>
<td>+</td>
</tr>
<tr>
<td>Fungi</td>
<td>++</td>
<td>+++</td>
</tr>
<tr>
<td>Resistant G-ive</td>
<td>+</td>
<td>+++</td>
</tr>
</tbody>
</table>

Subsequent fevers: longer in hospital (↑ hospital acquired infection), longer on antibiotics, etc

- If fever persists (72hrs):
  - Repeat the above exam and investigations – but unlikely to add anything new
  - Choices:
    - Change antibiotics
    - Consider antifungal: Amphotericin (maybe caspofungin or voriconazole)

Obscure Fevers
- Central venous line infection
- Occult sinusitis (check with CT)
- Hepatosplenic candidiasis (check with CT → abscess → biopsy)
- Pulmonary/disseminated aspergillus (check with CT; doesn’t respond to amphotericin)
- Viral
- Drugs (drug fever)
**Prevention**
- Avoid hospitalisation
- Strict hand washing
- Avoid invasive procedures
- Care of IV devices
- Consider prophylactic antimicrobials

**Prophylaxis**
- Anti-bacterial: selective gut decontamination (origin of many infections is bowel flora): *Ciprofloxacin* (fluorinated quinolone). Controversial
- Anti-fungal: imidazoles: *fluconazole, itraconazole* (OK for prophylaxis, not so good as amphotericin for established infection)
- Anti-viral: *acyclovir* (for HSV), *ganciclovir* (for CMV)
- Anti-pneumocystis: *co-trimoxazole* (but beware marrow suppression) or aerolised pentamidine
- Other possible treatments:
  - Granulocyte-CSF: try to ↑ marrow production of neutrophils
  - Maybe γ-globulin infusions
  - Transfuse granulocytes: emerging area
- **Isolation** is expensive, cumbersome and is *only really indicated if aspergillus* is a problem in a particular region; is not in Wellington, therefore isolation not used here

**Lymph Node Pathology**
- See neck lumps in paediatric section

**Anatomy**
- Accumulations of lymphocytes in discrete organised masses
- Have a structure (capsule, cortex, paracortex, medulla, subcapsular sinuses – portal of entry for lymph)
- Tcells on outside in parafollicular area, Bcells on inside in germinal centre
- Normal lymph node:
  - Cortical follicles = B cells
  - Paracortex = T cells
  - Medullary sinuses = histiocytes
  - B cells stain with *CD20*
  - T cells stain with *CD3*

**Mediastinal Lymph Nodes**
- 80% lie around the trachea, carina + main stem bronchi
- Divided into:
  - Visceral (draining intrathoracic structures)
    - Tracheobronchial
    - Anterior mediastinal
    - Posterior mediastinal
  - Parietal (draining chest wall structures)
    - Internal mammary
    - Posterior parietal
    - Diaphragmatic
- Lymph drainage:
  - RUL → hilum → R paratracheal + ant mediastinal nodes
  - RML → hilum → subcarinal → R paratracheal + ant mediastinal nodes
  - LUL → hilum → aorticopulmonary + para-aortic nodes
  - LLL → hilum → subcarinal → aorticopulmonary nodes

**Lymphadenopathy**
- Is it lymphadenopathy or other?
  - Reactive:
    - Sinus histiocytosis — ↑ activity of histiocytes (tissue macrophage or dendritic cells) in sinuses of LNs, can be seen in infection + malignancy
o Anthracosis – carbon deposition
o Sarcoïdosis – granulomatous, non caseous
o Connective tissue disorders – RA, SLE etc

➢ Infectious:
  o Viral – EBV, CMV
  o Bacterial – mycobacterium
  o Fungal
  o Protozoan – toxoplasmosis

➢ Granulomatous

➢ Neoplastic:
  o Primary:
    ➢ Leukaemia – widespread involvement of BM with large numbers of malignant cells in circulating blood
    ➢ Lymphoma – discrete tissue masses of malignant cells
  o Secondary: mets via lymphatic drainage of tumours, often seen in subcapsular sinus regions

• Lymphadenopathy:
  ➢ Localised or diffuse
  ➢ Tender or non-tender

• Local symptoms/signs:
  ➢ Sore throat
  ➢ Poor dentition
  ➢ Nearby skin rash

• Systemic symptoms/signs:
  ➢ Fever
  ➢ Sweats
  ➢ Weight loss

• Bilateral hilar LAN = either sarcoidosis, lymphoma, or TB

• Investigations:
  ➢ Hx and exam
  ➢ Bloods eg FBC, CRP/ESR, Serology [Ab for CMV/EBV if appropriate], quantiferon gold (or mantoux)
  ➢ Imaging → CXR if generalised; US
  ➢ Tissue diagnosis → cytology + histology. FNA: for cytomorphology, microbiology, and flow cytometry

Reactive Lymphadenopathy

• FNA findings:
  ➢ Cytomorphology = reactive lymph node pattern
  ➢ Microbiology = no growth
  ➢ Flow cytometry = mixture of T + B cells; polyclonal B cells

<table>
<thead>
<tr>
<th>Reactive pattern</th>
<th>Causes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Follicular hyperplasia</td>
<td>Non-specific, rheumatoid, HIV [see follicular hyperplasia picture above; bottom image is reactive germinal centre]</td>
</tr>
<tr>
<td>Paracortical T zone</td>
<td>Viruses</td>
</tr>
<tr>
<td>Sinus histiocytes</td>
<td>Non-specific, lymphangiogram</td>
</tr>
<tr>
<td>Mixed/other</td>
<td>Toxoplasmosis, dermatopathic lymphadenopathy, kikuchi’s lymphadenitis [see kikuchi’s picture here]</td>
</tr>
<tr>
<td>Granulomas</td>
<td>TB, sarcoïdal reaction [see picture here]</td>
</tr>
</tbody>
</table>

Toxoplasmosis

• Causes cervical lymphadenopathy in children + young adults
• Toxoplasma gondii protozoan parasite – seen in contact with cats
• Can cross placenta + → blindness/learning disorders in infants
• Confirm with serology → ↑IgM
• See:
  ➢ Follicular hyperplasia
  ➢ Granulomas
  ➢ Monocytoid B cell hyperplasia

Metastatic Squamous Cell Carcinoma

• FNA findings:

Haematology and Immunology
Cytomorphology = clumps of large pleomorphic squamous epithelial cells with focal keratin production

NB. Metastatic deposits tend to lodge in subcapsular sinus

**Lymphoproliferative Disorders**

**Multiple Myeloma**

- A neoplastic proliferation of plasma cells (ie B cells), characterised by lytic lesions, bone marrow failure and homogenous serum and urinary globulin elevations
- CRAB: calcium ↑, renal failure, anaemia, bone pain

**Epidemiology**

- 10-15% of haemopoietic malignancies (MGUS much more common)
- 12 – 16 new cases in Wellington each year
- Median age approx. 70 (rare under 40), male > female
- Remains incurable
- Association with lead, chemicals, agricultural work and FH of autoimmune disorders

**Pathogenesis**

- Monoclonal
- Arises in lymphoid follicle and disseminates to bone marrow. Plasma cells not seen in blood until terminal stage
- Stromal cells release IL6 → acts on osteoclasts to cause lytic lesions → crush fractures in spine, nerve compression, diffuse osteoporosis, hypercalcaemia. Treat vertebral fractures with radiotherapy

**Presentation**

- Bone pain, pathological fracture
- Anaemia
- May start with a solitary lesion (plasmacytoma) but most of these progress to full blown MM
- Amyloidosis in 10 – 15%: macroglossia, cardiomegaly, peripheral neuropathy. Diagnose with rectal/bone marrow biopsy. Stain with Congo Red
- Renal complications:
  - Presents with heavy proteinuria, also chronic renal failure – due to infiltration
  - Light chain nephropathy → worse prognosis. Casts of free light chains → obstruction and are directly nephrotic
  - Amyloid deposition → nephrotic syndrome
- Recurrent bacterial infections
- X-rays: multiple lytic lesions (myelomatosis) + osteoporosis
- Rarely ‘Hyper-Viscosity Syndrome’: due to ↑IgM or IgG → retinal haemorrhage

**Lab Findings**

- The increase in osteoclastic bone resorption in myeloma is usually associated with impaired osteoblast function and the rate of new bone formation is often markedly reduced. In contrast to other types of osteolytic bone disease such as breast cancer, serum ALP activity is decreased or within the normal range
- ACD: normochromic, normocytic anaemia
- Platelets in advanced disease
- ↑ESR
- ↑Serum uric acid
- Hypercalcaemia
- Bone marrow: ↑plasma cells
- Monoclonal band on electrophoresis
- Light chains (Bence-Jones Proteins) in urine
- X-rays: multiple punched-out lytic holes in the bone, no sclerosis
- Gross: ‘currant jelly’ – soft, red lesion
- Micro: resemble plasma cells but variability in cell shape, prominent nucleoli, multinucleation
- Differential: chronic osteomyelitis – but will have granulation tissue with at least a sprinkling of other inflammatory cells

**Pathology**

**Haematology and Immunology**
Macro:
- Multifocal destructive lesions, 1-4cm
- Entire skeleton
- Soft red tumour
- Gelatinous consistency

Microscopy:
- ↑ plasma cells (>30% of all cells)
- Neoplastic plasma cells (Russell bodies = cytoplasmic inclusions; Dutcher bodies = intranuclear inclusions)

Treatment
- General treatment:
  - >65: melphalan/prednisone
  - <65:
    - Several cycles of chemo (vincristine, adriamycin, dexamethasone)
    - Autologous stem cell transplant: generally poor response
- Emergency treatment:
  - Hypercalcaemia: pamidronate – coats bone surface to stop osteoclast reabsorption
  - Anaemia: transfusions
  - Hyperviscosity: plasmapheresis
  - Renal failure: dialysis

Prognosis
- Median survival 3 years
- Some develop AML or MDS
- Transplant (auto) may extend survival
- Allo-transplants may cure a select few

Monoclonal Gammapathy of Undetermined Significance
- = MGUS
- = Benign monoclonal gammopathy (old name)
- Common condition characterized by an accumulation of bone marrow plasma cells derived from a single abnormal clone:
  - 1% of those over 25 + 3% of those over 70 + 10% of those over 75
- Findings:
  - Monoclonal paraprotein band level < 30 g/L (low cf. MM)
  - No light chains in urine
  - Other Igs normal (cf. suppressed in MM)
- Difficult to distinguish from malignancy, especially in early stages. **Tend towards malignancy if:**
  - Serial M band levels are ↑
  - Bone lesions
  - IgG > 30 g/l or IgA > 20 g/l
  - Serum or urine light chains present
  - Normal Igs decreased
  - Marrow plasma cells > 10%
  - Renal failure
  - Hypercalcaemia
  - Anaemia
- **15-20% go onto MM** but may take 10 – 20 years

Aside: Causes of Paraproteinaemia
- MGUS
- Lymphoma or CLL
- Multiple myeloma
- Waldenstrom’s Macroglobulinaemia: monoclonal proliferation of B cell lineage (half way between lymphocytes & plasma cell). Slowly progressive lymphoma. Monoclonal IgM paraprotein. Present with big glands/liver/spleen – no bone lesions
Monoclonal Proteins

Monoclonal Bands

- Cases:
  1. 60 y/o man, rib # + back pain, anaemic, Cr ↑, TP 120, large monoclonal band + IgG was 50g/L, BM showed 50% plasma cells, urine had Bence Jones protein + skeletal survey revealed multiple lytic lesions → MM
  2. 56 y/o woman, tired, globulin gap 50, monoclonal band seen, normal Ig low + band was 24g/L → MGUS or MM
  3. 30 y/o man, FHx A1ATD, A1 band normal but very small band of monoclonal IgG → probably normal
- Monoclonal proteins become detectable when a single clone of cells produce sufficient quantities of a unique Ig to be seen as a discrete band on electrophoresis
- Monoclonal proteins are frequent findings on modern high res electrophoresis, detectable at <0.5g/L
- When present in absence of other clinical + lab features of malignancy (ie MM), condition is MGUS

Conditions Associated With Monoclonal Proteins

- Associated with uncontrolled proliferation:
  - Multiple myeloma
  - Solitary plasmacytoma: discrete, solitary mass of neoplastic monoclonal plasma cells in either bone or soft tissue [extramedullary]
  - Waldenstrom’s macroglobulinaemia
  - Lymphoma
  - Lymphocytic leukaemia
  - Heavy chain disease
  - Primary amyloidosis
- Associated with controlled proliferation:
  - MGUS
  - Chronic infections
  - Non-lymphoid malignancy
  - Connective tissue disorders
  - Transient (virus, drug reaction)
  - Peripheral neuropathy
  - Transplants

Chronic Lymphocytic Leukaemia

- Monoclonal proliferation of mature B cells (CD 19 & 20+). Being mature, will have surface expression of immunoglobulins
- Generally very good prognosis
- Autoimmune phenomena more common in CLL (is a malignancy of the immune system so is no wonder): see ITP + haemolytic anaemia (in 10%; see spherocytes) not uncommonly

Isolated Lymphocytosis

- Ie no other abnormality

Thought process:

- Non-malignant?
  - Infection:
    - Viral: CMV, EBV, adenovirus, HIV, hepatitis etc etc
    - Bacterial: pertussis, TB, syphilis, typhoid, brucellosis (ie the odd ones; most cause neutrophilia)
    - Protozoa: toxoplasmosis, malaria
  - Other:
    - Allergy
    - Splenectomy
    - Hyperthyroidism
    - Malignant?
  - CLL
  - Other malignant leukaemias (eg prolymphocytic leukaemia)

Epidemiology

- Commonest leukaemia: 25%
Primarily elderly
Male = 2 x Female

Clinical Features
- Asymptomatic (40 – 70%)
- Insidious, maybe weight loss, fatigue
- Symmetrical enlargement of superficial lymph nodes (50%)
- Splenomegaly and hepatomegaly
- ↓Platelets → bruising
- Defects in CMI and ↓Ig → infections: Herpes Zoster (shingles), fungal, bacterial, viral. Death usually due to infection

Diagnostic Criteria
- Blood lymphocytes > 5 x 10⁹/L
- Lymphocytes are B cells (CD19, 20 and 24)
- Marrow lymphocytosis > 30%

Differential Diagnosis
- Reactive lymphocytosis: EBV, CMV, HZV, Toxoplasmosis, Brucellosis (bacteria transmitted by animals; cause symptoms similar to the flu and may include fever, sweats, headaches, back pains, and weakness. See lymphadenopathy + hepatosplenomegaly. Severe infections of the CNS or heart may occur, Tb, Viral
- Other B cell tumours:
  - Prolymphocytic anaemia
  - Hairy cell leukaemia
  - Splenic lymphoma with villous lymphocytes
  - Mantle cell lymphoma
  - Follicular lymphoma

Tests
- Peripheral blood:
  - Blood film
  - Flow cytometry (CD19, 20, 24)
  - BM aspirate (not always done)
- Once a diagnosis has been made, is important to stage (see prognosis below)

Lab
- 20% diagnosed on routine blood test
- Lymphocytosis: > 5 x 10⁹/L, but may be 30 to 300. Small lymphocytes and smear/smudge cells (artefacts produced by lymphocytes damaged during slide preparation) common (cytoplasm fragile – breaks easily)
- Normal looking lymphocytes: small, little/no cytoplasm
- Anaemia in later stages due to marrow replacement and ↓survival. 15% have Coombs positive haemolytic anaemia
- Marrow: lymphocytic replacement
- 10% have haemolytic anaemia

Prognosis
- Uses the Rai system and documents which of the below are involved, going down the list (ie more of the body involved) worsens the prognosis (ie stage 0 has a 150/12 prognosis, stage 4 = 19/12):
  - Stage 0: peripheral lymphocytes
  - Stage I: lymph nodes (ie LAN)
  - Stage II: spleen/liver (ie splenomegaly)
  - Stage III: Hb
  - Stage IV: platelets

Treatment & Follow-up
- Depends on stage ie stage 0 will be followed annually by GP with no treatment
- Later stages can use:
  - Chemotherapy: chlorambucil, cyclophosphamide, steroids, fludarabine
SCT: need to consider prognosis, co-morbidities, functionality/performance of pt, if pt understands risks, can they make informed decision?

- **Supportive treatment** for infections, and radiotherapy for deposits causing pressure symptoms
- **Doesn't** convert to Acute Lymphoblastic Leukaemia
- Median survival from diagnosis: 4 years. But 15% live for 15 years with no treatment

**Complications**
- Infections, secondary to hypogammaglobulinaemia, neutropenia, drugs (immunosuppressive)
- Cardia dysfunction: secondary to chemo toxicity, etc
- DVT: hypercoagulable

**Lymphoma**
- Requires bx for:
  - Morphology (H & E)
  - Immunohistochemistry
  - Flow cytometry to look for clonal proliferations
  - Cytogenetics
- HL:
  - Enlargement of a group of nodes
  - Spreads in *orderly* fashion from *distal to proximal*: relatively straightforward to treat
  - See Reed-Sternburg cells (determines whether HL or NHL)
  - Much *less common* than NHL
- NHL:
  - Bcell lymphoma (85%) or Tcell lymphoma, all derived from a *single, monoclonal population of cells*
  - Less orderly spread, *widespread dissemination* as Bcells + Tcells recirculate throughout lymphatics + circulatory system therefore need systemic Rx
  - Presentation = enlargement of a *group* of LNs
- Distinction between HL + NHL → HL better prognosis due to HL being more predictable

**Lymphoma Classification**
- Hodgkin
  - Classical
  - Non-classical
- Non-Hodgkin
  - B cell or T cell
    - Low grade:
      - Follicular lymphoma
      - CLL/SLL
      - MALT lymphoma
      - Mantle cell lymphoma
    - High grade:
      - B cell = DLBCL + Burkitt lymphoma
      - T cell = ALCL + lymphoblastic lymphoma
- Lymphoid neoplasms:
  - Leukaemia (eg peripheral blood)
  - Lymphoma (eg discrete tissue mass; nodal or extranodal)
- Need tissue diagnosis → clinical staging
- Symptoms = fever, night sweats, weight loss
- **Ann Arbor** staging:
  - I = single lymphoid region
  - II = >= 2 lymphoid regions on same side of diaphragm
  - III = lymphoid regions on both sides of diaphragm
  - IV = extranodal sites
- Treatment can range from observation (low grade) → aggressive chemotherapy with BM transplant for high grade; radiotherapy can be used for local control

**Hodgkin Lymphoma**
- FNA findings:
Cytomorphology = Reed-Sternberg cells, often present in reactive lymphoid background (NB. R-S cells can be confused with paracortical T zone hyperplasia immunoblasts as seen in infectious mononucleosis)
- Microbiology = no growth
- Flow cytometry = mixture of T + B cells; B cells POLYclonal
  - ~30% of all lymphoma, more commonly seen in young pts
  - Cervical lymphadenopathy is common
  - Relatively few large tumour cells
  - Abundant mixed reactive background
- Types:
  - Classical = nodular sclerosis
    - 95% of HL cases
    - See mixed cellularity, and either lymphocyte rich or lymphocyte depleted
    - Sclerotic bands divide the node into nodules
    - Lacunar Hodgkin cells: CD15 + CD30 +ve; diagnostic R-S cells
    - Reactive background, often with eosinophils
    - Bimodal age peak: 15-35 years + elderly
    - A neoplasm of germinal centre B cells
    - EBV may have a role in pathogenesis
    - Curable in >85% of cases
  - Non-classical
    - 5%
    - Nodular lymphocyte predominant HL (NLPHL)
    - Vague nodules with a rich follicular dendritic cell network
    - Popcorn Hodgkin cells; CD15 + CD30 -ve
    - 30-50yrs, male > female
    - Generally indolent
    - Progression to high grade DLBCL in ~ 5% of cases

**NHL: Follicular Lymphoma**
- FNA findings:
  - Cytomorphology = reactive lymphoid pattern
  - Flow cytometry = monoclonal B cells
  - Monoclonal neoplastic B cells from germinal centres
  - Multiple neoplastic follicles
  - Mixture of centroblasts + centrocytes
  - ~20% of lymphomas; seen in adults
  - Graded 1-3 depending on number of centroblasts (need bx for grading)
  - Caused by t(14;18) BCL2 translocation
  - Can be difficult to distinguish between reactive follicular hyperplasia vs follicular lymphoma
    - → use flow cytometry (see monoclonal B cells [light chain restriction] in lymphoma + ↑ expression of bcl2 vs reactive polyclonal B cells)
  - → histology also helpful (immunohistochemistry shows upregulation of bcl-2 in lymphoma) + needed for grading

**NHL: Diffuse Large B Cell Lymphoma**
- FNA findings:
  - Cytomorphology = dispersed neoplastic large cells
  - Flow cytometry = monoclonal B cell population
  - GC B cells (centroblastic) or post GC B cells (immunoblastic) types
  - ~30% of NHL
  - Large neoplastic B cells
  - High proliferation index - >90%
  - High grade
  - Treat with anti-CD20 = rituximab
- GC subtype may have better prognosis
- Malignant lymphoma = **Clonal proliferation of lymphocytes arising in lymph nodes** (or other lymphoid tissue). Minor exceptions – can get them in spleen, gut, etc
- Differentiating lymphoma from leukaemia: was its **origin** in the bone marrow or lymph nodes?
- Clinical features:
  - Painless lymphadenopathy: non-tender, **rubbery**
  - Hepatosplenomegaly
  - Systemic symptoms: fever, night sweats, weight loss, tiredness
  - Involvement of other areas: skin, CNS, GI, salivary glands
  - If bone involvement (fairly rare) then preference for bones with red marrow, and may present with bone pain
- Diagnosis: **excision biopsy (not FNA)**. Special lab procedures, stains etc. Warn the lab it’s coming (fresh)

**Classification**
- Hodgkin’s vs non-Hodgkin’s: histological diagnosis only. Hodgkin’s responds better in general. In general, **Hodgkin’s spreads node to node, non-Hodgkin’s spreads to any node in the body**
- Low (indolent) vs intermediate vs high (aggressive) grade
- Staging: **Ann Arbor Staging System** (Ann Arbor is a place in the USA):
  - 1: one lymph node area only
  - 2: 2 or more lymph node areas on the same side of diaphragm
  - 3: 2 or more lymph node areas on different sides of the diaphragm
  - 4: disease in liver, bone marrow or other **extra-nodal sites**
  - Symptom status: A = absence of fevers, sweats, weight loss.  B = one of unexplained fever > 38.5 C, weight loss > 10 % in preceding 6 months, drenching night sweats [Unusual to include symptom status in cancer staging]
  - Staging investigations: CT of neck, chest and abdomen.  Bone marrow.  FBC, LFTs, ESR
  - Compared with leukaemia: if its in your bone marrow its everywhere

**Survival**
- **Hodgkin’s Disease**:

<table>
<thead>
<tr>
<th></th>
<th>5-year survival (%)</th>
<th>10-year survival (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage I</td>
<td>90</td>
<td>73</td>
</tr>
<tr>
<td>Stage II</td>
<td>87</td>
<td>69</td>
</tr>
<tr>
<td>Stage III</td>
<td>71</td>
<td>54</td>
</tr>
<tr>
<td>Stage IV</td>
<td>45</td>
<td>&lt; 37</td>
</tr>
</tbody>
</table>

- **Non-Hodgkin’s Lymphoma**:

<table>
<thead>
<tr>
<th></th>
<th>5-year survival (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Favourable histology Localised</td>
<td>61 – 90</td>
</tr>
<tr>
<td>Widespread</td>
<td>50 – 70</td>
</tr>
<tr>
<td>Unfavourable histology Localised</td>
<td>76 – 100</td>
</tr>
<tr>
<td>Widespread</td>
<td>80 – 85</td>
</tr>
</tbody>
</table>

**Treatment**
- Radiotherapy if localised (main side effect is tiredness)
- Chemo if disseminated
- Possible bone marrow transplant if chemo fails (permits more toxic dose of chemo)
- If treatment fails then gradual progression

**Hairy Cell Leukaemia**
- Indolent (very slow growing) B cell neoplasm
- Males to female = 5:1. Median onset age 50
- Splenomegaly
- Wispy changes to cytoplasm of B cell
- Purine analogues → 80% remission

**Data Interpretation: Leukaemia & Lymphoproliferative disorders**
- **Normal count but atypical lymphocytes → viral infection**. Check glands/spleen. Test for EBV, CMV, or HIV. Ensure time to seroconvert

---

*Haematology and Immunology*
- If only a few blasts in blood (e.g. 1%) and some nucleated red cells → not acute (blasts not dominant) but marrow under stress → chronic

**Immunodeficiency**

**Immunology**

<table>
<thead>
<tr>
<th>Circulating molecules</th>
<th>Innate</th>
<th>Acquired/Specific</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cells</td>
<td>Complement</td>
<td>Antibodies</td>
</tr>
<tr>
<td></td>
<td>Phagocytes: macrophages, neutrophils, NK cells</td>
<td>Lymphocytes</td>
</tr>
</tbody>
</table>

**Innate immunity:**
- *Integrity of skin* & mucosal surfaces
- Mucus in respiratory and GI systems
- pH of urine and skin and stomach secretions
- Clearance of surfaces (eg cilia)
- Antiseptic chemicals (eg lysozymes in tears, saliva, nasal secretions etc)

**Acquired/Specific immunity:**
- Has memory and specificity
- Turns on, then off
- **Humoral** (antibodies): generally extracellular bacteria. First exposure, mainly IgM. Subsequent exposures, more antibody, and mainly IgG
- **Cell mediated**/T-cells: intracellular

- The categories of things that go wrong:
  - Immune deficiency: can’t fight an external agent
  - Auto-immune: inappropriate reaction against an internal antigen
  - Allergy: inappropriate reaction against an external antigen

- Causes of immune deficiency:
  - Autoimmune Disease
  - Vitamin/mineral deficiency: B12/Zinc
  - Genetic patterns: autosomal recessive
  - Metabolic deficiency e.g. Adenosine deaminase deficiency
  - Arrest in embryogenesis

**Summary**
- Immunity can be either **natural** or **artificial**, **innate** or **acquired**=adaptive, and either **active** or **passive**
  - **Active natural** (contact with infection): develops slowly, is long term, and antigen specific
  - **Active artificial** (immunization): develops slowly, lasts for several years, and is specific to the antigen for which the immunization was given
  - **Passive natural** (transplacental = mother to child): develops immediately, is temporary, and affects all antigens to which the mother has immunity
  - **Passive artificial** (injection of gamma globulin): develops immediately, is temporary, and affects all antigens to which the donor has immunity

**Primary Immunodeficiency**
- Most single gene disorders: range of effects e.g. antibody or complement deficiencies
- Clinical features:
  - Highly suspicious: chronic, recurrent or unusual infections, incomplete response to treatment
Moderately suspicious: skin rash (eczema, candida), diarrhoea, growth failure, recurrent abscesses, hepatosplenomegaly

- Different infections associated with different disorders
  - ↓Antibodies: sino/pulmonary/gut problems
  - ↓CMI: multisystem (e.g. CMV), pulmonary (PCP, aspergillus, candida), viruses (e.g. Herpes)
  - Phagocytic problems: s. aureus
  - ↓Complement: recurrent neisserial infection

- Symptoms depend on where in the lineage the defect is:
  - Stem cell: eg SCID
  - Pre-B cell: X Linked Agammaglobulinaemia
  - Maturation Defect: eg can’t switch from IgM to IgG

**Group 1 – Combined Variable Immunodeficiencies (CVID)**
- Prevalence 1 in 20 – 50,000
- Symptomatic at 15 – 35 years (but long diagnostic delay)
- Recurrent pyogenic problems/autoimmune features/respiratory infections
- GI infections: giardia, campylobacter, HCV
- Normal B cells: but defect in maturation – no plasma cells
- Treatment: iv Ig (e.g. Intragam), prophylactic antibiotics

**Group 2 – Antibody Deficiencies**
- Diagnosis of primary antibody deficiencies:
  - Serum Ig’s
    - Quantitative measurement essential (electrophoresis insensitive)
    - Severe hypogammaglobulinaemia: serum IgG level below 3 g/L in adults
  - Response to vaccination (important test)
    - Tetanus and Pneumo-Vax
    - Do baseline, vaccinate, expect 4 times ↑ at 4 weeks
  - IgG subclass concentrations: interpretation difficult. Based on lymphocyte count. E.g. if lymphocytes normal then primary, if low lymphocytes then ?SCID
  - Lymphocyte Subsets:
    - Absence of B cells in Brutons
    - CVID: up to 30 % have T cell reductions
    - CLL - ↑CD5+ B cells
- IgA Deficiency (most common genetic deficiency)
  - Approx 1 in 700
  - Respiratory & GI infections
  - Risk of anaphylaxis with blood products due to reaction to exogenous IgA
  - Don’t treat with Ig
  - Runs in families with CVID
  - Can be associated with:
    - IgG subclass abnormalities
    - Impaired responses to vaccination

**Group 3 – Immunodeficiency Associated with Other Defects**

**Group 4 – Complement Deficiencies**
- Opsonisation: attachment of C3 to immune complexes
- ↓C3 →pyogenic infections due to ↓lysis

**Group 5 – Defects of Phagocytic Number or Function**
- E.g. severe congenital neutropenia, chronic granulomatous disease, IFN gamma receptor deficiency
- Can test for chemotaxis, adherence and phagocytic function
- Management: specific antibodies, G-CSF in neutropenia, etc
Secondary Immunodeficiency (Acquired)

Splenectomy
- RR of fatal infection ↑ by 200 times: e.g. meningitis, bacteraemia and pneumonia → OPSI (Opportunistic Post Splenectomy Infection)
- Biggest problem is encapsulated bacteria plus malaria and salmonella
- Treat with vaccination (negligent if you don’t, always record in notes) + prophylactic antibiotics
  - Pneumococcal vaccine
  - Hib vaccine
  - Meningococcal C vaccine
  - Influenza vaccine annually
- Aggressively investigate any post splenectomy patient with infection

Diabetes
- ↓ Function of neutrophils & macrophages
- Staph skin diseases common
- Compounded by ketoacidosis

AIDS
- Transmission: sex (↑ risk in receptive intercourse – male to male most significant, also in other STDs), blood and maternal transmission (↓ risk with AZT)
- 1 % of Europeans lack CXR-5 receptor: if homozygous then resistant
- Signs & Symptoms:
  - ↑ Temperature, wasting (chronic ill health)
  - Rashes: eg shingles, HSV (cold sores), candidiasis, may be drug response (heightened sensitivity to drug responses)
  - Lymph nodes
  - Signs of high risk behaviour: Injection marks, other STD
  - Mouth: infections, Kaposi’s Sarcoma (re-purple vascular non-tender tumours – mainly on skin)
  - Chronic cough common
  - Hepatosplenomegaly (infections, lymphoma)
  - Neuropathies: eg due to intracranial lesion (eg lymphoma), peripheral sensory neuropathies
  - Fundi: cotton wool spots, scars (eg due to toxoplasmosis, CMV)
- Early disease:
  - Serocconversion illness: in 50 – 90% of infected people. May include macular rash
  - Debate about usefulness of early treatment
  - Good evidence of value of prophylactic treatment (e.g. following needle stick)
- Screening:
  - 3 weeks before positive after infection
  - Elisa for HIV-1 and HIV-2 antibodies
  - False positive tests: 4/1000
- Confirmatory diagnosis: Western Blot
  - Can take up to 3 months to get Western Blot Positive
  - Can give indeterminate, weak positive or strong positive (3 bands)
- Course: measure based on viral load and CD4 count
  - Acute illness: 4 – 8 weeks
  - Asymptomatic: 2 – 12 years
  - Symptomatic: 2+ years. AIDS defining illness:
    - PCP infection (treat with co-trimoxazole): can → pneumothorax
    - Cryptococcus infection: mild headaches: lumbar puncture. Indian ink stain positive
    - Kaposi’s sarcoma: can present anywhere
    - Psychological: HIV related, secondary illness related, or depression
- Viral Load:
  - High T cell turnover: Virus replicates in 1½ days. Infected cell lasts 2.2 days
  - HIV in sanctuary sites: e.g. brain – hard to treat
- Measure through PCR of viral RNA: good indicator of progression. If viral load high, treat now
- Immune depletion: Based on CD4+ count:
  - > 500
- 200 – 500: Tb, herpes
- <200

- Subgroups of illness:
  - Constitutional: fever, diarrhoea, weight loss
  - Neurological: dementia, neuropathy, cognitive
  - Opportunistic infections: candida, PCP, toxoplasmosis, CMV, MAC, Tb
  - Malignancies: Kaposi’s sarcoma, non-Hodgkin’s lymphoma

- Drug Treatment:
  - Combination of drugs that inhibit various points of viral replication
  - Can improve CD4+ count from very low (e.g. 50) to e.g. 500-600
  - Side-effects: non-specific rashes, ‘buffalo hump’ – abnormal fat distribution

- Leading cause of death: Respiratory infection

**Testing for HIV**

- Guidelines for HIV pre-test counselling:
  - What the test for HIV antibodies means: not a test for AIDS
  - Significance of negative test (Window period)
  - Significance of positive test: medical implications (prognosis & treatment), social implications (coping, support, relationships, who needs to know, possible discrimination), notification requirements (HIV not notifiable, patient can use alias), implications for insurance
  - Safeguards to preserve confidentiality
  - Future preventative aspects: safer sex and IDU
  - How results are obtained
  - Any costs

- Guidelines for post test counselling:
  - Explanation of test results
  - If negative: 3-month window period – especially if recent high risk behaviour. Future prevention
  - If positive: repeat, confirmatory test organised, arrangement for counselling, support and specialist assessment

**Other Causes of Secondary Immunodeficiency**

- Malignancy
- Drugs e.g. steroids, cyclosporin, cytotoxics
- Nutritional Deficiency
- Post-viral
- Post-transfusion
- Alcoholism
- Chronic renal disease

**Allergy and Hypersensitivity Disorders**

**Hypersensitivity**

- A lay term
  - Stimuli that don’t cause symptoms amongst general population
  - Usually reaction of body surfaces (eyes, airways) to environmental factors

- Immunological Hypersensitivity Types:

<table>
<thead>
<tr>
<th>Problem With</th>
<th>Mechanisms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Immediate Hypersensitivity</td>
<td>IgE</td>
</tr>
<tr>
<td>Cytotoxic / Antibody mediated</td>
<td>IgM, IgG</td>
</tr>
</tbody>
</table>
Immune Complex Mediated

Antigens + Ig

Delayed Hypersensitivity / T cell mediated

CD4/8

- Antibody complexes are not cleared from the circulation and fix in capillary beds → WBCs → tissue damage. Eg serum sickness (foreign proteins and drugs – eg Ceeclor [cefaclor] – urticaria (hives, welts) 1 – 7 days later) and some glomerulonephritis

- TcR (T Cell receptor) binds to tissue antigens → clonal expansion and inflammatory cytokine release. Eg contact dermatitis, tuberculin sensitivity in Tb

Autoimmune disease can be any one of types II, III or IV

- Hyper-reactivity = ↑ sensitivity to non-specific stimuli (= irritants), eg cold, perfumes, etc

Allergy

- Cross references:
  ➢ See also Food Allergy, page 986
  ➢ See also Atopic Eczema, page 511
  ➢ See also Allergic Rhinitis, page 86
  ➢ See also Drug Allergy, page 855

- = Immunologic reaction to common substances which are harmless to most people
- Disease following an immune response to an otherwise innocuous glycoprotein (eg asthma, rhinitis, eczema, food/drug/insect allergy)
- Previous exposure → antibodies or specific lymphocytes against these substances
- Allergy + hygiene hypothesis = ↑ in autoimmune + allergic disease mirrored by the ↓ in infectious disease

Types

- Atopy:
  ➢ Tendency towards IgE mediated hypersensitivity to common environmental allergens
  ➢ Often a positive FHx
  ➢ Requires positive skin prick test for 1 or more common environmental allergens (dust mite, pollen, animal protein)
  ➢ “Atopic march”:
    o Progression of allergic manifestations w age eg food <1yr → atopic dermatitis 1-3 yrs → asthma/allergic rhinitis later
    o Sensitisation to allergens ↑ with age
  ➢ Order of incidence:

<table>
<thead>
<tr>
<th>Condition</th>
<th>Peak in years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eczema</td>
<td>1 – 2</td>
</tr>
<tr>
<td>Food allergy (eg milk, eggs)</td>
<td>2 – 3</td>
</tr>
<tr>
<td>Asthma</td>
<td>10</td>
</tr>
<tr>
<td>Seasonal Rhinitis (hay fever)</td>
<td>20 +</td>
</tr>
</tbody>
</table>

- Adults aged 20 – 44 in New Zealand: Asthma 15%, hay-fever 35%, Maori more symptomatic
- Mediators lead to vasodilation, vascular leakage (swelling), smooth muscle spasm (eg respiratory)
- Similar symptoms can occur from non-allergic hypersensitivity => non-atopic
- Contact Allergies: direct skin contact with nickel, chrome, rubber. Due to lymphocyte (delayed-type hypersensitivity, type IV) not IgE antibodies
- Allergic Alveolitis: lung inflammation. Eg farmer’s lung, pigeon fancier’s lung. Due to lymphocytes and IgG (not IgE)

Risk Factors

- Allergy predominates in young adults and children: while non-specific hypersensitivity is more common later in life
- Genetic Factors: one parent → doubled risk of child having atopic disease. Both parents → 4 times risk
- Early childhood factors important in subsequent development of allergic disease:
  ➢ High house dust mite/cat/pollen exposure in early months → ↑ risk

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Exposure to tobacco smoke in utero/infancy $\Rightarrow$ ↑risk
Early life infections $\Rightarrow$ ↓risk: improved shift from TH2 environment of uterus to non-allergic TH1 immune responses which dominate in most infections (especially intracellular pathogens)
First born children at greater risk

The workplace is a major source of allergen exposure

**Bee Sting Allergy**

- Don’t have to have atopic history
- If anaphylaxis as a child, 1 in 6 chance next time. For adult, 60% chance next time
- Carry adrenaline until desensitisation (serial antigen shots $\Rightarrow$95% effective)
- Anaphylaxis: give 0.5 m of 1:1000 adrenaline IM if in community setting (iv in hospital if you can give slow infusion). IM gives good diffusion, safer, effective and fewer problems with cardiac vasoconstriction cf bolus

**Anaphylaxis**

- For treatment of Anaphylaxis see Severe Anaphylaxis, page 796
- = Systemic inflammatory reaction due to release of substances from mast cells + basophils triggered by an IgE mechanism (or non IgE (anaphylactoid))
- Implies: sudden onset, systemic involvement (airway, respiratory, CV), medical emergency
- Incidence: 1/10,000
- Fatalities: rare ~ 1/1,000,000, 2/3 of those dying from insect stings + 4/5 of drug reaction had no previous indications of allergy
- Risk factors for fatal reaction = asthmatic, adrenaline unavailable, peanut allergy, age (age depends on trigger, i.e. cow’s milk ~ 8yrs, peanuts ~ 21)
- Death:
  - 50% due to shock (vasodilation, loss of VR, electro-mechanical dissociation, arrhythmias)
  - 50% respiratory arrest (laryngeal oedema, bronchospasm) – food + sting reactions more a/w upper airway swelling than drugs

**Pathophysiology**

- Prior antigen exposure $\Rightarrow$ Sensitisation $\Rightarrow$ Re-exposure:
  - Ag (allergen) binds to antigen-specific IgE attached to previously sensitized basophils and mast cells $\Rightarrow$ mediators are released almost immediately when the Ag binds
  - In an anaphylactoid reaction, exposure to an inciting substance causes direct release of mediators, a process that is not mediated by IgE
  - ↑mucous secretion and ↑ bronchial smooth muscle tone, as well as airway oedema, contribute to the respiratory symptoms observed in anaphylaxis
  - Cardiovascular effects result from ↓ vascular tone and capillary leakage
  - Histamine release in skin causes urticarial skin lesions

**Causes**

- Drugs:
  - Act as haptens (ie need to attach to a protein before IgE will recognise them – too small) or direct stimulants of mast cells
  - Penicillins (50-75%), NSAIDs, opiates (direct mast cell activators)
- Foods:
  - Adults (85% of food allergy) = peanuts, tree nuts, shellfish, fish
  - Children (90% of food allergy) = milk, egg, peanuts, wheat, soy, tree nuts
- Venoms:
  - E.g. bee sting
- Others: latex, contrast, vaccines, seminal fluid, exercise induced etc

**Diagnostic Tests**

- **Skin prick testing** (prick, prick + prick – for multiple potential triggers, intradermal)
- In vitro testing (specific IgE testing – RAST – radioallergosorbent test)
  - RAST – looks for specific IgE with blood
  - Less sensitive + immediate than SPT, more expensive too
- **Complement** studies (C3, C4 etc) if angioedema only – to dx acquired (in response to ACEi or ARBs) or hereditary angioedema
- Idiopathic in up to 1/3 cases, need to diary reactions + exposures + consider other dx
• **Serum tryptase** (released from mast cells):
  - Starts to rise at 15-30min, peaks at **1-2hrs** *(therefore best measured then)*
  - If raised, perform baseline post event to document return to normal levels – if remains high, consider mastocystosis (mast cell disorder)

**Clinical Features**
- Cutaneous = flushing, urticaria (hives – raised, itchy, red welts), **angioedema** (similar to urticaria but submucosal + subcutaneous in the skin + mucosa, especially lips + eyelids), pruritis etc
- CV = hypotension with shock + syncope, tachycardia etc
- Respiratory = wheeze + bronchospasm, cough, laryngeal oedema etc
- GI = n + v + d etc
- Other = aura/hallucinations, metallic taste, impending doom, general burning etc

**Differential Diagnosis**
- **Vasovagal**, vocal cord dysfunction (panic attack – sensation of throat closing over in response to trigger), hypoglycaemia, sepsis, hereditary angioedema, carcinoid syndrome, panic attack etc

**Management**
- NB. do not sit the pt up – lie flat w legs up – improves VR
- Discontinue offending agent
- Resus: **ABC** including inotropes + ICU support
- **Adrenaline:**
  - Give as early as possible.
  - IM – lateral aspect of thigh (better absorption), adults **0.3-0.5mg**, kids **0.01mg/kg**
  - IV – for cardiac arrest only. 10-20ug/min infusion
- **Antihistamines** – should be the **afterthought**, use oral **cetirizine**. *No good evidence* that these work
- **Corticosteroids** – need 12-24hrs to work + **not proven to save lives** but may ↓ overall duration of reaction.
  - 200mg IV stat then 100mg qid or 25mg bd PO
- Post treatment:
  - Mild – moderate reactions = observe 4-6hrs
  - Severe (hypotension, bronchospasm, laryngeal oedema) = hospitalise 8-24hrs
  - Discharge on = 3/7 antihistamines (cetirizine); 3/7 prednisone; if bronchospasm give salbutamol; injectable adrenaline
- **Basic principles:**
  - Avoid known triggers
  - Education
  - Use of epipen (adults 0.3mg, kids 0.15mg)
  - Medic alert bracelet
  - Immunomodulation/immunotherapy:
    - Injection immunotherapy = for systemic rx to insect stings
    - Oral desensitisation = for peanuts
    - Anti-IgE therapy for peanut allergy
    - Corticosteroids, antihistamines for recurrent idiopathic anaphylaxis

**Summary**
- Anaphylaxis is common, fatalities rare
- Adrenaline treatment of choice
- Causes:
  - Drugs (adults > children)
  - Foods (children > adults)
  - Stinging insects
  - 1/3 idiopathic

**Diagnosis**
- History: do symptoms occur in **particular environments**, particular **times or seasons**, what are **dominant symptoms** (eg sneezing/itching more likely to be allergy than chronic nasal blockage)
- Testing should be done:
  - To confirm suspicions;
When an allergic reaction has occurred + more than 1 trigger possible (eg child ate egg + peanut butter sandwich);
To assess risk of reaction to food in children w eczema + acute reactions;
To plan or advise on immunotherapy

Skin Prick Tests
• Need a positive (histamine) + negative (normal saline) control
• Can test aeroallergens (dust mites, animals, pollens, moulds) + food allergens (milk, wheat, peanut etc)
• Highly sensitive + reproducible, also safe, accurate and cheap
• Useful for atopic allergies: especially of the mucous membranes
• Use standard panel of allergen extracts (eg grass pollen, house dust mite, cat dander, etc)
• Read wheal (blanched raised area) and flare (erythema) reaction 10 – 15 minutes later
• If they have had an anaphylactic reaction → test in a hospital setting.  If very highly sensitive → systemic reaction.  If anaphylactic reaction, test tryptase (elevated for 1 – 6 hours)
• Skin prick tests will be negative in hypersensitivity that is not IgE mediated
• Pathophysiology:
  ➢ Allergen + specific IgE (attached to mast cells) → mast cell activation → degranulation → histamine and tryptase release + newly generated mediators (arachidonic acid metabolites eg leukotrienes and PGs) → local & systemic effects
  ➢ Eosinophils may also produce mediators of inflammation
  ➢ In the sensitisation process antigen presenting cells (dendritic cells, macrophages) present allergen fragments (epitopes) to T helper cells using MHC Class II.  Mainly Th2 cells involved in inducing allergic disease → IL4, IL5, IL3 → IgE production, eosinophil growth and differentiation and mast cell growth

Specific IgE Testing
• RAST – radioallergosorbent assay: the in vitro skin test; should be used in place of, not as well as
• Less sensitive + more expensive therefore less used but useful if skin tests not possible, history of anaphylaxis

Intradermal Testing
• Increases sensitivity but reduces specificity
• More dangerous; used most commonly for drug allergy + insect venom

Diagnostic Challenge Tests
• Routes: oral, nasal, bronchial, parenteral
• Allergens: aeroallergens, foods, venoms (eg bee)
• Types: open, single blind-placebo controlled, double-blind placebo controlled
• Mainly in research setting
• Food allergy: can do double blind, placebo-controlled food challenge. In small kids, removing food allergens from diet will improve severe eczema – but not in adults
• Inhalation of cold air, histamine or exercise may be useful in assessing bronchial hyper-reactivity in asthma

Contact Allergy
• Affect whole skin and are usually life long
• Diagnosed using patch testing on back for 48 hours.  Difficult to distinguish between allergic and irritant reactions

Allergy Management
• Avoid/minimise exposure to allergen
• Appropriate medication (antihistamines, adrenaline etc)
• Evaluate for allergen immunotherapy
• Educate

Autoimmunity
• See Coeliac Disease and SLE
• Predominantly young + middle aged
• F>M
• Pathogenesis unclear but auto-Abs often develop prior to clinical s + s
• IgG autoAb (+ IgA to lesser extent) most clinically significant autoAb, more so than IgM
• Treatment:
   Replace end organ function eg insulin, T4
   Immunosuppression eg corticosteroids, cytotoxics, monoclonal Abs etc
   Removal of stimulating Ag eg coeliac, drug induced autoimmune syndromes (eg lupus, vasculitis) etc

Basic Principles & Tests

Autoantibodies
• Those of clinical significance are IgG/IgA rather than IgM
• Clinical utility:
   Diagnosis (in the right clinical context)
   Screening, eg anti-tissue transglutaminase antibodies for coeliac disease in Type 1 diabetes
   Prognosis (some) eg anti-Scl-70 antibodies in scleroderma
   Monitoring (some)
• Autoimmune disease prediction:
   Increasing evidence that the presence of autoantibodies in asymptomatic persons predates disease:
    o Anti thyroid peroxidase antibodies (hypothyroidism)
    o Anti-double stranded DNA antibodies (Systemic Lupus Erythematosus)
    o Rheumatoid factor and anti-CCP (citulinated cyclic peptide) antibodies (Rheumatoid arthritis)
    o Anti-mitochondrial antibodies (Primary Biliary Cirrhosis)
    o Lupus anticoagulant (antiphospholipid syndrome and thrombosis)
• Allows opportunity for:
   Risk stratification and closer monitoring
   Assessment of treatment intensity
   Prevention

Anti-Nuclear Antibody
• The screening test: high positive rate (usually low level/titre) in the general population
• Clinical utility in the diagnosis of:
   SLE/Drug induced: see SLE section
   MCTD/Overlap
   CREST/Scleroderma
   Polymyositis
   Sjogren’s Syndrome
   Autoimmune hepatitis
   Juvenile Idiopathic Arthritis
• Request when clinical suspicion of an autoimmune disease:
   Systemic inflammatory signs
   Mouth ulcers, hair loss
   Chronic suggestive rashes or erythema (photosensitive, urticarial)
   Inflammatory Arthritis
   Sjica Symptoms (Xerostomia, Xerophthalmia)
   Unexplained serositis (pleuritis/pericarditis
   Possible autoimmune liver disease
   Glomerular disease (haematuria/casts, proteinuria)
   Myositis (raised CK and weakness)
   Skin thickening
   Raynaud’s phenomenon
   Interstitial lung disease
   Leukopenia, lymphopenia or haemolytic anaemia
   Psychosis

Haematology and Immunology
SLE clinical significance +ve titres:
- Screening test ~99% sensitive for SLE but not specific
- The higher the titre, in general the more significant
- “False positive” ANAs detected in 31.7% healthy individuals positive at titre 1:40; 13.3% 1:80; 5% 1:160; 3.3% 1:320

When not to order:
- For monitoring a connective tissue disease
- “Tiredness”
- Other forms of arthritis eg Gout, OA,
- If other causes of symptoms/signs explained

The antigen for the ANA test is dsDNA

4 common patterns reported:
1. Homogenous (diffuse):
   - Ag is ds-DNA; and histones/nucleosomes
   - Seen in SLE, drug induced lupus + autoimmune hepatitis
   - Anti-dsDNA:
     - Useful to monitor SLE pts
     - False positives in RA + AI hepatitis/PBC
     - Sens = 30% overall, 60-70% with active disease
     - Appears to vary with activity useful to monitor the majority (about 75%) patients with SLE
2. Speckled:
   - Fine or coarse pattern
   - Associated with specific ENA (see below):
     - With SSa/SSb (specific proteins) suggests Sjogren’s or some forms of lupus (neonatal [see heart block in neonatal lupus]
     - With Sm/RNP = SLE until proven otherwise (99% specific; 10-30% sensitive), RNP seen in MCTD
     - With Scl70: Systemic Sclerosis/Scleroderma (ANA can show speckled/homogenous + nucleolar patterns), but limited SS (ie CREST) shows anti-centromere pattern
3. Nucleolar:
   - Non-specific, not routinely tested
   - 20% of pts with scleroderma are positive
4. Centromere:
   - Ag = CENP-B
   - Associated with CREST (calcinosis, raynauds, esophageal dysmotility, sclerodactyly, telangiectasia)

Once ANA pattern determined, more specific ENA can be done to make/narrow the dx

Extractable Nuclear Antigen
- Useful post positive ANA test
- Uses direct ELISA
- Is more specific than ANA – to specific proteins (involved in different disease processes)

Six different types:
1. Anti-SSa (speckled), seen in Sjogren’s + neonatal lupus
2. Anti-SSb (speckled), seen in Sjogren’s + neonatal lupus
3. Anti-Sm (speckled), seen in lupus
4. Anti-SCI70 (speckled), seen in SS
5. Anti-RNP (speckled), seen in MCTD
6. Anti-Jo1, seen in myositis (ANA NEGATIVE; antibody is to proteins outside the cell nucleus)

Tissue Immunofluorescence
- Tissue immunofluorescence: (Ag + auto-Ab) + (anti-Ig with fluorescent label)

Other Important Autoimmune Disease
- Vasculitis:
  - Small vessel ANCA positive [Wegener’s] or negative
  - Medium vessel [polyarteritis nodosa]
  - Large vessel [giant cell arteritis]
- Anti-phospholipid syndrome (anti-phospholipid Ab; lupus anti-coagulant)
- Autoimmune liver disease:
  - Type 1 ANA, anti-smooth muscle Ab (SMA)
  - Type 2 anti-liver kidney microsomal Ab
  - PBC: anti-mitochondrial Ab (AMA)
  - PSC: pANCA
- IBD (auto-Ab not clinically useful)
- Coeliac (anti-tTG)
- T1DM (anti-islet cell Ab etc)
- Bullous skin disease (pemphigus vulgaris + pemphigoid)
- Thyroid disease (hashimoto’s thyroiditis + grave’s)

**Diseases Caused by Antibodies**

*Antibodies against tissue antigens*
- Cause disease specific for that cell/tissue
- Usually auto-antibodies: but may be a foreign antigen that is immunologically cross-reactive with a component of self-tissues
- Usually IgG or IgM
- Antibodies may be specific for cellular structures: eg receptors. May lead to interference in function, eg myasthenia gravis, Graves disease

*Immune complexes formed from a soluble antigen and specific antibody*
- Formed in the circulation, deposit typically in arteries, glomeruli, synovia
- Leads to local leucocyte activation and tissue injury
- Antigens can be foreign or self antigens, antibodies are usually IgG or IgM
Skin

- References:
  - Mainly Dr Lisa Judd’s notes in GP, Paediatrics and Musculo-skeletal
  - Prof Delahunt’s Pathology notes
  - Dr Stanley’s Paediatric eczema notes

**Dermatology Glossary**

- Annular lesion: ring shaped
- Erythema: *dilation of blood vessels* – colour goes away if pressed (blanching)
- Macule: an alteration in colour (e.g. macular erythema), flat and < 5mm
- Patch: a large macule (> 5mm)
- Papule: a small lump (raised), < 5mm in diameter
- Nodule: a large papule; lump (raised) > 5mm
- Plaque: elevated (maybe only very slightly) area of skin > 2 cm. Altered texture
- Erythematous-squamous: red and scaly
- Vesicles and bullae = fluid within or beneath epidermis (blister). *Vesicles < 5mm, bullae > 5mm*. Can have both. E.g. vesicular-bullae eruption from a plant allergy
- Pustule: accumulation of pus (can be just inflammatory not infectious, e.g. psoriasis)
- Cellulitis: inflammation of deep dermis and subcutaneous tissue
- Ulcer: loss of dermis and epidermis
- Scale: at edge of inflammatory lesion, can be fine, large, dark, silvery (psoriasis)
- Scar: fibrous tissue due to healing. *Atrophic* scar is thin and wrinkled. *Hypertrophic* scar is elevated
- Poikilodermia: cutaneous pigmentation, atrophy and telangiectasia
- Comedo – pl. comedones: a plug of keratin and sebum in a dilated pilosebaceous orifice. Open comedo = blackhead, closed comedo = whitehead
- Cyst: any closed cavity with a membranous lining containing fluid
- Petechiae – pl., petechiae: a haemorrhagic spot 1–2 mm diameter
- Purpura: haemorrhagic spot > 2 mm. Pressing down doesn’t blanch – red cells are extravascular → ?vessel damage. If purpura are palpable → vasculitis
- Ecchymoses: bruises – larger extravasations of blood
- Telangiectasias: permanently dilated small vessels
- Guttate: a profusion of small macules or plaques
- Serpiginous: a linear eruption which is S shaped or snake-like (e.g. larva migrans – a worm)
- Dermatitis: usually means eczema

**Structure of skin:**

- Epidermis:
  - o Stratum corneum
  - o Stratum lucidum
  - o Stratum granulosum
  - o Stratum spinosum
  - o Stratum germañitivum (base of epidermis = spinosum + basale)

- Dermis:
  - o Papillary dermis
  - o Reticular dermis

- Subcutaneous tissue

**Basic terms:** Non-specific reactive changes

- **Hyperkeratosis:** thickening of the *stratum corneum*. Eg due to trauma (e.g. callus; lump where you hold a pen)

- **Parakeratosis:** nuclei seen in the *stratum corneum* (would normally have died off, eg psoriasis)

- **Acanthosis:** thickening of the epidermis, eg due to irritation

- **Acantholysis:** breakdown of stratum spinosum

**Diagnosis**

- Where is it:
Psoriasis: likes scalp and extensor elbows/knees
Atopic eczema: likes flexor elbows and knees
Nose & cheeks: lupus, especially if it leaves a pigment behind

- Does it itch?
  - Atopic eczema (if it doesn’t itch it’s not eczema)
  - Chicken pox
  - Urticaria/allergic reactions
  - Contact dermatitis
  - Scabies
  - Insect bites
  - Fungal infections
  - Dermatitis herpetiformis
  - Pityriasis Rosea

Skin Infections

Bacterial Infections of Skin and Soft Tissue

Impetigo (School Sores)
- = superficial infection involving the epidermis
- Most common in children during summer months
- Non-bullous impetigo:
  - = Streptococcal impetigo
  - Vesicles on erythematos base → pustules (highly contagious) → yellow-brown scabs (CRUSTY), associated with regional lymphadenopathy
- Ecthyma is deeper version – cut out edge
- Commonly result of skin break such as insect bites or chicken pox. Especially if overcrowding and warmer climates
- Goes for limbs and face
- Fever uncommon. Check lymph nodes for lymphangitis
- Caused by S pyogenes with or without (generally with) co-infection with S aureus (can → Scalded Skin Syndrome, see page 505)
- Commonest cause of post-strep glomerulonephritis
- Rarely leads to scarring

- Bullous impetigo:
  - Due to Staph aureus of phage II (usually type 71)
  - Usually younger children
  - Lesions: begin as vesicles – turn into flaccid bullae in response to toxins. Following rupture of the bullae, a moist red surface remains and varnish like crust appears
- Neonatal Impetigo: Staph Aureus. Can spread to deeper tissues, umbilicus, bone and joints. If only one site, antiseptic bath once a day. If > 1 site then systemic antibiotics

- Treatment:
  - To relieve symptoms, stop new lesions, prevent complications (e.g. cellulitis, acute glomerulonephritis), and stop spread to others
  - Flucloxacillin, dicloxacillin, a cephalosporin, erythromycin or clindamycin are all effective
  - If MRSA: usually susceptible to co-trimoxazole (although not so good against S Pyogenes). Resistance to fusidic acid is also growing
  - Resistance is growing to topical agents (e.g. Mupirocin)

Scalded Skin Syndrome
- Due to staph aureus toxins – epidermolytic toxins A + B (may be distant site)
- Desquamation with little pressure (Nikolsky sign) – skin looks abnormal – damage from within
- Commonest in infancy
- May lead to major fluid balance problems (behaves like a burn)
- Treatment: flucloxacillin plus burn treatment (including fluid balance)

Folliculitis
- Usually caused by S aureus
- Pyoderma located within the hair follicle around mouth + nose, scalp and extremities
- Responds well to topical antibacterial measures

**Furuncle**
- Usually caused by S aureus
- A boil
- A deep inflammatory nodule
- In skin areas subject to friction and perspiration and containing hair follicles
- Often drain spontaneously (a draining abscess), especially with moist heat
- If recurrent, then nasal carriage of S aureus. Treat with topical intranasal mupirocin (bactroban) or systemic rifampicin
- May progress to a carbuncle: more extensive involving subcutaneous fat – may need incision + drainage
- If surrounding cellulitis or if on face then need iv antibiotics

**Cellulitis and Erysipelas**
- Infection of subcutaneous layer by S pyogenes
- Symptoms: inflammation, warmth, erythema, pain, fever
- Can → sepsis, bullae and small abscesses
- Also erythema around anus with pus and blood in stool
- Commonly see lymphangitis and lymphadenopathy
- May desquamate (late)
- Impaired lymphatic drainage predisposes to recurrent cellulitis (e.g. pelvic, joint, breast surgery)
- Erysipelas is a distinctive superficial cellulitis, primarily involves dermis. See a single, red, indurated, tender lesion. Raised and well demarcated. Prominent lymphatic involvement. May → chills, fever and malaise
- Treatment: S Pyogenes still very susceptible to penicillin

**Diabetic Foot Infections**
- Due to neuropathy, ischaemia, and infection
- Causes: often S aureus, also coagulase negative staphylococci and streptococci
- Often nasal carriage of S aureus
- Treatment: anti-staphylococcal agents. IV treatment if deep tissues or bone involvement

**Deep Tissue Infections**
- Necrotising Fasciitis: See Streptococcal Skin Infections

<table>
<thead>
<tr>
<th>Streptococcus pyogenes skin conditions</th>
<th>Rx</th>
</tr>
</thead>
<tbody>
<tr>
<td>Impetigo</td>
<td>Penicillin</td>
</tr>
<tr>
<td>Cellulitis</td>
<td>IV Penicillin G 4MU 4hrly – 1MU = 600mg</td>
</tr>
<tr>
<td>Erysipelas</td>
<td>Penicillin</td>
</tr>
<tr>
<td>Necrotising fasciitis</td>
<td>IV Penicillin G 4MU 4hrly + IV Clindamycin 600mg 6hrly</td>
</tr>
</tbody>
</table>

- Streptococcus Pyogenes (Group A, β -Haemolytic), page 814
- Superficial necrotising cellulitis or streptococcal gangrene (rare)
- Gas Gangrene (Clostridial myonecrosis): rapidly progressive and life threatening infection of muscle due to Clostridium Perfringens

**Scarlet Fever**
- See Scarlet Fever, page 815

**Lymphadenitis**
- May require drainage. Distinguish from lymphadenopathy
- Usually Staph aureus, also TB
- See Neck Lumps, page 987

**Toxic Shock Syndrome**
- See Streptococcal Skin Infections
Streptococcus pyogenes skin conditions

<table>
<thead>
<tr>
<th>Condition</th>
<th>Description</th>
<th>Rx</th>
</tr>
</thead>
<tbody>
<tr>
<td>Impetigo</td>
<td>Superficial pyoderma (pus of the skin) characterised by vesicular + crusted lesions</td>
<td>Penicillin</td>
</tr>
<tr>
<td>Cellulitis</td>
<td>Acute spreading subcutaneous tissue skin infection</td>
<td>IV Penicillin G 4MU 4hrly = 1MU = 600mg</td>
</tr>
<tr>
<td>Erysipelas</td>
<td>Distinctive superficial cellulitis (usually on the face) with lymphatic involvement</td>
<td>Penicillin</td>
</tr>
<tr>
<td>Necrotising fasciitis</td>
<td>Severe + spreading infection of SC tissues involving both superficial + deep fascia – toxic shock can ensue</td>
<td>IV Penicillin G 4MU 4hrly + IV Clindamycin 600mg 6hrly</td>
</tr>
</tbody>
</table>

- Streptococcus Pyogenes (Group A, β-Haemolytic), page 814
- See both a s pyogenes + a s aureus version
- S aureus:
  - Caused by TSS1 toxin
  - Presentation: 1-7 d of mild fever, myalgia, vomiting → abrupt high fever + systemic upset → skin diffusely erythematous (like sunburn) → conjunctivitis, red tongue, diarrhoea, renal failure, shock, ARDS, abdominal tenderness, peritonism, petechiae, oral ulcers
  - Desquamation a week later characteristic
  - Treatment: ABs, IV fluids + sometimes drainage of abscesses

Dog Bites
- Clean carefully (may need local anaesthetic)
- Treat with broad-spectrum antibiotic. Augmentin. NNT = 14. So limit to high risk of infection only. Consider anaerobe cover (eg metronidazole)
- Screen for post-traumatic stress disorder afterwards
- Report the dog

Lyme Disease
- Tick borne spirochete (Borrelia burgdorferi)
- Gives erythema migrans, headache, fever, myalgia, fatigue
- Leads to widespread systemic manifestations
- Discovered in Connecticut, USA. Not in NZ

Fungal Infections/Dermatophytosis
- Tinea
  - Fungal infections of animal (zoophilic) origin: These include “ringworm” (which causes a scaling macule – not a ring – and there is no worm!). Usually in children, for example from cows, dogs, cats or mice
  - Dermatophytes belong to the Microsporum, Trichophyton, and Epidermophyton genera
  - Common dermatophytes are M canis, T rubrum, T mentagrophytes

Clinical Description
- Fungal infections usually itch. Have a raised scaling margin that extends outwards
- There are several classical presentations:
  - Tinea Cruris: in the groin. Mainly affects men. Sharp margin. On thighs or buttocks may get follicular pustules. If feet involvement or folliculitis (indicating hair follicle invasion) as well then systemic treatment, otherwise topical

  - Athlete’s Foot/Tinea pedis: on the feet (usually lateral toe clefts – compared with eczema which in medial toe clefts). Usually T rubrum or T mentagrophytes. ↑ sweating predisposes to fungal infection. Fine powdery scaling extending to the sole. To hands by itching, where it presents with a dry, hot rash on one palm, with well defined lesions with a scaling edge
- **Tinea Corporis**: on the trunk, legs or arms. Presents with an erythema and itching, and a well defined, scaling edge. May not itch. May see alopecia. Topical antifungal (miconazole, econazole, terbinafine) should work.

- **Tinea manuum**: Hand. Almost always a pre-existing foot infection. Often only involve one hand (one hand, two feet). Little inflammation + scaling is fine + powdery

- **Onychomycosis** (Fungal infection of the nail): occur mainly in adults, usually in their toenails (fingernails uncommon, ?psoriasis), and especially following trauma. The nails become thickened, yellow, and crumble, usually asymmetrically. The changes occur distally, and move back to the nail fold (compared with psoriasis, which is symmetrical and moves distally from the nail fold)

- **Tinea Incognito**: fungal infection treated with steroids. Stops inflammation but fungus slowly spreads → follicular pustules etc.

  - **Tinea Versicolor**:
    - Infection due to a commensal yeast *Malassezia Furfur (= pityrosporum ovale. Not a fungus). In young adults (seen more in adults), causes hypo- or hyper-pigmented macules with powdery scale, on upper trunk, upper arms and neck. Slightly itchy. Distinctive appearance on microscopy (from scrapings) – don’t need culture
    - Differential diagnoses:
      - Vitiligo: but pure white lesion (amelanotic), no scaling
    - Treatment: Imidazole cream (eg miconazole) or itraconazole tablets, sporanox, selsun shampoo

**Diagnosis**
- Consider in any patient where isolated, itching, dry and scaling lesions occur for no reason (e.g. no history of eczema). Fungal lesions are usually asymmetric. Clippings or scrapings can be sent for culture
Pathogenesis

- Common: Microsporum Canis (from cats, fluoresce under Wood’s light), Trichophyton rubrum, and Trichophyton mentagrophytes
- Less common: Trichophyton tonsurans, Epidermophyton floccosum, Trichophyton erinacei
- Fungi consist of thread-like hyphae that invade keratin (yeasts do not have hyphae). Vegetative spores (conidia) develop in culture. When immune response is impaired, superficial infections may invade deeper tissues

Management

- Topical Treatment: imidazole preparations, such as clotrimazole and miconazole. Dusting preparations are also available. Terbinafine is available as a cream
- Systemic Treatment: diagnosis should be confirmed before commencing treatment. Terbinafine (250mg, once daily PO) for 2 to 6 weeks for skin infections and 3 months for fingernail infections, 6 months for toe nail infections. (Pregnancy and lactation are relative contraindications). Can take itraconazole 1 week per month for 3 months (200 mg bd) →↓side effects. Takes 12 – 18 months to grow a new nail. Given length of treatment, confirm with nail scraping for culture first.

Viral Infections

Molluscum Contagiosum

- Viral infection with pox virus
- Small solid papules with umbilication in middle. Stay fairly localised
- If you squeeze them then virus released (ie infective)
- Histology: acanthosis and molluscum bodies
- Disappear in under 9 – 12 months. Treat if severe

Verrucae (Warts)

- Papova virus: Papillary lesion + polyoma (lots of them) + vacuolation of cells containing the virus
- Locations:
  - Verruca vulgaris
  - Verruca plana: flat, eg on face
  - Verruca plantaris: on feet, can be painful
  - Verruca palmaris: on hands, can be painful
  - Condyloma accuminatum: Genital. Rarely premalignant
- Histology:
  - Hyperkeratosis/parakeratosis
  - Acanthosis
  - Nuclear and cytoplasmic inclusions
  - Perinuclear vacuolation

Other Viral Illness

- See Varicella Zoster
- See Herpes Simplex Virus (HSV), page 818
- See Common Paediatric Viruses, page 951

Other Infections

Paronychia

- Loss of cuticle (arrow; due to eczema, wet work, etc) allows growth of organisms beneath the proximal nail fold → inflammation and nail dystrophy. Acute usually staph, chronic usually candida
- Differential:
  - Onychomycosis
  - Lupus, psoriasis, chilblains
- Treatment: avoid wet work, treat eczema, dying agent, systemic antibiotic if bacterial, disinfect with daktarin tincture

Pitted Keratolysis

- Circular erosions (honeycomb)/small craters in the sole of the foot
- Asymptomatic. Leads to foot odour
• Variously attributed to *Corynebacteria*, *Dermatophilus*, *Micrococcus*
• Treatment: *keep feet dry*, avoid occlusive footwear, topical *erythromycin/clindamycin*, systemic tetracyclines

**Pityriasis Rosea**
• Usually 10 – 35. Starts with *herald patch* (**larger than later lesions**). After 5-15 days *general eruption* begins. *Oval, dull pink, with marginal scale*. Itch varies. On *trunk*, rarely on *face*
• Pityriasis rosea has a *collarette of scale* – a *ring of peely scale* a few mm in from the edge of the plaque
• Was thought to be viral, but *erythromycin* effective
• Fades after 3 – 6 weeks
• Differential: eczema (but no collarette of scale + plaques may be weepy), psoriasis (has silvery scale, no collarette of scale), seborrheic dermatitis (no collarette of scale), tinea versicolor

**Herpes Zoster**
• Clusters of flaccid vesicles, on an erythematous base
• *Dermatomal distribution* (pain + vesicles)
• Herpes zoster is reactivation of the chicken pox virus
• Usually elderly, but any age
• Recurrences rare
• Rx: *acyclovir* 800 mg 5 x daily for 7 days, starting within 3 days of onset.
• Differential diagnosis: dermatomal herpes simplex (uncommon)

**Candidiasis**
• Yeast infection
• Common in infants – either *mouth* (esp inside checks) and in *nappy area, maybe on hands if sucked*. More common in *damp areas*. Need to treat Mum’s nipple as well.
• Lesions whitish with satellite lesions characteristic
• Also with oral/inhaled steroids or broad spectrum antibiotics
• Systemic spread in immuno-compromised is nasty
• Treatment: see Antifungals, page 838

**Scabies**
• Infestation due to the *mite Sarcoptes scabiei*
• Passed by direct contact and occasionally fomites
• Female mite burrows just under surface skin layer and lays *eggs* – seen as *pinpoint black dot* (mite) at the *end of a thin curved line* (burrow)
• Seen in *fingerwebs, sides of fingers*, ulnar border of hand, sometimes periumbilical + elbows/feet
• *Irritation from hypersensitivity* (**“allergy”**) after 4 weeks of scabies mite burrowing – generalised *itching + rash* – can become secondarily infected
• Papular vesicular lesions
• **Treatment**: Scabicide – *permethrin or malathion* applied to all skin except head and left on for at least 12 hours
• DDx: Endogenous eczema, generalised pruritis of other cause

**Headlice**
• The insect = *pediculus humanus capitis*: 2 – 3 mm long, breeds all year round.
• They live in the scalp (the female *louse glues her eggs – nits to hair shafts* – does not burrow) and *suck blood* for food 5 or 6 times a day. They are only transmitted through close head contact. They don’t come off with swimming or washing.
• The eggs are a similar colour to scalp skin. The empty egg shells, known as nits, are white
• Life cycle: female lice lay about 7 – 10 eggs each night, these *hatch in 9 days*. A louse will live for 40 days
• Where to find them: around the hairline at the back of the neck, behind the ears, on the crown
• Treat:
  - If you find a live insect or an egg within 1 cm of the scalp (hair grows 1 cm a month, so more than 1 cm from head means they’re dead) then use *permethrin or malathion shampoo* from the chemist. Leave on scalp for 5 – 10 minutes. Don’t use too much water. Repeat a week later
• Don’t need to wash bedclothes: lice only lay eggs on hair. Instead check kid’s heads once a week
• **Prevention:** regular hair brushing, don’t share brushes, keep clothes separate, contact tracing

## Eczema

- **Dermatitis**
- **Formal definition:** pattern of **inflammatory response of the skin**, defined histologically by the presence of a predominantly **lymphohistiocytic infiltrate around the upper dermal blood vessels**, associated with **spongiosis** (= oedema between keratinocytes) and varying degrees of **acanthosis**.
- **Clinical features** include itching, redness, weeping, scaling and clustered papulovesicles
- **In acute eczema:** **erythema** is marked; **vesication** is likely (may look simply weepy); **bullae** may occur
- **In chronic eczema:** **erythema** + **vesication** are less marked and you may see:
  - Lichenification (epidermal thickening with exaggeration of skin markings)
  - Hypo or hyper **pigmentation**
  - Scaling/fissuring
- Papules may remain discrete or group into plaques
- **Endogenous forms:**
  - Atopic
  - Seborrhoeic
  - Discoid
  - Juvenile plantar dermatosis
  - Pompholyx
  - Pityriasis Alba
- **Exogenous forms:**
  - Asteatotic
  - Irritant contact dermatitis
  - Allergic contact dermatitis

### Atopic Eczema

- See Allergy and Hypersensitivity Disorders, page 496

## Symptoms

- **Common onset 2 – 6 months**
- **Acutely:**
  - Itchy
  - **Redness,** swelling, usually ill-defined border
  - **Papules,** **vesicles,** extremely large blisters, may look weepy
  - **Exudates** and crusting
  - Scaling
  - Can be papular
- **Chronic:**
  - Less vascular and exudative
  - More scaly, **pigmented** and thickened
  - Fissuring
  - More likely to be **lichenified** (epidermal thickening with exaggeration of skin markings) and develop painful fissures
  - If dark skin: post inflammation change in pigmentation
  - Pitting with ridging of nails
- **In babies:**
  - Common onset in **first few weeks**
  - Quite weepy/blistery
  - **Around face** (spares eyes and base of nose) and **trunk.** If extensor distribution think of contact sensitivity (eg house dust mite)
  - Can be due to allergens in breast milk
  - The **itch that rashes:** itchy skin is scratched and an eruption occurs – don’t see rash where child can’t reach
- **Children, and older:**
  - Bends of elbows, behind knees (flexor surfaces)
  - More leathery
Between **big toe and 2nd toe** (compared with tinea between 4 and 5; medial cf lateral)

- Occasionally can see erythrodermic type where all skin is diffusely red
- Associated with asthma and hayfever
- Associated with food allergy – commonly cows milk but this is **overstated**
- Atopic skin has lower threshold to irritation (eg soaps) and is more prone to staph infection
- Prognosis: **½ have cleared by 12**, few persist after age 30
- Increased tendency to: dry skin, urticaria, pityriasis alba, keratosis pilaris (bumps on outer arm), irritant contact dermatitis, etc

**Pathogenesis**

- Genetic predisposition
- Imbalance of Th1 and Th2 cells in the thymus **in favour of Th2**
- Early childhood infections → preferential induction of Th1 type cytokines and prevent atopic sensitisation
- ↓Infections → greater risk of atopy
- Inversely proportional to the number of older siblings (marker of exposure to infection)
- Atopy does not equal allergy:
  - Level of IgE, which may be elevated, **doesn’t** correlate with severity
  - Up to 50% of children with eczema do not have +ve skin prick tests (especially if mild eczema and no asthma)
  - Skin prick tests for histamine release (type 1 reaction) may be positive but the person may not have a reaction when exposed to that allergen
  - **RAST** test looks for *antigen specific* IgE
  - Type 1: normally asthma, rhinitis, urticaria, not usually eczema
  - Patch testing (Type 4) may be relevant to childhood eczema
  - Only 50% with severe eczema develop reactions when challenged with particular foods – most are delayed reactions
- See Allergy and Hypersensitivity Disorders, page 496

**Management**

- **Investigations:**
  - Patch testing
  - Is there infection? (Yellow crusts, weepy, failure to respond to treatment) → systemic antibiotics
- **Prevention:**
  - Don’t itch
  - Avoid aggravators:
    - **Light cotton clothes**, no scratchy woollens
    - Avoid excess humidity/dryness
    - Avoid local or systemic aggravators
    - **Care with soaps**, perfumes, solvents etc
    - **Baths not shower**, not too hot, pat not rub dry
    - Reduce stress
  - **Control dry skin: emollients** – aqueous cream, **emulsifying ointment**, white soft paraffin copiously
  - Use **emulsifying ointment** as soap replacement and in place of aqueous cream (longer lasting)
    - NB. ointments are oil with water as cf creams which are water with oil
- **Medical:**
  - Topical corticosteroids:
    - Reduce inflammation but doesn’t treat cause
    - **Use weakest possible** – 1% hydrocortisone OK for most
    - At night use in conjunction with **wet wraps** (containing emollient)
    - Not for too long otherwise skin atrophy, striae and rebound afterwards, **wrinkling, ↑vascular markings**, also dynamite to viral/bacterial infections. Even worse with systemic steroids – although sometimes need to use constantly in very poorly controlled eczema
    - Lotion for scalp, ointment for dry areas (may cause folliculitis), cream
  - **Strength:**
    a. **Face and flexures:** mild only
    b. Scalp, palms and soles: can tolerate very potent steroids (eg betamethasone dipropionate)
    c. Body and limbs: potent for short periods (a week or two), mild to moderate as maintenance
  - **Systemic steroids** for severe eczema, for a short time only
  - Tar compounds: esp. at night to prevent itching
- **Antihistamines**: stop itching (more in kids and for sedative effect) and urticaria
- Antibiotics for infection
- For severe eczema: phototherapy, azathioprine, cyclosporine

---

**Seborrhoeic Dermatitis**
- Erythematous plaques + greasy scaling, sharply circumscribed
- Scalp (not much erythema), eyebrows and nasolabial folds, moustaches + beards (bald scalp not affected)
- **Cradle cap** in babies whose scalp was clear at birth
- In kids = *another presentation of atopy*. Treat the same. Differential: Infantile psoriasis
- In adults = **hypersensitivity to Malassezia species** (commensal yeasts) which arrive with sebum gland activation at puberty
- **Dandruff** is a mild form
- Can be severe, even erythrodermic in those with AIDS, parkinsons + some drugs (phenothiazines + cimetidine)
- Differential:
  - Psoriasis. But doesn’t often affect the face
  - Discoid, and other forms of eczema
  - Pityriasis rosea (usually on trunk and not on the face)
  - Fungal infection: annular, scaling isn’t greasy
- Treatment (if required at all):
  - Scalp shampoo (eg selenium sulphide, tea tree oil)
  - Can use mid-potency steroid creams for severe involvement +/- antifungals
- **Leiner’s Disease**:
  - Rare condition whereby generalised seborrhoeic dermatitis-like eruption associated with FTT + diarrhoea
  - Defect in C5

**Contact Dermatitis**
- May be irritant or allergic or both. May co-exist with endogenous forms (eg atopic)
- Contact irritant dermatitis occurs as a result of irritant damage to the skin
- Contact allergic dermatitis occurs as a result of allergy to something in contact with the skin
• Can coexist (also with other endogenous forms of dermatitis eg atopic dermatitis)
• Differentiate from endogenous on the basis of history, distribution and maybe allergy testing, not morphology

**Contact Irritant Dermatitis**
• **Irritant:** a substance which induces dermatitis in anyone if applied in sufficient concentration for long enough → penetrates skin and produces cellular damage
• Individuals vary in their threshold
• Heat, occlusion and ↑ or ↓ hydration impair barrier function → more susceptible
• Cumulative effect of different irritants
• Irritants include: acids, alkalis, solvents, soaps, detergents, enzymes, abrasives
• **Diagnosis:**
  ➢ Is the pt exposed to irritants?
  ➢ Exposure to irritants for what duration and frequency and concentration?
  ➢ Are sites consistent with exposure?
  ➢ Does it improve after exposure stops?
  ➢ Any better explanation for signs and symptoms?
• **Management:**
  ➢ Steroid creams, emollients
  ➢ Reduce exposure, remove occlusion (ie sweat inside gloves → over hydration), other work

**Contact Allergic Dermatitis**
• **Type 4 cell mediated immune reaction** (see Allergy and Hypersensitivity Disorders, page 496)
• Often takes repeated exposure, so no previous symptoms may not be significant (same for type 1 reactions).
  Eg may have worn rubber gloves for years
• Once sensitised, further exposure to even minuscule amounts → reaction after a day or two. Takes 24 – 72 hours, compared to type 1 which takes 15 – 20 minutes
• Will involve primary sites, and maybe distant sites (eg due to hand spread: eyes, genitals)
• Photodermatitis = need exposure to allergen + UV light to cause rash.
  Eg sunscreens (chemical A in sunscreen is turned into chemical B by sunlight; the patient is allergic to chemical B )
• Common allergens: nickel (eg pierced ears), rubber additives, plants, chromate in cement, hairdressing chemicals, perfumes, colophony (Elastoplast), preservatives
• Rubber glove allergy can be:
  ➢ Type 1 due to rubber
  ➢ Type 4 due to rubber additives
  ➢ Contact dermatitis due to sweaty hands → ↑ risk of type 1 or 4 reaction (mediated by Langerhans cells) due to ↓ barrier function
• **Diagnosis:**
  ➢ Patch testing (is read at 48hrs and 96hrs)
  ➢ Is the patient exposed to plausible allergens?
  ➢ Are the sites of dermatitis consistent with the manner of exposure?
  ➢ Does the dermatitis go when exposure stops?
  ➢ Any better explanations?
  ➢ Patch tests positive?
  ➢ NB some sites resistant (scalp, soles)
• **Management:**
  ➢ Steroids, emollients, etc
  ➢ Avoid exposure

**Other Eczema Related Conditions**

**Discoid Eczema**
• = nummular dermatitis
• Descriptive term: round or oval, well circumscribed, red, scaly, +/- vesicular (= weepy)
• See one or multiple plaques on the trunk or limbs
• Usually adults, where cause is idiopathic; if in kids: often atopic
• May start following insect bites
• **Differential:**
  ➢ Ringworm: tends to be annular (worse at the edge). Often see have alopecia or follicular papules/pustules
  (as cf discoid eczema → see vesicles + fissuring etc). Take scraping for culture
- **Superficial BCC**: doesn’t usually itch, often a shiny surface, dots of pigment
- **Psoriasis**: silvery scale, not weepy
- **Bowen’s disease**: hyperkeratotic

**Juvenile Plantar Dermatosis**
- Fissured dermatitis of the plantar surface of the forefoot – red, glazed, cracked, symmetrical, toe clefts normal
- In children 3 – 14 years
- Usually atopic
- Treatment difficult: Urea creams, moisturisers, steroid creams. Has usually resolved by teens.

**Vesicular Palmoplantar Eczema**
- A group of conditions manifesting vesicles on palms +/- soles
- Pompholyx is an example of this

**Pompholyx (Dyshidrotic Eczema)**
- Not related to atopic eczema
- Vesicles +/- bullae on palms, soles, sides of fingers or toes
- Erythema or scaling absent. If present then just a vesicular eczema
- Usually itchy
- Heals with desquamation
- Worse with heat (summer)
- Differential: fungal infection (take a scraping)
- Treatment: ?steroids (poor response → will help itching though)

**Pityriasis Alba**
- Round/oval, hypopigmented, fine lamellar scaling, from 5 – 20 mm, commonly on face
- Usually age 3 – 16
- Associated with atopy – but may be independent
- No treatment – goes away by itself

**Asteatotic Eczema**
- Related to dry skin
- Usually on legs, usually elderly, often with diuretics, excessive washing or hypothyroidism
- Superficial fissures create a crazy paving pattern
- Treatment: soap substitute, moisturiser +/- topical steroid

**Intertrigo**
- Intertrigo is a dermatitis which occurs in body folds, where skin is against skin
- Some people use the term for any rash in a body fold eg psoriasis, candidiasis – whereas others use it for rashes in body folds where no other primary condition is diagnosed
- May be a form of atopic or seborrhoeic dermatitis
- Can be secondarily infected with candida or staph
- Treatment:
  - Reduce friction, avoid tight clothing
  - Mild steroid, antibacterial or anti-candida cream
  - Wet compresses

**Angular Cheilitis**
- Is a form of intertrigo, can be associated with atopic or seborrhoeic dermatosis
- Affects the fold of skin at the corner of the mouth. Especially in denture wearers
• It is most common in middle aged and older, when this crease becomes more prominent, but also occurs as a side effect of isotretinoin therapy – which also results in dryness of the lips
• May be infected with candida or staph, may be folate deficiency, a frequent complication of Roaccutane treatment

Keratosis Pilaris
• Common. More common in atopics. Seen in childhood or teens
• Small whitish plugs of keratin obstruct the follicle mouth. Usually extensor surfaces (upper outer arm especially). Feels like sandpaper
• Follicular horny papules +/- perifollicular erythema or pigmentation
• Facial involvement usually resolves in teens. Elsewhere can persist until middle age
• Autosomal dominant with variable penetrance
• Differential: acne (shouldn’t feel like sandpaper)
• Treatment: emollients, mild steroids, urea creams, retinoid creams etc

Nappy Rash

Napkin Dermatitis
• Irritant contact dermatitis caused by prolonged contact with wet nappies
• Spares the flexures (i.e. skin folds are white, not red)
• Bacterial conversion of urine to ammonia → alkaline irritant (nappy rash = urea + H₂O → ammonia + CO₂ – the ammonia produced causes caustic burn)
• Treatment:
  ➢ Frequent changing and careful washing and time out of nappies
  ➢ Zinc and castor oil ointment
  ➢ Disposable nappies (have silica gel to soak up H₂O therefore ↓ ammonia production)

Differential: Candidiasis
• Frequently superimposed on nappy rash
• Flexures involved + satellite lesions or superficial pustules on a background of erythema
• Treatment: antifungal cream (nystatin)

Treatment of Eczema
• If the history or distribution suggests contact allergy, investigate with patch testing
• If infected, treat both the infection and the eczema
• Avoid irritants (soaps – use aqueous cream, solvents, temperature extremes, irritating fabric)
• Moisturisers are often necessary (bath oils, urea cream, emulsifying ointment)
• If the area is weepy (maybe infected), try saline or KMnO₄ soaks
• Steroid cream appropriate to the site and planned duration of treatment
  ➢ Lotion for scalp
  ➢ Ointment for dry areas
  ➢ Cream
  ➢ Systemic for severe eczema
• Antihistamines for itch or urticaria (although itch is not always caused by histamines)
• Coal tar creams can help
• Pine tar may alleviate itch (eg pinetarsol in the bath)
• Phototherapy, azathioprine, cyclosporine for very severe eczema

A Guide to Steroids
• Mild:
  ➢ Hydrocortisone and Hydrocortisone acetate → Hydrocortisone
• Moderately potent:
  ➢ Clobetasone 17 butyrate → Eumovate
  ➢ Triamcinalone acetonide → Aristocort
• Potent:
  ➢ Betamethasone valerate → Beta
  ➢ Hydrocortisone 17 butyrate → Locoid
• Very potent:
  ➢ Clobetasol 17 propionate → Dermol
• Difficult to classify:
  - Methylprednisolone aceponate → Advantan
  - Mometasone furorate → Elocon

• Which steroid where?
  - **Face and flexures** – *mild steroids only*
  - **Scalp, palms and soles** – *tolerate very potent steroids for at least a few weeks; use mild to potent as maintenance treatment*
  - **Body and limbs** – *potent steroids for only a couple of weeks; mild to moderately potent as maintenance*

• More on steroids:
  - *Oclusion increases potency* eg covered by clothing, gloves, or a dressing; in a body fold; ointment base
  - *Continue treatment until eczema gone* – if you stop when it is eg 80% better, that patch of eczema will come back quite quickly
  - *Use the mildest treatment that will do the job* (although you may want to use a strong treatment briefly, to get things under control quickly)
  - Remember endogenous eczema is recurrent: choose treatments that are safe for continuous or repeated use

• Steroid side-effects:
  - Epidermal thinning
  - Striae
  - Skin fragility
  - Rebound flare?
  - Hypopigmentation
  - Systemic effects possible in some circumstances
  - Acneiform rashes on the face

**Sun Damaged Skin**

• Photo-damage = *Dermatoheliosis*
• Accelerates normal aging changes
• Increases risk of BCC, SCC, melanoma

• Damage results in:
  - Fine and coarse wrinkles
  - Altered pigmentation and texture
  - Comedones
  - Easy bruising: telangiectasia and purpura (thinned epidermis due to ↓basal cells + flattening out of dermo-epidermal junction → shearing forces rupture capillaries → bruising
  - Pseudoscars
  - Benign and malignant growths
  - Skin laxity
  - Diffusely thickened skin with yellowish micropapular appearance (especially temples), etc, etc

• Damage relates to life-time dose of UV:
  - Melanoma risk determined by age 15
  - ↑BCC and SCC risk

**Sunscreens**

• Sunscreens contain either chemical UV filters (cinnamates, PABA esters, salicylates, benzophenones, dibenzoylmethanes etc), or physical filters (titanium dioxide or zinc oxide)
• The vehicle (ie the kind of cream or gel or whatever that the filter is stuck into) also contributes to efficacy (is it photostable, does it rub off or sweat off?) and aesthetics (is it visible, sticky, etc)
• Behavioural changes – seeking shade, avoiding being outdoors in the middle of the day, clothing, hats etc are as important as sunscreen use
• The SPF factor refers to the sunscreen’s ability to block UVB, not UVA
• UVB : short wavelengths; causes sunburn
• UVA : longer wavelengths; less likely to cause sunburn
• Both UVB and UVA are implicated in photoageing and skin cancer
• UVB is more damaging, but UVA is harder to block out – it can penetrate sunscreens, cloudcover, clothing, glass. Choose a broad spectrum sunscreen effective in blocking both UVB and UVA
• The SPF is measured with sunscreen applied 2 mg/cm² thick, whereas the average punter actually puts on 0.5mg/cm² thick (because they don’t want to be covered in white gloop)
Heat and UV are not proportional

NZ (even Wellington) has much higher UV levels than Spain or the south of France, for example

The average UV Index in northern NZ in summer is over 12 with a peak of 15. In Southern Spain the median summer UVI is 9 with a peak of 11

How well clothes block UV depends on how tight the weave is – a crude test is to hold it up to the light: the better you can see through it the more UV it will let through

Lesions

- **Solar Keratosis:** = SK. See Premalignant Lesions, page 522
- **Cutaneous Horn:** horny outgrowth, arising from a SK, SCC or seborrheic keratosis. Treat according to underlying lesion
- **Disseminated Superficial Actinic Porokeratosis:** Caucasian. Autosomal dominant. First noticed in 40s. Up to 1 cm, slightly red/hyperpigmented on lower leg or forearms. Border has 2 parallel rows of scale
- **Bowen’s Disease:** See Premalignant Lesions, page 522
- **Chondrodermatitis:**
  - On sun damaged ears, may also be due to pressure
  - Common, M > F
  - Commonly on helix of pinna. *Painful* when pressed
  - Differential SCC (usually large and not as painful) or BCC (pearly, not often on rim of ear)
  - Treatment: excision (if annoying) including cartilage otherwise recurrence
- **Lentigines:**
  - Brown macules (look like large freckles)
  - Solitary, multiple or generalised
  - May be part of a syndrome (Peutz-Jegher)
  - In adults they are usually *sun induced*, on back of hand or back (but can see vulval/penile lesions – not sun-induced!)
  - Can get a solitary dark one on the lower lip after sunburn
  - Differential of dark ones: melanoma (use dermoscopy to differentiate)
  - May require excision to differentiate
- **Idiopathic guttate hypomelanosis:** pale spots in the shape and distribution of largish freckles on sun damaged skin (see pic above)
- **Freckle:** *brown macule*. Due to ↑ pigment production but anatomically normal. Fades if sun exposure ceases. Commoner in redheads

### Skin Neoplasia

<table>
<thead>
<tr>
<th>Type</th>
<th>Features</th>
</tr>
</thead>
</table>
| **Epidermal cyst**                         | - Derived from hair root shaft  
  - **Proliferation** of epidermis in the dermis  
  - Can become infected and **can recur** if not totally removed                                                                         |
| **Seborrhoeic keratosis** (basal cell papilloma) | - Derived from *stratum germinativum* cells  
  - **Confined to** epidermis  
  - Can see keratin horn cysts – round whorling lesions in the epidermis  
  - Exophytic keratinised, variegated  
  - Sits above skin surface  
  - Related to UV radiation                                                                                                           |
| **Keratoacanthoma**                        | - Starts as a lump **often on the lip**  
  - Grows and resolves rapidly  
  - **Inflammatory** cells seen at the base                                                                                               |
| **Dermatofibroma**                         | - **Fibrous tissue and blood vessels**  
  - Often seen on shoulders  
  - **Exophytic** with increased cellularity                                                                                               |
### Premalignant

**Solar keratosis (actinic keratosis)**
- UV exposure
- Dysplastic lesion (pleomorphic, high N:C, loss of normal architecture)
- Can progress to SCC (squamous)

### Malignant

**Basal cell carcinoma**
- Most common tumour, related to UV – elastin destroyed and thickened skin
- Common around the eyes
- Basal cell proliferation with dermal invasion – need a wide excision margin as can be multifocal
- Often see central ulceration with rolled edges
- See blue/purple dysplastic basal cells in nests, sometimes pallisading around BM
- Invades but rarely metastasises

**Squamous cell carcinoma**
- UV exposure, common around the lip
- Invades the dermis – seeds into blood vessels + lymphatics
- Late metastases
- Eosinophilic (pink) dysplastic squamous cells seen
- Keratin pearls seen – keratin seen as white scaling macroscopically

### Naevi and Melanoma

- Naevi = hamartomas (abnormal mixture of a tissue’s usual components) of the skin. With respect to melanocytes, a benign neoplasm
- Pigmented skin lesions:

<table>
<thead>
<tr>
<th>Lesion</th>
<th>Features</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Junctional naevus</strong></td>
<td>- Melanocytic proliferation at the epidermo-dermal junction</td>
</tr>
<tr>
<td></td>
<td>- Normal cellular morphology – no dysplasia</td>
</tr>
<tr>
<td><strong>Compound naevus</strong></td>
<td>- Melanocytic proliferation in the epidermis and dermis</td>
</tr>
<tr>
<td></td>
<td>- Normal cellular morphology – no dysplasia</td>
</tr>
<tr>
<td><strong>Intradermal/dermal naevus</strong></td>
<td>- Melanocytic proliferation in the dermis</td>
</tr>
<tr>
<td></td>
<td>- Normal cellular morphology – no dysplasia</td>
</tr>
<tr>
<td><strong>Lentigo maligna</strong> (Hutchinson’s melanotic freckle)</td>
<td>- In situ melanoma (no BM invasion)</td>
</tr>
<tr>
<td></td>
<td>- Often seen on side of face</td>
</tr>
<tr>
<td></td>
<td>- Neoplastic proliferation of melanocytes with melanin deposition in dermis</td>
</tr>
<tr>
<td></td>
<td>- Can progress to malignant melanoma</td>
</tr>
<tr>
<td><strong>Malignant melanoma</strong></td>
<td>- Neoplastic proliferation of melanocytes with melanin deposition in dermis</td>
</tr>
<tr>
<td></td>
<td>- Clinical features: irregular, variegated, bleeding/itching, shape change</td>
</tr>
<tr>
<td></td>
<td>- Asymmetry/appearance, Border, Colour, Diameter/depth, Elevation</td>
</tr>
<tr>
<td></td>
<td>- Histology features:</td>
</tr>
<tr>
<td></td>
<td>1. Cytologic features of malignancy:</td>
</tr>
<tr>
<td></td>
<td>- Malignant looking atypical melanocytes, seen in dermis also</td>
</tr>
<tr>
<td></td>
<td>- Dysplastic changes</td>
</tr>
<tr>
<td></td>
<td>2. Architectural features of malignancy:</td>
</tr>
<tr>
<td></td>
<td>- Pagetoid (upward) spread – tumour invading into epidermis</td>
</tr>
<tr>
<td></td>
<td>- Inflammatory infiltrate at the base</td>
</tr>
</tbody>
</table>
Melanocytic Naevi

- Acquired in childhood/early adulthood (genetic factors + sun exposure)
- Normal skin: epidermal cells, plus melanocytes, Langerhans cells (Antigen Presenting Cells – APC), prickle cells and melanocytes (sensory receptors)
- Moles tend to have a symmetrical shape + colour pattern; usually monotone or 2 colours
- Benign melanocytic naevi:
  - **Junctional**:
    a. Epidermis only, early active growth to <0.5 cm.
    b. Can be non-pigmented.
    c. Overgrowth of melanocytes in nests along the junction of the dermis and epidermis.
    d. Macular (ie not raised)
    e. Most common in children
  - **Compound**:
    a. Epidermis and dermis, older active growth (moles on palms, soles and genitalia stay junctional)
    b. Raised + generally lighter in colour than junctional naevi
  - **Intradermal**:
    a. Stopped growing, loss of tyrosinase → small and pale. Don’t have contact with the epidermal junction (ie are deep).
    b. Don’t become malignant – must have junctional activity to do this
- **Atypical mole syndrome** (dysplastic melanocytic naevi):
  - Uncontrolled proliferation without malignancy (> 100)
  - Mostly benign with possibility of malignancy
  - If have > 100 moles, 100 to 200 times normal risk
  - Risk of melanoma proportional to the number of moles, plus family history and degree of atypia
  - Management:
    o Self checking each month (at least **quarterly**)
    o Annual **doctor check** (to make sure they’re self checking)
    o Most moles that change aren’t melanoma, but if suspicious need to remove it
- Halo naevi:
  - Fairly common, especially in kids.
  - Depigmented symmetrical halo around the mole, but the mole is normal (cf depigmented melanoma where pigmented lesion is not normal and not central)
- **Pathogenesis**: ?Somatic mutation
- **Differential**:
  - Melanoma
  - Dermatofibroma: feels firm
  - Seborrhoeic keratosis: altered texture

Sebaceous Naevus

- Usually on the scalp
- Slightly raised, pinkish yellow, devoid of hair, often only a few cm
- At puberty, become more cobblestone in texture
- A variety of tumours arise in middle age, including BCC

Melanoma

- **Host Risk Factors**:
  - Skin colour
  - Naevi
  - Atypical mole pattern/syndrome
  - FHx (red hair/blue eyes)
Skin

- PHx non-melanoma skin cancer (doubles risk)
- Immune status

- Environment Risk Factors: UV light (geography, season, time), behaviour. Risk from sun determined by age 15. After that sunscreen mainly protects against squamous and basal cell carcinomas

- Epidemiology:
  - 1 – 3% of childhood cancers
  - Females 14/100,000, males 9/100,000. Difference is in the distribution on the legs

- Spotting them:
  - A: asymmetry
  - B: border irregularity – e.g. growing a peninsular
  - C: colour variability – 3 or more, colour not symmetrical, areas of black, variegated
  - D: diameter > 0.6 cm (although you can get smaller melanomas, and most larger lesions aren’t melanomas
  - E: elevation or enlargement → ↑ dermal penetration (but most are initially flat – superficial spreading melanomas

- Usually asymptomatic: don’t bleed until late (ie take bleeding seriously) and don’t usually itch

- Watch out for:
  - Lesions which look different to all the others – the odd one out
  - Geographic shaped moles (instead of round or oval)
  - Multicolored moles (ie 3 or more colors)
  - Black pigment
  - Change, bleeding etc
  - Bleeding, itching and halo (although can get two tone moles – OK if symmetrical)

- Lentigo maligna is a melanoma in situ; commoner in the elderly; often on the face or bald scalp; these usually progress very slowly

- Not all melanoma is pigmented – these are skin coloured secondary melanomas (amelanotic melanoma). Be suspicious about any odd looking lesion

- Progression:
  - Radial Growth Phase: initially growth is along the dermo-epidermal junction and within the epidermis
  - Vertical Growth Phase: Growth into the dermis → malignant cells in contact with lymphatics and capillaries → metastasis
  - Nodular melanoma: bad news
  - Acral Lentigenous Melanoma: on palms and soles

- Differential:
  - Benign mole
  - BCC
  - Seborrhoeic keratosis: stuck on appearance, monotone and symmetrical, greasy surface, numerous
  - Angiokeratomas
  - Dermatofibroma: firm, round, monotone
  - Any lesion under a nail (usually thumb) is a melanoma or SCC until proven otherwise

- Pathology:
  - Features of malignant cells: irregular, hyperchromatic, large N:C ratio, mitoses (blackberry nuclei), abnormal number of mitosis
  - Radical/Superficial/Horizontal growth phase: cells in contact with dermis, don’t metastasise
  - Vertical growth: mass of atypical melanocytes infiltrating dermis, lymphocytes, not necessarily pigmented, metastasises
  - Will always have junctional activity. If they only exist deeper in the dermis then they’re not malignant.

- Prognosis:
  - Breslow tumour thickness (> 0.76 cm bad) or Clarke’s levels (grade 1- 5, 3 ~ Breslow 0.76, bigger = worse)
  - Ulceration > 3 mm (bad)
  - High mitotic rate (bad)
  - Regression an indication of metastasis (bad)
  - Tumour infiltrating lymphocytes (bad)

- Treatment: surgical excision

- Hutchison’s Freckle: freckly ‘in-situ’ melanoma. Usually on face, tan macule that slowly enlarges and develops a geographic shape, multicoloured in time. Malignant change of melanocytes along the epidermis border but no infiltration. Takes years to become invasive. On sun damaged skin. On elderly watch for a while. Now showing up on younger people – excise before they get too big
Other Naevi

- Epidermal Naevi:
  - Defined according to their predominant cell type
  - Circumscribed distribution over a part of the body surface, usually dermatomal
  - Any size, never cross the midline, uncommon on face and head
- Sebaceous Naevi: hamartomas of predominantly sebaceous glands. Usually on scalp (lesion is bald). Raised, velvety surface, present at birth, usually small. ↑Risk of basal-cell carcinoma, but no longer prophylactically excised
- Dermal Melanocytic naevus (Mongolian spot): macular blue-grey pigmentation present at birth, over sacral area in Mongoloid and some other races. Looks like a large bruise. Rarely persist into adulthood.
- Congenital naevocellular naevus: Small is < 1.5 cm, intermediate = 1.5 – 20 cm, large is > 20 cm. If over lower sacrum →?spinabifida occulta. May arise or darken in puberty. Large ones have ↑risk of melanoma
- Spitz naevus: appears in early childhood as a firm, round red or reddish brown nodule. May bleed and crust. Benign. Local excision.

Other Tumours

Benign

- Epidermoid cyst:
  - Collection of epidermal cells within the dermis. Around the base of a hair follicle or from trauma (eg on a builders hands)
  - Face, neck, shoulders, chest
  - If it becomes infected → ulcerates and smells
  - May be tethered to the epidermis with a central keratin filled punctum (as in pic to right) + filled with smelly toothpaste like stuff
  - Treatment: surgical excision for cosmetic or nuisance reasons
- Seborrhoeic Keratosis (= Basal cell papilloma)
  - ↑Incidence with age, sun exposure, familial tendency, often associated with skin tags
  - Raised, sharply demarcated papule or plaque, shiny, bleeds easily if scraped Variable size, ‘stuck on’ appearance with cobblestone or leathery appearance, skin coloured, yellowish or greyish brown/black
  - Results from proliferation of squamous basaloid cells which sit on top of and do not invade the dermis (grow up, compared to BCC which grows down)
  - Histology: hyperkeratosis, well circumscribed, cystic structures within the epidermis filled with keratin
  - Treatment: liquid nitrogen for cosmetic reasons. Fairly harmless
  - Differential:
    - Melanoma – but different surface texture
    - Pigmented solar keratosis: treatment similar so differential not so important
- Keratoacanthoma:
  - Uncommon
  - Sun exposed sites eg on lip, up to 1 cm. Other areas up to 2 cm
  - Round skin colored nodule that grows in a few weeks to 1-2 cm
  - SCC can look exactly the same, but don’t usually grow this rapidly (but....they can do)
  - A ‘self healing squamous cell carcinoma’. Inflammatory reaction at the base – body is rejecting it
  - The keratoacanthoma develops a plug, like a cork, which increases in diameter until there is only a thin fleshy rim at the periphery. Then the plug falls out, leaving a shallow scar
- Dermatofibroma (= sclerosing haemangioma):
  - Slightly elevated and pink or brown. Firm, button-like dermal lesion. Usually female
  - Histology: expands into dermis
  - Not malignant – but recurs if not all cut out

Premalignant Lesions

- Actinic keratosis (= Solar Keratosis)
  - Common: 50% of NZers over 65
  - Dysplastic change in the epidermis (in situ proliferation of dysplastic squamous epidermal cells caused by UV light)
  - Not well circumscribed
  - Usually 3-5mm
  - Hyperkeratotic, rough surface (adherent scale, difficult to pick off)
  - Sun exposed site (face common)
- Usually a fair skinned person
- Although technically an intraepidermal SCC, the natural history of SK’s seems to be one of high turnover with new ones popping up and existing ones disappearing
- There is no evidence that treatment of SK’s reduces the risk of invasive SCC developing (it’s possible – but there is as yet no evidence for this)
- The conversion rate of solar keratoses to invasive SCC is thought to be << 1%
- A patient with lots of solar keratoses has a significant skin cancer risk and deserves some sort of surveillance
- It is appropriate to advise re sun protection
- Histology: large, irregular nuclei, overgrowth of epidermis, hyperkeratosis and parakeratosis
- No evidence that removal reduces the incidence of cancer – don’t need to treat but often do for cosmetic reasons
- Differential:
  - Bowen’s Disease: usually larger with a sharper margin
  - Discoid Lupus: erythema or pigmentation more marked, may have a pitted surface, more common in Polynesians
- Treatment:
  - Reduce sun exposure
  - Examine skin regularly for cancer
  - Remove lesions which are atypical, growing, annoying, unsightly
  - Liquid nitrogen or efudix (5-FU cream) or cryotherapy (painful, blistering, crusting, white mark) if few in number
- Bowen’s Disease:
  - Common
  - 75% are on the leg
  - Erythematous, well circumscribed, hyperkeratotic plaque (10-15mm)
  - Slightly raised plaque with irregular hyperkeratosis. Compared with BCC it’s not so shiny and has no pearly rim. May be bright red
  - SCC arises in 3%
  - May remain stable for a long time. If growing or bleeding or young patient → treat
- Differential:
  - Solar keratosis
  - BCC: shiny surface, pearly border, few dots of pigment
  - Psoriasis: silvery scale
  - Eczema
- Treatment:
  - Excision
  - Leave and watch

Malignant
- Basal cell carcinoma:
  - Most common malignant tumour
  - Because of their variable and sometimes subtle appearance, they can be tricky to diagnose
  - Commonest in fair freckly people
  - Risk factors: genes, and sun exposure in childhood
  - Location:
    - Face, neck, back of the ear
    - Back, chest
    - Leg, thigh
    - Forearm, arm
    - They are rare on the scalp (even if bald), and dorsum of the hand
  - Nodular BCC:
    - Flat and paler than surrounding skin, pearly or translucent, shiny. May have telangiectasia over the surface
    - Progresses to ‘rodent ulcer’ (ulcer with raised, rolled edges)
    - Often on bridge of nose where glasses sit
    - Differential:
      - Intradermal naevus: Don’t have the shiny, stretched look of a BCC
- SCC: usually in badly damaged skin, and not translucent
- **Superficial BCC:**
  - Red plaque +/- atrophy +/- dots of pigment. Usually well circumscribed. Raised rim. Less shiny. Commonest on back, arms, legs, behind ears
  - Can be **linear**, multiple, subtle, pigmented
  - **Most common** form of BCC
  - **Differential:**
    - Eczema: weep-y, fissured surface, itchy (BCC isn’t), atypical sites for a BCC
    - Psoriasis: silvery scale
    - Bowen’s disease: duller surface with more hyperkeratosis, also superficial BCCs are common on the back and Bowen’s is not (both are common on the legs). Bowen’s tends to have a rough surface, BCC is shiny or atrophic, BCC may be pigmented
- Don’t metastasise but does **invade**. Won’t kill you (at least quickly)
- Histology: basophilic (blue) cells, palisaded around the edge
- **Squamous cell carcinoma:**
  - Skin coloured or purplish nodule/plaque which may ulcerated
  - Nodular, with a dull, hyperkeratotic surface (margins less well defined than BCC)
  - SCC tend to occur on chronically sun damaged skin eg head, dorsa hands, forearms, legs and tops of feet (BCC’s uncommon on these sites)
  - **SCC don’t have the shiny look** that BCCs do + no telangiectasia
  - May have cutaneous horn. Fleshy layer at the base of the horn differentiates it from benign lesions
  - Commonly misdiagnosed as BCC
  - If neglected will invade (claw-like infiltration)
  - 4% metastasise
  - On sun exposed areas, may have cutaneous horns
  - Histology: hyperkeratosis

**Treatment of Skin Cancers**
- Melanoma’s are **always excised** (except for lentigo maligna in a very elderly patient – one may choose to wait and watch, given their slow progression into invasive melanoma)
- BCC’s and SCC’s are **usually excised**
- Both can be treated with **radiotherapy**
- Superficial multifocal BCC’s (which clinically are flat or nearly flat lesions) can sometimes be treated with **cryotherapy, efudix cream (SFU), imiquimod cream, or photodynamic therapy**

**Ulcers**

**Venous Stasis Ulcers**
- 70 – 90% of ulcers on lower extremities are due to venous insufficiency (eg varicose veins)
- Below the knee, never on the sole of the foot, usually around the malleoli
- Unlike ulcers due to arterial insufficiency, will have good peripheral pulses and no peripheral neuropathy
- Usual isolates: S aureus and/or various G –ive bacilli (including Pseudomonas aeruginosa and other aerobic G-ive’s)
- Treatment: in absence of extensive surrounding cellulitis or systemic signs, there is no role for systemic antibiotics

**Pressure Ulcers**
- = Skin necrosis and ulceration as a result of pressure induced ischaemia
- Incidence over a 3 week period of bed and chair bound patients is about 8 %
- **Critical factors in their development:**
  - Pressure: Muscle and subcutaneous tissue are more vulnerable than epidermis. Pressure leads to venous, arteriolar and lymphatic occlusion. Especially over bony prominences
  - Shearing: Sliding of adjacent surfaces (eg sacral skin on underlying bone) → vulnerability to pressure induced obstruction
  - Frictional forces: Eg from being pulled across sheets → intra-epidermal blisters
  - Moisture: eg urinary incontinence, also sweat and faeces. ↑Risk of pressure sores 5 times
  - **Risk factors:** age (loss of blood vessels, epidermal atrophy etc) and immobility
  - Staging:
1: irregular, ill-defined area of soft tissue swelling, induration and heat. Reversible
2:Plus inflammatory and fibroblastic response. Extends through dermis and into subcutaneous fat. Reversible
3:Plus undermining of edges
4:Plus underlying muscle and bone

- Infection. All pressure areas become contaminated. Impairs healing. Can lead to bacteraemia (usually polymicrobial) with high mortality
- Site: most at the sacrum, heel, ischial tuberosities and greater trochanter

Management:
- Prevention (responsibility of all involved professionals)
- ↓pressure: change of positioning, padding, alternating air cell mattresses
- ↓Friction: appropriate bed clothes, no particles in bed (eg food)
- ↓Moisture: Pads, catheters, reduced sweating
- ↓Shearing: avoid shearing positions (eg propped up in bed)
- Established sores: Good nutrition, oral vitamin C, topical antibiotics (but ↑resistance), saline dressings + variety of preparations/dressings. If stage 3 or 4 then consider debridement or skin grafts

**Other Ulcers**
- Ischaemic ulcers:
  - Large artery disease: usually lateral side of the leg, pulses absent
  - Small vessel disease (eg vasculitis): palpable purpura
- Malignant ulcer: eg basal cell carcinoma (pearly translucent edge), squamous cell carcinoma (hard everted edge), etc
- Neuropathic ulcer: painless penetrating ulcer on the sole of the foot due to peripheral neuropathy (eg diabetes, leprosy)
- Underlying systemic disease: Diabetes, pyoderma gangrenosum, rheumatoid arthritis, lymphoma

### Inflammatory Skin Lesions

<table>
<thead>
<tr>
<th>Condition</th>
<th>Description/features</th>
<th>Histology</th>
</tr>
</thead>
</table>
| **Psoriasis vulgaris** | - Infl condition associated with rapid epidermal turnover (3-4d cf 28d)  
- May be inherited, ass. with trauma/infection/childbirth  
- Elbows/knees/scalp | 1. Parakeratosis  
2. Acanthosis  
3. Microabscesses in stratum corneum  
4. Dermal papillae oedema |
| **Pustular psoriasis** | - Infl condition associated with rapid epidermal turnover (3-4d cf 28d)  
- Can be an emergency – secondary infection + electrolyte disturbance  
- Can be generalised or localised | As above + abscess formation within the epidermal layer |
| **Pemphigus (pemphigus – confined to epidermus – is worse)** | - Intraepidermal bullous (blisters) lesions  
- Auto-Ab against stratum spinosum (junctions b/w epidermal cells)  
- Consequent acantholysis – breakdown of stratum spinosum  
- Oral, nasal mucosa and skin  
- 40% mortality | 1. Acantholysis  
2. IgG seen ABOVE BM (seen using immunofluorescence) |
| **Pemphigoid (bullous pemphigoid)** | - Subepidermal bullous (blisters) lesions  
- Auto-Ab against junctions of basal epidermal cells  
- Skin  
- Usually self-limiting, chronic relapsing | 1. IgG + C3 IN BM (seen using immunofluorescence)  
2. Blisters seen as cavities – below the epidermis  
3. Eosinophils (pink) |
### Verrucae

- **Warts** – HPV
- **Verruca vulgaris** (common warts), plana (flat warts), plantaris (feet), palmaris (hands), condyloma acuminatum (genital)

- 1. Hyperkeratosis/parakeratosis
- 2. Acanthosis
- 3. Nuclear and cytoplasmic inclusions
- 4. Perinuclear vacuolation

### Molluscum contagiosum

- **Pox virus** causing papular skin rash
- Resolves on its own

- 1. Acanthosis
- 2. Molluscum bodies

### Impetigo

- **Staph or strep**
- Blisters, later forms ulcers, may scar

### Psoriasis

- **Epidemiology:**
  - Begins at any age but two peaks: *late teens + late 50s*
  - ~2% of the population
- Chronic characterised by rich red, *erythematous silvery scaly plaques*. May or may not itch
- May be inherited (autosomal dominant with mixed penetrance)
- Precipitated or aggravated by:
  - Cigarette smoking and alcohol consumption
  - Strep infection
  - Trauma (Koebner phenomenon; turns up in areas of damaged skin eg sun burn)
  - Hypocalcaemia
  - **Drugs:** lithium, beta blockers, Antimalarials, withdrawal of systemic steroids
  - Stress
- Characterised by rapid turnover of epidermis. *Normally 28 days, reduced to 4 days → parakeratosis*
- ~10% (10-40) have associated *arthritis*
- Histology: epidermal squamous cell hyperplasia, neutrophil accumulation
- **Psoriasis vulgaris:**
  - Elbows, knees, scalp
  - Histology: *parakeratosis, acanthosis*, focal thinning, oedema of dermal papillae, *micro-abscesses* in the stratum corneum
- **Pustular psoriasis:**
  - Abscess formation within the epidermal layer → widespread sloughing → risk of infection/electrolyte imbalance
  - Common on the palms and soles. The pustules are usually sterile, and result from accumulation of neutrophils in the epidermis
  - DDx of pustules is a pustular drug reaction
  - **Generalised** (rare and life-threatening) or **localised** (most commonly palms and soles)
    - Generalised:
      - Often abrupt onset with fever and malaise
      - Erythema with *thousands of tiny pustules*. *No* silvery scale
      - Most likely to occur if a patient with severe or unstable psoriasis has been treated with **systemic steroids** – which is why systemic steroids are relatively contraindicated in psoriasis
- Nail involvement: pitting, discoloration, subungual hyperkeratosis and onycholysis (especially *lateral*)
- May be erythrodermic, in which case the typical silvery scale is lost
- **Differential:**
  - Bowen’s disease: usually over leg
- Superficial BCC
- Eczema: may show lichenification or fissures or vesicles
- Lichen planus
- Fungal: do a scraping
- Discoid Lupus: face, leaves scars, has plugs of follicular hyperkeratosis
- Seborrheic dermatitis

- Treatment:
  - Mild steroid creams for face and flexures
  - Stronger steroid creams for short periods on trunk and limbs (but rebound flare up)
  - Coal tar creams: messy and smells
  - Dithranol + salicylic acid in white soft paraffin
  - Scalp: steroid of Betnovate strength to shift scale then a maintenance cream
  - Narrow band UVB treatment or PUVA (photochemotherapy): Psoralen tablets to photosensitise 2 hours prior to UVA treatment
    - Phototherapy is done 2 or 3 times a week
    - The success rate is about 80% with NBUVB and PUVA
    - The patient has to go somewhere eg the hospital, or a private clinic, in order to have their treatment
    - There is an increased risk of skin cancer with PUVA after 200 or so treatments.
    - Generally the patient has to attend for several weeks to clear their psoriasis
  - If severe: methotrexate, neotigason, azathioprine, cyclosporin, etc
  - Treatment of psoriasis by site:

<table>
<thead>
<tr>
<th>Site</th>
<th>First line therapy</th>
<th>Second line therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Scalp: thick scale</td>
<td>Moderate to potent topical steroid cream for several days</td>
<td>Calcipotriol or tar creams; mixtures of tar/salicylic acid/steroid.</td>
</tr>
<tr>
<td>Scalp: mild scaling, or scalp maintenance treatment</td>
<td>Steroid scalp lotion; calcipotriol lotion; tar shampoo; anti-dandruff shampoo</td>
<td>Calcipotriol (sometimes irritates), tar (smelly), pimecrolimus cream (costly)</td>
</tr>
<tr>
<td>Flexural or facial psoriasis</td>
<td>Mild steroid cream</td>
<td></td>
</tr>
<tr>
<td>Palms and soles</td>
<td>Potent steroid cream</td>
<td>PUVA, Methotrexate, Neotigason</td>
</tr>
</tbody>
</table>

- Treatment of psoriasis by extent of involvement:

<table>
<thead>
<tr>
<th>Severity</th>
<th>First line therapy</th>
<th>Second line therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 25% body surface involved</td>
<td>Steroid cream (potency depends on site); calcipotriol cream</td>
<td>Tar cream; narrow band UVB</td>
</tr>
<tr>
<td>Generalised plaque psoriasis</td>
<td>Steroid cream; tar cream; calcipotriol cream; narrow band UVB</td>
<td>Methotrexate, Neotigason, PUVA; Azathioprine, Cyclosporin</td>
</tr>
<tr>
<td>Erythrodermic</td>
<td>Methotrexate; Neotigason</td>
<td>Azathioprine, Cyclosporin</td>
</tr>
</tbody>
</table>

**Bullous Lesions**

- Epidermis sloughs off dermis
- **Intraepidermal**: if any of the epidermis is left attached
  - Burns
  - Herpes
  - Pemphigus (epidermis; wurse):
    - 40 – 60 years, very fragile blisters skin, and also on oral and nasal mucosa
    - Bullae are fragile + flaccid
    - Less common than Pemphigoid but more serious (40% mortality)
    - Often starts with oral lesions (can precede skin eruptions by months)
    - A generalised phase may occur within a few months
    - Even with treatment the mortality is 10%
    - Histology: BM is intact, acantholysis
    - Pathogenesis: autoimmunereaction to desmosomes in the epidermis → infection etc. IgG above the basement membrane. Chicken-wire pattern on immunofluorescence within the epidermis
    - In pemphigus foliaceous, acantholysis (and antibody deposition) occurs only in the superficial layers. In pemphigus vulgaris the full thickness of the epidermis is involved. That’s why in pemphigus vulgaris the bullae are so fragile – the epidermis literally falls apart
    - Pemphigus vulgaris:
- **Suprabasal** lesions. More serious of the two.
- Mucosal and scalp involvement, more fragile blisters, looks like burn
- Generalised bullous phase ~ 5 months after the onset of oral lesions
- Heals *without* scarring. Patients are ill
- Fluorescence extending throughout *entire* epidermis

  - Pemphigus foliaceous:
    - Acanthosis only in the *superficial* epidermis; superficial variant, involving the *upper layers* of the epidermis
    - *It can look a bit like eczema* – it can be localised, generalised, even erythrodermic
    - Is a ‘benign’ form of pemphigus. Like pemphigus vulgaris one can induce lesions with pressure and slight shearing force on unaffected skin (**Nikolsky sign**)
    - Small flaccid blisters, rupture leaving erythematous lesion, heals with crustung and scarring
    - Face, scalp, chest and back. Oral lesions *not* common
    - Fluorescence in *upper part* of epidermis only

- Treatment of Pemphigus:
  - Pemphigus vulgaris: *high dose* steroids (80mg/d)
  - Pemphigus foliaceous may respond to *topical* steroids or low dose prednisone
  - Other immuno-suppressing agents also used eg methotrexate, cyclosporin

- **Subepidermal:**
  - **Pemphigoid:**
    - Due to binding of IgG autoantibodies to hemidesmosomal proteins, causing the *epidermis to separate from the dermis* (the cleavage is in the dermo-epidermal junction)
    - *Tense*, localised, sturdy, grape-like blisters, generally rest of skin remains intact
    - Because the whole intact epidermis forms the blister roof, the blisters are sturdy, and can grow to a large size. They don’t break easily, but if they do the blister base is dermis ie raw, and sore.
    - Ruptured lesions heal rapidly. *No* oral involvement
    - Usually one gets large *tense* blisters, and itch
    - May begin in a localised fashion and become widespread
    - May be preceded/accompanied by urticarial or erythematous areas
    - Usually self-limiting, chronic relapsing, > 60 years. Can become generalised
    - Histology: epidermis lifts in total at the dermo-epidermal junction
    - Pathogenesis: IgG in the BM, linear pattern with direct immunofluorescence (seen in 90-100%)
    - About 70% of patients have circulating antibodies
    - **Differential:**
      - Diagnosis of bullae difficult. Usually need to refer, and histology (*prior* to treatment) usually necessary
      - Reactions to plants and insect bites, other autoimmune diseases such as pemphigus and linear IgA disease to name a few
      - In advanced old age it is a common condition. In any other age group it is best to seek advice re biopsy etc
      - Eczema (but not itchy)
      - Russian hog weed et al
    - Treatment:
      - Systemic steroids: may need 20 – 40 mg per day. Unsuitable for long term use → problem especially in the elderly
      - Potent topical steroids if localised
      - Tetracycline 1 – 2 g per day, especially in elderly
      - Other immunosuppressive treatment (eg methotrexate)
Treatment is generally continued for 1-5 years

- Pemphigus vs pemphigoid:
  
<table>
<thead>
<tr>
<th>Pemphigus</th>
<th>Pemphigoid</th>
</tr>
</thead>
<tbody>
<tr>
<td>Epidermal cells float apart (acantholysis) because of antibody ‘attack’ on intercellular (epidermal) substance. In pemphigus foliaceous only the superficial epidermis is involved.</td>
<td>The split is in the basement membrane zone because of antibody attack on BMZ protein. The epidermis is intact and forms a sturdy blister roof.</td>
</tr>
<tr>
<td>Fragile flaccid bullae</td>
<td>Usually large tense sturdy bullae</td>
</tr>
<tr>
<td>Often oral involvement</td>
<td>Don’t often get oral involvement</td>
</tr>
<tr>
<td>In pemphigus vulgaris patients may appear ‘ill’ and there is significant mortality.</td>
<td>Low mortality, although can be debilitating in the elderly</td>
</tr>
</tbody>
</table>

**Lupus Erythematosus**

- Interaction of genetic, environmental, hormonal factors
- There is a spectrum of clinical forms
- Skin involvement occurs in about 75% - it can be specific or nonspecific; it can be localised or generalised; it can occur by itself or in association with systemic symptoms
- The specific skin manifestations can be classified as:
  - Acute (eg the butterfly rash of SLE)
  - Sub-acute
  - Chronic (the commonest of which is discoid lupus erythematosus)
- The most common non specific skin manifestations are leukocytoclastic vasculitis, and livedo reticularis (dilation of capillary blood vessels and stagnation of blood within these vessels causes mottled discolouration of the skin. It is described as being reticular cyanotic cutaneous discolouration surrounding pale central areas). These are nonspecific because they occur in other conditions too.

**Discoid Lupus Erythematosus (DLE)**

- = mild end of Lupus spectrum and much much more common than SLE
- Mild skin rash, normal serum ANAs and ENAs
- Rash usually on the face, usually crosses the nose, sometimes scalp, ears, nose, arms
- Erythematous plaques varying from several mm to several cm. Adherent scale (not flaky like eczema) and pitted surface. Rough feel, doesn’t itch. May heal with hyperpigmentation or white scar. Scarring alopecia
- Alopecia in scalp lesions which is normally permanent
- More common in Polynesians and Maori, F > M
- Only about 5% have systemic involvement
- Characteristic histology and direct immunofluorescence (DIF) +ive
- Differential:
  - Eczema (doesn’t scar, uncommon to get discoid eczema on face, eczema can be weepy)
  - Solar keratosis or Bowen’s (but patient usually too young for these + SK are less inflammatory + don’t have a pitted surface – the hyperkeratosis is more irregular)
- Treatment:
  - Topical or intralesional steroids: fairly potent ones but be careful on the face. Systemic if widespread
  - Sun protection
  - Antimalarials (eg hydroxychloroquine. SE: eye problems → regular check-ups)
  - Topical Retinoids – also ↑ penetration of topical steroids
- See also Systemic Lupus Erythematosus, page 439

**Scleroderma**

- Like lupus, scleroderma is a continuum of disease. Like lupus, the commonest form of scleroderma is cutaneous, without systemic involvement.
- Morphea is characterised by fibrosis in the dermis and/or subcutaneous tissues. Unlike systemic sclerosis there is no sclerodactyly, Raynaud phenomenon or telangiectasia.
- Occasionally it is associated with arthralgia or dysphagia. Less than 5% progress to systemic scleroderma

**Morphea**

- Localised cutaneous scleroderma, occurs any age but especially 20 - 40
- Thickened dermis with dense collagen, progressive loss of subcutaneous fat

**Skin**
Skin

- The fibrosis destroys sweat glands and hair
- Plaques have a waxy texture with a grey-lilac color. Often hyperpigmentation at the margin. Usually asymptomatic
- Linear forms of scleroderma may extend along a limb or down the face
- Vary in size from 2 – 15 cm with lilac coloured edge
- Any site, especially the trunk
- Tend to improve over time (years)
- Treatment: intralesional steroid
- See Progressive Systemic Sclerosis (PSS), page 442

Vitiligo

- Slowly progressive amelanotic macules, initially on sun exposed areas
- Usually symmetrical. Face, axillae, hands, groin, elbows and knees, are the common sites
- Affected areas prone to sunburn
- Associated with family history (30-40%) and other autoimmune disorders (e.g., alopecia areata: AI hair loss)
- In 50% develops before age 20
- Differential:
  - Tinea versicolor (but hypopigmented, not amelanotic, and scaly)
  - Pityriasis alba (but hypopigmented, not amelanotic, and scaly)
- Treatment: usually unsatisfactory
  - Phototherapy: PUVA or narrow band UVB (may need 2 or 3 treatments a week for a year)
  - Various surgical procedures

Acne

- Inflammatory disease occurring in and around the sebaceous glands, affecting the face (99%), also the chest (60%) and back (15%)
- Characterised by comedones, papules and pustules, or by cysts and other more specific lesions
- Comedones are not inflamed: a closed comedone is a whitehead (below left), and an open comedone is a blackhead (below middle); both (in below right)

  - Deeper lesions are associated with scarring: hypertrophic, keloidal or depressed
  - In most cases acne starts in adolescence and resolves in mid twenties
  - Acne can also occur in infants (usually male)
  - 12% of women over the age of 25 have some degree of acne
  - Acne, especially in women, may start in the 20's or 30's
  - Rarely, acne can persist into the 50's or 60's, or older
  - Presentations:
    - Papulopustular acne
    - Nodulocystic acne
  - Differential:
    - Rosacea
    - Perioral dermatitis
    - Acneiform drug eruptions

Pathogenesis

- Four factors:
  - 1. Increased sebum production by the sebaceous glands (normally produced to maintain epidermal hydration)
  - 2. Cornification (→ blockage) of the pilosebaceous duct: abnormal keratinisation and desquamation of follicular epithelium combine with increased amounts of sebum production to obstruct the duct
3. **Bacterial proliferation** - abnormal colonisation of the follicle duct by *Propionibacterium acnes*. But severity is not proportional to number of bacteria. *Propionibacterium acnes* may produce inflammatory mediators which contribute to the production of inflammatory lesions

4. **Inflammation**

- If the obstruction is closer to the skin surface it will form open comedo and oxidation of the fatty material causes discoloration (blackhead). A closed comedo (white head) occurs when the duct is blocked at a deeper level

- Acne is dependent on:
  - **Genetic** factors (high concordance in monozygotic twins); inherit the propensity for follicular epidermal hyperproliferation, plugging the follicle
  - **Hormonal** factors: *androgens* → sebum production
  - **Environmental** factors: blockage of the pilosebaceous orifice by topical agents, or swelling of corneocytes in humid conditions, may aggravate acne
  - Diet rarely implicated

- Usually starts in adolescence and resolves by mid 20s (starts earlier in females and is more persistent)

**Management**

- **Reassurance**: Treat as a physical and psychological disorder. Undermines patient’s self-confidence, especially in the adolescents. **Myths of poor diet and hygiene make patients feel responsible and/or guilty - reassured** that they are not the cause

- **General advice**:
  - Avoid humid conditions
  - Avoid occlusive creams and sunscreens
  - Only use moisturisers if the skin is dry
  - **Sunshine** may help

- **Topical agents**. For mild to moderate acne:
  - Comedolytics: most effective option is **Tretinoin (topical retinoid [vit A derivative]:** result in proliferation and reduced keratinisation of skin cells independent of their functions as a vitamin)). Normalises desquamation of the follicular epithelium promoting drainage of pre-existing comedones. This increases penetration of antimicrobial agents
  - Antibiotics such as **benzoyl peroxide** (AB + helps to unblock the pilosebaceous ducts) and **erythromycin/clindamycin** gel reduce bacterial numbers and inflammation

- **Oral agents**. Are generally used for severe or persistent acne in addition to topical agents:
  - **Antibiotics** such as tetracycline, **doxycycline**, minocycline, trimethoprim and erythromycin suppress inflammation by inhibiting neutrophil chemotaxis and production of bacterial lipases and proteases. For a minimum of six months with an 80-90% improvement expected after this time. Often recur. **SE of Minocycline**: vertigo, discolouration of teeth, grey skin pigmentation, discolouration of teeth, flatulence, diarrhoea
  - Oestrogens. They have a **direct effect on sebaceous gland activity**. They are combined with progesterone in an oral contraceptive, which may counteract the effects of the oestrogen
  - **Antiandrogens** (in a female only) such as cyproterone acetate and spironolactone act peripherally to inhibit androgen stimulation of sebaceous glands and hair follicles. They are useful in mature presenting acne
  - **Isotretinoin** (**Roaccutane**)
    - A synthetic Vitamin A derivative that inhibits sebaceous gland activity, reduces P. acnes cell numbers, alters follicular keratinisation and is anti-inflammatory
    - Isotretinoin is about **97% successful**
    - It is the only treatment that produces long term or permanent remission of acne
    - All other treatments need to be used long term until acne resolves of its own accord
    - Other treatments have much fewer side effects
    - **Highly teratogenic**: Women need to be fully informed of the risks, need to have a negative pregnancy test before starting treatment, and need to be on reliable contraception throughout course (i.e. belt and braces) and one month after
    - Causes **liver damage** and hyperlipidaemia: baseline bloods and then after one month
    - Causes **dry lips and maybe nasal mucosa** (→ epistaxis), skin and eyes, **angular cheilitis**, sun sensitivity
    - < 10% will get aching muscles, depression, hair loss, headaches
    - See Retinoids, page 537

**Rosacea**

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**Skin**
Cardinal signs in order of importance:
- Erythema
- Telangiectasia
- Papules
- Swelling
- Tiny pustules

On cheeks, chin, forehead, nose and neck, sun exposed sites. Flushing may precede other signs

Many theories as to cause

Usually seen in middle aged or older fair skinned people with other evidence of sun damage

It is very rare in Asians and Polynesians

May be associated with rhinophyma (bulbous swelling of the nose)

Minor ocular involvement in 50%: especially conjunctivitis, maybe blepheritis, etc

Treatment:
- Systemic or topical antibiotics (as per acne) such as erythromycin/clindamycin
- Retinoids
- Metronidazole (systemic or topical)
- Commonly one uses a tetracycline antibiotic for a month or two, and then perhaps a topical agent to prevent recurrences

Perioral Dermatitis

- Not a dermatitis at all
- Mainly young women
- Cause a mystery. Can be caused by topical steroids
- Starts in nasolabial fold + spreads to involve the perioral area. Micropapules + pustules on an erythematous base with some scaling
- No comedones
- Treatment: Systemic tetracyclines or erythromycin until rash gone then for another couple of weeks

Other Skin Lesions

Erythema Multiforme/Stevens-Johnson Syndrome/Toxic Epidermal Necrolysis

- Confusion/overlap between Erythema Multiforme (EM), Stevens Johnson Syndrome (SJS; severe fever + mucosal involvement eg mouth, eye, genitals) and Toxic Epidermal Necrolysis (TEN) [Later two at the severe end of the spectrum]
- Varying degrees of mucosal involvement and rash
- Typical lesion: target lesion – dull red macule or maculopapule 1 – 2 cm across, erythematous rim with cyanotic or purpuric centre. May be blistering. Typically affects acral areas (dorsal hands, feet, palms, soles, forearms, legs)
- Usually crop over a couple of days and fade after 3-6/52
- Trunk only in extensive reactions. Also if severe: erosions, haemorrhagic crusting, lesions uncomfortable (not usually painful). May affect cornea. May get systemic upset (fever, anaemia, etc)
- Histology: vacuolar degeneration of lower epidermis
- Provoking factors:
  - HSV – major cause. Rash worst at periphery (+/- oral mucosa). Will get it with subsequent outbreaks as well. History: Do you get cold sores?
  - Mycoplasma (<1% of EM)
  - Drug reactions – more likely if severe outbreak. Not typical targets (eg red blotches), on trunk as well as acral, may be blistered. Implicated drugs: penicillins, anticonvulsants: phenytoin, barbiturates, carbemazepine, sulphonamides, NSAIDs, allopurinol. Stops drugs if at all possible. Treat like a burn. Steroids controversial
  - Idiopathic

Erythema Nodosum

- Lesions: 2 –4 cm, erythematous, tender, especially on shins but also on thighs or forearms. A little raised. Look like purplish bruises
- Number from 2 – 50 (usually 5 – 6), erupt over 10 days and subside over 3 – 6 weeks
- Regress with bruise like yellow/green colour changes
- Systemic signs: fever, generalised aching and malaise
- Due to deposition of immune complexes in and around venules in the deep dermis
- Causes:
  - Kids: Streptococcal infection
  - Sarcoidosis (rare in kids)
  - TB
  - Cat scratch disease
  - Yersinia
  - Some drugs
- Differential:
  - Nodular vasculitis (tend to ulcerated, don’t heal with bruise like changes)
  - Meningococcal or gonococcal septicaemia (smaller lesions, often purpura, ill patient)

**Erythema Toxicum Neonatorum**
- Up to 50% of full term infants (less if preterm), occur up to 4th day
- Erythematous macules, wheals, papules and pustules – few to several hundred
- Face, buttocks, torso, proximal limbs, not palms or soles
- Usually resolves in several days
- Cause unknown
- Differential: HSV

**Urticaria**
- = Hives or welts. Intensely itchy.
- Transient erythematous/oedematous swellings on dermis/subcutis (increased permeability of capillaries)
- Normally last <24hrs
- Can be due to immune mechanisms but at least 50% are not allergic
- Relationship to allergy and atopy:
  - More likely in atopy
  - 50% related to allergy – type 1 only ⇒ exposure 15 – 30 minutes prior to onset and last < 24 hours ⇒ careful history
  - Allergy likely to be all over, and no further outbreak for weeks/months
  - Most chronic urticaria is non allergic
  - Some foods/drugs may cause urticaria without immune involvement (ie histamine release without IgE involvement)
- Common causes:
  - Idiopathic – common
  - IgE mediated:
    - Food: peanuts, strawberries, dairy, eggs
    - Animal dander: horses, cats
    - Other: drugs, latex, stings
  - Physical: pressure, cold, heat
  - Complement mediated: hereditary angioedema and blood transfusion reactions
  - Mast cell releasing agents: opiates, penicillins
  - Prostacyclin inhibitors: Aspirin, NSAIDs
  - Infections: cause of 80% of acute childhood urticaria (eg hepatitis)
  - Serum sickness: type 3 reaction. Drugs, especially penicillin. Fever, raised ESR, starts within 5 – 20 days of exposure and lasts 5 – 28 days. See Allergy, page 497

**Papular Urticaria**
- Reaction to an insect bite
- Itchy, urticarial weal → firm itchy papule (see ‘crops’ of 3-5 urticarial papules)
- Each crop resolves in about 10 days but may persist for months
- Treatment: try insect repellent
- If dark skin, may be post-inflammatory hypopigmentation

**Alopecia Areata**
- Circumscribed areas of hair loss but skin normal.
- Presentations:
- Often scalp – with a few bald areas 1 – 3 cm
- Loss of all scalp hair is alopecia totalis
- Loss of hair at all sites is alopecia universalis
- Not a diagnosis
- Autosomal, autoimmune dominant disorder with variable penetrance
- Duration < 1 year in 50 %, relapse common. Kids get it worse
- Associated with Atopy, Downs, Hashimoto’s Disease, Pernicious Anaemia, Addison’s Disease, Vitiligo
- Treatments include local steroids, topical minoxidil (antihypertensive), etc
- Differential diagnosis: all produce circumscribed hair loss, but skin itself is abnormal
  - Fungal infections
  - Anything causing scarring (eg skin cancer)

Graneloma Annulare
- Ring of smooth, firm, skin coloured or slightly purplish papules from 1 – 5 cm. No scaling (cf ring worm which is) or blistering (= epidermis fine)
- Enlarged centrifugally, with beaded rim gradually flattening until it disappears without trace within 2 years
- Dorsal surfaces of feet, hands and fingers are the commonest sites
- Lymphohistiocytic granulomata
- Mainly children and young adults
- Can treat with intra-lesional steroids

Lichen Planus
- Occurs in 30 – 60 year olds. Insidious onset, can be explosive, localised or generalised. In 80% resolves in 18 months
- Is thought to be due to an abnormal immune reaction provoked by a viral infection
- Inflammatory cells seem to mistake the skin cells as foreign and attack them
- Clinically: flat topped papules, discrete or coalescing. Lacy network of white lines on papules = Wickham’s Striae. Can also get annular, hypertrophic, atrophic or even bullous forms. Often form linear lesions (Koebner phenomenon). Itch variable. Rash resolves with hyperpigmentation. Can be painful on lips or genitals
- Looks like everything else. Differential:
  - Plane warts
  - Eczema
  - Drug reaction: gold, quinine, thiazides, etc
- Treatment: Acitretin (retinoid), steroids, miscellaneous

Koebner phenomenon:
- Is where a skin disease preferentially occurs in an area of damaged skin
- It may occur in scratch marks (which results in linear rash), or in other areas of trauma (surgery, sunburn etc), or it may overlap other kinds of rash
- Psoriasis, lichen planus, and vitiligo may all display the Koebner phenomenon
- For example, someone with psoriasis who develops chicken pox may find that their chicken pox rash transforms into patches of psoriasis

Tuberous Sclerosis
- Disorder of haematoma formation: especially in eye, brain, skin, kidney and heart
- Skin lesion:
  - Angiofibromas: appear from 3 – 10, firm, discrete red/brown telangiectatic papules, 1 – 10 mm, cheeks and chin
  - Periungual fibromas: smooth skin coloured excrescences emerging from the nail folds
  - Shagreen patch: skin coloured plaque in lumbosacral region
Oval white macules (Ash-leaf-macules) seen under Woods light. But also similar lesions common in normal kids.

- Classically (but not invariably) seen with epilepsy and mental retardation (‘zits, fits and nit-twits’)
- Autosomal dominant with variable penetrance, 50% are new mutations
- Prevalence ?1/10,000

**Neurofibromatosis**

- Neurocutaneous syndromes (others = tuberous sclerosis, von hippel-lindau syndrome)
- Look like intradermal naevi but soft

**Type 1:**

- Commonest, 1/3000, *Autosomal dominant*, 30% new mutations
- See:
  - Multiple neurofibromas arising from peripheral nerves
  - Café-au-lait spots
  - Astrocytoma of optic nerve

**Type 2:**

- 2 or more of:
  - 6 or more café-au-lait macules over 5 mm in pre-pubertal patients
  - 2 or more neurofibromas
  - Freckling in axillary or inguinal regions
  - Optic glioma
  - Others
- Characterised by bilateral acoustic neuromas (acoustic neuromas – CNVIII; spindle cells; biphasic – loosely + densely aggregated tissue)
- May lead to short stature, macrocephaly, kyphoscoliosis, intellectual handicap, endocrine problems (precocious puberty, acromegaly, Addison’s), neuro tumours (optic nerve glioma, astrocytomas), etc
- See Other Congenital Skeletal abnormalities, page 419

**Ichthyoses**

- All genetic
- Ichthyosis vulgaris: common, usually mild. Entire skin is scaly. Controlled with moisturisers
- Rare sorts: Collodion Baby, Bullous and non-bullous ichthyosiform erythroderma, lamellar ichthyosis, X-linked ichthyosis, Harlequin fetus

**Erythroderma**

- *Inflammatory skin disease involving 90% or more of the body surface.* Don’t call it Exfoliative Dermatitis – meaning is unclear
- May have sudden onset over weeks or days. Scaling varies in degrees
- Can see alopecia, ectropion, nail changes
- Skin often feels hot but they may feel cold
- Itch varies
- Well or unwell, feel hot or cold even though temperature normal
- Associated with hypoalbuminaemia and oedema common (due to ↑ capillary permeability)
- Fatal in 20 – 40% due to pneumonia, septicaemia, cardiac failure
- Erythrodermic psoriasis patients do not have the silvery scale that is typical of psoriasis – the diagnosis in this case is based on history: the patient had severe typical plaque psoriasis that worsened until they were erythrodermic
- Cause:
  - Eczema: 40%
  - Psoriasis: 25%
  - Lymphoma, leukaemia: 15%
  - Drug reaction: 10%
  - Unknown: 10% (usually elderly)
- History usually helpful, histology usually unhelpful
- Management: monitor fluid balance, rest, nutrition (shedding lots of protein), moisturiser, careful use of steroids, methotrexate, etc.
Epidermolysis Bullosa

- All rare
- Variety of inherited forms. An acquired form exists
- Can be localised or generalised
- Types:
  - Generalised simple autosomal dominant epidermolysis bullosa
  - Junctional EB
  - Autosomal Recessive Dystrophic EB
  - Autosomal dominant dystrophic EB

Incontinentia Pigmenti

- X-linked dominant, usually lethal in males
- Presents within first 2 months
- Tense bullae on limbs then red nodules or plaques on limbs and trunk
- Pigmentation ranges in colour from blue-grey to brown

Pharmacology

- Topical treatment →↓systemic side effects
- Penetration of drugs into the skin depends on:
  - Barrier function (↓with age and disease)
  - Nature of the vehicle (greasy better)
  - Interaction of the drug and vehicle
  - Hydration
  - Patient compliance (especially if sticky, smelly or staining)
- Types of vehicles:
  - Liquids: solutions, emulsions (oil in water or water in oil), emulsion, suspension
  - Semi-solids: ointments (no water), gels, creams, pastes
  - Greases: oils, waxes, mineral greases (eg vasoline), macrogols

Treatments

- Coal tar: in psoriasis, sometimes eczema. Therapeutic agent unknown

Topical Steroids

- Double the concentration doesn’t necessarily double the efficacy
- Potency related to receptor binding. Modulates messenger RNA production
- Anti-inflammatory effects involve a wide range of mediators
- Side effects:
  - Epidermal thinning
  - Melanocytic inhibition
  - Reduction in collagen synthesis and ground substance →striae and intradermal haemorrhage
  - Vascular effects: initial vasoconstriction →rebound vaso-dilation →oedema, inflammation
  - Inhibition of pituitary-adrenal axis if excessive use or potent
- Grouped into 4 classes according to “potency” – based on vasoconstrictor assays not efficiency

Antifungals

- Griseofulvin
  - Only one till recently
- Poorly absorbed orally, carried to skin through sweat
- Fungistatic
- Rapidly cleared from the skin → have to continue till condition cleared
- Headaches and nausea common
- Only effective against dermatophytes, not yeasts (eg candida)
- Lamisil and itraconazole: effective against fungi + yeasts

**Itraconazole (= Triazole)**
- Fungistatic
- Absorption dose dependent, take with a fatty meal
- Persists in skin for 4 weeks and in nails for up to 6 months after 3 month course
- P450 interaction
- GI side effects in 7%

**Terbinafine (= allylamine)**
- Fungicidal
- Well absorbed orally
- Adverse effects in 10%, no P450 effect

**Use:**
- Cochrane review: no evidence that topical antifungals are of value in fungal toenail infections
- Skin infections of the feet: allylamines better than azoles, but much more expensive

**Retinoids**

- Retinol (vitamin A): metabolised by the liver to retinal, then oxidised to retinoic acids. β carotene can also be converted into retinol
- A hormone: binds to nuclear receptors
- Modifies the expression of a variety of genes involved in cell growth and differentiation
- Induces epidermal hyperplasia and desquamation (efficacy without peeling unlikely)
- Thins the stratum corneum, ↑ dermal capillaries, etc etc, promotes hair growth

**Isotretinoin (= Roaccutane, Oratane, 13 cis retinoic acid)**
- Lipophilic (⇒ take with food)
- Teratogenic: contraception till 1 month afterwards
- Side effects: dry skin, mucosa, photo-sensitive, aching muscles, headaches

**Acitretin (= neotigason)**
- Inhibits formation of retinoic acid from retinol.
- Used in Psoriasis
- Teratogenic for 2 – 3 years afterwards, also reduces efficacy of oral contraceptives
- Plus dry skin, mucosa, photo-sensitive, aching muscles, headaches
### Gynaecology

#### Reproductive function and dysfunction

<table>
<thead>
<tr>
<th>Development:</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Pulsatile secretion of GnRH</strong> (10AA-rapidly degraded requiring separate portal blood stream) <strong>starts at puberty</strong>. This stimulates FSH and LH stimulation of the gonads. **–ve fb by sex hormones (progesterone [especially], oestrogen) controls the secretion of GnRH (females have oestrogen threshold triggered <strong>+ve fb loop for ovulation).</strong></td>
</tr>
<tr>
<td><strong>LH</strong> stimulates caudal mesoderm (females = thecal cells, males = leydig cells) to produce androgens (testosterone)</td>
</tr>
<tr>
<td><strong>FSH</strong> stimulates <strong>primitive</strong> follicles</td>
</tr>
<tr>
<td>- Females = <strong>granulosa</strong> cells → produce <strong>aromatising enzyme</strong> (convert testosterone to oestrogen – ↑oestrogen conc around oogonia [within follicle]).</td>
</tr>
<tr>
<td>- Males = <strong>sertoli</strong> cells → <strong>androgen binding protein</strong> (ensures high androgen concentration around the sperm)</td>
</tr>
<tr>
<td><strong>Development of the internal sex ducts</strong>: Y chromosome has gene encoding <strong>anti-mullerian hormone</strong> (= mullerian inhibiting factor [MIF]; prevents formation of the fallopian tubes), <strong>wolffian duct forms epididymis, vas deferens, seminal vesicles and prostate</strong>.</td>
</tr>
<tr>
<td><strong>Male gonadal differentiation</strong>:</td>
</tr>
<tr>
<td>- Follicles develop during foetal life by mitosis starting with &gt;200</td>
</tr>
<tr>
<td>- At puberty presence of LH and FSH drives spermatogonium production.</td>
</tr>
<tr>
<td>- Nerve stimulation:</td>
</tr>
<tr>
<td>- Parasympathetic NS → Prod and Piss.</td>
</tr>
<tr>
<td>- Sympathetic NS → Shoot and Store!</td>
</tr>
<tr>
<td><strong>Female gonadal differentiation</strong>:</td>
</tr>
<tr>
<td>- Primitive follicles (from <strong>yolk sac</strong> divide by mitosis until week 32 (7,000,000 follicles formed).</td>
</tr>
<tr>
<td>- Under control of <strong>X chromosome</strong> a few follicles develop each day becoming sensitive to FSH but with the lack of FSH until puberty/pregnancy these undergo atresia. By <strong>birth only 3.5 million</strong> remain and by age 9 only &lt;150,000 (onset of puberty- start of GnRH mediated FSH release).</td>
</tr>
<tr>
<td>- GnRH stimulated FSH stimulates <strong>granulosa</strong> cells to produce <strong>aromatizing enzyme</strong> which converts <strong>testosterone</strong> produced by the <strong>thecal cells</strong> (under influence of LH) to oestrogen causing the egg to grow and has systemic effects (endometrial proliferation).</td>
</tr>
<tr>
<td>- When the follicle reaches ~20mm (oestrogen levels ~1000pmol/L) the +ve fb switch is triggered, LH surge occurs → ripening the follicle and causing ovulation.</td>
</tr>
<tr>
<td>- The remnant follicle forms the <strong>corpus luteum</strong> which produces <strong>progesterone</strong> AND oestrogen but is programmed to <strong>regress unless stimulated by HCG</strong>.</td>
</tr>
</tbody>
</table>

### Male sexual function:

- LH → Leydig cells → **androgens** (testosterone).
- FSH → Sertoli cells → Androgen binding protein (ABP) → ↑testosterone around the sperm promoting spermatogenesis.

### Male reproductive function:

- **Hx**: recent **paternity**, surgical (eg UDT, vasectomy etc), drugs (steroids), mumps
- **Libido**: (sex/masturbation >3xweek, spontaneous erections).
- **Examination**: male phenotype, **gonadal size** (>12ml volume – walnuts not peanuts).
- **Semen analysis**: normal 2-6ml with 20,000,000 motile sperm.
- **Blood tests**: FSH, LH, Thyroid function, Prolactin, Testosterone.
- **Mixed antiglobulin reaction (MAR)**: detects soluble **sperm antibodies in seminal plasma** by using healthy donor spermatozoa as antigen. Do in infertile couples esp post vasectomy.
Male dysfunction:
- **H/P:** ↓GnRH (hypogonadotrophic hypogonadism), trauma, neoplastic (prolactinaemia), drugs (steroids, antipsychotics).
- **Testis:** Developmental (UDT), trauma, infection (mumps, Tb), cancer, drugs (smoking).
- **Sex ducts:** vasectomy, STI, SNS (shoot – ejaculation failure).
- **External genitals:** developmental, injury, STI, obesity, PNS (prod – erectile dysfunction).

Male infertility treatment:
- **Lifestyle:** ↑GnRH by ↑ sexual frequency + erotic stimuli; Menevit (antioxidants + vitamins)
- **Intrauterine insemination:** mild oligospermia (5-10 million motile sperm per ejaculate).
- In vitro fertilisation (IVF) with intracytoplasmic sperm injection (ICSI): moderate to severe oligospermia or MAR.
- **Donor insemination:** if no sperm able to be aspirated from testis.

Female sexual function:

**Menstrual Cycle:**
- **Follicular phase:** the follicle under the stimulation of FSH and LH produces oestrogen which causes the follicle to grow. This suppresses LH and FSH although FSH receptors are increased allowing follicle growth to continue. As it gets larger it produces more oestrogen until ~20mm when oestrogen levels reach ~1000mmol/L when it triggers the +ve Fb loop and stimulation of the LH surge.
- **Ovulation:** The LH surge causes the follicle to ripen and ovulation to occur.
- **Luteal phase:** the ruminant follicle forms the Corpus luteum which produces progesterone (& oestrogen) responsible for maintaining the uterine wall for implantation of the egg. The CL is programmed to die after 10-14 days unless rescued by HCG which is produced if the egg is fertilised by the sperm. hCG production signals the corpus luteum to continue secreting progesterone to prevent shedding of the endometrial lining. When the CL dies progesterone and oestrogen levels fall and menstruation occurs (endometrium: oestrogen = grow [proliferate]; progesterone = mature [secrete])

Normal cyclical changes:
- **Bleeding:** regular every 26-32 days lasting < 7days with only 1 day’s spotting. Volume should be <80ml without clots and not occur after sex or between periods or after menopause.
- **Record as:** k(measurement) = 4(days bleeding)/28-29 LMP(2/12/11)
- **Pain:** only normal just before and 1st day of period (not incapacitating) due to prostaglandin release. Midcycle “Mittelschmerz” a/w ovulation can be normal.
- **Swelling:** breast and lower abdominal swelling (progesterone effect – fluid retention).
- **Discharge:** late follicular phase and during ovulation (↑oestrogen).
- **Fertility:** fecundity < 35yrs on average 20% per cycle (ie chance of getting pregnant per month)

Female reproductive dysfunction:
- Hypothalamic-pituitary-ovarian axis dysfunction: hypogonadotrophic hypogonadism, PCOS, prolactinoma
- Ovarian dysfunction: dysfunctional uterine bleeding (DUB), Endometriosis, Menopause, premature ovarian insufficiency (POI), PID
- Internal sex ducts: IUD, Gynae surgery, PID, STD, Neoplasm, Endometriosis
- External sex ducts: Imperforate hymen, STD, Prolapse

**Anatomy**
- Adenexae = fallopian tubes, broad ligament and ovaries

**Physiology & Embryology**
- GnRH:
  - Is a **peptide**: 10 amino acids – only lasts seconds \(\Rightarrow\) requires portal circulation
  - Pulsatile release
  - Stimulates release of FSH + LH
  - **Inhibited by progesterone** (strongest inhibitor), PRL (stress, breastfeeding, adenoma, hypothyroidism \(\uparrow\) TRH), drugs, inhibin, testosterone, oestrogen, stress
- FSH: **glycoprotein**; acts on germ cells:
  - Male: primitive follicle \(\rightarrow\) promotion of spermatogenesis + sertoli cells to produce **androgen binding protein** (ABP) to “soak” up the testosterone which is then pumped around the sperm to promote spermatogenesis
  - Female: granulosa layer within the follicle \(\rightarrow\) **aromatising enzyme** (aromatase) \(\rightarrow\) testosterone (LH stimulates this) \(\rightarrow\) oestradiol
- LH: **glycoprotein**; acts on supporting tissue:
  - Male: Leydig cells \(\rightarrow\) testosterone
Female: **Thecal** cells → **testosterone** → acted on by aromatase (produced by granulosa cells in response to FSH) → **oestradiol**

- **Oestrogen:** three types:
  1. **Oestradiol (E2):** ovary
     - Produced by follicles
     - →↑Mucus
     - →ve feedback on FSH
     - Above a threshold →↑LH
     - Unopposed oestradiol causes endometrial hyperplasia – growth without the maturing effect of progesterone
  2. **Oestriol:** placenta
  3. **Oestrone:** metabolised from androgens (eg testosterone) by adipose tissue

- Female foetus has several million eggs, **by puberty has 300 – 400 eggs**
- Follicle at ovulation is **2cm**
- Infection control:
  - Sperm carry bacteria and viruses into uterus. If mucus inhibits sperm → ↓infection, which would otherwise cause inflammation and ↓chances of implantation
  - ↑Oestrogen → vaginal epithelium thickens during cycle → ↑glycogen → ↑lactobacilli → ↑acidity → ↓other bacteria

**Embryology**

- Normal reproductive function in male and female depends on co-ordination between five specific organs:
  1. Hypothalamus
  2. Anterior pituitary
  3. Gonads
  4. Internal genitalia
  5. External genitalia:
     - Piss + prod with PSNS
     - Shit + shoot with SNS

- Understanding the development of these organs can assist understanding of normal and abnormal reproductive function:

  **Development of the hypothalamus:**
  - The hypothalamus controls the reproductive system in mature humans by secreting, in a pulsatile fashion, a decapeptide, gonadotrophin releasing hormone (GnRH), which requires its own portal system to minimise degradation by blood proteases.
  - Before puberty, there is no GnRH produced by the hypothalamus, and hence the anterior pituitary and gonads are switched off. At puberty, this hypothalamic “clock” is switched on and GnRH secretion commences, with resultant FSH and LH production stimulating the gonads to produce gametes and sex steroids.
  - In mature males and females, the centre within the paraventricular region of the hypothalamus becomes sensitive to negative feedback: if this centre is exposed to stress hormones, sex steroid hormones (particularly progesterone), prolactin or certain drugs, the pulsatile secretion of GnRH is inhibited.
  - Unlike males, females also have a positive feedback centre in the hypothalamus that once exposed to a certain high threshold of oestrogen, secretes tonic levels of GnRH into the pituitary portal system, (and this then results in tonic secretion of LH from the anterior pituitary that matures the egg, and then expels it from the follicle = ovulation, after which the follicle becomes the corpus luteum). Once the follicle ruptures, oestrogen levels fall below the threshold for positive feedback and so GnRH secretion from this centre is inhibited, and so LH secretion in large amounts ceases.

- **Development of the anterior pituitary:**
  - The anterior pituitary gland develops as an outpouching of the pharynx = Rathke’s pouch. As a rudimentary alimentary gland, its hormones are all glycoproteins, with half lives comparable to insulin. It responds to the GnRH stimulus from the hypothalamus by the production of follicle stimulating hormone (FSH) and luteinising hormone (LH), although the relative amounts of each depend on other factors such as which hypothalamic centre is producing the GnRH – at the time of a period, with little oestrogen around, more FSH is produced whereas at ovulation more LH is produced.

- **Development of the gonads, internal sex ducts and external genitalia:**
  - The primitive gonads are formed by the migration of follicular cells (enclosing primitive germ cells) from the yolk sac.
LH acts on caudal mesoderm cells into which primitive follicle embeds itself: male = leydig cells, female = theca cells. Convert cholesterol → androgen

FSH acts on primitive follicle cells which migrate from yolk sac. Granulosa cells = female. Sertoli cells = male. Follicle cells encase primitive germ cells.

Sertoli cells = androgen binding protein/SHBG

Granulosa cells = aromatising enzyme

The follicle cells use androgen produced in theca/leydig cells to promote high concentration of androgen around spermatogonia, or high concentration of oestrogen around oogonia.

Y chromosome: androgen secretion + AMH during intrauterine life = suppresses development of mullerian duct. Increasing androgen causes at 30 weeks the migration of gonad into scrotum.

Once testis stimulated by LH starts producing testosterone - promotes secretions from prostate gland.

Testosterone by testes promotes development of Wolffian duct to form epididymis, vas deferens, seminal vesicles, prostate.

Testosterone from testis promotes development of primitive penis

No FSH/LH around until puberty = no sperm/ testosterone is produced

At puberty hypothalamic clock switched on + increase in LH/FSH= male phenotype and function occurs as increase in testosterone – some around spermatogonia, some leaks out into systemic circulation causing male phenotype + external genitalia development.

Testosterone stimulates autonomic system: PNS = piss and prod (pee and erection), SNS = shit and shoot (defecate and ejaculation)

Female (no Y) gonads develop into ovary by default.

Primitive germ follicles divide until 32 week gestation = 7mill follicles then undergo controlled apoptosis by X chromosome as no FSH. By puberty 90% eggs lost

Primitive female gonad/ovary produces no testosterone + no AMH thus mullerian duct develops into fallopian tubes, uterus and cervix. + external genitalia (vulva and vagina)

At puberty when ovary stimulated by FSH and LH (usually age 9) – proliferation of internal sex ducts ie proliferation of endometrium.

FSH rescues follicles and stimulates granulosa cells – increased oestrogen – LH surge

Other Stuff

- NB. Inflamed ovaries → see regular midcycle pain (mittelschmerz should be irregular); seen in endometriosis + PID/STI
- Vasectomy → ↑ pressure in epididymis → leakage into lymphatics → passage to liver → anti-sperm Ab → secreted through prostate → ↓ sperm motility
- Prostatitis: ↑ ejaculate (~ 10ml as cf normal = 2-6ml)
- Need 20 million motile sperm in ejaculate for fertility
- In females:
  - ↑ FSH:LH ratio → multiple pregnancy as more follicles are recruited
  - ↑ LH:FSH ratio → ↑ testosterone (which kills off follicles) → cysts, acne, hirsutism, obesity = PCOS
Menstrual Cycle

Reproductive and Obstetrics

- Progesterone (and oestrogen) tails off:
  - Menses
  - ↑GnRH + LH + FSH
  - ↑LH → thecal cells → testosterone
  - ↑FSH → granulosa cells of follicle (stimulates growth of follicle + prevents apoptosis which is what would happen to the follicle otherwise) → aromatising enzyme
  - Aromatising enzyme converts testosterone → E2 (oestradiol)
  - ↑ oestrogen →
    - Changes in cervical mucus to allow sperm in (becomes stringy: spinnbarkeit; sperm swim into it and up it)
    - ↓GnRH + FSH + LH
    - Growth of endometrium (proliferation)
    - Positive FB (at ~ 1000) to switch on LH to ripen + pop the egg out of the follicle
  - Follicle collapses to form corpus luteum → ↓ oestrogen + ↓LH
  - Thecal cells of CL now produce progesterone & oestrogen (luteal phase) →
    - Negative FB to pituitary → ↓FSH + LH
    - Changes in cervical mucus to disallow sperm entry (progesterone effect)
    - CL produces progesterone responsible for maintaining the uterine wall for implantation of the egg
    - The CL is programmed to die after 10-14 days unless rescued by HCG which is produced if the egg is fertilised by the sperm.
    - hCG production signals the corpus luteum to continue secreting progesterone to prevent shedding of the endometrial lining.
    - When the CL dies progesterone and oestrogen levels fall and menstruation occurs.

Ovarian & Other Hormones

- **Oestrogen**: steroids secreted by the ovaries that prepare the endometrium for implantation; increase motility of fallopian tubes and have other effects on the breasts, behavior and pituitary secretions.
  - a. Estradiol is the major secreted estrogen. Other types are estrone and estriol.
  - b. Inhibits FSH and LH secretion during the early follicular phase.
  - c. Rise in estrogen 24 hours prior to ovulation initiates the “LH surge” that produces ovulation.

- **Progesterone**: a steroid secreted in large amounts by the corpus luteum. Effects:
  - a. Induces progestational effects on the endometrium.
  - b. Stimulates development of lobules and alveoli in the breast.
  - c. Provide feedback to the hypothalamic and pituitary regulation of the hormonal feedback mechanism.
  - d. **Causes rise in BBT** at time of ovulation.

Individual hormone actions:
- **Oestrogen** – endometrial proliferation, forms sperm favouring mucus.
- **Progesterone** – stabilises endometrium, inhibits development of new follicle, stimulates PG secretion (causing spiral artery vasoconstriction and spasm), forms unfavourable sperm mucus
- LH – triggers ovulation and development of CL.
FSH – stimulates follicle growth, rescues CL from apoptosis.
Inhibin from developing follicle suppresses FSH compared with LH → LH surge
Human Chorionic Gonadotrophin (hCG) from implanted zygote signals corpus luteum to continue progesterone production

**Clinical Indicators of Ovulation**
- **1. Secretory pattern** in endometrium seen on biopsy
- **2. Rise in basal body temperature (BBT).** BBT is the temperature taken on awakening and before activity. *Persistent elevation of 0.5° - 1.0° F reflects ovulation* (a progesterone effect)

**Uterine Response**
- Phases for uterus endothelium: menstrual → proliferative/follicular → secretory/ progestational
- **Menstrual phase (Days 1-5)**
  - Physiologic changes: endometrial and degenerative changes cause tissue necrosis at the end of the secretory phase.
  - Basalis layer remains
  - About 2/3 of endometrium are lost with each ovulatory cycle and by the time brisk flow ceases, most tissue loss has occurred from shedding of the superficial or functionalis layer.
- **Proliferative phase (Days 6-14)**
  - Physiologic changes: under the influence of estrogen
  - Regeneration of surface and glandular epithelium
  - Thickness increases as phase continues.
- **Ovulatory**: no appreciable change seen in endometrium in the 24-36 hours following ovulation. Changes become noticeable after progesterone levels increase with the evolution of the corpus luteum.
- **secretory** (Progestational) phase
  - Physiologic changes: progesterone secretion induces maturational changes in endometrial lining.
  - Increasing stromal oedema to its maximum which is reached at about 22nd day of cycle when corpus luteum activity reaches its maximum level.
  - In the absence of fertilization and implantation, corpus luteum activity regresses; estrogen and progesterone levels drop; rapid regressive changes in the endometrium occur → menstruation begins.

**Ovarian Response**
- **Follicular phase**: varying number (usually 5 - 8) of follicles may be identified with EV sonography in each ovary. Dominant follicle may be identified by about day 8 and measures approximately 10mm. Its size begins to exceed that of other antral follicles. Other sonographic considerations of a dominant follicle:
  - Any follicle measuring > 11mm will most likely ovulate
  - Grows linearly (approx. 2 - 3 mm/day)
  - Maximum diameter varies between 15 - 30mm
  - Line of decreased reflectivity around follicle suggest ovulation will occur within 24 hours
  - Presence of cumulus oophorus suggests ovulation will occur within 36 hours
- **Ovulatory phase**: Chronologically, *ovulation occurs within 24 - 36 hours after onset of the LH surge*. Sonographic findings that ovulation has occurred may include:
  - Sudden decrease in follicular size
  - Fluid in cul de sac
- **Luteal phase**: Involution of the follicle into a corpus luteum (yellow body). This structure produces progesterone which will maintain the secretory endometrium should implantation occur. In the absence of hCG, the corpus luteum regresses after 14 days. Sonography may reveal:
  - Replacement of dominant, cystic follicle with *echogenic structure representing thrombus*
  - Small, irregular cystic mass with crenulated borders

**Abnormal Uterine Bleeding**
- Terminology: abnormal menstrual patterns may be characterized as *abnormalities of volume or frequency*:
  - **Volume:**
    - Hypermenorrhea: excessive volume during cyclic menstrual bleeding
    - Hypomenorrhea: an abnormally small amount of menstrual bleeding
  - **Frequency:**
    - Polymenorrhea: frequent menstrual bleeding occurring at less than 21 days apart
    - Oligomenorrhea: menstrual bleeding occurring more than 35 days apart
  - **Both:** Menometorrhagia: bleeding that is *irregular in both frequency and volume*
- **Dysfunctional uterine bleeding**: vaginal bleeding **NOT** related to menstrual cycle or endometrial pathology.
  - Causes: many and varied include: functional or organic problems; endocrine disorders; endometrial disorders; others
- **Amenorrhea**: the absence of menstrual flow:
  - **Primary**: failure of the onset of menstrual periods by age **16**.
  - **Secondary**: the lack of menstrual periods for **6 months** in previously menstruating woman

### History

<table>
<thead>
<tr>
<th>Gynae Hx</th>
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<tbody>
<tr>
<td><strong>(SMOCS)</strong></td>
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<tr>
<td>- PC/HPC</td>
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<tr>
<td><strong>Symptoms</strong> <em>(Pink Bats Do It Standing)</em></td>
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<tr>
<td>- Pain</td>
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<tr>
<td>- Pain with periods, mittelschmerz, <strong>dyspareunia, dysuria</strong>, pain on <strong>defecation</strong></td>
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<tr>
<td>- Uterine pain is felt in the sacrum and groin, often colicky</td>
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<tr>
<td>- Ovarian pain is felt in the iliac fossa and anterior thigh</td>
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<tr>
<td>- Bleeding</td>
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<tr>
<td>- PMB (post-menopausal) / <strong>IMB</strong> (inter) / <strong>PCB</strong> (post-coital)</td>
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<tr>
<td>- Any other time?</td>
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<tr>
<td>- Symptoms of anaemia/other bleeding problems (easy bruising, dentist etc)</td>
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<tr>
<td>- Discharge</td>
</tr>
<tr>
<td>- When? colour/odour/volume/associated symptoms</td>
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<tr>
<td>- Incontinence and prolapse</td>
</tr>
<tr>
<td>- <strong>Bladder symptoms</strong> – frequency/nocturia/incontinence (stress vs urge)/dysuria/haematuria</td>
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<tr>
<td>- Bowel symptoms – incontinence/difficulty/pain/worsens prolapse</td>
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<tr>
<td>- Sex – dyspareunia, difficulty due to prolapse obstructing vagina</td>
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<tr>
<td>- Actual symptoms of prolapse eg ‘<strong>fullness, golf ball between my legs</strong>’ or ‘dragging sensation’</td>
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<tr>
<td>- Swelling</td>
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<tr>
<td>- External genitals eg warts, <strong>lumps</strong>, ulcers, lesions etc</td>
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<tr>
<td>- Internal <strong>lumps</strong> eg abdominal or pelvic masses (cancer), uterine fibroids</td>
</tr>
</tbody>
</table>
- **Menstrual**:
  - LMP/cycle/period duration
  - Pain – severity, timing
  - Bleeding – severity, timing
- **Obstetric**:
  - Ever been pregnant? G ⇒ P/M/E/T
    - When?
    - Gestation, problems, puerperium, outcomes?
  - Want more? Tried long (infertility)?
- **Contraception and Sex**:
  - Sexually active? Plans for pregnancy?
  - Contraception now/previous/future
- **STIs and Smears**:
  - Ever had an STI or symptoms of? Now? Concerned?
  - Smears in the past? **Ever abnormal**? Procedures? Due?
- **PMH / PSH / Drugs and allergies / FHx**
- **Social hx – smoking and drinking** / family / job / partner / happiness in relationship / ever threatened or forced into sex etc
- **Review of systems**
  - CVS, RESP, ENDOCRINE, NEURO

**OSCE Focussed History Taking**
- **Urogynaecology**:
  - Symptoms:
    - Stress or urge **leakage**
    - Frequency / nocturia / key in door / protection / interference with lifestyle
    - Symptoms of **prolapse**
    - Symptoms of **UTI**
• Obstetric history: weight / mode of delivery / complication

• Other history:
  o History of urinary infection
  o **Weight gain.** Any increase abdominal girth (?pelvic mass)
  o Caffeine and fluid intake
  o Smoking

• Menstrual disorders:
  ➢ Remember urgent priority is to exclude: Pregnancy, Cancer of cervix or endometrium, Infection
  ➢ Symptoms:
    o Heavy or irregular bleeding. Intermenstrual bleeding. Post coital bleeding.
    o Sanitary Protection / interference with lifestyle
  ➢ Smear history
  ➢ Contraception
  ➢ Symptoms of anaemia
  ➢ Symptoms of menopause
  ➢ **Other bleeding symptoms** – dentist, easy bruising
  ➢ Symptoms of infection
  ➢ Medication? COCP / progesterones/ other
  ➢ Symptoms of PCOS – irregular menses / hirsutism / skin changes / weight gain
  ➢ Thyroid / visual / other endocrine symptoms if amenorrhoea

• Pelvic pain:
  ➢ Remember urgent priority is to exclude: Ectopic, Ovarian cyst accident/torsion, Infection, Appendicitis, Renal colic
  ➢ Dyspareunia
  ➢ Interference with lifestyle
  ➢ Menstrual cycle and LMP
  ➢ Contraception
  ➢ Symptoms of infection.
  ➢ Medication? COCP / progesterones/ other
  ➢ Previous Gynae history – cysts / laparoscopy / other.

• Antenatal history:
  ➢ Age
  ➢ Gestation. Certain LMP?
  ➢ Past medical history: BP/DM/VTE/Epilepsy/Asthma/etc
  ➢ Past obstetric history
  ➢ Family history DM/VTE/Pregnancy complications/Anomalies
  ➢ Booking **bloods**
  ➢ Had scan yet? Nuchal scan result and / or detail scan result?
  ➢ Any **problems to date**? Bleeding / UT symptoms / BP problems / Scan problems / baby moving?
  ➢ **Social:** Good Support? Safe at home?

• Past obstetric history:
  ➢ Number of pregnancies
  ➢ Outcomes, which include miscarriage, TOP, mid trimester loss, livebirths, stillbirths.
  ➢ Spontaneous or induced
  ➢ Gestation at delivery of children
  ➢ Mode of delivery
  ➢ Birth weights
  ➢ Any complications e.g. PET, PPH, VTE

**OSCE Education Stations**

• Smear result
• Vaginal birth after Caesarean Section
• Detrusor instability
• How to use COCP / POP
• Options for contraception
• Testing for chromosomal anomaly
• Genital herpes simplex in pregnancy
• Recurrent miscarriage
• Rhesus isoimmunisation
• Positive Chlamydia swab
• Diabetes in Pregnancy
• Options for treatment menstrual disorders

Introduction Data

• Age
• Gravidity = total number of pregnancies
• Parity = # of deliveries (multiple births = 1 delivery – but definitions vary…). E.g. P1(SB) = one stillbirth. P1(twins). Eg: G4P2 (+TOP + SAB). SAB = Spontaneous Abortion.
• LMP
• +/- Marital status

Presenting Complaint

• Recorded as direct quote from the patient. Give them time to tell you. Stop and listen!

HPC

• BUPV (bleeding, urinary sx, pain, vaginal discharge)
• Bleeding:
  ➢ Quantity (eg # of pads per day – but ask why they change – 1 per hour too much), double protection needed (eg tampon and pad), soaking through, etc
  ➢ Duration
  ➢ Timing: with menses, inter-menstrual, post-coital
  ➢ Always consider anaemia, look for signs, do FBC if indicated
• Pain:
  ➢ Location (be specific)
  ➢ Radiation
  ➢ Circumstances (related to menses, meals, activity, time of day). Want to differentiate from bowel and bladder pain
  ➢ Character: sharp, dull, continuous, intermittent, severity
  ➢ Reliving factors: position, medication
• Vaginal discharge:
  ➢ Duration
  ➢ Relationship to menses
  ➢ Colour, odour, consistency
  ➢ Associated symptoms: itch, burn, dyspareunia, vulvar irritation
  ➢ Response to treatment, if any
• Urinary symptoms:
  ➢ Incontinence: stress or urge
  ➢ Frequency, urgency
  ➢ Dysuria
  ➢ Haematuria

Past Gynaecological History: Menstrual History/Fertility History/Infertility History/Sexual History

• Menstrual history:
  ➢ Age of menarche – probably not a big deal – were you significantly younger or older than friends
  ➢ Menstrual cycle (normal 21 – 35 days) and duration (normal 3 – 7 days), regularity (some variation normal). NB:
    o First day of bleeding = 1st day of menstrual cycle. Teenagers will often give their period length as first day without bleeding to first day of bleeding – check understanding
    o Ovulation is 12 – 16 days before the start of the next period (determined by timing of the following period, not the prior period). Fertile for 5 – 7 days before ovulation
  ➢ Abnormal bleeding:
    o Menorrhagia: random bleeding
    o IMB (intermenstrual bleeding): at set times in cycle
Menorrhagia: change/↑ in bleeding with clots
- Post-coital
- Dysmenorrhoea: and relationship to cycle
- Contraception
- Menopause (6/12 period free [should be no bleeding] with climacteric symptoms)
- If post-menopausal, when did periods stop and are there any symptoms

- Fertility history:
  - Sexual history
  - Dyspareunia (superficial, deep, relation to menstruation)
  - Abnormal d/c (colour, itchy, smell, hx of STIs)
  - Smears
- Infertility:
  - Sexually active? Contraception?
  - Sex around time of ovulation (signs = stringy mucus, mittelschmerz)
  - Previous STIs/surgeries (→ scrarring)
  - Endometriosis/fibroids
  - Previous pregnancy?
- Past gynaecological problems or procedures
- Incontinence
- Smear history: last smear date, any abnormal
- Past Obstetric History (mainly for obstetric history): See History and Antenatal Booking, page 602
- Past Medical and Surgical History (and maybe very brief systems review)
- Medications:
  - Remember vitamins and non-prescription meds – may be bad in pregnancy
  - Allergies
- Family History: Sister or mother with fertility, pregnancy or gynaecological problems
- Social History:
  - Marital/relationship status
  - Sexual activity, sexual orientation (‘Are you in a relationship with a man or a woman’), number of partners. To avoid embarrassment, just ask straight
  - Cigarette, alcohol and recreational drug use
  - Occupation
  - ?Victim of interpersonal violence (but don’t introduce it in a crisis situation). See Suspicion of Abuse or Interpersonal Violence, page 555
- Gynaecological write-up:
  - Mrs X is a 44 year old G3P2 LMP (24/5/11) who presents complaining of (PC)
  - Then HPC, including all pertinent (+) and (–) and any relevant past medical, surgical or gynaecological information

Exam
- Check bladder is empty
- Explanation while dressed. Check experiences with past exams
- Ensure chaperone if male
- Have available: light, additional light source and mirror for the patient
- Clear instructions to patient on what clothes to remove and position. Cover with sheet
- Position: flat on back on firm surface, unless prolapsed, obese or on a soft bed, in which case left lateral position (like recovery position) with right knee drawn up
- Pulse: indicator of anxiety
- BP
- General physical exam as indicated
- Whilst still covered: “I’ll just get you to bring this leg out to the side, and now the other”
- Inspection of external genitalia
- Vaginal Exam:
  - Bivalve Speculum:
    - “I’m going to just touch on the outside of your leg first”
    - Warm and check temperature
    - Part labia minora
    - Introduce at 45 degrees then rotate
Use narrow speculum for nulliparous, wider speculum for multiparous, and paediatric for child or sometimes post menopausal. Use Sim’s Speculum for prolapsed. Warm blade, little lubricant if doing a smear.

Check size, shape, position and appearance of cervix, view transformation zone and os. Nulliparous or multiparous cervix

Also undertake STI swabs:

1. High vaginal for BV, trichomonas, candida
2. Endocervical for chlamydia
3. Endocervical for gonorrhoea

Bimanual:

“I’m going to do the pelvic/vaginal examination now. We routinely do this to assess the uterus + ovaries for any abnormalities. It involves placing one hand on the tummy and a finger inside the vagina to feel for any abnormalities.”

“I’m going to just touch on the outside of your leg first”

Check uterus for size, shape, consistency, tenderness and mobility

Check adnexa for abnormal swelling or tenderness

Normal tube and ovaries are not palpable

Offer tissues/sanitary pads

Explain results when fully dressed

OSCE Exam Stations

Pelvic exam:

Introduce yourself

Wash hands

Put on gloves

Examine abdomen first in all cases

Explain pelvic exam to patient

“Let me know if it hurts and I will stop”

Observe patient’s face for discomfort as you examine

Examine vulva and vagina for prolapse/atrophy/infection/ulceration/leukoplakia/white skin/injury/scars

Try a cough to look for prolapse or urinary leakage if appropriate

Pass speculum. Use lubricant. Look for atrophy/discharge/Blood/appearance of cervix (if present)

Take swabs/smear if indicated

Bimanual examination. Use lubricant. Comment on uterus — size, anteverted/retroverted, mobile, tender. Any cervical excitation? Are there any adnexal masses (remember a large mobile ovarian cyst may be missed on a bimanual exam which is why we always perform an abdominal examination first)?

Antenatal exam:

Introduce yourself

Check blood pressure and urinalysis results

Make sure you know the gestation

Wash hands

Explain abdominal palpation to patient

“Let me know if it hurts and I will stop”

Observe patient’s face for discomfort as you examine

Observe abdomen first in all cases. Look for scars, striae, unusual masses or distension, fetal movement

Measure the symphysis-fundal height with tape

Ballot the abdomen to determine:

1. The lie of the fetus (longitudinal/oblique/transverse)
2. The presentation (cephalic or breech usually)
3. Engagement of the fetal presenting part (usually head)
4. Which side the back is on
5. An estimate of whether the liquor volume is normal

Listen to fetal heart with doppler over fetal anterior shoulder

Contraception

Ideal contraceptive is 100% effective, only desirable side-effects, readily reversible, and able to be used unsupervised

Reference: OHCS + numerous pamphlets
For a younger person wanting to start on the pill:
- Discuss the possibility of coercive sex, especially if under 15
- Discuss the emotional and physical consequences of sex
- Ask about prior contraceptive use
- **Ask whether they want to become pregnant** – establish a context for motherhood in terms of the next 5 years
- Find out their thoughts about birth control (many myths: birth defects, ↓fertility)
- Inform about all methods → what else have you considered?

**Risk assessment questions:**
- Current sexual history
- Past problems with weight gain
- Acne
- Headaches/migraines
- Dysmenorrhoea/irregular menses
- Nausea/abdominal pain
- Diabetes
- Smoking
- Personal or family history of DVT
- Hypertension or IHD

**Effectiveness of Family Planning Methods**
- Most effective (less than 1 pregnancy per 100 women per year): sterilisation, vasectomy, IUD, implants
- Slightly less effective: injectables, OCP, patch, lactation method
- Slightly less effective again: condoms (male + female), diaphragm, fertility awareness methods
- Less effective (about 30 pregnancies per 100 women per year): withdrawal, spermicides

**Natural Family Planning**
- No intercourse from **6 days before to 2 days after ovulation** – free and no drugs
- Monitor fertility by:
  1. **Checking cervical mucus** – clear and stretchy when fertile
  2. **Temperature ↑ 0.3 C** after ovulation (affected by fevers, drugs, drink)
- Success if regular cycles, dedication and self-control
- Peak effectiveness is 2% - usually 10 - 20% (pregnancies per woman years)

**Barrier Methods**
- Low health risk, **need high motivation**, some STD protection
- Condoms, Caps +/- spermicide, Female condom (Femidom)
- Don’t use oil-based lubricant or anti-thrush cream with condom
- Spermicide gives extra protection

**Long-Acting Reversible Contraception (LARCS)**
- Implants
- Injection
- IUCDs

**IUCD**
- Very effective (failure rate 1-2 per 1000 woman years)
- Inhibit implantation and may impair sperm migration
- Need replacing every 3 – 5 years
- Best in older, parous women in stable relationships
- Contraindications: Pregnancy, high risk for STD, undiagnosed vaginal bleeding, very heavy periods
- Complications:
  - Can be expelled from a nulliparous or distorted (eg fibroids) uterus
  - Ectopic pregnancy more likely (1 in 2000)
  - Associated with PID following insertion or STD
- If she becomes pregnant then must take the IUCD out (little risk of inducing miscarriage). If it’s left in then↑risk of chorioamnionitis, miscarriage or pre-term labour
Mirena – carries levonorgestrel (a progesterone) → ↓ risk of implantation and lighter periods (Good for menorrhagia). Lasts 3 years. 20% experience reversible amenorrhoea. Expensive. Can use with oestrogen only HRT (no ↑ risk of endometrial hyperplasia) and avoid progesterone side effects

Contraceptives

**Combined oral contraceptive pill**

- Types (all contain oestrogen + a varying type of progesterone):
  - **Norimin** – norethisterone (prog) + ethinyl-estradiol
  - **Levlen / monofeme** – levonorgesteral (prog) + ethinyl-estradiol
  - **Estelle/Ginet** – cyproterone acetate (prog) + oestrogen (good for PCOS & acne due to anti-androgen properties)
  - **Yasmin/Yaz** – droperinone (prog) + oestrogen (has diuretic properties so good for those who retain fluid on COCP)

- MOA:
  1. Suppress ovulation
  2. ↓ sperm penetration through cervical mucous
  3. ↓ likelihood of implantation (altered endometrium)

- Non contraceptive benefits:
  - ↓ Cancer risk 50% (ECCO: cervical, endometrial, ovarian, colorectal)
  - Note: if HPV +ve long term use a/w 4x ↑ in cervical carcinoma risk
  - Improved acne, ↓ menstrual pain, ↓ bleeding, ↓ functional cysts, regulates periods

- Contraindications:
  - CVD → ↑ risk MI, CVA (amplify existing risk factors – smoking, diabetes)
  - VTE or arterial thrombosis
  - Liver disease, breast cancer, migraines with aura
  - Not safe in breastfeeding & may ↓ breast milk supply
  - If contraindicated, can use Copper IUCD

- Starting the COCP:
  - Detailed Hx and examination (Hx: migraine, epilepsy, smoking, obesity, DM, HTN, dyslipidemia, previous CVD/VTE. Exam: BP, BMI)
  - Instructions:
    - **Start on day 1 of cycle**
    - **If starting on days 1 to 5 of cycle** (ie during menstruation; day 1 = 1st day of bleeding) → contraceptively safe straight away
      - **If starting after day 5**: use other contraception as not safe until 7 hormone pills have been taken (7 day rule)
    - Take one pill per day until pack is finished and start new pack in same place as first pack
    - Don’t take with St John’s Wort
    - Withdrawal bleed will occur in sugar pill part of the pack, can skip these if want and avoid withdrawal bleed
    - May experience nausea, breast tenderness, lighter menstrual flow, ↓ libido
    - **Missed pills/ABs/diarrhoea >24hr/vomiting within 3hr of pill:**
      - If miss 1 pill take it as soon as possible (this may mean taking 2 at once)
      - If miss >2 pills or 1 pill when haven’t had 7 days of hormone pills in a row beforehand, vomiting, diarrhoea, other medications → follow 7 day rule
    - Report any problems immediately: chest pain, swollen ankles, sudden SOB
Monitoring:
- Review at 3/12 then every 6/12 after that (BP, check for SE, new RFs eg smoking)
- Side effects: fluid retention, chloasma (facial pigmentation), nausea
- Causes of breakthrough bleeding: late or missed pill, d & v, meds, STI, pregnancy, 1st few months of new pill, running packs together
- COCP withdrawal symptoms: 7d pill free interval (ie sugar pills) a/w: pelvic pain, HA, breast tenderness, bloating/swelling
- New COCP regimes:
  - Yaz – take for 24 days with 4 days sugar pills.
  - Seasonal (4 bleeds per year) take 3 months hormonal pills back to back.
  - Continuous pill taking
  - Advantages of new regimes: ↓ hormone withdrawal sx, ↓ ovarian cysts, ↓ breakthrough ovulation, ↓ PMS
- Interactions:
  - Antibiotics and enzyme inducers (rifampacin, St johns wort, anticonvulsants, anteretrovirals, griseofulvin) do interfere and the 7 day rule should be applied post stopping drug.
  - For women on enzyme inducing meds (eg anticonvulsants), can use 50ucg pills (20-30ucg is normal), but best to use another method
- Stopping:
  - 66% menstruate within 6 weeks, 98% by 6 months
  - At menopause: Stop at 50 with > 1 years amenorrhoea. CoC masks menopause, so stop at 50 and use non-hormonal method. Little evidence that it’s not safe to continue to menopause

Progestogen only pill
- Types:
  - Noriday (norethisterone)
  - Microlut (levonorgestrel)
  - Cerazette (desogestrel)
- CI:
  - Pregnancy
  - Breast malignancy
  - History of ectopic pregnancy
  - Liver disease
  - Enzyme inducing drugs
- Uses:
  - 1. Breastfeeding women (limited transfer to milk – equivalent of 1 pill in 2 yrs breast feeding).
  - 2. Contraindications to oestrogen – previous or FHx endometrial cancer, VTE, older smokers (ie >35)
  - 3. Sensitivity to high dose progesterone (depression, ↓ libido, weight gain) or oestrogen (nausea, bloating, fluid retention, chloasma, migraine, HTN) during COCP use
- MOA: note: faster action than COCP also faster wearing off.
  - 1. Makes cervical mucus impenetrable
  - 2. Suppression of ovulation
  - 3. Altered uterine endometrium
- Efficacy:
  - ↑ with ↑ age (25-29:3% failure [ie 3 out of 100 women will fall pregnant in 1 year], 40+:0.3% failure)
Starting the POP:
- Detailed Hx and examination.
- Instructions:
  - Can start at **any** stage of the cycle
  - If starting **days 1 to 5** of cycle (during menstruation) – contraceptively safe straight away.
  - If starting **after day 5**: not safe until 7 hormone pills have been taken; use other contraception until then (**7 day rule**)
  - NB. No sugar pills
  - **Missed pills**:
    - Miss/late (counts if not taken within 3hr of normal time, vomit within 3hr of taking, diarrhoea >24hr)
    - → then **2 day rule**: continue taking for 2 days before contraceptively safe
- **NB.**: No problems with ABs

Missed pills:
- Miss/late (counts if not taken within 3hr of normal time, vomit within 3hr of taking, diarrhoea >24hr)
- → then **2 day rule**: continue taking for 2 days before contraceptively safe
- **NO** problems with ABs

Side effects:
- Menstrual irregularities – esp 1st few months: **irregular bleeding**, amenorrhoea (improves w time, can take 2 POP per day, do pregnancy test)
- ↑ functional ovarian cysts.
- PMS sx, acne, bloating, hunger (weight gain)
- **Interactions**:
  - Antibiotics **don’t** interfere
  - Enzyme inducers **do** interfere (read label)

Long acting reversible contraception (LARC)

Implants:
- Types:
  - Jadelle (lasts 4-5 years; levonorgestrel), subsidised
  - Implanon (lasts 3 years; etoneorgestrel), not subsidised
- **MOA:** thickens cervical mucous + inhibits ovulation.
- **+ve:** extremely effective (<1% failure rate), fit and forget, reversible
- **-ve:** requires clinician to insert, enzyme inducers do effect, irregular bleeding.

IUCD:
- Actinomyces and actinomyces-like organisms can be seen in smears of women with IUCDs; if symptoms → refer
- **Copper IUCD:** lasts 5 or 10 years
  - MOA: **impairment of sperm function** to prevent fertilisation
  - Contraindications: pregnancy, PID, cervicitis, current STI, malignancy, undiagnosed bleeding
  - Side effects: **heavier/more painful periods**, 1/1000 risk of **perforation** at insertion, 1/20 **risk of expulsion, ectopic** risk, infection
- **Mirena** (lasts 5 years)
  - Levonorgestrel releasing intrauterine system
  - MOA: prevents fertilisation, chemical sperm barrier, ↓ endometrial proliferation, ovulation **usually continues**
  - **+ve:** very effective <1% failure rate, ↓ menstrual bleeding, **effective therapy for menorrhagia**
  - **-ve:** only subsidised for menorrhagia (special authority)

Injection:
- **Depo provera** (lasts 3/12) but can have 2/52 window at end of 3/12 for re-injection during which contraceptively safe.
- MOA:
  - 1. Inhibits ovulation (100%)
  - 2. Thickens cervical mucous.
3. Endometrial alterations: unfavourable to implantation
- Significant contraindications: CVD, Liver Disease, undiagnosed vaginal bleeding, pregnancy, breast cancer
- SE: weight change (readjust upon stopping depo), depression, irregular bleeding, ↓libido, headaches
- ↓ risk of endometrial ca, slightly ↑ risk for breast ca in women < 35
- ↓ Bone density 5-7% over 1st 2 yrs use but then plateaus (return to normal after stopping depo) → ensure not smoking and calcium and folate sufficient.
- If bleeding experienced: exclude pregnancy, infection. If at end of injection period (12/52) then have DP 10 weekly, else can try NSAIDs or give oestrogen pills
- Periods return ~ 6/12 after injection expires = 9/12 after last injection. By 2 years conception rate = non-DP users (ie longer than IUCDs or implants)

Instructions:
- 1st injection:
  - If on day 1-5 of menses, no additional contraception required.
  - > Day 5, not safe for 7d (7 day rule), therefore abstinence or alternative barrier method
- Injections every 3/12 + 2/52 treatment window.

Emergency contraception
- 2 types: pharmacological and IUCD.
- Chemical:
  - Up to 72hrs post sex
  - Postinor: requires prescription. Take with food. Vomiting within 3hr requires repeat dose. Enzyme inducers need 2 pills.
  - Levonelle-1: can get from pharmacies over the counter.
  - MOA:
    - Interfere with sperm motility.
    - Delay ovulation.
  - SE: N+V (14%)
  - Efficacy:
    - < 24hrs – 0.5% failure, < 48hrs – 1% failure, < 72 hrs – 2.5% failure.
    - Always perform pregnancy test 3-4 weeks post ECP.
- Post coital IUD: Copper IUD
  - Works up to 5 days after possible fertilisation (ie around ovulation; depends on point in cycle; ~100% effective)
  - MOA: prevents implantation.
  - Need to screen for STIs and give prophylactic ABs

Sterilisation
- Reversal is only 50% successful ⇒ see it as irreversible
- Tubal ligation has 1% failure (1:200) – 10 times worse than vasectomy and same as IUCDs
- Vasectomy – easier than tubal ligation, but takes up to 3 months before stored sperm used up. Need to be tested and have 2 sperm-free ejaculates. Has been discussion of ↑ risk of prostate cancer – best evidence says no association.

Emergency Contraception
- Ask why: unprotected intercourse, condom broke, etc. If no condom, then check why. If indicated: ‘Are you worried about infection?’ and ‘Was it OK with you that it all happened the way it did’ [checking for non-consensual intercourse]
- Ask:
  - How long ago was sex?
  - LMP
  - Regular partner (→ ↓ risk of STD)
  - Medications
  - Previously had an ECP – any side effects. Sometimes nausea +/- vomiting with Progesterone only ECP
  - Other conditions
- Discuss:
  - How to take it
  - Pregnancy test in three weeks
  - Ongoing contraception, other advice
Emergency IUCD: inserted within 120 hours (5d) of unprotected intercourse. Screen for STDs. Prophylactic cover if suspected

Suspicion of Abuse or Interpersonal Violence

- It is common and victims are high users of health services
- Epidemiology: 20% of women report sexual abuse before 16, full intercourse reported by 4%. Sexual abuse of boys is about 1/3 as common as for girls.
- Adult women: 25% report sexual abuse, 12% rape
- Men: 5% report sexual abuse, 3% rape (?under-reporting)
- 10 – 16 % of rapes reported to police

Effects:
- Acute and long term effects are related to age of victim, extent and duration of abuse, relationship with abuser and response of others
- Acute effects: numbness, shock, disbelief, anxiety
- Long-term effects: feelings of helplessness, depression, sleep disturbances, nightmares, flashbacks, guilt, self-blame, shame. Measurable long-term psychiatric sequelae in 25%

What is patient’s age:
- < 14: all suspected cases should be referred to CYPFS, or if older but abuser still has access to young people. See also Child Abuse, page 998
- 14 – 17 don’t make a decision about what to do on your own ⇒ need to put caveats on confidentiality

History questions (but don’t introduce it in a crisis situation)
- Suspect if physical injuries, chronic undiagnosed pelvic pain, heightened anxiety about an examination, STD’s without being worried about health risks
- They will be reluctant to discuss it
- Physical: ‘have you ever been hit, slapped or shoved by a parent or partner. Ever had bruises or had to stay in bed…
- Sexual: Did anything sexually frightening happen to you as a child or young adult, have you ever been made to participate in sexual activity that made you feel uncomfortable. Was it your choice, or were you forced or coerced?
- Psychological: Does your partner ever ignore you, call you names, make fun of you, threaten to leave you, punish the children when he is angry with you, are you fearful of anyone at the moment?
- Most helpful response is: being believed, being supported, not being blamed, being helped not to feel odd or alone

Rape/Non-Consensual Intercourse

- Rape: = sexual contact without consent (including consent under threat) which involves oral, genital or anal penetration, otherwise unlawful sexual contact

Therapeutic role:
- Recognise & treat physical injury
- Attention to emotional trauma
- Prevention of pregnancy – offer ECP. Legal requirement under the Contraception, Sterilisation and Abortion Act.
- Check for infection (NB incubation of chlamydia is 21 days) and offer prophylaxis (but may interfere with ECP – do it after)
- Referral to support services
- If not sure about making a police complaint, bring in crisis counselling team
- Victim compensation – inform re ACC entitlement

Forensic role:
- When did it happen: If less than 7 days then may be forensic requirements. If very recent then nil-by-mouth and collect all urine and toilet paper until forensic examination. Ring forensic specialist (DSAC = Doctors for Sexual Abuse Care)
- Keep detailed records at the time of examination
- Forensic specialist will do genital exam, blood tests, urine (drug screen), colposcopy (for genital injury), finger nail scrapings, etc and appear as expert witness

Supportive role:
- Communicate empathy: ‘that sounded really unpleasant for you’
- ‘You are safe now’ (don’t say if not true)
- Reinforce ‘its not your fault’ – victims blame themselves
- Follow-up at 1 week, 1 month and 3 months (pregnancy, HIV test, Hep B and C, Syphilis)
Infertility

- Inability to establish a pregnancy within a year of unprotected intercourse or > 2 consecutive miscarriages or still births
- For the average couple, there is only a 20-25% chance of conception per month
  - After six months, 60% of fertile couples will have conceived
  - After 12 months the figure is 80%
  - After 24 months, the figure is 95%
- Incidence – approx 10% of couples
- Aetiology:
  - Male factors: 30%
  - Female: 30%
  - Idiopathic/unexplained: 20%
  - Both: 20%
- A range of lifestyle factors can influence overall fertility, these include:
  - Diet and exercise (weight)
  - Smoking/drugs/alcohol
  - Stress
  - Sexually transmitted infections
  - Medical problems
  - Environmental toxins
- History:
  - Male: surgery (eg hernia), trauma to the nads, undescended testes, mumps, etc
  - Female: surgery, menstrual history, BMI, symptoms of endocrine disorders, nasty polyps, STI, PID, ectopic pregnancy, nasty appendicitis
  - Both: general medical and reproductive history, smoking, medications, family history
- Exam: include general assessment of endocrine disorders: PRL (→ Galactorrhoea), thyroid disorders (goitre, etc), Polycystic ovary (→ hirsutism, obese, etc)
- Investigations:
  - Male:
    - Semen analysis, sperm antibodies
    - Plasma FSH (primary or secondary testicular failure) & LH, androgen deficiency (testosterone), TSH, PRL
  - Female:
    - Possible causes: Endometriosis, stress/anorexia/exercise, early menopause, PCOS, thyroid, ↑PRL
    - Ovulation: if regular menstruation then ovulation likely
    - HCG, TSH, PRL, FSH + LH, Oestrogen (day 2), progesterone (day 21) for 3 cycles to check for consistent ovulation
    - Post-coital test of cervical mucus
    - Pelvic assessment: US
    - AMH: For most women, age best predicts the chance of conception each month. 10% lose their fertility earlier than expected. AMH helps to estimate what is called ‘ovarian reserve’ by measuring the number of follicles developing in the ovary at a particular time. Once the test is complete, we compare the results with those of other woman of the same age. AMH is a hormone made by small follicles as they grow in the ovaries.
- Management:
  - Induce ovulation: risk of multiple pregnancy, also narrow TI.
  - Anovulatory cycles: treat with Clomiphene – stimulates ovulation but risk of multiple pregnancy
  - Clomiphene action in the induction of ovulation is that it binds to the F2 receptors in the hypothalamus (antagonist) to create a state of hypoestrogenicity, thereby causing an enhanced GnRH release followed by an ↑ secretion of gonadotropins which induces ovulation
  - IVF (also better for tubal blockage than surgical repair). 1 in 3 have life birth.
    - Fertilisation of the eggs and the first few days of embryo development occur outside the body
    - Hormonal drugs are administered to increase the number of eggs growing within the ovaries
    - At the appropriate time maturation of the eggs is triggered by another drug and the eggs are aspirated from the ovary using a needle guided by ultrasound
    - The eggs are then placed with sperm and both are cultured together overnight in carefully controlled conditions.
    - Eggs that have fertilised are then cultured for a further 1-4 days
One or two embryos are selected for transfer into the uterus.

- **Oligospermia**: intracytoplasmic sperm injection, donor sperm, artificial insemination
- **Male**: Menevit capsule contains vitamin C, zinc, vitamin E & folic acid (antioxidants)

- Lots of psychosocial implications of infertility
- Workup to point of diagnosis is funded. Criteria based funding for treatment
- Also prepare for pregnancy: take folate, do booking bloods, check rubella status and offer vaccination

### Male Infertility

- **Maldevelopment of gonads, internal sex ducts and external genitalia:**
  1. If **male gonadal development is suboptimal** (such as by the migration of less than the usual 150-200 primitive follicle/germ cells), will see:
     - Small testis
     - Production of testosterone during fetal development suboptimal
     - Suboptimal descent of testis (UDT)
  2. The **absence of an intracellular receptor for androgen**, to mediate androgen's action, means that the internal mesonephric sex ducts cannot differentiate:
     - Androgen insensitivity syndrome/testicular feminisation syndrome
     - Decreased intracellular R for androgen = internal sex ducts can’t differentiate: female-like but no female genitalia
     - XY = male gonad formed but no male sex ducts or external genitalia as this needs testosterone.
     - AMH (anti mullerian hormone) thus no female differentiation either.
     - Gets peripheral conversion of androgen to oestrogen
     - Blood test for testosterone shows testosterone levels higher than a male due to peripheral conversion of gonadal androgen to oestrogen by aromatising enzyme
     - Well developed female genotype but no secondary hair.

- **History:**
  - Previous children?
  - Surgical hx?
  - Drugs, sex, steroid hx?
  - Libido? Sex/masturbation 3-4x weekly?
  - Spontaneous erections?
  - Orgasm?

- **Examination:**
  - Male phenotype?
  - Testes? Gonadal size? Penis?

- **Investigations:**
  - Semen analysis – collect sample within 2/3 days of ejaculation
  - Normal ejaculate 2-6mls + 20 million motile sperm
  - FSH/LH – hypothalamus/pituitary function
  - Thyroid
  - PRL – hypothalamus/pituitary function
  - Testosterone – leydig cell function

- **Potential causes:**
  - Hypothalamus/pituitary:
    - Hypogonadotrophic hypogonadism i.e. Kallmans
    - Sphenoidectomy?
    - Prolactinaemia?
    - Antipsychotics
  - Testis:
    - Maldescent
    - Hypoplasia
    - Scrotal torsion
    - Teratoma
  - Internal sex ducts:
    - Vas aplasia
    - Vasectomy
    - STD
  - External sex ducts:
    - Hypospadias
Management:

1. Enhance GnRH production – increase sexual frequency, erotic stimuli, weight loss
2. FSH/LH production suboptimal
3. Erection/ejaculation issues – sildenafil
4. IUI if mild oligospermia
5. IVF with ICSI – moderate/severe oligospermia
6. Donor insemination if azoospermia (no sperm), hypoplastic testis

Female Infertility

Normal/PC:

- **Bleeding** – regular every 26-32d, no postcoital bleeding, IMB, or postmenopausal bleeding
- **Pain** – due to release of PGE. Abnormal if: after sex, during sex, with defecation, with micturition
- **Swelling** – breast and lower abdominal swelling, progesterone induces decreased gut motility and fluid retention
- **Discharge** – late follicular phase prior to and during ovulation as oestrogen induced vaginal transudation
- **Fertility** – increased libido midcycle

Normal female function is determined from the **history:**

- Recent pregnancy
- Previous surgical and drug history
- Menarche, menstrual cycle length, loss, predictability, discomfort/cramps with the onset of the loss, and mucus at midcycle

Examination:

- Female phenotype
- Lower genital tract examination

Investigations:

- A **transvaginal ultrasound** may be performed
- **Day 2 FSH and oestradiol**
- **Day 21 progesterone** performed to confirm luteinization (and thus ovulation). If these results are abnormal, then dysfunction may be suspected

Potential causes:

- Hypothalamus/pituitary
  - Hypogonadotrophic hypogonadism
  - Sphenoidectomy
  - Prolactinoma
  - PCOS
- Ovary
  - Hypoplasia
  - Torsion
  - Surgery
  - PID
  - PCOS
  - Endometriosis
- Internal sex ducts (Tubes/uterus/cervix)
  - IUD
  - Gynae surgery
  - PID
  - STD
  - Neoplasm
  - Endometriosis
- External sex ducts (Vagina/vulva)
  - Imperforate hymen
  - STD
  - Prolapse

Ovarian failure: All women by 55y exhausted their ovarian follicles – menopause

- Estrogen creams, patches, HRT – combine with progesterone unless had a hysterectomy to prevent endometrial hyperplasia and endometrial cancer risk + breast cancer risk.
• HRT CI in thrombophilia, hypertension

• Premature ovarian insufficiency:
  • Menopause < 40y
  • Due to previous ovarian surgery or X chromosome issue where premature follicle atresia occurs (fragile X syndrome)
  • Low levels of FSH and oestrogen like those seen in post-menopausal women
  • Amenorrhoea + shorter cycles
  • AMH level = indicator of reserve of follicles
  • Low inhibin levels
  • Transvaginal USS may see fewer follicles

• Hypogonadotrophic hypogonadism:
  • Kallman’s syndrome = anosmia – hypogonadism due to pituitary failure and don’t develop phenotype and sexual characteristics
  • Negative feedback doesn’t initiate an FSH response
  • Positive feedback doesn’t induce LH release and ovulation
  • Infrequent and irregular periods
  • Infertility
  • Investigations:
    o Thyroid
    o PRL – pituitary failure due to hyperprolactinaemia
    o USS – ovaries with follicles and of good volume
  • Treatment
    o COC if fertility not an issue
    o Clomiphene – oestrogen antagonist – increased GnRH + FSH

• Dysfunctional uterine bleeding:
  • Irregular bleeding/ periods but no organic problem
  • Dysfunction = hormonal – pituitary not making FSH/LH regularly or ovaries not responding to FSH/LH regularly
  • PCOS is a form of DUB
  • Follicular cysts may develop
  • Treatment:
    o Progesterone – IUD, POP
    o Clomiphene/FSH therapy if fertility desired

• Defective Luteal phase:
  • Normal luteal phase 12d
  • Defective if <10d or level of progesterone is insufficient to cause secretory changes in endometrium needed for fertility
  • Day 21 progesterone should be > 30nmol/l
  • Defective corpus luteum due to defective follicle development
  • Treatment: Clomiphene – to increase FSH production and better follicle development

Infertility of a Couple

• Infertility = not conceived in 12 months
• 1 in 6 couples
• Primary infertility
• Secondary infertility (conceived previously)
• 30% female, 30% male, 20% both, 20% other
• Male:
  • Maldescent of testes
  • Destruction of sertoli cells
  • Defective ejaculation (Vasectomy, hypospadias)
• Female:
  • Anovulation/infrequent ovulation (PCOS, Hypogonadotrophic hypogonadism)
  • Endometriosis
  • Tubal scarring – endometriosis, STD
  • Uterine (Endometrial polyps, Fibroids)
  • Cervical (Scarring)
• History:
  • Relationship – live apart, duration
- Occupations
- Contraception – depo provera can take up to 2 years to return
- Sexual practises – frequency, timing, any difficulties?
- Age – ovarian follicle depletion?
- **Weight** – obesity halves chances, PCOS? vs. underweight: hypogonadotrophic hypogonadism
- Previous pregnancies?
- Smear Hx?
- Previous surgery?
- Previous STD?
- PMHx? Thyroid problems? GI disease?
- Medications? Any teratogens?
- Smoking?
- LMP? Cycle length and regularity?
- Pelvic pain? Endometriosis? PID?
- Changes in bowel/bladder? Endometriosis?
- Skin acne? Hirsutism?
- FHx?

- Male:
  - Age? Weight?
  - Previous surgery? Vasectomy?
  - Previous chemotherapy?
  - PMHx?
  - Ejaculation? Erection problems?
  - Smoking?

- Examination:
  - Male phenotype?
  - Testes size? Maldescent?
  - Hypospadias?
  - Ejaculate volume? Norm 2-6ml if >10ml = prostatitis
  - Masculinisation in female?
  - Thyroid?
  - Abdominal exam, pelvic, bimanual, speculum

- Investigations:
  - Swabs for STDs
  - **Day 2 FSH/oestrogen** – follicle dysfunction?
  - **Day 21 progesterone** – luteal phase defective?
  - PRL, T4, TSH – hypogonadotrophic hypogonadism
  - Testosterone, LH – PCOS
  - Pelvic USS – ovaries, cysts, PCOS
  - Semenanalysis – sperm count and morphology
  - AMH – ovarian follicle reserve

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**When to Refer**

- Check:
  - Female rubella status
  - Taking folic acid
  - Weight gain if anovulatory
  - Occupational and drug history
  - Cervical smear history

- Advice:
  - Weight loss if BMI is more than 28
  - Stop smoking
  - Minimal alcohol and caffeine intake
  - Regular intercourse (3-4 times a week)

- Investigations:
  - Length of cycles, progesterone 6-8 days before menses (~day 21)
  - FSH and oestradiol day 2-4 of cycles
  - Semen analysis – repeat in 4-6 weeks unless totally normal
  - Prolactin and thyroid function only if irregular cycles

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Reproductive and Obstetrics
Further investigation (Required for public patients):
- Laparoscopy if duration more than one year, unless severe ovulation or sperm factor

Referral:
- No success after 12 months unprotected intercourse
- Any abnormal results on investigation

Early referral if:
- Extreme anxiety about fertility
- Woman more than 35 years of age
- Ovulation factor
- Severe sperm factor
- Previous abdominal / pelvic / urogenital surgery
- Previous STI / PID
- Recurrent miscarriage (two or more consecutive miscarriages)
- Abnormal pelvic / genital examination (woman or man)
- Family history of menopause of less than 40 years of age
- Significant systemic illness
- Genetic conditions (eg. Cystic fibrosis, muscular dystrophy or Huntington's disease)

Immediate Referral for Sperm, egg, ovarian tissue or testicular tissue stored before starting cancer treatment.

Treatment

1. If both partners: IVF, with ICSI (intracytoplasmic sperm injection)
2. IUI intrauterine insemination:
   - Ejaculation problems
   - Mild oligospermia
   - Ovulation detected by blood – LH surge and sperm injected into uterine cavity
   - 15% success per treatment
3. Clomiphene (oestrogen antagonist):
   - Anovulation
   - Oestrogen antagonist given orally day 3-7 (if given after day 9 then impaired cervical mucous and endometrial development)
   - Day 21 progesterone test
   - 40% success after 3 cycles of treatment
4. Gonadotrophin therapy:
   - If unsuccessful treatment with clomiphene
   - Anovulation due to hypogonadotropic hypogonadism
   - Give daily FSH injection from day 3-5 of cycle – monitor to see if follicles developing with daily blood oestrogen and LH.
   - Ovulation then triggered with LH injection. Couple advised about timing of coitus – 40h after LH surge
   - 20% success per treatment cycle
5. Mild hyperstimulation with IUI:
   - Unexplained infertility
   - Mild endometriosis
   - Give clomiphene then gonadotropin therapy (FSH) to induce development of 2-3 follicles. When ovulation induced with LH = IUI occurs.
   - 15% success per cycle
6. IVF:
   - If both in couple infertile or IUI or gonadotropin therapy unsuccessful
   - Female tubal disease
   - Moderate – severe endometriosis
   - Severe oligospermia (will need ICSI)
   - Unexplained infertility
   - Process:
     - 1. Administer GnRH agonists or antagonists by injection to block pituitary stimulus to ovary
     - 2. Daily administer FSH to induce 6-10 follicles (10-12d)
     - 3. Measure response by blood oestrogen levels + USS
     - 4. Trigger ovulation by LH admin once oestrogen level 6000 – 10000 (ie 6 – 10 follicles)
     - 5. Oocyte pick-up by USS guided transvaginal needle aspiration 36h after ovulation
     - 6. 4h later insemination of oocytes naturally or ICSI
     - 7. Culture of fertilised embryos for 3-5d
8. Replacement of cleaved embryos/blastocysts through cervix into uterus
9. Luteal phase by progesterone administration
10. Cryopreservation of surplus cleaved blastocysts
   - For 1 embryo = 40% success per cycle
   - Ovarian hyperstimulation syndrome (OHSS) where >10 follicles recruited and increased production of estrogen and progesterone leads to excess fluid in gut and chest. Occurs 5 days after oocyte pick up.
     - Symptoms: abdominal pain, SOB
     - Condition resolves after corpus luteum dies but if IVF works and conceives then may become worse!

7. Thawed embryo replacement:
   - Cryopreserved embryos from IVF

8. Donor insemination:
   - Azoospermaia or absent sperm
   - Female normal – bloods done to determine ovulation and cryopreserved sperm thawed and IUI

9. Donor oocyte therapy:
   - Females who have poor follicle numbers (low AMH, high FSH, poor response to FSH)
   - Same as IVF but after oocyte pick up the eggs are donated to recipient women whose partners sperm is used to fertilise eggs before replacement into recipient women
   - >50% success

10. Surrogacy:
    - Absence of uterus
    - Can’t safely undergo pregnancy

Dyspareunia
- = Pain with sex
- Causes:
  - Superficial pain: vulvitis (e.g., HSV), introital shrinkage (atrophy, scarring), vaginismus
  - Vaginal pain: post-menopausal atrophy, medication (e.g., antihistamines), arousal phase dysfunction
  - Deep pain: pelvic disease (endometriosis, adenomyosis), shortened vaginal vault post-hysterectomy, retroverted uterus
- May be cycle of anticipation of pain → tense muscles and lack of lubrication → further pain
- Treatment if no aetiology uncovered:
  - Lubricants
  - Oestrogen replacement
  - Position modification
  - Counselling
- Vaginismus: involuntary spasm of the levator ani muscle making penetration difficult. May be related to prior trauma/abuse. Pain-vaginismus-pain cycle develops. Treatment: behaviour modification, progressive vaginal dilatation

Menstrual Disorders
- Key distinction:
  - Ovulatory cycles: regular
  - Anovulatory cycles: irregular
- Also consider thyroid and ↑PRL (PRL inhibits FSH + LH)

Abnormal Uterine Bleeding

- Definition: Bleeding outside of normal parameters.
- Abnormal if:
  - 1. <2days/>7days
  - 2. Menstrual interval <21days/>35days
  - 3. >80ml blood loss
- Terms to describe AUB:
  - Menorrhagia: excessive bleeding each cycle (>80ml bleeding per cycle) tend to be ovulatory
    - > 7 days in length
    - Increase in blood loss
    - Increase in no of times pads need changing (having to change a pad/tampon every 1-2hrs)
    - Passing of blood clots
- Anaemic symptoms
  - Metorrhagia: irregular bleeding between cycles, tend to be “anovulatory” (no ovulation)
  - Menometorrhagia: irregular, prolonged bleeding between cycles (i.e. fibroids, polyps).
  - Oligomenorrhoea: scant menstruation (>35d)
  - Polymenorrhoea: frequent menstruation (<21d)
  - Dysmenorrhoea: painful (mid-cycle “mittelschmerz” a/w spotting).

- Aetiology:
  - Organic (functional)
    - Systemic disease: Coagulation disorders, vWD, thrombocytopenia, Liver disease, Thyroid disease, PCOS, Exogenous hormones – COC, HRT, Prolactinoma
    - Reproductive tract disease: Pregnancy/ectopic pregnancy, Infections, Malignancy, Endometriosis, Polyps, Fibroids, Trauma

- Inorganic (dysfunctional/DUB)
  - Defined as AUB in the absence of organic disease
  - Occurs when the normal cycle of menstruation is disrupted, usually due to anovulation (90%; failure to ovulate) that’s unrelated to another illness.
  - Ovulatory: regular heavy bleeding
    - Loss of local endometrial haemostasis:
      - Shift in the ratio of vasoconstrictor (prostaglandin F2α) to vasodilator (prostaglandin E2 and prostacyclin I2)
      - Enhanced fibrinolysis due to excessive production of plasminogen activator
      - Dysfunction of corpus luteum and inadequate progesterone production
    - Bleeding is typically cyclic, but heavy or prolonged
  - Anovulatory:
    - In anovulatory DUB, oestrogen is continually secreted but an egg never ripens in the follicle. Because an egg is never released, progesterone is never produced from the corpus luteum to counteract the uterine lining proliferation. Eventually the uterine lining outgrows its blood supply and sloughs off at irregular intervals.
    - Because an egg was never produced, the premenstrual and menstrual symptoms associated with
ovulation and progesterone don’t occur, and the uterine bleeding is usually painless.

- **Irregular** heavy bleeding: **HPO axis dysfunction** – luteal phase dysfunction (ie progesterone not being produced), Secondary to anovulation – pre-menopause, pre-menarche, idiopathic, stress and exercise, obesity/rapid weight change

- **Pathophysiology of anovulatory DUB:**
  - In the follicular phase: oestrogen unopposed by progesterone → proliferative unstable endometrium which sheds easily
  - Get oestrogen withdrawal bleeding
  - Increased oestrogen: progesterone ratio
  - ↑ risk of endometrial hyperplasia and malignancy
  - No moliminal (pre-menstrual) symptoms (as progesterone is responsible for these)
  - Common at the extremes of reproductive age:
    - **Perimenarchal** girls due to immaturity of HPO axis
    - **Perimenopausal** women (as menopause approaches, ovarian function wanes, ovulation occurs less often, increased variability of the cycle length)

**History:**
- SMOCS
- Should cover **anaemia symptoms** (SOB, CP, tiredness, pre-syncpe)
- Should include **PMHx + FHx of bleeding problems** (dentist, post surgery, bruising etc)

**Investigations:**
- **Pregnancy test:** if fertile age – always determine if pregnant
- Severity of bleeding: **FBC +/- ferritin**.
- STI check.
- Guided by Hx:
  - Prolactin
  - Day 21 progesterone (if >30, definitely ovulating)
  - FSH: ovarian failure or hypothalamic dysfunction
  - LH & testosterone: PCOS
  - TSH
  - LFTs

- **U/S:** trans-vaginal U/S (in post menopausal endometrium <5mm rules out endometrial cancer).
- **Endometrial biopsy (pipelle):** if persistent IMB or > 45 unexplained bleed
- **Hysteroscopy +/- D & C:** gold standard for evaluation of intrauterine pathology

**Classification:**
- **FIGO classification system** for causes of AUB in nongravid women of reproductive age
- Structural abnormalities on the left, non-structural on the right

**Treatment:**
- Rx any underlying organic cause
- RCOG recommends **tranexamic acid and mefenamic acid** as first line drugs for women who do not require contraception or prefer non-hormonal treatment
- Medical management (preferred) vs surgical (when MM fails; endometrial ablation, hysterectomy)
- “Regular” ovulatory menorrhoea (menorrhoea = bleeding):
  - Stop the bleeding!
    - Mefenamic acid: ↓ endometrial vasodilating prostaglandin levels. 25% ↓ in menstrual blood loss. Need to be taken regularly & should be commenced as soon as bleeding starts
    - Tranexamic acid (↓ bleeding 40%) note: use only when bleeding. Given on first 4 days of cycle
    - COCP: makes cycles regular and reduces bleeding.
    - Mirena: progesterone stabilises endometrium.
    - If completed family:
      - Endometrial ablation.
      - Hysterectomy.
- “Irregular” anovulatory menorrhoea:
  - Replace the progesterone (if not ovulating, not producing progesterone; progesterone stabilises endometrium & ↓ endometrial cancer risk)
- **RCOG recommends long acting progestogens or COCP as a first-line treatment** for the management of menorrhagia in women requiring contraception
- **Medroxyprogesterone acetate** – 1st 21 days of cycle (then sugar pills to allow withdrawal bleed)
- COCP
- Mirena – low dose progesterone release
- Depot provera
- Fe supplements

**Age related common diagnoses & treatment**

<table>
<thead>
<tr>
<th>Age-group</th>
<th>Cause</th>
</tr>
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<tbody>
<tr>
<td>Pre-puberty</td>
<td>Pre-Menacme: trauma, vulvovaginitis, tumours, precocious puberty</td>
</tr>
<tr>
<td>Adolescence</td>
<td>DUB: secondary to immature pituitary-hypothalamic axis</td>
</tr>
<tr>
<td>Reproductive Age</td>
<td>Pregnancy</td>
</tr>
<tr>
<td></td>
<td>Malignant</td>
</tr>
<tr>
<td></td>
<td>Fibroid, endometriosis, adenomyosis</td>
</tr>
<tr>
<td></td>
<td>Endocrine, Hormonal, hyperprolactinemia, excess</td>
</tr>
<tr>
<td></td>
<td>Endometrial DUB</td>
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<tr>
<td></td>
<td>Infection</td>
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<tr>
<td></td>
<td>Haematologic</td>
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<tr>
<td></td>
<td>Exogenous hormones</td>
</tr>
<tr>
<td>Perimenopause/ Menopause</td>
<td>Cancer</td>
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<tr>
<td></td>
<td>Anovulatory bleeding</td>
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<tr>
<td></td>
<td>Polyps/Fibroids</td>
</tr>
<tr>
<td></td>
<td>Endometriosis</td>
</tr>
<tr>
<td></td>
<td>Vaginal or endometrial atrophy</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>age:</th>
<th>12</th>
<th>15</th>
<th>45</th>
<th>51</th>
</tr>
</thead>
<tbody>
<tr>
<td>a</td>
<td>b</td>
<td>c</td>
<td>d</td>
<td>e</td>
</tr>
</tbody>
</table>

- **A. Pre-menstrual**: trauma, vulvovaginitis, tumours, precocious puberty
- **B. Peripubertal**:
  - Usually menorrhagia due to immature HPO (Anovulatory DUB “irregular”): anovulation with ↓ CL → ↓ progesterone (no stabilising of the endometrium) with oestrogen producing friable unstable endometrium.
  - Rx: give progesterone!
    - Medroxyprogesterone acetate (MPA) – 1st 15-21 days of cycle
    - COCP
    - Mirena – low dose progesterone release.
- **C. Reproductive age**:
  - Usually a haemostasis (AUB E [endometrial]) issue (vasodilators > vasoconstrictors)
  - Regular:
    - Ovulatory DUB “regular menorrhagia”: imbalanced vasodilating/vasoconstricting prostaglandins required for flushing of spiral arteries (COX mediates vasodilatory PG’s hence black COX → ↓ blood loss).
      - NSAIDS (↓ bleeding 20%): Mefenamic acid
      - Tranexamic acid (↓ bleeding 40%) note: use only when bleeding.
      - COCP: makes regular and reduces bleeding.
      - Mirena: progesterone stabilises endometrium.
    - If completed family:
      - Endometrial ablation.
      - Hysterectomy.
    - Organic AUB: Systemic disease → coagulopathies + liver disease.
  - Irregular:
    - Anovulatory DUB “irregular”: HP axis dysfunction (peri-menarche, peri-menopausal), stress, idiopathic). Rx with progesterone!!
    - Organic disease: hormonal (PCOS, thyroid, HRT, Prolactinoma), or reproductive tract (pregnancy, infection, malignancy, Endometriosis, Polyp, fibroids). Treat cause! i.e. fibroids → myomectomy.
- **D. Perimenopausal**:
  - Failure of HP axis due to primary failure of ovaries producing irregular production of oestrogen and progesterone as responses to FSH and LH vary.
    - NSAIDS (COX inhibitor ↓ bleeding 20%), Tranexamic acid (↓ bleeding 40%) note: use only when
Reproductive and Obstetrics

bleeding.
- Cyclical progesterone
- Mirena
- Endometrial ablation/hysterectomy
- HRT

- E. Postmenopausal:
  - DDx:
    - Endometrial carcinoma (~10%)
    - Atrophic vaginitis (Rx: topical oestrogen, ablation)
    - Endometrial hyperplasia.
    - Endometrial polyp
    - Cervical malignancy.
  - Ix: have to rule out malignancy
    - Hx, Exam and FBC (severity of blood loss)
    - Speculum examination with C-smear.
    - Transvaginal U/S.
    - Biopsy (pipelle).
    - Note: endometrial carcinoma
    - Simple without atypia: 1% → malignancy.
    - Simple with atypia: 5% → malignancy.
    - Complex without atypia: 10% → malignancy.
    - Complex with atypia: 30% → malignancy.

Amenorrhoea

- Defn:
  - Primary amenorrhoea: lack of menses by age 14 without secondary sexual characteristics or at age 16 in the presence of normal growth and secondary sexual characteristics
  - Secondary amenorrhoea: cessation of menstruation for >6months other than pregnancy.

- Aetiology:
  - Main 3 causes:
    - 1. Failure of HPO axis
    - 2. Absence of end organs (developmental, iatrogenic)
    - 3. Obstruction of outflow tract (imperforate hymen [haematocolpos], cervical stenosis)
  - Anatomical: pregnancy, obstruction, congenital abnormality
  - Ovarian failure: menopause, iatrogenic, chromosomal.
  - Endocrine: H-P tumour, gonadotrophin deficiency, hyperandrogenism (PCOS), Hyperthyroid, Cushings.
  - Other: Stress, anorexia, illness, exercise.

- Ix:
  - Progesterone challenge (tests oestrogen status)
  - Karyotype.
  - US: rule out PCOS and Structural abnorms.
  - Serum LH and Testosterone (↑in PCOS), FSH (↑in premature menopause), TFT, prolactin.

- Rx:
  - Hypothalamic dysfunction: clomiphene citrate (if fertility desired), OCP (induce menstruation).
  - Hyperprolactinaemia: bromocriptine - ↑dopamine- inhibit Prl.
  - Premature ovarian failure: Tx cause, HRT to prevent osteoporosis.
Oligomenorrhoea

Polycystic Ovarian (PCO) Syndrome
- **Epi:** 5-10% reproductive women.
- **Aetiology:** ↓ aromatisation due to imbalanced pituitary secretion of LH and FSH or oversensitivity of theca cells to LH → androgen excess & oestrogen deficit causing multiple follicles to become stuck at the 2-10mm stage with chronic anovulation resulting
  - Imbalanced pituitary secretion of LH and FSH → ↓Aromatisation.
  - Oversensitivity of theca cells to LH → ↓Aromatisation.
- **Sx:**
  - Infrequent irregular periods (prolonged amenorrhoea followed by menorrhagia).
  - Acne, hirsutism, darker skin on flexors (acanthosis nigricans – hyperprolactinaemia).
- **Dx:** 2 of the following need to be met (U/S being the gold standard).
  - Transvaginal U/S – pearl necklace appearance.
  - Chemical: ↑LH, ↑Androgens (testosterone).
  - Sx – infrequent irregular periods due to chronic anovulation.
- **Rx:**
  - Lifestyle: ↑CV and diabetic risk (due to ↑androgens), ↑endometrial cancer.
  - COCP (using anti-androgen): anti androgen effects as progesterone lowers the levels of effective testosterone.
  - Spirinolactone acts as a weak anti-androgen.
  - Progesterone IUD - induce menstruation (prevent endometrial hyperplasia and lower the risk of endometrial carcinoma).
  - Metformin – reduce diabetes risk and improve Sx (↓ insulin levels - ↓testosterone (↓hirsutism and CV risk)).
  - If want to conceive – Clomiphene (oestrogen agonist blocks hypothalamic oestrogen inhibition of FSH and LH → ↑FSH and LH, due to endocervical effects (prevents endometrial proliferation prior to ovulation) limit to days 3-7 of cycle (any longer than this will see unwanted effects on endometrium [and unfavourable conditions for implantation] – ie no proliferation as endometrium has E2-receptors).

Hypogonadotropic hypogonadism:
- **Defn:** failure of normal response to ovarian hormone feedback
  - ve fb failing to initiate FSH response
  - +ve fb failing to initiate LH surge
  - Note: Kallman’s syndrome is pituitary failure (no FSH or LH) a/w anosmia.
- **Sx:** infrequent/irregular periods or infertility.
- **Dx:**
  - Thyroid tests, prolactin (could be primary cause of pituitary failure).
  - LH and FSH: low in HH due to pituitary failure.
- **Rx:**
COCP – if fertility not desired, replaces hormones.
Clomiphene +/ FSH therapy – have to monitor follicle development to prevent multiple pregnancies.

**Menorrhagia**

- **DDx:** "I DEAL P"
  - IUCD
  - Dysfunctional Uterine Bleeding
  - Endometriosis/endometrial cancer
  - Adenomyosis
  - Leiomyomata (fibroids)
  - Polyps

**Dysfunctional Uterine Bleeding (DUB)**
- Occurs at extremes of fertile life, no asc pathology, usually anovulatory (In teens usually settles with start of ovulation).
- **Aetiology:** irregular LH/FSH production or unreliable response to LH/FSH this can cause excessive follicle growth (overproduction of oestrogen and hyperproliferation of the endometrium)
- **Dx:** exclude hypothyroidism
  - If desiring fertility: clomiphene +/ FSH
  - Long term progesterone therapy → mirena / oral cyclical progesterone.

**Endometriosis**
- **Epi:** 10% of all women, 30-50% of all infertile women.
- **Definition:**
  - 1. Ectopic proliferation and growth of endometrial tissue with
  - 2. abnormal immune response driving inflammation.
- **Aetiology:** Unknown – multifactorial
  - Retrograde menstruation: shed endothelium → fallopian tubes → peritoneum.
  - Abnormal immune response to refluxed tissue (normally absorbed with no inflammation).
  - Growth/metaplasia within the pelvic tissue (possibly disposed at birth).
  - Longer survival of shed epithelium.
- **Sx:** majority are asymptomatic.
  - Pelvic pain – cyclical at the time (dysmenorrhoea) of periods or constant due to inflammation and adhesions, commonly asc with sex (deep dyspareunia). *Pain on defecation* suggests colonic/bladder depositions.
  - **Bleeding:** *due to hypervascular endothelium*, premenstrual spotting or menorrhagia.
  - **Infertility:** multiple reasons
    - ↓freq of sex due to dyspareunia.
    - Inflamed pelvic tissue digest sperm.
    - Ovarian follicle failure to develop, rupture and release (*inflammation*).
    - Scarring of fallopian tubes.
    - Ovarian cyst impede fibrial pick up of oocyte.
  - **Ovarian cysts:** ectopic ovarian endometrial growth. Bleeding leads to formation of *chocolate cyst*.
- **Dx:**
  - Laparoscopic investigation under LA → characteristic flared, haemorrhagic lesion.
- **Rx:**
  - Laparoscopic ablation and removal of inflamed growths (during diagnosis). Allows for pregnancy during period of reduced symptoms.
  - Continuous progesterone/ GnRH antagonists (prevents fertilisation).
  - Fertilisation may require Intra-uterine insemination or IVF.

**Adenomyosis**
- **Definition:** Extension of endometrial tissue into the myometrium.
- **Epi:** 15% females <35yrs.
- **Sx:** Menorrhagia, dysmenorrhoea, pelvic discomfort, dyspareunia.
- **Dx:** Uterus symmetrically bulky/boggy (Exam + US) note: definitive diagnosis on excised uterus pathological examination.
- **Rx:**
  - D&C to rule out other pathology.
  - Symptomatic: Iron supplements, Pain relief (NSAIDS, Paracetamol).
  - Low dose danzol (synthetic androgen).
  - Hysterectomy.
Reproductive and Obstetrics

Fibroids (leiomyomata):
- **Defn:** benign smooth muscle tumours of the uterus (leiomyomas).
- **Epi:** 20% of women ↑with age.
- **Aetiology:** *oestrogen dependent growth* (↑pregnancy + COCP), rarely (1/1000) undergo *sarcomatous change* (ie malignancy; Sx: pain, malaise, bleeding, ↑ size)
- **PC:**
  - *Menorrhagia* (heavy + prolonged periods)
  - Fertility problems (interfere with implantation).
  - *Pain* (torsion of pedunculated fibroid, "red degeneration" due to thrombosis of blood supply)
  - Mass (urinary sx, venous efx (varicose veins), obstruct labour)
- **Rx:**
  - Many women no treatment is needed → if asymptomatic.
  - Menorrhagia:
    - Mirena – progesterone IUCD.
    - Hysterectomy (older with no desire for pregnancy).

Endometrial polyps:

Cases
- Case 1. 25y IMB
  - Hx, exam, FBC, HCG, STI swabs, smear, hormone levels, TV-USS
  - Ddx: mid-cycle oestrogen drop, organic cause, IUD
- Case 2. 48y heavy periods
  - Hx, Exam, bloods, swabs, TV-USS, endometrial biopsy?
  - Ddx: fibroids, polyp, cancer, anovulatory DUB
  - Treat with iron supplements, NSAIDS or hormonal treatment to regulate cycles if anovulatory
- Case 3. 16y to ED complaining of dizziness, irregular PV bleeding for 6 months
  - Hx + exam
  - Ddx: DUB, infection, coagulation disorders
  - Treat with iron replacement, antifibrinolytics, NSAIDS, COC
- Case 4. 55 y spotting for past month post-menopausal
  - Hx, exam, endometrial biopsy?
  - Ddx: cancer – need to rule out!

Amenorrhea
- **Primary** amenorrhea:
  - Failure to start menstruating
  - Has she got external secondary sexual characteristics? Are internal genitalia developing properly?
  - If not developing then karyotyping may reveal Turner's syndrome/ testicular feminisation (CAH)?
  - Has she got an imperforate hymen? → cyclical pelvic pain but no bleeding
    (haematocolpos/haematometra)
- **Secondary** amenorrhea:
  - Periods stop for >6 months not due to pregnancy
  - HPA axis dysfunction – exams, stress, weight loss, high-performance athletes (exercise). ↑PRL, severe disease. Test with a 7-day progesterone challenge. If withdrawal bleed following, then there is enough oestrogen to produce an endometrium
  - PCOS
  - Premature ovarian failure
- Investigations:
  - LH, testosterone
  - FSH increased in premature menopause
  - PRL
- Oligomenorrhoea: infrequent periods: common in the young and the nearly menopausal. Consider PCOS, rapid weight change, ↑PRL, hypothyroidism or primary oligomenorrhoea

Menorrhagia
- Increased blood loss unusual for woman (= Excessive blood loss (technically > 80ml lost/cycle – but hard to measure)
> 7 days in length
Increase in blood loss
Increase in no of times pads need changing (having to change a pad/tampon every 1-2hrs)
Passing of blood clots
Anaemic symptoms

- Causes:
- 1 DEAL P (IUD, DUB, endometriosis/endometrial cancer, adenomyosis, leiomyomata, polyp)
- Dysfunctional uterine bleeding:
  - If no abnormality of uterus found
  - 50% women with menorrhagia
  - Diagnosis of exclusion
  - Need to rule out: blood dyscrasias, thyroid dysfunction, malignancy, endometriosis, PCOS, PID and fibroids.
  - >90% of DUB due to anovulation as failure of ovulation results in lack of progesterone → increased endometrial hyperplasia and overgrowth
  - Remaining 10% of DUB due to dysfunction of corpus luteum i.e. defective luteal phase
- Fibrin: 1 in 3 women
- Endometrial polyps: benign growths on uterus lining — may cause spotting
- Endometrial hyperplasia
- Adenomyosis: enlargement of uterus due to a growth into endometrium in endometriosis
- CAH: increased androgens, decrease in mineralcorticoids – give dexamethasone
- Uncommon causes: thyroid imbalance, IUDs esp copper, liver/kidney conditions, clotting disorders i.e. warfarin therapy
- ENDOMETRIAL CANCER (but more likely to cause IMB, post menopausal bleeding)

- Investigations
  - Pelvic examination
  - Pap smear
  - βHCG: are they pregnant
  - FBC: anaemic?
  - USS – endometrial hyperplasia, uterine cancer, fibroids, cysts
  - Hysteroscopy to look inside uterus
  - Laparoscopy

- Treatment
  - NSAIDs first line for reducing bleeding in adolescent.
  - COCP or POP
  - Tranexamic acid
  - Danazol
  - IUD – mirena
  - Surgery: endometrial ablation, myomectomy – removal of fibroids, hysterectomy

Inter-Menstrual Bleeding
- May follow mid-cycle ↓in oestrogen (i.e with ovulation)
- Also cervical polyps, ectropion, carcinoma, cervicitis and vaginitis, IUCD, hormonal contraception (spotting)
- If post-coital, then ↑ suspicion of more serious pathology (e.g. cervical cancer)
- Appropriate to do an exam and smear – but it is NOT appropriate to reply on the smear result (false negatives, etc). Should act on clinical suspicion

Dysmenorrhoea
- = Painful periods, may be associated with sweating, tachycardia, headache:

<table>
<thead>
<tr>
<th>Primary</th>
<th>Secondary</th>
</tr>
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<tbody>
<tr>
<td>Age</td>
<td>&lt; 20</td>
</tr>
<tr>
<td>Onset of pain</td>
<td>With bleeding</td>
</tr>
<tr>
<td>Duration</td>
<td>First 1 – 2 days of menses</td>
</tr>
<tr>
<td>Intensity</td>
<td>Begins with ovulatory cycles, remains constant</td>
</tr>
<tr>
<td>Aetiology</td>
<td>Probably PG-F2α mediated</td>
</tr>
<tr>
<td></td>
<td>Pain without organ pathology</td>
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</tbody>
</table>
### Chronic Sepsis (e.g., Chlamydia)

Conditioned behaviour

**Treatment:**
- Reassurance
- **CoC:** at least 3-month trial, combine with **NSAIDs** if necessary
- Progestogens: day 5 – 25
- PG inhibitors
- Exercise
- De-conditioning, eliminate secondary gains

### Endometriosis

**Two components:**
- 1. Growth of endometrium in tissues outside uterus = “**ectopic**”
- 2. + **Inflammation** of tissues

**Due to hypervascular endometrium (causes bleeding) + increased retrograde reflux of endometrium at menses into peritoneum** – abnormal inflammatory response NOT absorption causing pain + adhesions

**Chronic and progressive:** inflammation and local haemorrhage → fibrosis and scarring

**Common:** 10% females between 12-50y

**Usually inactive following menopause**

**Mild – Moderate – Severe**

**Site:**
- Ovaries MOST COMMON 60%
- Broad ligament
- Uterosacral ligament
- Rectosigmoid colon
- Appendix
- **Adenomyosis** = endometriosis within the wall of the uterus

**Symptoms:**
- Classic triad = pelvic pain, deep dyspareunia, dysmenorrhoea
- **Pain:** inflammation + PGE
  - Dysmenorrhoea (endometrial growths)
  - Deep dyspareunia (uterosacral/pouch of Douglas growth)
  - **Pain during defecation/peeing** (growth on sigmoid colon/bladder)
  - **Midcycle pain** (growth on ovary)
- **Bleeding** – menorrhagia
- **Infertility** – 30-40%. Due to:
  - Sex less frequent
  - Inflamed pelvic tissues digest sperm
  - Lack of ovarian follicles
  - Scarring of fallopian tubes
  - Ovarian cysts – endometrioma/chocolate cyst
  - Less optimal implantation at endometrium
- **Ovarian cysts – endometrioma**

**Diagnosis:**
- At laparoscopy:
  - **Red brown nodules on surface of ovaries and pelvic structures**,* and other sites (appendix, peritoneal scars, etc).
  - Can develop large cysts, lined by endometrial stroma and glands and containing changed blood (chocolate cysts).
- Tender nodularity on pelvic examination, fixed retroverted uterus, firm fixed adnexal mass
- US: free fluid

**Treatment:**
- Medications:
  - COC to relieve pain
  - Progestagen – relieve symptoms
  - **GnRH agonists** – **suppress release of oestrogen from ovaries and decrease menstruation** (may need add back therapy = oestrogen + progesterone) only short term use. GnRH analogues are equally as effective as Danazol (a modified testosterone; *inhibits ovarian steroidogenesis* resulting in decreased secretion of estradiol and may increase androgens) in relieving the severity of symptoms of
endometriosis. They induce a state of hypogonadotrophic-hypogonadism or pseudomenopause with low circulating levels of oestrogen → ↓ growth of ectopic endometrial growth

- If woman wanting to conceive → can’t opt for medical tx must have surgery

- Surgery:
  - Laparoscopy – removal of tissue (relieve pain and improve fertility)
  - Laparotomy – if bowel resection etc needed.
  - Hysterectomy – severe cases if no future pregnancies planned

- Wishing to conceive: IUI, IVF
- Some women heal on their own.

- Genesis of endometrial response in normal women cf women with endometriosis:

<table>
<thead>
<tr>
<th>Normal Women</th>
<th>Women with Endometriosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ovarian egg follicle grows</td>
<td>Ovarian egg follicle grows</td>
</tr>
<tr>
<td>Oestrogen is secreted</td>
<td>Oestrogen is secreted</td>
</tr>
<tr>
<td>Endometrium grows</td>
<td>Endometrium grows abnormally</td>
</tr>
<tr>
<td>Ovarian egg follicle dies (4w)</td>
<td>Ovarian egg follicle dies (4w)</td>
</tr>
<tr>
<td>Oestrogen level falls</td>
<td>Oestrogen level falls</td>
</tr>
<tr>
<td>Endometrium sloughs</td>
<td>Hypervascular endometrium sloughs</td>
</tr>
<tr>
<td>Most endometrial sloughing revealed as period</td>
<td>Less endometrial sloughing revealed as period</td>
</tr>
<tr>
<td>Some endometrium refluxes up the tubes and into the pelvis</td>
<td>More endometrium refluxes up the tubes and into the pelvis</td>
</tr>
<tr>
<td>The peritoneum absorbs the refluxed endometrium without allowing growth or an inflammatory reaction (Normal immunity)</td>
<td>The peritoneum reacts to the refluxed endometrium by allowing growth and an inflammatory reaction causing pain, adhesions and/or ovarian cysts (Hyper-immunity)</td>
</tr>
</tbody>
</table>

**Fibroids**

- *Benign smooth muscle tumours of myometrium* (ie underneath the proliferative layer), also referred to as leiomyomata or myomas
- Very common, especially in overweight and infertility
- Uterine fibroids are the most common benign tumour of the female genital tract
- The lifetime risk for a woman > age 45 of having fibroids is >60%
- Peaks in 5th decade, reduces after menopause
- **Oestrogen → enlargement**, so grow in pregnancy and shrink after menopause
- Aetiology unknown but fibroid growth is known to be hormone dependent (FSH/LH → oestrogen) and therefore medical therapy involves regulating this pathway
- Fibroids have higher concentration of oestrogen receptors, progesterone receptors and aromatase – grow in response to estrogen and progesterone
- Risk factors: early age of menarche + obesity + family hx (1st degree), nulliparous
- Protective factors: having children, smokers, use of progestins
- Symptoms:
  - Asymptomatic
  - Menorrhagia (no IMB or PCB)
  - Painful periods
  - Urinary frequency, constipation
  - Majority of fibroids are not painful (pelvic pain is not a common complaint from patients, pressure is)
**Reproductive and Obstetrics**

- **Exam**: pelvic exam, bimanual + speculum
- **Diagnosis**: abdominal +/- transvaginal ultrasound → hysteroscopy
- **DDx**: remember to consider other causes of menorrhagia: endometrial polyps, endometrial hyperplasia, cancer, cervicitis etc

**Treatment:**
- Treatment of fibroids should be based on symptoms, **no role for treating asymptomatic fibroids**
- Essentially: anti-oestrogenic drugs (eg GnRH based drugs to saturate pathway), surgery, angio
- **Medical:**
  - GnRH analogues/antagonists: **Saturate/inhibit FSH/LH pathway and reduce levels of oestrogen**.
    - Given IM or as implant. However, can only be used in the short term, due to the risks of long term treatment, for:
  - Peri-menopausal woman for brief symptomatic relief
  - To ↓ size of fibroid prior to surgery – reduced blood loss and makes surgery easier + faster + more conservative
    - Sometimes **add in oestrogen/progesterone** (analogues or the real stuff) to counteract side effects caused by suppression of FSH/LH. This added oestrogen/progesterone does not prevent the action of GnRH analogues on the fibroid.
    - Disadvantages: Menopausal symptoms, Bone demineralisation with prolonged use, Used pre-operatively may increase risk of fibroid recurrency.
      - **Cabergoline**: Dopamine agonist. *Increasing dopamine levels leads to reduced levels of GnRH* (inhibits its release). Shows significant fibroid regression. Less side effects that GnRH analogue
      - **Oestrogen Receptor Modulation**: Most commonly used in carcinoma of the breast (tamoxifen). Have the ability to act as oestrogens in some tissue and block oestrogen action in others. To date, only **Raloxifene** has shown to reduce fibroid volume in post-menopausal woman. Tamoxifen is not used as it has a hyper-plastic effect on endometrium and may actually increase the size of fibroids. These are not being used clinically due to insufficient evidence over efficacy.
      - Aromatase Inhibitors: This would also prevent oestrogen production seen in adipose tissue, thereby having a greater potential in both pre and post-menopausal woman. However, use to date is only in case reports which report positive results. These tend to be well tolerated and can be given orally. Long-term use could again result in bone demineralisation and therefore need bisphosphonates.
      - **Levonorgesterol Intra-Uterine Device**: Effective at reducing menstrual blood loss and may be alternative to surgery. Limited side effects due to being released in target organ. Prevents endometrial proliferation to thereby reduce volume and length of bleeding.
      - **Antiprogesterones**: Progesterone may promote fibroid growth as well. These antagonists improve quality of life, anaemia and reduce uterine volume. There is also reduced side effects as low dose is used.
      - **Danazol**: Synthetic steroid with androgen effects. Suppresses sex hormone binding protein and exerts antiprogestational effects.
      - **Gestrinone**: Anti-oestrogen and anti-progesterone activity at receptor level. Also inhibits pituitary. Used to treat endometriosis and as an oral contraceptive.
      - **Non-Hormonal Options**: This is currently the main aim of research, to find compounds that will inhibit growth factors.
        - Heparin-binding factors have been found in fibroids leading to the possibility of using heparin to treat fibroids
        - **NSAIDs, Progesterone and HRT** don't shrink fibroids
      - **Angio**: uterine artery embolization: ↓ in sx usually lasts 3-5yrs but painful at the time
    - Surgical:
      - **Hysterectomy** (fibroids are leading cause of hysterectomy): leads → earlier menopause, ↑ risk of stress incont + vaginal prolapse
      - **Myomectomy** (↑risk of uterine rupture in subsequent pregnancy): allows fertility to be retained but can re-grow
      - Surgeries are risky and can drastically influence future fertility → aim to try and find a **medical management**
      - **Endometrial ablation**: may not get complete resolution of sx

**Adenomyosis**
- = Growth of endometrial glands and stroma into the myometrium
- Does not undergo cyclic changes and is **not hormone responsive**
- Symptoms: dysmenorrhea, menorrhagia, deep dyspareunia
- Incidence: age 35 – 50, parous
- Exam: globular, boggy, enlarged uterus, most tender peri-menses
- Treatment: NSAIDs, OCPs, GnRH agonists, Hysterectomy

**Premenstrual Symptoms & Syndrome (PMS)**

- Negative and/or positive changes in mood, behaviour, physical wellbeing + body shape that appear in the days prior to menstruation
- Multifactorial
- Main symptoms:
  - Depression, irritability, tiredness, headache, bloating, breast tenderness.
  - Classify as mild, moderate or severe on the basis of interference with daily function
  - Use of a symptom diary over 2 months is very valuable
- Diagnosis:
  - History
  - Symptom diary (see sx worst before periods, relieved with periods, at least 1 symptom free week afterwards)
  - Exam to exclude gynaecological and endocrine disorders
  - Tests: rule out thyroid, PRL, secondary dysmenorrhea (eg endometriosis)
  - Follow-up outside the pre-menstrual phase for objectivity – else pt might be irrational!
- Differential:
  - Psychiatric: depression or anxiety with premenstrual exacerbation
  - Medical: anaemia, hypothyroidism, cancer, SLE, menopause if > 45, renal causes, polycystic ovary
- Some more premenstrual symptoms:

<table>
<thead>
<tr>
<th>Most frequent negative symptoms</th>
<th>Most frequent positive symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abdominal distension</td>
<td>More energy</td>
</tr>
<tr>
<td>Anxiety and/or stress</td>
<td>Zest to finish pending matters</td>
</tr>
<tr>
<td>Pain and tension in breasts</td>
<td>More efficient at work</td>
</tr>
<tr>
<td>Crying spells</td>
<td>More interest in things in general</td>
</tr>
<tr>
<td>Depression</td>
<td>Sense of more control over one’s life</td>
</tr>
<tr>
<td>Fatigue, lack of energy</td>
<td>Socially more able</td>
</tr>
<tr>
<td>Less libido</td>
<td>More libido</td>
</tr>
<tr>
<td>Unprovoked anger or irritability</td>
<td>Breast more attractive</td>
</tr>
<tr>
<td>Problems concentrating</td>
<td>Younger face</td>
</tr>
<tr>
<td>Headaches</td>
<td>More affectionate</td>
</tr>
<tr>
<td>Changes in drinking and eating patterns</td>
<td>More relaxed</td>
</tr>
<tr>
<td>Oedema in extremities</td>
<td>More self assured</td>
</tr>
</tbody>
</table>

- Clinical identities of the premenstrual alteration:
  - Normal
  - Abnormal
  - Premenstrual symptoms
  - Premenstrual syndrome, with marked loss of quality of life through physical and psychological impact
  - Abnormal
  - Premenstrual Dysmorphic Disorder, with functional impairment through mood or psychosomatic impact
- Evidence-based treatments of premenstrual anomalies:
  - **1. Oral contraceptives** – multicentre studies show reduced dysmenorrhea and PMS in general
  - **2. Antidepressants** – RCT show positive results up to 60% with fluoxetine etc. Non-serotonergic antidepressants did not produce same results. FDA approved fluoxetine for PMDD in 2002.
  - **3. Psychological treatment** – an Oxford study showed that CBT resulted in near total remission of psychological and somatic symptoms in the medium term.
  - **4. Hysterectomy and bilateral oophrectomy** – lasting, but not everyone wants this.
  - **Ca2+, Mg2+ and vitamin B6 supplements** – reduction in symptoms rating more than placebo
  - **Spironolactone** – some studies showed no clinical impact or elimination of oedema superior to placebo, some later studies reveal a moderate positive effect
  - **Primrose oil** – from theory that patients with PMS suffer from a deficiency in the metabolism of fatty acids and hence primrose oil was recommended. Studies show NO difference from placebo
  - **Progesterone** – well-designed studies found neither progesterone nor placebo improved symptoms
  - **Dietary habits** – ↑intake of carbohydrates or other foods high in tryptophan reduce mood symptoms.
    - ↓refined sugars and salts ↓liquid retention. ↓intake of methylxanthines (coffee, tea, coke, chocolate)
    - ↓breast discomfort. Soy isoflavones act on estrogen and may reduce cramps and oedema
Phytotherapy – with agnus castus, well proven in EBMHealth. A study showed comparable efficacy with fluoxetine, though agnus castus reduced physical symptoms more.

Post Menopausal Bleeding (PMB)

- Bleeding > 1 year after the last period (check it is vaginal bleeding, not urethra or rectal)
- Causes:
  - Vaginitis (often atrophic): fragile → trauma, and ↓secretions → ↑infection
  - Foreign bodies (eg pessaries)
  - Endometrial or cervical polyps, endometrial fibroids (bleed a lot – leiomyoma, adenomyosis, hyperplasia)
  - Oestrogen withdrawal (HRT or ovarian tumour)
  - Carcinoma of the cervix
  - Endometrial cancer
- Distinguish from peri- or post-menopausal on HRT
- Investigation: Trans-vaginal US (looks at thickness of endometrium) and trans-abdominal US (finds other masses); pipelle biopsy
- If bleeding on non-cyclical HRT or intra-cyclical bleeding on cyclical HRT, be a bit more aggressive in investigation (HRT → slight ↑ risk of endometrial cancer)

Polycystic Ovary Syndrome (PCOS)

- Think of: a never-pregnant fat diabetic female with greasy skin, moustache and smoking (risk factors)
- Common 5-10% female
- Age 15-35y
- Over-response of theca cells to LH → ↑ androgen → aromatising hormone from follicular cells can’t keep up → excess androgen.
  - LH>FSH 2.5:1
  - Inhibits follicular growth pre-antral stage → necklace of follicles
  - Abnormal menstrual cycle
  - Androgen effects: greasy skin, central adiposity, acne, hirsutism
  - If rapid viralisation then look for tumour – not PCOS
- Associated with:
  - Obesity
  - Type 2 diabetes – insulin resistance → hyperinsulinaemia
  - Lipid abnormalities → vascular disease (eg 7 times risk of MI)

Symptoms

- 1. Disruption to menstrual cycle:
  - Infrequent periods
  - Irregular
  - Menorrhagia
  - Polycystic ovaries
- 2. Infertility
- 3. Alopecia
- 4. Hirsutism + acne + weight gain

Sequelae

- 1. Increased risk of gestational diabetes, pregnancy related hypertension, premature labour
- 2. Increased risk of endometrial cancer – no progesterone → endometrial hyperplasia

Diagnosis

- 1. US of polycystic ovaries > 12 antral follicles (“pearl necklace”)
- 2. Evidence of LH excess
- 3. Infrequent periods
- Differential: tumours of the ovary (eg granulosa and thecal cells) → chronic anovulation

Investigations

- Pelvic USS
- Fasting glucose (increased risk of DM)
- LH/FSH/Testosterone levels
Treatment

- 1. Lifestyle changes:
  - **Lose weight** (↓ peripheral oestrogen + insulin resistance)
  - Regular exercise and diet healthy

- 2. Medications:
  - **COC** to **regulate menstrual cycle** and reduce risk of endometrial cancer
  - Spironolactone (Yasmin) → control high BP and anti-androgen effects
  - Oral hypoglycaemics → metformin (↑ insulin sensitivity, ↓ menstrual disturbance and ↑ ovulatory function)
  - Progestagen → Provera, POP, IUD

- 3. If wishing to conceive: fertility drugs ie. **Clomiphene** (oestrogen antagonist) → ↑ FSH (+ therefore induces ovulation), given at **beginning** of cycle (day 3 – 7)

- 4. Surgery: Laparoscopic ovarian drilling

Menopause

- **Primary ovarian failure** → ↓ oestrogen feedback → ↑↑ FSH
- Continue contraception for **one year following last period** (eg PoP, IUCD, condoms)
- Usually age **50 – 51**. Cycles start to slow from 47 – 48. Usually follows **pattern of her mother**. Factors affecting age:
  - CoC delays menopause (less ovulation therefore lots of eggs left over)
  - Earlier if chronic disease or toxins (eg radiation, chemo, etc)

- WHO definition: the permanent cessation of menstruation resulting from loss of ovarian follicular activity determined retrospectively from the date of the last menstrual period, after **12 month amenorrhoea**, with no other attributable cause.

- Menopausal transition: **climacteric/perimenopause** phase. Early transition is characterized by changes in the normal menstrual cycle of > 7 days. In the late transition, women experience two or more skipped menstrual cycles and at least one intermenstrual interval of 60 days or more.

- Lifestyle changes in menopause:
  - Exercise: reduces cardiovascular risk
  - Menopausal women are advised to adopt healthy lifestyle modification

- Symptoms of menopause:
  - **Vasomotor symptoms** – hot flush, accompanied by other symptoms including anxiety, irritability, sweating, palpitations. Management:
    - 1. **Non-hormonal** – clonidine (centrally alpha agonist). Side effects: sleeplessness, constipation, drowsiness, dry mouth. SSRI paroxetine, SNRI venlafaxine: side effect: nausea and vomiting, reduced appetite, decreased libido, dry mouth and constipation.
    - 2. **Hormonal therapy – oestrogen therapy**. All types of oestrogen and routes have been found to be equally efficacious for relief of hot flushes.
    - 3. **Alternative**: environment factors (light clothing, use fan), physically active, paced respiration, herbal and botanical.

  - **Sleep disturbance**: after ruling out other causes of sleep disruption, sleep hygiene and behavioural changes should be addressed. HRT has long been used for improvement of sleep at menopause

  - **Depressed mood**: common in the menopausal transition phase. Risk factors for development of depression: hx of depressive disorders, poor physical health and life stressors, hx of surgical menopause and long perimenopausal transition. Management:
    - 1. Carefully evaluate to rule out clinical depression.
    - 2. Psychotherapy, antidepressants
    - 3. Oestrogen therapy might be effective in relieving the symptoms.

  - **Vulvovaginal symptoms**: most commonly reported symptoms. Vaginal dryness, dyspareunia, decreased sensitivity to touch.
    - Prevention: reduce smoking, vaginal health is better maintained in women with higher circulating levels of androgen and in women who are more frequently sexually active.
    - Management of atrophic vaginitis:
      - 1. **Exogenous oestrogen** particularly vaginal oestrogen
      - 2. Vaginal moisturizers, containing non hormonal moisturizing gel of water, glycerine etc.
      - 3. All formulations of local oestrogen-cream, ring or low dose tablet had efficacy in relieving symptoms of dryness, pruritus and burning.

  - Aches and pain:
Some of the most troubling symptoms are joint pain and stiffness.

**Management:**
- **1. Physical activity** – exercise that promotes flexibility and stretching such as yoga.
- **2. Glucosamine** provides symptomatic relief for women with arthritis and can be useful for menopausal joint symptoms.

**Sexuality** – decline in sexual interest and function:
- The cornerstone of management is to treat any underlying disorders, educate and help to set reasonable expectations, and to intervene with behavioural and lifestyle changes, counselling, or sex therapy.
- Oestrogen therapy relieves vaginal dryness and is associated with increase in sexual ideation, desire, arousal, and satisfaction.

- **Signs:**
  - Hot flushes, palpitations
  - Night sweats
  - Mood swings/depression
  - Vaginal atrophy → dyspareunia, post-coital bleeding
  - Urinary frequency/incontinence
- Test for high TSH if wanting to exclude thyroid and psychiatric problems

**Hormone Replacement Therapy**
- Replacing normal physiological dose of oestrogen (cf CoC which is higher)
- **Contraindications:**
  - History of breast or endometrial cancer (not ovarian or cervical)
  - Undiagnosed vaginal bleeding
  - Liver disease (it’s metabolised in the liver)
  - Pregnancy or breast-feeding!
  - Past PE
  - High cholesterol is NOT a contra-indication – it’s protective (compared with OC dose of progesterone which is bad)
  - Smoking is NOT a contra-indication – it’s protective
  - DVT is NOT a contra-indication (whereas OC dose of oestrogen is bad for clots)
- **Benefits:**
  - Especially good for those with hysterectomy, bilateral oophorectomy, ↑risk of osteoporosis, IHD, ↑cholesterol, DM, RA
  - **Oestrogen effects:** ↓menopause symptoms, ↓osteoporosis, ↓CV disease (↓LDL, ↑HDL, vasodilates coronary arteries)
  - **Progesterone effects:** ↓risk of endometrial cancer (if they have a uterus) by preventing proliferation of endometrium by unopposed oestrogen
  - ??Protective against colon cancer and Alzheimer’s
- **Side-effects:** irregular bleeding, ↑weight, PMS, cholestasis, vomiting
- **Risks:**
  - Minimal breast and ovarian cancer risk if taken for less than 5 years
  - Gallbladder disease
  - If severe heart disease then slightly ↑risk of CV problems in 1st years
- **Types:**
  - **Cyclical:** continuous oestrogen, progesterone for any 10 days per cycle (with bleeding 2 – 3 days after its finished). Good if immediately post-menopausal – cycle them for a while and if no break through bleeding then → continuous HRT after a year
  - **Non-cyclical:** Continuous oestrogen and progesterone. No period as oestrogen and progesterone oppose each other → stable endothelium. Don’t start until after menopause. Ovary may still be ‘surging’ from time to time → break through bleeding that you’ve got to investigate

**Chronic Pelvic Pain (CPP)**
- **NB.** See Pelvic Inflammatory Disease
- Ongoing chronic pain in the lower abdomen/pelvis, not related to pregnancy, ovulation or sexual intercourse
- Affects 1 in 6 women
- Diagnosis of exclusion
- Causes/differentials:
  - Disorders of female pelvic organs:
Disorders of 
- Endometriosis
- PID
- Adhesions
- Retained ovary syndrome
- Ovarian cysts

Disorders of urinary tract:
-Interstitial cystitis (most common urologic cause of chronic pelvic pain)
- Bladder neoplasm
- Urethritis

Disorders of GI tract:
- IBS
- Chronic constipation
- Diverticular disease
- Celiac disease

Also fibromyalgia, pudendal neuralgia, ovarian, bone and bladder cancer

Physical examination/ix:
- Pelvic examination
- Abdo, vaginal USS
- Urinalysis - infection
- Bloods – inflammation, infection
- STI check

Treatment:
1. Pain relief: NSAIDS
2. COC esp if dysmenorrhoea
3. GnRH agonists – prevents ovaries from making hormones – decrease estrogen and endometrial pain
4. ABs
5. Antidepressants

Pelvic Mass

<table>
<thead>
<tr>
<th>Pelvic Masses</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Aetiology:</strong></td>
</tr>
<tr>
<td>• Uterine: pregnancy (symmetrical), fibroids (leiomyomata)</td>
</tr>
<tr>
<td>• Fallopian tubes: tubo-ovarian abscess, ectopic pregnancy, neoplasm.</td>
</tr>
<tr>
<td>• Ovaries: functional cyst, neoplastic cyst, dermoid cyst (commonly bilateral), endometriosis (endometrioma).</td>
</tr>
<tr>
<td>• Surrounding tissues: distended bowel, hernia, colon cancer.</td>
</tr>
<tr>
<td><strong>Clinical assessment:</strong></td>
</tr>
<tr>
<td>• If incidental finding → indicates benign nature.</td>
</tr>
<tr>
<td>• Hx: disturbance of other bodily functions (weight loss → malignancy).</td>
</tr>
<tr>
<td>• FHx, Exam</td>
</tr>
<tr>
<td><strong>I/x:</strong></td>
</tr>
<tr>
<td>• U/S (trans-vaginal, trans-abdominal) → good for imaging the uterus (endometrial thickness) and fibroids.</td>
</tr>
<tr>
<td>• CT/MRI – gold standard but expensive.</td>
</tr>
<tr>
<td><strong>Tumour markers:</strong></td>
</tr>
<tr>
<td>• CA125 antigen – ovarian tumour marker – produced by many inflammatory or neoplastic ovarian diseases – useful for monitoring or if very high indicate abnormality present.</td>
</tr>
<tr>
<td>• HCG – tumour marker for gestational trophoblastic diseases (hydatidiform mole and choriocarcinoma) + germ cell tumours of the ovary. Also elevated in pregnancy (good for comparing pre and post treatment). Normally doubles every 2 days in 1st 8/40. If not doubling or is decreasing before 8/40 implies non-viable pregnancy.</td>
</tr>
<tr>
<td>• CEA: colon cancer tumour marker.</td>
</tr>
<tr>
<td>• Cytology</td>
</tr>
<tr>
<td>• Guided biopsy</td>
</tr>
</tbody>
</table>

**Fibroids (uterine leiomyomata)**
- Defn: smooth muscle tumour of the uterus
- Epi: affects 20% women (black>white), 50% symptomatic.
- Aetiology:
  - Oestrogen dependant (↑pregnancy, ↑COC, ↓menopause),
  - Regression: either slow or rapid. Rapid = “Red degeneration” painful and asc with N&V and fever.
Reproductive and Obstetrics

Sx:
- **Menorrhagia** – most common reason for seeking treatment.
- **Infertility** – can cause miscarriage or obstruction due to encroaching on uterus.
- **Pain** – torsion of pedunculated fibroid or red degeneration.
- **Mass effects** – bladder (↑ frequency) bowels (↑ constipation), discomfort, varicose veins.

Ix:
- Physical examination
- U/S

Tx:
- Surgical:
  - **Myomectomy**: laparoscopic removal – maximum preservation of uterus and fertility, ~50% recurrence within 5 yrs.
  - **Endometrial ablation**: infertility, 75% success rates.
  - **Hysterectomy**: 100% success but infertile as result.
  - **Uterine artery embolisation**: minimally invasive but painful and only produce ~50% reduction in size of fibroids.
- Medical:
  - **Pain**: paracetamol, NSAIDS
  - **Mirena**: used to attempt to shrink and maintain fertility.
  - **LHrH analogue**: ↓ oestrogen reducing size and fertile when stop tx.

History:
- Pain, bleeding, urinary and bowel symptoms, constitutional symptoms (weight loss, night sweats, etc)
- Parity and gravidity, menstrual, contraceptive, and cervical smear status
- Check for family history of tumours: ovarian, breast (BRCA family) and GI. Also fibroid family history.
- Malignancy features: fast growing, GI upset, weight loss, patient noticed ↑ in skirt size
- Fibroids features: dull pelvic/back ache, stress incontinence

Exam:
- **Lymphadenopathy**, abdo exam, record features of mass (size, fluctuance, mobility, irregularity), speculum and bimanual exam of vagina and cervix (note relationship of mass to uterus and adnexae).

Differential Diagnosis

- **Use surgical sieve**
- **Uterine**:
  - **Pregnancy**
  - **Fibroids** – pedunculated/intraligamentous
- **Tubal**:
  - **Ectopic pregnancy**
  - **Tubo-ovarian abscess**
  - **Paraovarian cysts** (remnants of Wolffian duct)
  - **Neoplasia**
- **Ovarian**:
  - **Functional cyst** – (can be 10cm) common, follicular/corpus luteum, theca lutein (infertility treatment)
  - **Endometriomas** – ovary common site (chocolate coloured <12cm), can be indistinguishable from neoplasm
  - **Neoplasm** – 20% malignant – solid (fibroma, thecoma, adenocarcinoma) or cystic (cystadenoma, cystic teratoma, cystadenocarcinoma)
- **Non-gynaecological**:
  - **Bowel** – faecal, inflammatory (diverticulitis, abscess, ileitis, GI malignancy)
  - **Bladder**
  - **Kidney** – pelvic
  - **Retroperitoneal** – sarcoma, lymphoma

**Symptoms Pointing to a Diagnosis**

- Pain related to an adnexal mass is usually secondary to distention of the ovarian capsule or compression of adjacent structures
- In premenopausal women, midcycle pain suggests ovulation or mittelschmerz
- Pain following intercourse may be related to a ruptured follicular or corpus luteum cyst
- Pain during intercourse is suggestive of endometriosis
Abdominal or pelvic pain in the setting of an adnexal mass and a positive pregnancy test is almost always due to an ectopic pregnancy.

Sudden onset of severe pain or intermittent severe pain, often associated with nausea and vomiting, implies ovarian torsion.

Severe dysmenorrhoea and menorrhagia can signify endometriosis or leiomyomas.

A history of prolonged amenorrhoea followed by menorrhagia and the finding of multicystic ovaries is characteristic of polycystic ovarian syndrome.

Bleeding in the premenarchal or postmenopausal patient with a solid ovarian mass increases the likelihood of a granulosa cell tumor.

Other important symptoms are dyspepsia, early satiety, a sensation of abdominal bloating or fullness, and constipation or a change in the calibre of the stool.

Patients with ovarian carcinoma frequently present with vague gastrointestinal symptoms.

In women with an adnexal mass, a breast examination is particularly important because the ovary is a common site of metastasis for carcinoma of the breast.

Location

Physiological: full bladder, flatus, faeces, pregnancy, obesity

Congenital: uterine anomaly, pelvic or polycystic kidney

Trauma: rectus abdominis haematoma

Infective: pyosalpinx, pelvic abscess, diverticulitis, TB peritonitis, lymph nodes

Neoplastic: fibroids, tumours of colon, rectum cervix or endometrium, ascites, retroperitoneal tumour, mesenteric cyst

Hormonal: non-neoplastic cysts

Mechanical: hydropneumosis

Pregnancy associated: pregnancy in uterine horn or ectopic, trophoblastic disease, corpus luteum of pregnancy

Exam: hydration, anaemia, supraclavicular, lymphadenopathy, pleural effusion, abdominal scars, mass, ascites, pelvic exam (sensitivity/specificity 50%)

Investigations

Pregnancy test

Tumor markers:

- **CA125** (epithelial ovarian carcinoma) +ve in 1% normal population, 6% benign disease (endometriosis, PID, pregnancy, liver cirrhosis, pancreatitis), 28% non-gynae malignancy, **82% ovarian cancer**. Useful to monitor response to chemo.
- **CA19.9**: main use is pancreatic cancer marker. Also a marker for cancers of: breast, lung liver, uterus and ovary.
- **Alpha Feto Protein**: marker in ovarian germ cell tumours. Also raised in other tumour types, hepatitis and cirrhosis.
- **HCG**: germ cell tumour marker and gestational trophoblast disease. Also raised by many other cancers, non-malignant diseases and pregnancy.
- **Carcino-Embryonic Antigen (CEA)**: primarily to monitor colorectal Ca treatment. Also raised in ovarian Ca and other non-malignant diseases. Prognostic not diagnostic.

Other investigations: Aspiration and cytology, guided biopsy (for advanced disease with unknown primary source)

- ESR, FBC
- Laparoscopy, colonoscopy
- Transvaginal USS
- Transabdominal USS

Benign tumors – smooth walled, cystic, mobile, unilateral, small than malignant.

Malignant tumors – solid, bilateral, irregular, fixed, nodules in pouch of douglas, ascites

Pre-Menopausal Pelvic Mass

- <16y → 20% malignant
- 30y → 18% malignant
- 40y → 26% malignant
- >10cm should be surgically explored
- 95% <5cm non-neoplastic
Management:

Post-Menopausal Pelvic Mass
- In postmenopausal women with adnexal masses, both primary and secondary neoplasms must be considered, along with leiomyomas, ovarian fibromas and other lesions such as diverticular abscesses
- CA125 very sensitive in post-menopause
- CA72-4
- RMI (risk of malignancy) = CA125 + (USS score x menopausal status) = >200 malignant
- USS score = points given for loculated cysts, bilateral, solid areas, ascites, metastases
- Management:

Pregnancy Pelvic Mass
- Common (usually dermoid or ovarian cysts) – most resolve by 2nd trimester (surgically evaluate if persist – 17/18wk abortion risk very low). 3rd trimester – 2-5% malignancy
- Ovarian tumors can complicate labour, rupture cyst, haemorrhage, infection, torsion

Uterine & Vaginal Prolapse & Urinary Incontinence
- Hymenal remnant is the reference point
- Uterus prolapses either down into or out of vagina
- Pubic body (region b/w anus + vagina) can bulge post traumatic delivery + appear as a prolapse

Uterine/vaginal prolapse and Urinary incontinence
- Essentially: either cystocele/rectocele/uterine prolapse secondary to birthing trauma/obesity etc exacerbated by menopause, causing fullness, urinary & bowel symptoms, treated with anterior/posterior repair (colporrhapy)/pessaries/laxatives etc
- Aetiology:
Pregnancy related stretching of supporting structures (poor perineal repair reduces support)
Congenital abnormality (inherited pelvic floor weakness).
Exacerbated by: **menopausal atrophy, obesity**, straining (chronic cough/constipation).

- **Sx:**
  - Feeling of mass; dragging or sensation of prolapse descending
  - **Urinary Sx:** frequency, stress incontinence
  - **Bowel sx:** difficulty defecating – requiring manual assistance.

- **Prolapse history taking:**
  - **Urinary symptoms** – frequency, urgency, nocturia
  - **Incontinence** – stress vs. urge – increased frequency, nocturia, key-in-the-door syndrome (urgency), small vol voiding, dribbling, detrusor instability
  - Pain during intercourse
  - Pain during defecation

- **Ix:**
  - Internal examination with **Sim’s speculum + straining**
  - POPQ: classification system

- **Types of prolapse:**
  - **Front wall of vagina – cystourethrocele** (most common form of prolapse) when bladder and urethra fall towards vagina
    - **Cystocele:** when bladder prolapses against front wall of vagina
      - Causes: frequency, urgency, nocturia, stress incontinence, incomplete bladder emptying
      - Treat with kegel exercises, vaginal pessary, anterior vaginal repair
    - **Urethrocele:** when urethra prolapses against front wall of vagina
  - **Back wall of vagina**
    - **Rectocele:** rectum bulges against back wall of vagina – causes: difficulty passing stool. Treat with laxatives, posterior repair
    - **Enterocele:** part of SI which usually sits behind uterus slips into pouch of douglas.
  - **Prolapse of uterus** – 2nd most common form of prolapse after a cystourethrocele. Grades depending on the degree the uterus drops into vaginal canal.
    - **Grade 1.** Uterus has dropped into lower half of vagina
    - **Grade 2.** Uterus has dropped into vagina and cervix and is near the opening of the vagina
    - **Grade 3.** Vagina, uterus and cervix are protruding partially outside the vaginal opening
    - **Grade 4.** Most severe, vagina, uterus and cervix completely fallen out of vaginal opening.

- **Note:** prolapse of the vaginal vault occurs in women who have had hysterectomy – vagina involutes on itself and can protrude out.

- **Rx:**
  - **Pessaries** can be used for support
  - **Colporrhaphy:** repair of Rectocele (posterior Colporrhaphy), cystocele (Anterior Colporrhaphy) or lateral prolapse by excision of excess vaginal wall and insertion of mesh supports.
  - Uterine prolapse repair:
Sacrohysteropexy: surgery to suspend the uterus to the sacrum.

Hysterectomy: in women who have completed families.

Vaginal vault prolapse repair:

- Sacrospinous ligament fixation: superior vagina is fixed to the sacrospinous ligament providing support of the vaginal vault (can be used after hysterectomy)

Urinary Incontinence

- **Storage** = SNS hypogastric n → relaxes detrusor m. Pudendal n → constricts external sphincter.
- **Peeing** = PSNS pontine micturition centre descending inputs which cause peeing
- Alpha R. – sphincter contraction. MAch R. – detrusor m contraction
- In treatment of detrusor m instability: anticholinergics and alpha agonists.
- **Epi**: 10% at 20yrs to 35% at 50yrs.
- **Defn**: involuntary leakage of urine causing a social or hygiene problem
- **RF**: pregnancy/NVD, DM, obesity, oral oestrogen therapy, stroke, constipation, ?menopause
- **Hx**:
  - Symptoms: use SMOCS, just concentrate on urinary symptoms first
  - **Bladder diary**: fluid intake and urinary output
  - Rule out transient reversible causes:
    - DIAPER
    - Delerium, infection (UTI), atrophic vaginitis/urethritis, psychological/pharmacological, restricted mobility, stool impaction

- **Examination**:
  - **Abdominal**: for masses, distended bladder
  - **Vaginal**:
    - Inspection for atrophy, abnormal anatomy, prolapse
    - Palpation & speculum for prolapse
  - **Neurological**:
    - Perianal sensation – cauda equina syndrome
    - Gait
    - S2-4 myotomes (anal sphincter/pelvic floor strength) & dermatomes
    - Reflexes: ankle jerk
  - **Stress test**: ask patient to cough while holding labia apart on full bladder to observe for leakage.

- **Ix**:
  - Urinalysis
  - US for pre & post void volumes (if retention suspected)
  - **Urodynamic study** (GOLD STANDARD)
    - Via catheter fill bladder and measure:
      - 1. Intraurethral pressure
      - 2. Intravesical pressure
      - 3. Intra-abdominal pressure (via probe in rectum)
    - **Stress incontinence**: bladder capacity normal, pressure rises just before capacity.
    - **Urge incontinence**: intravesicular pressure rises early with reduced capacity

- **STRESS incontinence**: involuntary leakage of urine when increased abdominal pressure occurs due to weak pelvic floor muscles with prolapse of urethra resulting in shortening of the intra-abdominal urethra.
  - **Sx**: Leakage of small volumes of urine with ↑ intra-abdominal pressure: exertion, cough, sneeze
  - **Causes**: multiple childbirths, urological procedures, obesity, chronic cough
  - **Rx**:
    - **Lifestyle**: weight loss, smoking cessation, regulate food and fluid intake.
    - **Physiotherapy**: **Bladder retraining** (hold on for longer), pelvic floor retraining (<90% success rate after 3 months for stress incontinence).
    - **Vaginal pessary** – pressure + oestrogen effects on bladder neck.
    - **Medical**: Duloxetine: 5HT3 + NA reuptake inhibitor: ↑ 5HT3 + NA in pons which ↑ Onuf’s nucleus tonic contraction of the urethral sphincter
    - **Surgery**:
      - 1. Mid-urethral “transvaginal” tape: minimally invasive. Transobturator approach used now
      - 2. **Pubovaginal sling**: sling elevates bladder neck attached to rectus sheath.
      - 3. **Open/laparoscopic Burch colposuspension**: anterior vagina suspended from the side walls of
the pelvis supporting the bladder neck (>80% success rates).

- URGE incontinence/overactive bladder: involuntary leakage of urine a/w sense of urgency due to detrusor overactivity in response to uninhibited PSNS innervations.
  - **Note:** older women have detrusor hyperactivity with impaired contractility → urge incontinence with residual volume predisposing to UTI's.
  - **Sx:**
    - Involuntary leakage asc with urgency (day and night)
    - Frequency
    - Nocturnal enuresis
  - **Cause:** Stroke, alzheimers, parkinsons, BPH with overflow (males).
  - **Rx:**
    - Anticholinergic drugs:
      - **Oxybutinin** (Less specific more SE’s)
      - Tolteradone (more specific to detrusor M3 Ach receptors)
    - Botox injection
    - Surgery: sacral nerve stimulation or other surgical techniques; rarely done + last resort
- Can also see mixed (urge + stress) incontinence patterns: important to ask the pt which symptom is the most bothersome
- **Rare cause of incontinence:** vaginovesical fistula. Can be seen post hysterectomy or obstructed labour
- **Normal physiology:**
  - **SNS:** storage (α receptors on sphincter, β receptors on detrusor muscle)
  - **PSNS:** pee via activation of muscarinic receptors causing contraction of detrusor m (& relaxation of IUS)
  - As bladder fills → SNS activated, allowing filling without increased intravesical pressure.
    - **Hypogastric nerve** → relaxation of the detrusor muscle while contracting the internal sphincter.
    - **Pudendal nerve** → contracts external sphincter
    - **Higher centres** – inhibit pontine micturition centre (PSNS).
  - **Voiding:** bladder fills to close to capacity (~350mls) before pelvic nerve stimulates cortical micturition centres that activate the pontine micturition centre. This inhibits SNS activation and causes activation of the PSNS contraction of the detrusor muscle.
  - **Pelvic floor:**
    - Sling-like support for organs of the lower pelvis
    - Contributes to the action of the EUS
    - Made up of levator ani + pubococcygeus
    - 2 important reflexes:
      - 1. Perineodetrusor inhibitory reflex: tone of the pelvic floor promotes reflex relaxation of the detrusor
      - 2. Detrusosphincteric inhibitory reflex: contraction of detrusor relaxes pelvic floor & EUS

![Diagram of types of incontinence](image)
The NEURORECEPTORS that control the micturition reflex are PARASYMPATHETIC (cholinergic) and SYMPATHETIC (Alpha or Beta).

The PARASYMPATHETIC (cholinergic) receptors are throughout the “body” of the bladder, trigone and bladder neck.

The SYMPATHETIC (beta) receptors are throughout the bladder, more densely populating the “dome” and less dense in the trigone.

The SYMPATHETIC (alpha) receptors are densely located in the bladder neck (proximal urethra) and more sparsely populate the trigone.

During storage:
1. Parasympathetic (cholinergic) receptors are inhibited, prohibiting detrusor muscle contraction.
2. Sympathetic receptors are stimulated, resulting in:
   - Relaxation of beta controlled detrusor muscle and increased stretch capacity of the bladder dome.
   - Contraction of the alpha controlled bladder neck.

During emptying:
1. Sympathetic receptors are inhibited, resulting in:
   - Cessation of the beta assisted stretch of detrusor muscle.
   - Relaxation of the alpha controlled bladder neck.
2. Parasympathetic (cholinergic) receptors are stimulated, strengthening the detrusor contraction.

Vulval Lesions

- Non-neoplastic epithelial disorders:
  - **Lichen Sclerosis**:
    - 1/3 of lesions, commonest after menopause
    - Pruritic, affecting any part of the vulva
    - Multiple irregular white patches, shiny wrinkled atrophic skin
    - ↑ Risk of SCC
    - Microscopy: subepithelial homogenous collagen + band of lymphocytes
    - Autoimmune aetiology → treatment with steroids
  - **Squamous Hyperplasia**:
    - Non specific thickening of the epithelium + inflammatory reaction below the BM: acanthosis, hyperkeratosis
    - Non specific diagnosis
  - Other dermatoses: Lichen simplex chronicus, spongiotic dermatitis (contact dermatitis eg perfumed toilet paper), psoriasis, lichen planus

- Vulval Intraepithelial Neoplasia (VIN):
  - Often multi-focal white-pink-red raised lesions which itch/burn/asymptomatic
Preinvasive dysplastic squamous lesions
- Dysplasia is graded VIN1, VIN2, VIN3
- Untreated 7/8 progress to SCC (unlike CIN)
- Risk factors similar to cervical carcinoma
- 60% have lesions in other areas

- Squamous Cell Carcinoma:
  - 90% of vulval and 5% of gynae cancer
  - Two types:
    - Elderly women (70+): 65%, related to Lichen Sclerosis & squamous hyperplasia, well differentiated – islands of invading cells
    - Younger women (40+): 35%, related to HPV, Cervical cancer risk factors, poorly differentiated
  - Raised white warty mass
  - Micro: resembles SCC at other sites
  - Often present late
  - Prognosis depends on stage. Factors in order of importance are:
    - Lymph node metastasis
    - Depth of invasion
    - Size

- See also Non-Sexually Transmitted Genital Skin Lesions, page 679

Gynaecological Pathology

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<th>Cancer</th>
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<tr>
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<td>SCC, adenocarcinoma</td>
<td>HSIL</td>
<td>1. Smear</td>
<td>LLETZ</td>
</tr>
<tr>
<td></td>
<td></td>
<td>ASCUS – H</td>
<td>2. Colposcopy using acetic acid (enhances TZ) + iodine (non-glycogenated cells if malignant don’t take up I &amp; are pale), biopsy, endocervical curettage</td>
<td>Cone bx</td>
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<tr>
<td></td>
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<td>AGC</td>
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<td>ACIS</td>
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<tr>
<td>Endometrial</td>
<td>Adenocarcinoma</td>
<td>Oestrogen dependent</td>
<td>1. TVUS</td>
<td>TAH + BSO</td>
</tr>
<tr>
<td></td>
<td></td>
<td>HNPCC related Older</td>
<td>2. Biopsy (pipelle)</td>
<td>Maybe chemo</td>
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<tr>
<td>Ovarian</td>
<td>Serous cystadenocarcinoma</td>
<td>&gt;10cm, bilateral,</td>
<td>1. US + Ca125 + menopausal status (RMI)</td>
<td>Refer</td>
</tr>
</tbody>
</table>
|            | (most common)                | multiloculated,           |                                                    | TAH + BSO + omentectomy |}
|            | Borderline, Brenner          | ascites, thick septations | 2. CT chest/abdo/pelvis                            | Maybe chemo        |
|            | Germ cell eg teratoma, dysgerminoma, choriocarcinoma etc | | 3. LFTs for liver mets | |
|            |                              |                           | 4. Urea/Cr prior to chemo                          |                    |
|            |                              |                           | 5. hCG, inhibin, AFP, LDH                          |                    |
|            |                              |                           | Not bx                                             |                    |

Cervical Dysplasia

HPV
- There are over 200 HPV subtypes; approximately 40 types are specific for the anogenital epithelium but most HPV infections are transient and asymptomatic.
- HPV subtypes:
  - High risk HPV subtypes: HPV 16 and 18, are strongly associated with high grade lesions (HSIL and CIN 2,3), persistence, and progression to invasive cancer, although they may also be associated with low grade lesions. HPV 16 and 18 accounts for 25% of low grade lesions, 50-60% of high grade lesions, and 70% of cervical cancers. High grade lesions are usually flat, but cancers can be nodular, ulcerative, exophytic, or endophytic.
  - Low-risk subtypes, such as HPV 6 and 11, do not integrate into the host genome and only cause low grade lesions (eg, LSIL and CIN 1) and benign condylomatous genital warts. Overall, HPV 6 and 11 account for 10% of low grade lesions and 90% of genital warts.
- Risks:
  - First sexual experience at young age, multiple partners, partner with HPV.
  - Not attending screening appointments.
  - Women > 40, MAP, low SES.
- Cofactors in pathogenesis:
Reproductive and Obstetrics

- **Immunosuppression** e.g. HIV, steroids, organ transplant
- **Smoking:** Cigarette smoking and HPV infection have synergistic effects on the development of CIN and cervical cancer. Breakdown products e.g. nicotine, are concentrated in cervical mucous, where they may induce cellular abnormalities in cervical epithelium and decrease local immunity.
- Use of COC’s. NOTE: Microglandular hyperplasia can occur with OCP use – it may look red and be painful/bleed but is benign.

**Pathology:**
- Essentially: HPV infection → koilocytosis → virus inserted into genome of cells → oncogene activation → uncontrolled cell growth
- HPV (6, 11, 16, 18) virus infects cells of the cervical epithelium through integration of its genetic material into the cell (creating an episome).
- The episome (viral genetic material) causes **koilocytosis** (squamous cell that has undergone structural changes due to HPV infection; cells on the right, cells on the left are normal) but no dysplastic changes.
- If the episome can insert into the nucleus and integrate into the cell DNA (integrating genes **E6** (retinoblastoma gene- regulating entry into cell cycle) and **E7** (apoptotic regulator)) it can **produce proteins that activate oncogenes** resulting in **uncontrollable cell growth**.
- This can occur with any of the oncogenic HPV strains but is more likely in the high risk strains such as 16 or 18.
- Occurs at the transformation zone due to ↑ mitotic activity here
- Ectocervical abnormalities: squamous cells = epithelial
- Endocervical abnormalities: columnar cells = glandular

**Screening:**
- **Pap smear** (designed for squamous changes, can still pick up glandular changes): cells scraped from TZ.
- Preparing slides:
  - **Conventional smear** (Pap) test: Cells are smeared onto slide and stained (not done any more)
  - **Liquid based cytology** (LBC) test: Cells put into liquid medium – machine puts cells on slide and stains like above (↓ unsatisfactory smear rate)
  - If results are ‘unsatisfactory’ e.g. couldn’t see cells due to blood/mucus, must do again
  - Inflammation/infection may be noted.
- Screening Process:
  - Start at 20 (if sexually active) – **re-smear at 1 year** (in case anything missed ↓false -ve). Women < 20 not screened as **very rare to see cancer in this age group**
  - Screening (every 3 years after until 70 [unless abnormal previous smear]) reduces risk to the individual by >90%
  - If unsatisfactory smear (likely due to TZ movement into endocervix) in 70 year old, give 10-14 days oestrogen then repeat
  - NB If > Syrs between smears start process again e.g. 1 year then 3 years (need two clear smears before can 3yrly screen)
  - If HIV+ve: screen yearly
  - If had hysterectomy (both uterus and cervix) – only have smear if had abnormal cells confirmed by biopsy, surgery due to abnormal cells e.t.c (=vaginal vault smear).
- Reflex HPV testing:
  - If abnormality found on smear, lab will reflexly do HPV testing in those over 30
  - Performed in any liquid smear reported as abnormal in individuals over the age of 30 (if <30 most likely to regress therefore not done).
  - If High risk HPV +ve (HrHPV) → refer for colposcopy, Low risk HPV → further observation
  - If HrHPV –ve → repeat smear at 12/12
Classification:

Squamous intraepithelial lesions (SIL) for CYTOLOGICAL changes (SMEAR)

- **LSIL**: Low grade SIL. Occurs when the virus persists in the cytoplasm of epithelial = usually CIN1 (koilocytosis).
- **HSIL** (and cancer): High grade SIL. Occurs when the virus integrates into the human genome = usually CIN2, CIN3
  - HSIL are typically diagnosed in women 25 to 35 years of age, while invasive cancer is more commonly diagnosed after the age of 40, typically 8 to 13 years after a diagnosis of a high grade lesion.
  - HSIL: < 2% have invasive cervical cancer at that time, however about 20% would progress to having invasive cervical cancer without treatment.

Cervical intraepithelial neoplasia (CIN) for HISTOLOGICAL changes (BIOPSY)

- **CIN 1** (low grade lesion) = dysplastic cellular changes confined to the basal 1/3 of the epithelium.
- **CIN 2** (high grade lesion) = dysplastic cellular changes confined to the basal 2/3 of the epithelium.
- **CIN 3** (high grade lesion) = dysplastic cellular changes encompassing >2/3 of the epithelial thickness, and includes full-thickness lesions (formerly called severe dysplasia and carcinoma in situ and adenocarcinoma...
The Bethesda System (TBS) (System for reporting smear results “CYTOLOGICAL CLASSIFICATION”)

- Squamous cell abnormalities (ectocervix - epithelium):
  - 1. Atypical squamous cells of undetermined significance (ASCUS)
  - 2. Atypical squamous cells - cannot exclude HSIL (ASCUS-H)
  - 3. Low grade squamous intraepithelial lesion (LSIL) → corresponds to CIN1
  - 4. High grade squamous intraepithelial lesion (HSIL) → corresponds to CIN2/3
  - 5. Squamous cell carcinoma (SCC) or features of invasion

Management of abnormal squamous findings (ASCUS as LSIL and ASCUS-H as HSIL)

- If -ve for atypical change → repeat test in 3 yrs (unless 1st → repeat 1 yr)
- ASCUS/LSIL:
  - <30 re-test in 12 months unless previous abnormal smear (colposcopy if changes persist)
  - >30 reflex HPV test on fluid cytological sample
- +ve for high risk HPV → colposcopy.
- -ve for high risk HPV → resmear in 12 months.
  - ASCUS-H/HSIL: Colposcopy + biopsy (exceptions may occur if pregnant)
  - SCC: Colposcopy ASAP!

- Glandular cell abnormality (endocervix)
  - Atypical glandular cells not specified (AGS-NS)
  - Atypical glandular cells suspicious of endocervical carcinoma in situ (AGS-neoplastic)
  - Adenocarcinoma in situ (AIS).

- Management of abnormal glandular findings (lower sensitivity test so more cautious)
  - Refer all abnormalities for colposcopy or gynaecological assessment with HPV testing → sensitivity of a smear to detect glandular abnormalities is poor cf epithelial abnormalities
  - Abnormal colposcopy → cone biopsy + D&C (dilation of cervix and curettage)
  - NOTE: Inflammation (i.e. due to infection) can make cells look slightly abnormal – may mimic LSIL.

Pathology:
- **LSIL** (CIN1): Koliocytes present, thickened epithelium, dysplastic cells confined to basal 1/3 (Koliocytes have perinuclear clearing, nuclear irregularity, hyperchromasia)
- **HSIL**: (CIN2/3) Mitotic figures seen, nuclear pleiomorphism, increased N:C, >2/3 affected

Diagnosis:
- LSIL Lesions (warts): Most go away by themselves (just transient)
  - Premenopausal women: immediate colposcopy (high risk of underlying CIN 2, 3 or more).
  - Adolescents: repeat cytological evaluation in 12 months as LSIL generally represents a transient HPV infection and both the infection/LSIL usually resolve over time. Furthermore, the rate of invasive cervical cancer in this age group is near zero.
  - Postmenopausal women: options for further evaluation include: immediate colposcopy, repeat cytoplogic evaluation at 6 and 12 months, and HPV testing (can avoid colposcopy).
  - Note: Endocervical curettage is NOT performed in pregnancy OR young females.
HSIL Lesions:
- All non-pregnant women with HSIL are immediately evaluated by colposcopy with biopsy of all visible lesions and endocervical curettage (ECC) or by a diagnostic excisional procedure.
- Endocervical curettage is NOT performed in pregnant women because of potential trauma to the gestational sac and heavy bleeding (also younger females).

Colposcopy:
- Provides an illuminated, magnified view of the cervix, vagina, and vulva to identify precancerous and cancerous lesions so that they may be treated early.
- Indications:
  - 2 low grade smears (at least 12 months apart), 1 high grade smear, suspicion of cancer, ACIS (adenocarcinoma in-situ) or any glandular abnormality (as smear not accurate for this).
  - Also: Symptoms (IMB, post-coital bleed) or abnormal looking cervix – REGARDLESS of a normal result.
  - NB: Abnormal cervix often just nabothian cysts or angry ectropion.
  - If persistent low grade – colposcopy within 6 months, high grade – 1 month, invasive carcinoma – 1 WEEK!
- Procedure:
  - External visual inspection of the vulva.
  - Speculum examination.
    - The cervix is first viewed (areas of erosion, true leukoplakia, pigmented lesions, or areas of obvious ulceration or exophytic growth).
    - Acetic acid is then applied to enhance definition of the squamo-columnar junction (TZ) – It dehydrates cells so that squamous cells with relatively large or dense nuclei (hypernuclear regions) reflect light and thus appear white.
    - Lugol’s or Schiller’s solution (iodine based) may be applied to aid in detection. Uniform uptake = no lesion is present. Glycogen containing cells (ie normal cells) will take up iodine and become dark brown. Non-glycogenated cells, such as HSIL, and many LSIL, will not take up iodine and remain light yellow.
    - The TZ represents area of rapid cell turnover and of squamous metaplasia (from columnar).
    - Biopsies:
      - Performed on the most abnormal areas or Endocervical curettage (ECC) or sampling in some patients e.g. HSIL

Treatment:
- Must Rx high grade within 2 months and low grade within 6 months
- Large loop excision of the transformation zone (LLETZ): “GOLD STANDARD TREATMENT”
  - Colposcopic electrical wire loop removes abnormal cervical cells under LA for HSIL or persistent LSIL.
- Ablative: Laser therapy, Diathermy and cryotherapy: Had high recurrence so not done anymore
- Cone biopsy (under anesthetic) – done if persistent disease following LLETZ (after 2 – as likely abnormal cells lie in canal) or ACIS → poor obstetric outcomes with no better prognosis than LLETZ.
- Radiotherapy (+/- adjunctive chemotherapy): shown to be equally as effective as hysterectomy + radiotherapy.
- Hysterectomy: If growth extends beyond LLETZ and cone biopsy margins. Hysterectomy: only considered if not desire to child bear.
- Risks: Bleeding, cervical stenosis or incompetence (risk of affecting future pregnancies)
• If satisfactory (visual/biopsy) & normal: repeat smear at 12 and 24 months
  ➢ If normal, return to 3 yearly smears
  ➢ If abnormal, repeat colposcopy
• If satisfactory & abnormal, carry out target biopsy for:
  ➢ CIN I → repeat smear at 6 and 12 months
  ➢ CIN II and III → LLETZ

Information for pt with LSIL
• Most likely not cancer: smears pick up at risk, abnormal cells
• Caused by warts virus
• At risk cells can return to normal or progress slowly to cancer (ie over 15 years), we don’t know which they will do so need to watch
• Very common: 1 in 5 women have the changes, 1 in 20 go on to further Ix
• Cells extremely unlikely to change between appointments
Follow-up for ASC-H/HSIL:
- If satisfactory & normal, cyto-histo review:
  - If normal, repeat in 3 months
  - If high grade, repeat colposcopy & cytology in 3 months. Treatment is indicated here.
- If satisfactory & abnormal, perform target biopsy:
  - CIN II & III: LLETZ (greater risk of recurrence with ablation)
  - CIN I: management based on MDT decision
- If pregnant + HSIL → colposcope during pregnancy to r/o malignancy then Rx following delivery

Follow-up for Cervical Glandular Abnormalities:
- If the colposcopy is satisfactory and normal, it is recommended that cytology be reviewed.
  - If abnormal glandular cytology is confirmed on review, cone biopsy and dilatation and curettage (D&C) are recommended.
  - If abnormal glandular cytology is not confirmed on review, management should be based on a MDT decision.
- If the colposcopy is satisfactory and abnormal, and consistent with cancer, punch biopsy and refer to a gynaecological oncologist.

Cervical Cancer

Epidemiology
- 200 women diagnosed, 70 die per year

Benign lesions:
- Nabothian Cyst/inclusion cyst: No rx required
- Cervical ectropion
- Endocervical polyps: Rx = polypectomy

Malignant lesions:
- Any malignant change requires colposcopy
- Adenocarcinoma (5%): Occurs in columnar cells (endocervix)
- Squamous cell carcinoma (95%): Occurs at TZ

Staging:
- FIGO classification:
  - 0 Carcinoma In Situ (CIS)
  - I (A, B) Confined to cervix.
    - A = up to 5mm deep.
    - B = >5mm deep/7mm wide or visible <4cm.
  - II (A, B) Beyond uterus but not pelvic wall, doesn’t involve lower 1/3 of vagina.
    - A = upper 2/3 vagina.
    - B = upper 2/3 vagina + extension into parametrial tissue.
III (A, B) Extends to pelvic wall and/or lower 1/3 vagina and/or causes hydronephrosis or non-functioning kidney
- A = lower 1/3 vagina.
- B = lower 1/3 vagina + pelvic side wall or hydronephrosis.
IV (A, B) Beyond true pelvis +/- spread
- A = Bladder, rectum.
- B = Distant metastases.

**Scans:**
- MRI
- PET/CT: Good at pinpointing areas of abnormal metabolic activity within the body e.g. primary and secondary cancers. Shows isotope uptake – good at seeing affected nodes also.

**Treatment:**
- IA: Cervical Cone biopsy if desire future fertility otherwise simple hysterectomy (5-year survival 95%)
- IB or IIA: Radical hysterectomy + pelvic lymphadenectomy, ovaries can be spared, radiotherapy if >4cm (5-year survival 70% to 85%)
- II, III, IV: Radiotherapy + Cisplatin based chemotherapy (5 year survival 65%, 40%, 20% respectively).
- VB: Chemo +/- pelvic radiation (5 year survival 10%)

**Symptoms:**
- **Bleeding** (often spotting or post coital), **pain**, discharge
**Prevention:**
- HPV VACCINE: Gardasil
  - Quadrivalent vaccine (serotypes 6, 11, 16, 18)
  - Give to U16 (before sexually active)
- Note: HPV Typing: This is now more common – used to see if have low or high risk HPV to tailor therapy

### Endometrium

**Postmenopausal bleeding is endometrial cancer until proven otherwise (90% present with vaginal bleeding)**

**DDx:** “I DEAL P”
- IUD
- Dysfunctional Uterine Bleeding
- Endometriosis/endometrial hyperplasia/endometrial cancer
- Adenomyosis
- Leiomyomata Fibroids
- Polyps
- Endometrial hormones:
  - Oestrogen: makes it GROW
  - Progesterone: makes it MATURE (thins the endometrium – switches off the signal to grow)

**Benign causes of menorrhagia:**
- Post-menopausal: vaginal atrophy (often PCB)
- Leiomyomata/fibroids: within myometrium
**Endometrial polyps:** In endometrium (often occur due to progesterone resistant area) – 99% are just simple hyperplasia

**Endometrial hyperplasia:**
- **Definition:** abnormal proliferation of the endometrium in excess of the normal proliferation that occurs during the menstrual cycle
- *Endometrial hyperplasia may develop into endometrial carcinoma.*
- **Risk factors:**
  - Age > 40 (average age = 60)
  - Unopposed estrogen (i.e. not modified by progesterone) e.g. oestrogen only HRT, obesity, PCOS
  - Nulliparity, late menopause (>52)
  - Hereditary non-polyposis colon cancer (HNPCC)
  - Tamoxifen (is anti-estrogenic on breast but pro-estrogenic at endometrium (increasing cancer) and bone (decreasing osteoporosis)).
- **Pathogenesis:**
  - There are four types of endometrial hyperplasia: Simple, Complex, Simple atypical, Complex atypical (Complex atypical is most likely to lead to cancer)
  - 90% of simple and complex hyperplasia regress spontaneously.
- **Histology:**
  - **Simple hyperplasia:** increased glands, dilated and lined with crowded epithelia, cells normal.
Complex hyperplasia: larger irregularly shaped glands but cells normal.
Atypical hyperplasia: crowded glands (packed close together) lined with atypical, dysplastic cells (25% risk cancer)
Carcinoma: INVASION (confluent glands, atypical cells)

Investigations:
1. TVUS
2. Biopsy (pipelle)
3. D+C and hysteroscopy

Treatment:
Simple hyperplasia usually responds to high dose progestogens (can be effectively delivered by the levonorgestrel intra-uterine system).
Surgically, endometrial ablation or hysterectomy (especially if atypical hyperplasia)

Malignant causes of menorrhagia:

Endometrial carcinoma:
Note: Mainly adenocarcinoma (ie glandular) and is oestrogen dependent
Risks:
1. Age > 40 (average age = 60)
2. Unopposed estrogen (i.e. not modified by progesterone) e.g. oestrogen only HRT, obesity, PCOS
3. Nulliparity, late menopause (>52), Hereditary non-polyposis colon cancer (HNPCC)
4. Tamoxifen (anti-estrogenic on breast but pro-estrogenic at endometrium (increasing cancer) and bone (decreasing osteoporosis)).
5. Note: Taking COC decreases risk in later life

Ix:
TV U/S: Fibroids, Polyps and endometrial thickening (<5mm very low risk malignancy).
Biopsy: Pipelle biopsy (syringe like – sucks endometrium out – high false –ve if miss area)
D+C and hysteroscopy (BEST!)
Smear: Although not designed to pick up glandular changes, these are often found

Sx: Bleeding (post menopausal or AUB pre-menopausally)

Staging: FIGO classification:
STAGE DESCRIPTION
CIS Confined to corpus (body – endo/myometrium)
I (A, B, C) Involves corpus and cervix
II (A, B) Outside uterus but not beyond true pelvis
III (A, B, C) Beyond true pelvis +/- distant spread, bladder, rectum (A) Distant metastases (B)

Rx:
Depends on stage
IA,B - total abdominal hysterectomy with bilateral salpingo-oophorectomy (TAH/BSO)
IC, II, III – TAH/BSO, pelvic/periaortic node dissection, radiotherapy (can do this alone is unfit for surgery)
IV: Generally hormone (Progestosterone) therapy - no surgery
Other adjuvant chemotherapy is also used.

Endometrial sarcoma: rare, develop from fibroid.

Ovaries:

Pre-menopausal ovarian mass DDx:
1. Functional ovarian cyst:
   1. Follicular cyst: arise when rupture and ovum release does not occur → follicle continues to grow.
   2. Corpus luteal cysts: occur when the corpus luteum fails to involute and continues to enlarge after ovulation.
   3. Simple cysts: <2.5 cm in diameter are considered to be normal physiologic cysts (usually <10 cm in size).

2. PCOS: should be considered in the reproductive age pt found to have multicystic ovaries

3. Pregnancy related:
   1. Ectopic pregnancy: Suspect if missed menstrual period, abdominopelvic pain, + vaginal bleeding.
   2. Theca lutein cysts: Luteinized follicle cysts present as bilateral multiseptated cystic adnexal masses.
Due to:
- **Overstimulation from high hCG levels** (gestational trophoblastic disease, multiple gestation)
- Hypersensitivity to hCG.

3. **Corpus luteum of pregnancy**: Normal in pregnancy typically <2.5 cm. CL may occasionally become enlarged and painful due to hemorrhage.

4. **Luteoma**: Luteoma is a non-neoplastic ovarian change associated with pregnancy that can simulate a neoplasm. Luteomas involute spontaneously after delivery or are surgically treated. Suspect in the presence of a solid adnexal mass and maternal hirsutism or virilization.

5. **Inflammatory**:
   - **PID**: if poorly treated, results in scarring or "clubbing" of the tubal fimbriae. This leads to a collection of either tubal secretions or pus, resulting in a hydropsalpinx or pyosalpinx, respectively. When the ovary is also involved, a tuboovarian abscess or complex can form (TOA/TOC)
   - Suggestive findings: abdominopelvic pain, fever, purulent cervical discharge, cervical motion tenderness, adnexal mass and a prior history of STD.

6. **Malignant ovarian neoplasms** (similar to testicles):
   - Features: >10cm, bilateral, cystic, uniloculated and thin septations
   - **Epithelial tumours** e.g. Borderline, Serous (most common ovarian tumour – most benign; see papillae), mucinous, endometroid, clear cell, Brenner tumour
   - Germ cell tumours e.g. Dysgerminoma (LDH), Immature teratoma (yolk sac tumour (AFP), Embryonal carcinoma (AFP and hCG), Choriocarcinoma (hCG))
   - Sex cord stromal ovarian tumours e.g. Granulosa-theca cell tumours, Sertoli-leydig cell tumours

7. **Metastatic disease**: the ovary can be involved especially from breast cancer or Krukenberg tumours (mets from the GIT, usually stomach with 'signet ring' cells)

- **Post-menopausal** adnexal mass DDx:
  - Incidence of ovarian cancer ↑ with age (greatest RF) → consider adnexal mass malignant until proven otherwise!
  - 1. Benign ovarian cysts: High levels of gonadotrophins or androgens may cause small epithelial lined structures cysts. Common, especially in the first few years after menopause.
  - 2. Ovarian carcinoma:
    - Serous cystadenocarcinoma most common
    - Epi: Average age 50-60, 85-95% are epithelial cell tumours
    - Sx: Usually asymptomatic until disseminated (most present at stage III), → Late presentation.
    - Pc: Pleural effusion, ascites, abdominopelvic mass, and groin adenopathy.
    - Rectovaginal examination will often reveal cul-de-sac nodularity
    - Dx: US + Ca125 together → 90% sensitive
    - Laparoscopic: enlarged nodular ovaries and diffuse intraperitoneal disease.
    - RF:
      - Increasing age (greatest risk)
      - FHx (x2), BRCA gene (40-50% risk), HNPCC (<10% risk)
      - Oestrogen only HRT >5 years, early menarch/late menopause (COCP decreases risk as not ovulating)
      - History of infertility/infertility drugs e.g. clomiphene
      - Endometriosis (due to inflammation)
    - Staging: FIGO classification for primary carcinoma of ovary
<table>
<thead>
<tr>
<th>STAGE</th>
<th>DESCRIPTION</th>
</tr>
</thead>
<tbody>
<tr>
<td>I (A, B, C)</td>
<td>Growth limited to ovaries</td>
</tr>
<tr>
<td>II (A, B, C)</td>
<td>Growth involving one/both ovaries with pelvic extension</td>
</tr>
<tr>
<td>III (A, B, C)</td>
<td>Growth involving one/both ovaries with peritoneal implants outside pelvis and/or +ve retroperitoneal or inguinal nodes</td>
</tr>
<tr>
<td>IV</td>
<td>Distant metastases beyond peritoneal cavity</td>
</tr>
</tbody>
</table>

- **Treatment:**
  - Stage:Early (IA,B): TAH/BSO + omentectomy + peritoneal washings + staging
  - Advanced: debulking surgery and chemotherapy (platinum based: cisplatin + paclitaxel)
  - Do prophylactic BSO for BRCA mutation carriers
  - Often palliative due to late presentation

- **3. Metastases**
- **4. Leiomyomata:** may persist into the menopausal years, but new myomas typically do not develop.
- **5. Diverticular disease:** common in elderly. During an episode of diverticulitis, a tender mass is palpable in about 20% and abdominal distension is common. Symptoms: fever, abdominal pain (usually left lower quadrant), nausea/vomiting, constipation, diarrhoea, and urinary symptoms

- **Adnexal mass management (OSCE!):**
  1. **US**
  2. **Ca125**
  3. **Refer**

- **Staging (OSCE!):**
  - CT chest/abdo/pelvis
  - LFTs for liver mets
  - Urea + Cr pre-chemo

**Summary:**
- Characteristics that increase the likelihood of malignancy include:
  - Pre-pubescent or postmenopausal female
  - A complex or solid appearing mass on ultrasound
  - Presence in a woman known to have a non-gynaecological cancer (eg, breast or gastric cancer)
  - Ascites
- **Note:** NEVER do FNA on ovarian mass as can seed malignant cells

**Pelvic Pain**
- **Acute:**
  - *Pregnancy-related:* miscarriage, ectopic pregnancy, rupture of corpus luteum cyst; causes in later pregnancy include premature labour, placental abruption and uterine rupture.
  - *Gynaecological:* ovulation (mid-cycle, may be severe pain), dysmenorrhoea, PID, rupture/torsion of ovarian cyst, degenerative changes in a fibroid (Must also consider possibility of a pelvic tumour or pelvic vein thrombosis).
  - *Other causes:* appendicitis, diverticulitis, irritable bowel syndrome, UTI, adhesions, strangulated hernia.
- **Chronic:**
  - Endometriosis, Adenomyosis, Fibroids, PID, Adhesions, Gastrointestinal, e.g. irritable bowel syndrome, diverticular disease, Urological, e.g. cystitis, chronic urethritis, urinary tract calculi, Musculoskeletal pain, e.g. low back pain, fibromyalgia, Post-herpetic neuralgia, Psychological and social issues

**Cancer antigen 125 (CA 125):**
- Most useful as a marker for **non-mucinous ovarian epithelial cancer**, present in ~80% of cases of **advanced ovarian cancer** - often -ve earlier in the disease.
- **Conditions which may have elevated CA-125:**
  - **Malignant disease:** Ovarian Cancer, Uterine Cancer, Other intra-abdominal cancers (pancreas, stomach, colon, rectum) and metastases from other sites (eg breast).
  - **Non malignant conditions:** Benign ovarian tumour (eg Meig’s), *Endometriosis, Pelvic inflammatory disease* / salpingitis, Pregnancy and menstruation, Leiomyoma, Ascites - eg liver disease (cirrhosis) and renal failure, Diverticulosis, Pleural and pericardial disease, Pancreatitis and Heart failure
- **Note:** Meig’s syndrome (fibroma, acites and right pleural effusion) often associated with Benign stromal cell tumour.
- **Uses:**
  - Monitoring patients with known ovarian cancer for relapse, determining primary ovarian cancer with mets (ie from colon – may have CEA but not CA 125)
  - Can be combined with USS and menopausal status to give risk of malignancy index (RMI)
  - >200 = gynae oncology referral!!
- RMI determines extent of surgery eg low RMI → cystectomy; high RMI → TAH/BSO/omentectomy
- **Other biochemical markers:** Inhibin, hCG, AFP, LDH

### Gestational Trophoblastic Neoplasia (GTN)

- **Proliferative abnormalities of trophoblast** (placental cells = trophoblast). Aka “Mole” untreated a **hydatidiform mole** (= molar pregnancy) can continue to **grow and invade surrounding organs**.
- **Epi:** Occurs in 1/1000 pregnancies, 80% benign, 5% metastatic and cure rate >90%
- **RF:** Age >40, multiple pregnancies, previous molar pregnancy, vit A deficiency
- **Pc:**
  - Large for date uterus
  - **Vaginal bleeding** (often with ‘grape-like’ vesicles – due to dilated chorionic villi)
  - Early pre-eclampsia, prominent theca-lutein cysts
  - Less common are hyperemesis gravidarum (↑Beta Hcg), hyperthyroidism
- **Ix:**
  - **1. USS:** Classic ‘snow-storm’ pattern (complete), or a vesicular pattern.
  - **2. B-hCG** (usually **abnormally high** - better for use in follow up).
  - **3. CXR, CT, MRI** for metastatic disease.

#### Benign GTN:
- **Hydatidiform mole:**
  - **Complete** mole (Most common): **Androgenetic** (all genes from father; paternal genes code for placenta): vast majority of complete moles.
    - ~80%: empty egg is fertilized by a single sperm → duplication of all chromosomes / genes = diploid.
    - ~20%: empty egg fertilised by two sperms (diploid).
    - No evidence of fetal tissue, grape like
  - **Partial** (incomplete) mole:
    - Majority are **triploid** → normal haploid egg is fertilized by two sperms. Thus the nucleus contains one maternal set of genes and two paternal sets (can be XXX, XXY, XYY).
    - These have **less dramatic clinical features**
    - Usually **evidence of fetal tissue** (i.e. F RBCs)

#### Malignant GTN:
- **Invasive mole or persistent GTN:** Mets are rare, often diagnosed by rising or plateau in B-hCG
- **Choriocarcinoma:**
  - **Pc:** Sx from metastases (lung and brain most common). Most commonly follows a molar pregnancy (also abortion, ectopic or normal)
  - **Placental site trophoblastic tumour:** Rare aggressive choriocarcinoma, usually low B-hCG but high hPL and insensitive to chemo.
- **Metastatic:** Via hematogenous spread:
  - **Lungs** (80% cough, haemoptysis), **Vagina** (30% bleed), **Pelvis** (10% if bowel, rectal bleed), **Liver** (10% elevated LFTs), **Brain** (10% headaches, dizziness, symptoms of space occupying lesion)
  - May be highly vascular and bleed
  - Poor prognosis factors: Mets → brain/lung, high b-hCG titre, >4months since pregnancy.
- **Staging** (FIGO staging system)
  - **Stage I:** Confined to the uterus.
  - **Stage II:** Extends outside the uterus but is limited to the genital structures
  - **Stage III:** Extends to the lungs with or without genital tract involvement.
  - **Stage IV:** All other metastatic sites.
- **Rx:**
  - **Chemotherapy for ALL stages:** Start with MTX and use others if don’t respond
  - Shouldn’t need hysterectomy. If persistent, re-evaluate (may need MTX)
- **Follow-up:** Contraception!!! So that B-hCG levels not affected – for all stages weekly B-hCG until 3 consecutive normal results then monthly (12 months for stage I-III and 24 months stage IV)
- **Future pregnancies:**
  - Only try to conceive when B-hCG levels normal for 6 months and 12 months post chemo
  - If previous molar pregnancy, at very low risk of another and 98% have normal pregnancy and no complications – if get it again, most likely to be same histological type.
Cervical Cancer

**Epidemiology**
- In NZ, about **200 new cases per year, 60 deaths** (⇒ relatively rare compared with other cancers)
- One in 90 women without screening will get CC, 1/570 with screening
- 75% of cases and 80% deaths are over 35, but CIN lesions can develop young (ie many woman coming for colposcopy after abnormal smears are 25 – 30).

**Aetiology**
- Human Papilloma Virus (HPV):
  - HPV 6, 11: condyloma acuminate
  - HPV 16 or 18: Genital dysplasia. Is a necessary but not sufficient condition for cervical cancer
  - **Koilocytes**: HPV infected keratinocytes with a perinuclear halo. Episomal viral DNA
  - Dysplasia: pleiomorphic, hyperchromatic mitotically active, high nuclear/cytoplasmic ratio. Integrated DNA (Kettle fry nuclei)
  - HPV Carcinogenesis:
    - Not typical mechanisms
    - E6 binds to p53 (tumour suppressor and accelerates its degradation)
    - E7 binds to RB displacing transcription factors usually sequestered by RB
- Other risk factors:
  - Early age at first intercourse
  - Multiple sexual partners
  - High risk male partners
  - Smoking
  - Herpes
  - Immunosuppression
- Occurs in the **transformation zone**: junction in the endocervix between squamous cells of the vagina and columnar cells of the uterus (**squamocolumnar junction**). Completes development at age 18 – 20, shifting into the endocervix. Previously in the exocervix and more vulnerable to damage/infection ⇒ significance of age at first intercourse

**Classification**
- **Bethesda classification system**: classified as squamous or glandular
  - **Squamous**:
    - Atypical cells of uncertain significance (ASCUS)
    - ASCUS – cannot exclude HSIL (ASCUS – H)
    - Low-grade squamous intraepithelial lesion (LSIL) which = CIN 1
    - High-grade squamous intraepithelial lesion (HSIL) which is predictive of CIN 2 or CIN 3
    - SCC
  - **Glandular**:
    - Endometrial cells
    - AGUS
    - Adenocarcinoma
- Low grade changes: Low Grade Squamous Intraepithelial Lesion (LSIL) (=CIN1 – Cervical intraepithelial neoplasia. More likely to be HPV types 6 & 11). Nucleus is slightly enlarged and irregular. In bottom third of cells on top of base membrane in transformation zone. If found on screening ⇒ more regular smears. 50 – 60% return to normal
- High Grade Changes: HSIL (covers CIN 2 and 3/CIN – carcinoma-in-situ. More likely to be HPV 16 & 18). Nucleus of every cell is very enlarged and irregular in shape. High nuclear:cytoplasmic ratio. Affected cells right to surface. If found on screening ⇒ refer for colposcopy. Treated the same but CIN3 more likely to progress than CIN2
- Invasive cancer: basement membrane has been breached. Can get glandular extension in CIN3 – metaplasia down glands – but still not invasive as the BM is not breached

**Progression**
- Cervical Dysplasia: grade depends on the proportion of the epithelium occupied by malignant cells
- Cervical Carcinoma:
  - Micro: islands of infiltrating neoplastic squamous cells that may show keratinisation
  - Outcome: depends on stage
- Size and depth of invasion. > 10 mm invasion → poorer outcome
- Lymph node involvement → poorer outcome
- Stage 1: confined to cervix. 90 – 95% 5 year survival
- Stage 3: lymph node positive: 30% 5 year survival

- Cervical glandular neoplasia:
  - Also HPV related, but much less common than cervical squamous carcinoma (which has a higher rate of replication)
  - Invasive adenocarcinoma has infiltrating neoplastic glands
  - Comprises 20% of tumours in a screened population vs 5% in unscreened

**Cervical Screening**

- Came about as a result of the **Cartwright enquiry**
- Pap smears collect exfoliated cells from the cervix
- Currently reported using the **Bethesda system** (see above)
- Register:
  - National database with **reminders + recalls**
  - **Quality control** of smear takers undertaken
  - Results used in **research** (but no identifiers)
- NZ Protocol:
  - **3 yearly screening** should be offered to all women aged 20 – 69 years who have been sexually active
  - Screening should be **yearly for 2 years from 20** (some advocate starting earlier if > 2 years since commencing regular sex – but as cancer in this age group is very uncommon, it’s not good screening practice. If you think cancer is a possibility, you shouldn’t use a screening test to diagnose it)

**Cervical Smear Procedure**

- Best done **mid-cycle** (↓blood and ↓bacteria which are a causes of cytolysis)
- Explain first. Ask about LMP, abnormal bleeding, post-coital bleeding, abnormal discharge, if pregnant, and previous smear history and experiences
- Patient Education: discuss feelings about having a smear, emphasise preventative nature, explain what cervix is, show equipment
- Ensure screen/curtain for patient and sheet
- Either:
  - **Broom** does both well (sample of choice for all age groups) – turn **5 times**
  - **Brush**: insert into endocervix and turn 1-2 times
  - **Spatula**: **one full turn** (only turn one turn otherwise bleeding → obscures sample)
- Put into appropriate containers (**liquid cytology**)
- Data on lab form includes LMP and clinical details.
- Biggest cause of ↓sensitivity is poor sampling. Smears can be unsatisfactory if blood, inflammatory cells or lubricant present. Smears taken 4 – 5 days prior to the next period may show cytolysis (cellular degeneration due to ↑ bacilli)

**Relationship Between Screening Results and Lesions**

- Normal or benign/reactive changes:

<table>
<thead>
<tr>
<th>Satisfactory</th>
<th>Satisfactory but limited</th>
<th>Unsatisfactory smear</th>
</tr>
</thead>
<tbody>
<tr>
<td>Previously normal</td>
<td>First smear, or more than 5 years since last smear</td>
<td>Abnormal smear in last 5 years</td>
</tr>
<tr>
<td>Smear in 3 years</td>
<td>Smear in 1 year</td>
<td>Smear in 6 months</td>
</tr>
<tr>
<td>Previously normal</td>
<td>Previous abnormal smears</td>
<td>Abnormal in last 5 years</td>
</tr>
<tr>
<td>See below</td>
<td></td>
<td>Smear in 6 months</td>
</tr>
<tr>
<td>Previously normal</td>
<td>First smear, or more than 5 years since last smear</td>
<td></td>
</tr>
<tr>
<td>Smear in 1 year</td>
<td></td>
<td>Smear in 1 – 3 months</td>
</tr>
<tr>
<td>Previous abnormal smears</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- Abnormal:

<table>
<thead>
<tr>
<th>CIN1 or HPV</th>
<th>CIN 2 or 3 → Colposcopy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Previous normal smear</td>
<td>If LSIL or less</td>
</tr>
<tr>
<td>Smear in 6 months</td>
<td>Smears at 6 months, 1 year, 1 year, 3 yearly</td>
</tr>
<tr>
<td>Previous abnormal smear</td>
<td>If HSIL</td>
</tr>
<tr>
<td>Smear in 6 months, if normal then 2 * 1 year, if abnormal then colposcopy</td>
<td>Smear at 6 months then annual until 70,</td>
</tr>
</tbody>
</table>
Effectiveness of Screening
- Sensitivity of a single smear is 80% for low and high grade lesions (ie not sufficient for diagnosis, only for screening)
- PPV of HGSIL cytology report: 30 – 40%
- NPV of a normal smear is 80% ⇒ if abnormal appearing cervix (lesion with raised edge, nodular feel, hard, bleeds when touched) or persistent abnormal bleeding they need a colposcopy not a smear: DON’T RELY ON THE SMEAR
- Maximum prevention: 91-92% of squamous cancers with 3 yearly screening. ↑ to 92 – 93% with annual screening. ↓ to 87% with 5 yearly screening
- Less than 100% because of:
  - Less than 100% enrolment
  - False negatives in sampling (eg a lesion is more likely to bleed and compromise the sample)
  - False negatives in laboratory diagnosis
  - Interval cancers: minimum time from infection to invasive is ~ 18 months. Normal is ~ 10 to 15 years
- Success rate for adequate treatment of pre-cancers is 98 – 100%
- Women most likely to get cervical cancer are those not regularly screened
- Much less effective at glandular lesions: clinical suspicion should overrule a ‘normal’ smear

Other Cancers
Ovarian Cancer
- Three hereditary cancer syndromes associated with ovarian cancer:
  - Site specific syndrome
    - Develops ovarian ca 10-20 years younger than those with non-familial ovarian ca
  - Breast-ovarian syndrome:
    - FHx of multiple relatives with breast/ovarian ca
    - Genetic testing for BRCA1/BRCA2 needed
    - 80% lifetime risk of breast ca
    - 45% lifetime risk of ovarian ca
  - Lynch II syndrome
    - History of breast, ovarian, endometrial GI and GU ca
- NB: recommended that patients with a history of hereditary ovarian cancer have yearly recto-vaginal examinations, CA-125 and transvaginal USS until age 35 or completion of childbirth.
  - Then prophylactic bilateral salpingo-oophorectomy recommended.
- Risk factors: nulliparity, infertility, early menarche, family history, no past pill use
- Presentation:
  - 75% asymptomatic until advanced
  - Swelling with palpable mass
  - Pressure effects (eg on bladder)
  - Infarction, haemorrhage, peritonism
  - Ascites
  - Torsion
  - Endocrine: virilisation, menstrual irregularity, PMB
- Lower incidence than endometrial cancer, but higher death rate due to late presentation
- 5 Yearly survival ~ 30 – 35% (varies from 80 – 100% for FIGO I to 5 – 10% for FIGO IIIC/IV)
- Types:
  - Epithelium: 70%
    - Benign (60%): younger – serous cystadenoma, mucinous cystadenoma. If cysts have smooth internal epithelium likely to be benign
    - Borderline (20%): mucinous tumour of borderline malignancy. 6% recurrence (but still treatable) so need long term follow-up
    - Malignant (20%): serous cystadenocarcinoma
  - Ovum: 20%
    - Dermoid cyst (teratoma)
    - Occur in children and young women, in contrast to epithelial tumours
    - Commonest is benign, but in young children they are often malignant
Reproductive and Obstetrics

- Micro: variety of mature cell types: skin, gut, neural tissue, etc
  - Others: 5%
    - Stroma: lymphoma, fibroma
    - Granulosa cell tumour → ↑ oestrogen → amenorrhea and breakthrough bleeding
    - Thecal cell tumour → ↑ androgen → infertile, hirsutism, amenorrhea
- Investigations: Ca125, FBC, electrolytes, LFTs, US + CT (for mets or possible primary elsewhere)
- Should identify and screen those with high risk – those with genetic tendency (ie BRAC1, BRAC2, HPNCC). If family history then screen with US plus CA125 – more informative together. NB ↑ lead time bias
- Treatment: Surgery for staging +/- debulking, chemo (usually platinum)
- Other ovarian cysts:
  - Present with mass effects of torsion:
    - Follicular cyst
    - Corpus luteum cyst
  - Polycystic ovaries
  - Endometriosis

**Endometrial Neoplasia**
- Most common gynaecological cancer, but early presentation → better prognosis
- Endometrial hyperplasia:
  - Simple hyperplasia: cystic glands with pseudostratified mitotically active cells. No atypia, minimal risk of carcinoma
  - Complex hyperplasia: More crowded gland with budding and infolding. With atypia, 5% progress to carcinoma
  - **Complex hyperplasia with atypia**: crowded, folded gland in which the lining cells are pleomorphic with loss of polarity and increased nuclear cytoplasmic ratio. > 25% progress to carcinoma
- **Endometrial polyps**:
  - Most are hyperplastic polyps
  - Often seen with generalised hyperplasia
  - Due to an area responding to oestrogen but resistant to progesterone
  - Micro: a polypoid collection of cystic hyperplastic glands in a fibrotic stroma
- Endometrial cancer:
  - Presentation: irregular PV bleeding, often post menopausal
  - Risk factors: obesity, nulliparity, diabetes, unopposed oestrogen therapy, pelvic irradiation, endogenous unopposed oestrogen (functioning ovarian tumour, anovulatory cycles, fat), family history for breast, ovarian or colon cancer
  - Peak age 55 - 60
  - Investigate **endometrial thickness with TV ultrasound**:
    - Reproductive endometrium: 0.5 – 1.5 cm
    - Menopausal endometrium: < 5 mm. If bleeding, repeat US in 4 – 6 months and look for change
    - If menopausal and 5 – 9mm, do endometrial sample. 90% are normal proliferative endometrium. 5% are atypical (pre-cancerous), 5% are carcinoma
    - If > 9 mm, straight to D&C to get good endometrial sample (high suspicion of cancer). Not hysteroscopy (can force malignant cells into the peritoneum)
  - Macro: fungating mass in the fundus
  - Micro: adenocarcinoma
  - Treatment: hysterectomy and oophorectomy + chemo and radiotherapy
  - Prognosis:
    - Stage 1: invade wall, 90% 5 year survival
    - Stage 2: invade cervix, 50% 5 year survival
    - Stage 3: lymph nodes, 20% 5 year survival
Obstetrics

History and Antenatal Booking

**Obstetric history**
- How’s baby going? Any issues or concerns? Baby moving?
- SMOCs
- S: History of a current pregnancy → DR TVS (TOSH!)
  - D - Dates: work out her LMP, EDD, gestational age.
R - Red flags (bleeding, discharge, leak/ruptured membranes, contractions, no fetal movements).
T - Tests: screening or diagnostic tests etc and the results of these.
V - Visits so far: to obstetrician mainly but also GP, midwife etc.
S - Symptoms she is experiencing now: SOB, fetal movements, oedema, urinary frequency.
- M: if relevant
- O: Past obstetric history:
  - When?
  - Gestation
  - Delivery
  - Weight
  - Complications
- C: Complications of pregnancy: DAMS DEPTH
  - Diabetes, anaemia, miscarriage, strep infection, distress (?not moving), emesis, pressure/placenta (rising + low lying placenta), toxaeaemia (proteinuria), haemorrhage
- S: past gynae hx: smears, STIs, surgery etc
- PMHx/PSHx:
  - HTN, DM, epilepsy etc etc
- Meds/allergies:
  - Vitamins too
  - Should be on folate from conception → 13/52
- Fx: of same named conditions above
- SHx: smoking, ETOH, other substances
- Pregnancy write-up:
  - Mrs X is a 30 year old G1P0 LMP (15/3/2012) EDD (5/12/2012)/EDC (estimated date of confinement) at _ weeks by [LMP or US at _ weeks] who presents for/complaining of etc
  - Her prenatal course has been uncomplicated/complicated by....
  - Should also include (gestation dependent): contractions, abdominal pain, bleeding, ROM – discharge or leakage, foetal movement (1st baby about 20 weeks, 2nd baby maybe as early as 18 weeks)
- Examination
  - BIPSA
  - Check BP, BMI, urinalysis done; OEDEMA, PALLOR, HR, RR, chest, resp, thyroid
  - Inspection: linea nigra, SG etc
  - Palpation: leopold’s
  - SFH
  - Auscultation
  - Presentation of findings:
    - There is a uniformly distended abdomen consistent with a singleton pregnancy
    - There is/is not linea nigra/striae gravidarum/low transverse scar consistent with CS
    - SFH measures xx cm and this is consistent with dates (+/- 2cm [or 3 if you’re Dr Sood])
    - Baby’s lie is ... eg longitudinal
    - The presentation is ... cephalic/breech/transverse
    - Baby’s position is... eg left occiput anterior
    - The head is ... fifths above the symph (ie engagement)
    - The fetal HR is ...
- Antenatal booking visit:
  - Should be done in 1st trimester – prior to 12/40
  - By dr or midwife
  - Objectives of antenatal care:
    - Assessment and monitoring of maternal and fetal well-being
    - Preparing woman and family for childbirth
    - Preparing woman and family for parenthood
- Introduction Data:
  - Age: NB ‘Old’ at 35:
    - Hypertension/diabetes/DVT more common
    - Down’s: Past aged 35 risk of Down Syndrome > risk of amnio (approx 1 in 200)
  - LMP – date of first day of bleeding in last period. Cycles regular? How long?
• +/- Marital status

• History of current pregnancy:
  • Due date = LMP + 7 days + 9 months (Naegele’s rule), if 4 weekly cycle. If 6 weekly cycle, add 2 weeks (ovulation set by end of cycle not beginning)
  • Date it well. Management decisions later in pregnancy depend on dates being accurate. U/S more accurate early on:
    o 1st trimester (< 12 weeks) accurate +/- 5 days
    o 2nd trimester (12 – 24ish weeks) accurate +/- 10 days
    o 3rd trimester (24+ weeks) accurate +/- 2 – 3 weeks
  • Has pt prepared? eg folate/iron supplements (neurokare)
  • Experienced any symptoms of early pregnancy: morning sickness, pica etc
  • Progress of pregnancy/red flag symptoms:
    o Pink Bats Do It Standing
    o Pain/contractions
    o Bleeding
    o Discharge
    o Incontinence = urinary sx
    o Swimming = movement

• Past Obstetric History: For each pregnancy:
  • When was it
  • If TOP then:
    o How many weeks. If 6 – 8 then likely to be choice. If after first trimester maternal or congenital problem more likely so need to ask the reason for the TOP
    o Any problems (bleeding, infection, etc)
  • Antenatal problems/complications: hypertension, diabetes, PTL (Pre-term labour), medical problems
  • Gestation (how close to your due dates were you)? If pre-term then ↑ risk this time. Was there a reason?
  • How delivered? If caesarean need to check surgical report for type of incision. If it was low transverse (LTCS) can trial labour, if vertical then not. Skin incision not reliable indicator.
  • Weight of baby: big → ?diabetes (were they screened for diabetes – they will remember the sugar load), small → ?smoking or growth problem
  • Post partum bleeding, infection, depression
  • Breast feed, if so how did it go
  • How’s the baby now?

• Past Gynaecological History. If indicated. See History, page 545
  • Actively treat any infection
  • Any chronic infections (eg Herpes)
  • Polycystic ovaries, uterine abnormality or surgery →↑ risk
  • Gynaecological cancer: pregnancy hormones may exacerbate the disease
  • Contraceptive history – talk about restarting after pregnancy
  • Smear history: last smear date, any abnormal

• Past Medical and Surgical History (and maybe very brief systems review):
  • History of hypertension (any signs of renal disease?), DM, heart disease, asthma, epilepsy, RF, bleeding tendency, clots, previous STIs, TB, Hep B, gynaecological problems, kidney disease, clinical depression, autoimmune disease, thyroid
  • Previous surgery

• Medications:
  • See also Pharmacology of Pregnancy and Breast Feeding, page 852
  • Remember vitamins and non-prescription meds. Vitamin tablets not recommended in pregnancy (OHCS, p 95).
  • On folate (should be from before conception to 13 weeks)
  • Allergies

• Family History:
  • As for medical history
  • Clotting problems/DVT
  • Hereditary anemias: Thalassemia (Mediterranean), Sickle Cell Anaemia (African)
  • Birth/Congenital defects (including congenital dislocation of hips)
  • Multiple births
  • Sister or mother with fertility or pregnancy problems (HT, miscarriages, DM, premature labour)

• Social History (key element in determining pregnancy outcome):

Reproductive and Obstetrics 604
- Adopted
- Marital/relationship status, subject to domestic abuse
- Support system
- Cigarette, alcohol and recreational drug use
- Occupation. Interested in exposures. Also stay away from high impact activity and keep HR < 140 (→↓placenta perfusion)
- Financial well-being
- Low socio-economic status →↑pregnancy complications (eg poor nutrition, lack of antenatal care, etc)
- Enquire about anxieties, etc

- Offer advice on:
  - Questions or concerns (especially if first pregnancy or previous miscarriage)
  - Antenatal screening
  - Antenatal classes
  - Dental check-up
  - Smoking and alcohol
  - Diet, including folate, iron, listeria (nothing from the Deli unless it’s piping hot, no imported soft cheeses - unpasteurised)
  - Morning sickness: keep glucose up (ie morning barley sugar)
  - Rest
  - Knowledge of social security benefits
  - Mild exercise
  - Intercourse OK if there is no vaginal bleeding

**Obstetric Exam**

- **General observation**: including BP, urinalysis, HR, RR, CVS, RS, thyroid, oedema, anaemia etc

- **Inspection** of abdomen:
  - Distension
  - Striae gravidarum
  - Linea nigra
  - Surgical scars
  - Umbilicus
  - Vessels
  - Hernias
  - Fetal movements
  - Any other

- **Palpation** - Leopold’s manoeuvres:
  - First Maneuver – **Fundal Grip** (Upper pole for head/bum)
    o Examiner faces woman’s head
    o Palpate uterine fundus
    o Determine what fetal part is at uterine fundus
    o Using two hands and compressing the maternal abdomen determine height of fundus + what’s in the upper pole
    o Also determine approximate height of fundus (in cm NOT weeks):

  - Second Maneuver – **Lateral Grip** (Sides of maternal abdomen for spine)
    o Examiner faces woman’s head
    o Palpate with one hand on each side of abdomen
    o Palpate fetus between two hands
Assess which side is spine and which extremities

- **Third Maneuver** - *Pawlik or Pelvic Grip* *(Presenting part evaluation w duck grip)*
  - Examiner faces woman’s head
  - Apply downward pressure on uterine fundus
  - Hold presenting part between index finger and thumb
  - Assess for cephalic versus breech presentation

- **Fourth Maneuver** – *Reverse Pawlik Grip* *(Lower pole for descent/engagement)*
  - Examiner faces woman’s feet
  - Palpate just above symphysis pubis feeling for brow
  - Palpate fetal presenting part between two hands
  - Assess for fetal descent/engagement

- **Auscultation**: either with US or stethoscope over baby’s spine

- **Symphyseal-fundal height measurement (SFH):**
  - Fundal height is used to indirectly measure fetal growth in relation to gestational age.
  - Fundal height measured in centimetres, should equal the number of weeks gestation +/- 2 cm. A discrepancy between fundal height and gestation may indicate a fetus small or large for gestational age and should be further investigated
  - Fundal height is measured and recorded at each visit on an empty bladder. Measurement should start at the variable point (the fundus) and continue to the fixed point (the superior symphysis pubis) using a non-elastic tape measure.
  - The centimetre side of the tape should be face down to avoid a biased measurement.
  - Between 20-36 weeks gestation, a SFH measurement equals the number of weeks gestation +/- 2 cm.
  - A discrepancy of 3 cm or more after 20 weeks should be referred ASAP for further investigation involving CTG, AFI, Dopplers and growth ultrasound.
  - Measure only once
  - Plot on customised chart, record in notes
  - Record the metric measurement and plot it on the growth chart *(SFH normogram)*

**Presenting Obstetric Examination Findings**

- There is a uniformly distended abdomen consistent with a singleton pregnancy
- There is/is not linea nigra/striae gravidarum/low transverse scar consistent with CS
- SFH measures xx cm and this is consistent with dates (+/- 2cm [or 3 if you’re Dr Sood])
- Baby’s lie is … eg left occipitolateral
- The presentation is … cephalic/breech/transverse
- The head is … fifths above the symph (ie engagement)
- The fetal HR is …

**Booking Exam and Investigations**

- **Exam:**
  - Pulse, blood pressure
  - Weight and height → BMI
  - Signs of thyroid disease
  - Signs of anaemia
  - Heart and lungs (eg wheeze, mid systolic murmur common, pan systolic and diastolic abnormal) → need baseline
  - Breast exam, including nipples
  - Abdominal (masses, large liver, etc)
  - Oedema
  - Varicose veins
  - Fundal height
  - Fetal Heart rate by monitor (if old enough)
  - Pelvic exam: only in early pregnancy to assess uterine size/smear/adnexal abnormalities + swab for STIs; in late pregnancy to determine pelvic dimensions/assess cervix/presenting part
    - Vaginal
    - Bi-manual – uterus size consistent with dates and no adnexal masses. Uterus becomes an abdominal organ (rather than pelvic) at 12 weeks

- **Tests:**
NB. Oestradiol + PRL are raised in pregnancy with suppression of FSH + LH

Blood:
- FBC: check for anaemia
- Blood group: check if Rh –ve. If so, mark clearly in notes. Give Anti-D following birth or invasive procedure
- RBC Antibodies (eg Anti-D, Anti-ABO, etc)

Serology:
- Syphilis (VDRL): treat with course of penicillin IM
- Hepatitis B: if +ve, test and immunise partner and close contacts. At birth give Hep B IgG and Hep B vaccine to baby (repeat at 1 and 6 months)
- Rubella: If negative for Rubella and pregnant then NO vaccine (it’s a live vaccine). Stay away from kids. If she gets sick, repeat serology 2 – 3 weeks later to see if it was Rubella. 70% fetuses affected in 1st trimester, drops to < 5% by 16 weeks.

- HIV

MSU for protein, bacteria and glucose

High vaginal/endocervical swab where indicated for chlamydia, gonorrhoea, bacterial vaginosis, candida, trichomoniasis

If indicated:
- Smear if not up-to-date
- Ultrasound if dates unsure
- Tb if high risk (immigrant, family contact, etc)
- Sickle cell anaemia if black
- α-feto protein/triple test if at risk of Down
- If > 35 then offer amniocentesis

Subsequent visits: see Assessment of Fetal Growth and Well-Being, page 609

- Further bloods @ 28/40 including polycose for ?DM + FBC + Abs
- Further bloods @ 36/40: FBC + Ab

Minor Symptoms of Pregnancy

- Pregnancy testing: requires a few drops of urine, +ve from first day of missed period until week 20, false +ves low
- Early: amenorrhoea, nausea, vomiting, bladder irritability
- Nausea: At 20 weeks, 20% may still vomit. Reassure, small meals and ↓stress
- Headaches, palpitations and fainting due to peripheral dilation. Drink lots
- Urinary frequency (exclude UTI)
- Abdominal pain
- Breathlessness
- Constipation due to ↓motility. Give fibre and lots of fluid
- Reflux oesophagitis
- Backache in 3rd trimester
- Carpal tunnel syndrome (due to fluid retention)
- Itchy rashes
- Ankle oedema – almost universal. Exclude ↑BP and proteinuria (⇒ pre-eclampsia)
- Leg cramps

“At Risk” Pregnancies

- Adolescent Pregnancy (usually considered < 16):
  - Usually no problems with size of pelvis
  - Psychological and social problems: stability of relationship, financial (no DPB until 16), may conceal pregnancy or have poor access to care, if very young may involve incest → criminal offence, need ↑support after birth

- Obstetric problems:
  - Inaccurate dates
  - Compliance issues
  - Pre-diagnosis exposure to alcohol/drugs
  - Smoking
  - ↑Risk for pre-eclampsia (more likely to have less immunological tolerance to partner)

- Elderly Primagravid (> 35):
- ↑Risk of chromosomal abnormality, twins, pre-eclampsia (more likely to have essential hypertension, SLE or renal disease), DVT, thyroid disease, gestational diabetes, labour problems
- IVF pregnancy →↑risk of prematurity, IUGR, multiple pregnancy
- ↑Risk of fibroids (which double in size in pregnancy) → malpresentation, outgrow blood supply (→ pain) but usually little problem to pregnancy
- Grand Multip (≥ 5 pregnancies)
  - Fe deficiency
  - Precipitate labour: can → uterine rupture due to ↑ efficiency
  - Post-partum: relaxes quickly → PPH
  - Lie can be very unstable

Multiple Pregnancy

*Causes of Large Uterus for Dates*
- (in order of occurrence)
- Incorrect date for LMP
- Distended bladder
- Multiple fetuses
- Polyhydramnios
- Adnexal mass
- Large for gestational age fetus
- Fetal macrosomia (in diabetes)
- Hydatidiform mole

*Epidemiology*
- NZ rate of multiple births ~ 15/1000 (1/80)
- Hellin hypothesis: if the incidence of twins is n, the incidence of triplets will be n^2, quadruplets n^3 and so on
- Multiple pregnancies are increasing due to older maternal age at childbirth and increased use of fertility treatments

*Symptoms & Signs of Multiple Pregnancy*
- First clue is given by hx:
  - FHx of twins
  - Fertility treatment
  - Higher age + parity
  - Excessive vomiting
  - Excessive fetal movement & back ache
- Exam:
  - Larger than anticipated uterus
  - Excess weight gain + abdominal girth
  - Later in gestation:
    - Large & globular abdomen
    - 2 (or more) fetuses palpated
    - 2 (or more) heart beats

Dizygous Twins
- Siblings that happen to share the uterus at the same time: separate placentas, amnions, and chorions
- 2/3 of twins
- Risk factors: > 35 years, high parity, ethnicity and assisted conception

Monozygotic Twins
- Family history has minimal risk for monozygotic
- Splitting before day 5 gives separate placenta, amnion and chorion (dichorionic diamniotic)
- Splitting between days 4 & 8 gives common placenta & chorionic sac, but separate amnions (monochorionic diamniotic; most common)
- Splitting later than this gives common placenta, amnion and chorion (monochorionic monoamniotic)
- Problems:
Cord entanglement: only if MA; highest risk < 30 wks → occlusion and fetal death
IUGR
Conjoined twins (1% of monozygotes): incomplete splitting of primitive node
Twin-to-twin transfusion syndrome: one twin develops at the expense of the other due to unbalanced placental intertwin vascular anastomoses (one donor twin and one recipient twin)

Complications
- All complication rates are increased
- Maternal:
  - Pre-eclampsia: 3 x risk
  - ↑ risk of antepartum and postpartum haemorrhage
  - Preterm labour: on average 3 weeks early
  - Malpresentation: only 45% present cephalic/cephalic
  - Hypertension
  - Miscarriage
  - Iron and folate deficiency
- Fetal:
  - Fetal growth restriction (~500 g less than expected in 25%)
  - Complications associated with preterm delivery eg RDS, IVH, PVL
  - ↑ risk of cerebral palsy
  - ↑ still births and infant mortality
  - ↑ congenital malformations, mental retardation and neurological damage

Management
- Standard pregnancy care PLUS
- More regular monitoring: MDT/obstetrician + US (frequency depends on chorionicity)
- Screening for chromosomal abnormalities:
  - Serum markers for Down syndrome are not applicable to twin pregnancies because the mean sensitivity is associated with a high false-positive rate and the screening test does not provide the separate risk for each fetus.
  - Nuchal translucency can be used for screening. CVS or amniocentesis can be used but loss rates are greater in sampling a twin pregnancy (possibly due to double puncture) and there is a possibility of inaccurate diagnosis due to sampling the same sac twice
  - Fetal reduction or termination is possible in cases of congenital anomaly in one or both twins
- Multiple pregnancy support groups and education
- Hospital delivery: obstetrician, midwife, paediatrics etc; ↑ chance of caesarean section

Fetal Welfare
Assessment of Fetal Growth and Well-Being
- Clinical assessment. Key issue is serial measurement:
  - Mother:
    - Blood pressure
    - Maternal weight
    - Test urine from 20 weeks for proteinuria and glucose
    - Oedema
    - Check Hb and Rh antibodies (eg at 28 weeks) and do glucose challenge
  - Baby:
    - Symphyse-fundal height (SFH)
      - Indicator of weeks gestation – roughly 1 cm per week. Drops a bit at term
      - Measure from top of pubic bone to top of uterus
      - NB – can just palpate uterus on the abdomen at 12 weeks. At 20 weeks up to umbilicus
    - Lie and presentation from 32 weeks
    - Fetal heart: use Doppler (mum can hear it too). Normal is 110 to 160 bpm.
    - Fetal movements (from 19 – 20 weeks in primips, earlier in multipps): if no movement then asleep or sick. Awake foetuses are active
  - OSCE tips:
    - First introduce yourself, wash hands, get sheet to cover legs
    - Explain what you’re going to do
    - BP in sitting/semi-reclined position (to ↓ aortocaval compression)
Prenatal Testing/Diagnosis

**Prenatal diagnostic testing**

- **1st prenatal:**
  - FBC & maybe Fe tests
  - Type, Rh and antibody screen
  - Syphilis, Rubella, HIV, Hep B
- First trimester combined screen (FTCS) (9-13 weeks) – screening test for chromosomal abnormalities i.e. Down syndrome.
  - PAPP-A - Pregnancy-associated plasma protein A – if low indicates aneuploidy (abnormal number of chromosomes)
  - Free βHCG
  - Nuchal translucency – 11-13+6 weeks to assess risk of chromosomal abnormality – measure thickness of nuchal fold – fluid produced by fetus increased if fetal heart abnormalities.
  - Maternal age
  - Calculate risk of chromosomal abnormality: >1:300 → **Chorionic villous sampling.**
- Second trimester maternal serum screen 2 (Quadruple test; 15-20 weeks) - screening test for chromosomal abnormalities & NTDs. Only done if FTCS not done. Does not include NTS
  - aFP - major plasma protein produced by the yolk sac equivalent to fetal albumin (↑NTDs & ↓ in Down syndrome)
  - Estriol - "unconjugated estriol" if low may indicate chromosomal or congenital anomalies.
  - Inhibin A - ↑asc with downs syndrome.
  - βHCG
  - Maternal age
  - Calculate risk of chromosomal abnormality: >1:300 → **Amniocentesis.**
- Morphology scan (18-20 weeks gestation) – structural abnormalities (neural tube, brain, heart, limbs), provides accurate gestational age, inspects placenta.
- Chorionic villous sampling: (9/10-14 week).
  - Diagnostic for chromosomal abnormalities (culture → karyotype)
  - U/S guided trans-abdominal or trans-cervical needle biopsy of the placenta (chorionic villi).
  - 97.5% accurate with a 1% risk of miscarriage.
  - Other risks: *rhesus immunisation* (give anti-D if Rh –ve), bleeding, perforation, infection.
- Amniocentesis: 15th week onwards (after fusion of the amniotic sac to the wall of the uterus).
  - Diagnostic for chromosomal abnormalities + inherited disorders.
  - U/S guided trans-abdominal needle biopsy of the amniotic fluid.
  - 99%+ accurate with <0.5% risk of miscarriage.
  - Other risks: *rhesus immunisation* (give anti-D if Rh –ve), bleeding, infection, damage to fetus, premature labour
- Further investigations: Most have high false positives ⇒ interpret in light of clinical picture
  - SFH: screening test for fetal growth. Normally approximates gestation after 20/40. SFH 4cm below expected is a/w IUGR (27% sensitive; 48% sensitive if using customised SFH charts)
  - Fetal kick chart: screening test for fetal wellbeing, from 28/40 on. Mother counts fetal movements – should feel 10 in 12hr period (normally done from 9am → 9pm). Sensitivity 50% + specificity 80% for fetal mortality
  - Cardiotocography (CTG - fetal heart rate monitoring). See Cardiotocography, page 636
  - Umbilical artery doppler (not routine): to assess the physiology of the maternal-fetal unit
  - Ultrasound scan: fetal size (biparietal diameter, abdominal circumference, femur length), amniotic fluid estimation, assess fetal breathing (eg ↓in hypoxia)
  - Biophysical Profile: Only if high risk. **Combines CTG with US findings.** Score of fetal heart rate,
~3% of babies have congenital anomalies/malformations + 1/3 of those are severe

**Prenatal testing** is the use of screening or diagnostic tests to find out if a baby has (diagnostic) or is at risk of having (screening), a congenital problem due to a genetic disorder or to a chromosomal (abnormalities of the number or structure of chromosomes → problems of development and functioning) disorder, or to some other error of development

**Reasons** for prenatal diagnosis:
- 1. If an abnormality is detected, **termination** may be considered
- 2. Knowledge of an abnormality may give time to **adjust/prepare**

**Indications:**
- 1. A parent affected by a known genetic disorder which may be passed on to the baby
- 2. A previous child or more distant FHx of a child affected by some congenital anomaly
- 3. A woman taking medication which may affect the baby

For Down syndrome see **Down Syndrome**, page 906

**Screening tests** (higher false +ve, especially if low risk women) — used to modify existing risks:
- Info delivered by a screening test is a **risk estimate**
- A low risk does not guarantee absence of congenital anomalies, only that the chance is small (and vice versa)
- A high risk result may lead to a diagnostic test
- There is **no risk of miscarriage a/w** screening tests, most of which are non-invasive
- **First trimester combined screen (FTCS):**
  - **Blood test** (measures serum PAPP-A + free BHCG; *markers of placental health*) at 9-13 weeks +
  - **Nuchal translucency scan** (transabdominal US) at 11-13+6 weeks gestation (will also check gestation via crown-rump length, BPD etc)
  - NTS is only 60% sensitive with 5% FPR + odds of being affected with a positive result (OAPR) are 1:104; combined with blood test = 85% sensitive with 5% FPR, OAPR = 1:32
  - Results available at 24-48 hrs after NTS (NTS + blood results combined [no use on their own] with baby’s gestation + mother’s age to calculate a risk estimate)
  - No risk of harm
  - A risk estimate of **1:300** indicates there should be discussion whether to have a diagnostic test (usually amnio)
    - Blood test is government funded but NTS costs up to $100
- **Second trimester maternal serum screen (MSS2):**
  - **Screening test for major chromosomal disorders, especially Down syndrome + NTDs**
  - Done at 14-20 weeks gestation (ideally 14-17/40) + results available within 48hrs
  - Blood test taken for BHCG, inhibin A, oestriol + alpha-FP; these are measured and combined with mother’s age → risk estimate
  - At 1:300 risk estimate, is 85% sensitive with OAPR = 1:32
  - No risk to baby
  - A high risk estimate (eg 1:50 for Down) for chromosomal anomalies indicates there should be discussion re diagnostic test (usually amnio)
  - A high risk estimate for NTDs indicates there should be discussion re US scan for definite info
- **Fetal nuchal translucency** (= nuchal fold): at 11–13+6 weeks, measure soft tissue thickening on posterior neck, normal < ~ 3 mm. ↑Thickness (adjusted for maternal and fetal age) associated with chromosomal abnormalities. Combine with other risk factors (eg age). Fetal risk 0%

**Diagnostic tests** (higher false –ive):
- **Indications:** positive results from screening, previous child affected by a congenital/genetic disorder or family history, maternal age > 35, maternal condition or medication with possible effect on baby
- All introduce risk of Rh isoimmunisation ⇒ give anti-D afterwards if Rh –ve
- Rapid testing (using either PCR or FISH) can be done with both amniocentesis + CVS for trisomy 13, 18, or 21 or for known translocations (FHx) or sex chromosomes
- **Amniocentesis:** from **15 weeks** (ie 2nd trimester test; 10 – 13 weeks → 5% miscarriage)
  - Needle passed through uterus into amniotic sac
  - Culture amniotic cells for 2 – 3 weeks then **karyotype** detects **chromosomal abnormalities and neural tube defects**
  - Risk 0.5% miscarriage
  - Gold standard but late. Difficult if anterior placenta or oligohydramnios
- **Chorionic villous sampling:** from 10/40 (ie 1st trimester)
  - Detects chromosomal disorders eg Down via [karyotype](#) (can also do DNA genetic tests for eg CF)
  - Results in 2-3/52
  - Needle passed through uterus (under US guidance; or via cervix) to remove small piece of placenta
  - 1% miscarriage rate
  - Marginally less accurate than amnio but can be done earlier and useful for testing inherited genetic disorders (can test DNA). Can’t detect neural tube defects

- **Routine (detailed/morphological) US:**
  - At 18-20/40
  - Diagnostic for some problems (major structural eg NTD, limbs, heart)
  - Screening for others (chromosomal disorders; see “soft” signs indicating ↑ risk)

  - **20-week morphology scan.** Fetal risk 0%. Operator dependent. Assesses:
    - Fetal number, lie and cardiac activity
    - Fetal anatomy: CNS, CVS, GIT, GU, musculoskeletal anomalies (eg neural tube)
    - Gestational age (BPD, head/abdomen circumference ratio, femur length)
    - Amount of amniotic fluid (poly or oligo-hydramnios)
    - Placental location (low lying?)
    - Pelvic pathology: fibroids, cysts, etc
    - Give reassurance: ↓parental anxiety

- **Further investigations:** Most have high false positives ⇒ interpret in light of clinical picture
  - SFH: screening test for fetal growth. Normally approximates gestation after 20/40. SFH 4cm below expected is a/w IUGR (27% sensitive; 48$ sensitive if using customised SFH charts)
  - Fetal kick chart: screening test for fetal wellbeing, from 28/40 on. Mother counts fetal movements – should feel 10 in 12hr period (normally done from 9am → 9pm). Sensitivity 50% + specificity 80% for fetal mortality
  - Cardiography (CTG - fetal heart rate monitoring). See Cardiography , page 636
  - Umbilical artery doppler (not routine)
  - Ultrasound scan: fetal size (biparietal diameter, abdominal circumference, femur length), amniotic fluid estimation, assess fetal breathing (eg ↓in hypoxia)
  - Biophysical Profile: Only if high risk. Combines CTG with US findings. Score of fetal heart rate, breathing movements, fetal movement, fetal tone and amniotic fluid volume. Not often done in NZ

- **Preimplantation genetic diagnosis:** IVF → remove 1 cell at 8 cell stage → test for mutation → abort/continue

- **Ethics of prenatal diagnosis:**
  - Respect for autonomy requires facilitating good decisions (ie supported by sound clinical/ethical reasons) about which tests to have (if any)
  - Beneficence + non-maleficence require good info, communicated effectively in a supportive setting
  - Info provided should be reliable (accurate + up to date), helpful and comprehensive
  - Professional empathy affirms the positives + acknowledges anxieties
  - HPCA requires that clinicians must provide info /or actively facilitate access to a sound source of info as well as referral to another service provider
  - H&D consumers code of rights is applicable to women consulting about prenatal screening/dx

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Intrauterine Growth Restriction (IUGR)/Fetal Growth Restriction (FGR)

- = Intra-Uterine Growth Retardation (IUGR)
- = Failure to achieve full growth potential.
- Not quite the same as small for gestational age (< 10th percentile)
- Causes of ↓SFH: descent, changes in lie, IUGR, oligohydramnios
- Common cause of perinatal death (along with prematurity and congenital malformation)
- Associated with NIDDM, hypertension, heart and thyroid disease in later life
- Types:
  - Asymmetrical:
    - Most common pattern
  - Chronic placental insufficiency – head preferentially protected
  - Caused by extrinsic factors: occurs in maternal illness/smoking/eTOH, twin-twin, multiple preg, idiopathic, PET
    - → ↓ Abdominal circumference cf the head (head sparing), ↓amniotic fluid
  - Symmetrical:
    - Less common but more worrisome
    - Globally smaller
- Seen in: **chromosome abnormalities, early placental dysfunction**, congenital infections or toxins (ie TORCH), multiple pregnancy, malnutrition

**Diagnosis:**
- US scan
- SFH
- Umbilical artery doppler

**Consequences:**
- Vulnerable to *foetal distress* in labour
- *Hypoglycaemia* in first few days of life
- *Polycythemia due to intrauterine hypoxia*, maternal smoking (look plethoric)
- Long-term = depends on underlying cause; need to follow as other diagnoses may emerge

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**Small for Gestational Age**

- Birth weight < 10th centile for gestational age
- Causes = premature infant, IUGR, healthy but constitutionally small infant
- Use **customised growth charts** to assess (ie take into account size of parents)
- Dx: as above

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**Termination of Pregnancy (TOP)**

**Crimes Act 1961**

- Child by definition is not a child until delivered
- Killing an unborn child: prison term not exceeding 14 years
- Unlawful to unlawfully procure an abortion for a woman
- It is a criminal offence to terminate the life of an embryo or fetus unless one of the abortion grounds in Section 187A Crimes Act 1961 exists
- **Section 187a**: It is *not* unlawful to procure an abortion for a women if:
  - Not more than 20 weeks gestation and either:
    - Continuing the pregnancy would result in *serious danger* (not being danger normally attendant upon childbirth) to the *life, or physical or mental health* of the woman or girl
    - That there is a substantial risk that the child, if born, would be so *physically or mentally abnormal as to be seriously handicapped*
    - That the pregnancy is the result of *incest* that is an offence against section 131(1)
    - The girl or woman is severely *subnormal*
    - If the woman is *near the beginning or end of child bearing years*, or if there is *reasonable grounds to consider the pregnancy was the result of rape*, then these factors may be taking into account (although are not sole grounds for termination)
  - More than 20 weeks, and the termination is *necessary to save the life of the woman or girl or to prevent serious permanent injury to her physical or mental health*

**Contraception, Sterilisation and Abortion Act 1977**

- Specifies the **process, not the criteria**, for getting an abortion
- Abortions must be certified by **two certifying consultants (CC)**
- CC chosen by the **abortion supervisory committee**, with a view to expeditious access by any woman seeking an abortion
- Supervisory committee also appoints/approves counselling services
- Every medical practitioner requested by a pt must consider + deal with request
- If able to perform, must refer to another CC for consultation
- If not prepared to do, must refer to two consultants for their consideration within certain timeframe (14d)
- If one or other certifying consultants refuse, case is refused or referred for second opinion
- If lack mental capacity to consent, consultants can make the decision to abort (**section 33**) after consultation with doctor responsible for their care
- **Procedure where woman seeks abortion:**
  - any doctor must arrange to have an abortion request considered under the prescribed procedures
  - if the request is thought to fall under **Crimes Act 187A**
  - an operating surgeon needs to be identified
  - **two CCs**, of whom one is a **designated O/G**, make a determination of whether the abortion may be authorised
 each CC considers the request asap and interviews the woman if she requests (may be accompanied by own doctor)
 with woman’s consent, her own doctor and the operating surgeon may make representations to each CC
 any CC may, with woman’s consent, consult with anyone
 no CC can be obliged to determine without first interviewing and examining woman

The Care of Children Act 2004
 Consent to abortion is not restricted by age, subject to the child having the capacity to understand the nature and the consequences of the treatment.

Ethics
 Killing is wrong unless we can produce a good reason to the contrary
 Why is killing wrong:
   1. Violates the moral integrity of the entity killed
   2. It has negative consequences
   3. Evidences moral flaws in the killer
 Reasons for killing: to end suffering, to protect the innocent, lesser of two evils, to express societal condemnation
 A fetus is obviously human but most of the features which make a human being morally significant [rationality, intelligence, self-awareness, ability to form relationships, artistic creativity, emotional sophistication etc] are either not present in a fetus, or only very late in its development, or only in rudimentary form
 Different views of the moral status of the fetus:
   1. Fetus has the same moral status: absence of a dividing line between a baby and a fetus does not show lack of difference
   2. Fetus has no moral status: Is seeking an abortion for trivial reasons wrong?
   3. Fetus has some moral status: As the fetus develops, reasons have to be increasingly weighty

Procedure
 Medical abortion (<9/40):
   Day 1: use of mifepristone (progesterone receptor antagonist) to block progesterone (required for pregnancy)
   Day 2: misoprostol (prostaglandin analogue) to induce contractions and expel the fetus
 Surgical abortion: for later pregnancies:
   Cervical softening before surgical abortion: misoprostol
   D & C

Infections in Pregnancy

Vertically Transmissible Pathogens and Usual Routes of Transmission

<table>
<thead>
<tr>
<th>Pathogen</th>
<th>Intrauterine</th>
<th>Intrapartum</th>
<th>Breastfeeding</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rubella virus</td>
<td>++</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>Parvovirus B19</td>
<td>++</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Treponema pallidum</td>
<td>++</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Toxoplasma gondii</td>
<td>++</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Cytomegalovirus</td>
<td>++</td>
<td>++(g, h)</td>
<td>+</td>
</tr>
<tr>
<td>VZV</td>
<td>+</td>
<td>++(h)</td>
<td>-</td>
</tr>
<tr>
<td>Listeria monocytogenes</td>
<td>++</td>
<td>+ (g, h)</td>
<td>-</td>
</tr>
<tr>
<td>HIV</td>
<td>+/-</td>
<td>++(h)</td>
<td>+</td>
</tr>
<tr>
<td>HBV</td>
<td>+/-</td>
<td>++(h)</td>
<td>+</td>
</tr>
<tr>
<td>HCV</td>
<td>+/-</td>
<td>++(h)</td>
<td>-</td>
</tr>
<tr>
<td>HSV</td>
<td>+/-</td>
<td>++(g, h)</td>
<td>-</td>
</tr>
<tr>
<td>Streptococcus agalactiae</td>
<td>+/-</td>
<td>++(g, h)</td>
<td>-</td>
</tr>
<tr>
<td>Chlamydia trachomatis</td>
<td>-</td>
<td>++(g)</td>
<td>-</td>
</tr>
<tr>
<td>Neisseria gonorrhoeae</td>
<td>-</td>
<td>++(g)</td>
<td>-</td>
</tr>
</tbody>
</table>

Key:
 ++ = main route of transmission
 + = recognised route, less common
Reproductive and Obstetrics

Routine Antenatal Screening

<table>
<thead>
<tr>
<th>Test</th>
<th>Comment</th>
<th>Intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rubella IgG antibody</td>
<td>Continue screening at each pregnancy</td>
<td>If negative, vaccinate post-partum</td>
</tr>
<tr>
<td>HBsAg</td>
<td>To detect chronic infection (carriers)</td>
<td>Vaccinate infant at birth + give HB immune globulin if mother HBe +ve</td>
</tr>
<tr>
<td>Syphilis (VDRL, TPHA)</td>
<td>To detect active infection</td>
<td>Give penicillin if active syph suspected</td>
</tr>
<tr>
<td>HIV antibody</td>
<td>Offered as routine</td>
<td>If positive, give antiretroviral therapy at start of 2nd trimester plus C-section</td>
</tr>
<tr>
<td>VZ IgG antibody</td>
<td>Not routine; should be offered to women of child-bearing age</td>
<td>If negative, vaccinate post-partum</td>
</tr>
<tr>
<td>Urine culture</td>
<td>Treatment will ↓ adverse pregnancy outcome</td>
<td>Treat if asymptomatic bacteriuria. Repeat culture after treatment</td>
</tr>
<tr>
<td>Vaginal/rectal swaps for GBS</td>
<td>Recommended at 36/40; self-swab. NB. Intrapartum Abs also recommended for GBS isolated from urine during preg, those who have previously given birth to an infant with invasive GBS disease, those whose status is unknown at onset of labour + are &lt; 37/40 or membrane rupture &gt; 18hrs or temp &gt; 38°C</td>
<td>Intrapartum penicillin if carrier</td>
</tr>
</tbody>
</table>

- Tests not recommended for routine antenatal screening:
  - CMV IgG antibody – no treatment available for seronegative women
  - Toxoplasma IgG antibody – primary infection in pregnancy is rare
  - Parvovirus IgG antibody – risk of maternal and fetal infection is low
  - Hepatitis C antibody – only indicated for high-risk groups (eg drug users)

Pre-Pregnancy Testing and Counselling

- Couple should ideally consult GP when planning pregnancy
- Testing:
  - Routine antenatal screening (see above) plus
  - Rubella antibody – vaccinate if negative
  - VZV antibody – vaccinate if negative
  - CMV antibody if woman in close contact with toddlers (eg childcare worker) – if negative:
    - Careful handwashing after nappy change
    - Avoid contact with babies’ saliva
    - Test monthly for CMV antibody for first 3-4 months of pregnancy
- Dietary advice (to reduce risk of listeriosis or toxoplasmosis):
  - Avoid raw or undercooked fresh meat
  - Avoid refrigerated ready-to-eat food (eg cold meats, salads, soft cheese, pate) that is not freshly prepared
  - Peel or wash raw fruit and vegetables to remove contaminating soil
  - Wash hands after disposing of cat (kittens really) litter or after gardening

Management of Symptomatic Infective Illness During Pregnancy

<table>
<thead>
<tr>
<th>Presentation</th>
<th>DDx</th>
<th>Tests</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Flu-like illness:</td>
<td>Primary CMV infection (will see atypical mononucleosis – as with EBV)</td>
<td>IgG/IgM</td>
<td>Nil (termination)</td>
</tr>
<tr>
<td>→ lethargy, fever, myalgia, +/- headache, lymphadenopathy</td>
<td>Primary toxoplasmosis (prominent lymphadenopathy)</td>
<td>IgG/IgM</td>
<td>Spiramycin</td>
</tr>
<tr>
<td>Listeriosis</td>
<td>Blood culture; faeces culture</td>
<td>EBV serology</td>
<td>None</td>
</tr>
<tr>
<td>Maculopapular rash:</td>
<td>Primary EBV infection/other viral URTI</td>
<td>EBV serology</td>
<td>None</td>
</tr>
<tr>
<td>→ +/- fever, arthritis/arthritis</td>
<td>Rubella</td>
<td>IgG/IgM</td>
<td>Nil (termination)</td>
</tr>
<tr>
<td></td>
<td>Parvovirus B19</td>
<td>IgG/IgM</td>
<td>Nil (monitor for hydrops)</td>
</tr>
<tr>
<td></td>
<td>Enterovirus (eg echo)</td>
<td>Throat swab/faeces culture</td>
<td>Nil</td>
</tr>
</tbody>
</table>
Reproductive and Obstetrics

<table>
<thead>
<tr>
<th>Vesicular rash</th>
<th>VZV</th>
<th>IgG/IgM swab vesicle</th>
<th>Acyclovir</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hand, foot, and mouth disease (Coxsackie A)</td>
<td>Throat swab/faeces</td>
<td>Nil</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Genitourinary symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>→ frequency, dysuria</td>
</tr>
<tr>
<td>→ +/- join pain, fever, ulcer, vaginal discharge</td>
</tr>
<tr>
<td>UTI</td>
</tr>
<tr>
<td>Chlamydia, gonorrhoea</td>
</tr>
<tr>
<td>Genital HSV (HSV2)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Maternal fever near term</th>
</tr>
</thead>
<tbody>
<tr>
<td>→ +/- premature labour</td>
</tr>
<tr>
<td>→ +/- premature rupture of membranes</td>
</tr>
<tr>
<td>UTI</td>
</tr>
</tbody>
</table>

Specific Pathogens

- Rubella:
  - **Route of transmission:**
    - Droplet spread from respiratory secretions
    - Most infectious during eruption of rash
    - May shed virus from throat from 10 days before onset of rash to 15 days after
  - **Clinical manifestations – post-natal rubella** (ie mother) – most cases are sub-clinical but clinical signs include:
    - Maculopapular rash (starts on face + moves down the body – lasts 3-5d)
    - Arthritis/arthralgia (30% of women with primary rubella)
  - **Clinical manifestations – congenital rubella:**
    - Spontaneous abortion
    - LBW
    - Deafness
    - Cataract or glaucoma
    - Congenital heart disease (eg PDA)
    - Mental retardation
  - **NB.** Up to 10% of women of child-bearing age are susceptible to rubella because not vaccinated or vaccine failure or vaccine-induced immunity has waned
  - **Primary maternal infection in first trimester → high risk of fetal infection + damage**
  - **Maternal infection in months 1-2 → 90% risk of fetal infection**
  - **Maternal infection in month 3 → 50% risk of fetal infection**
  - **Risk of damage is negligible after 16/40 gestation**

- CMV:
  - **Route of transmission:**
    - Blood – transfusion, needle-sharing, mother to fetus (intrauterine; less common)
    - Cervical secretions – perinatal transmission to neonate (more common), sex
    - Semen – sex
    - Saliva – close contact between children (esp in daycare centres)
    - Urine – infants to adults
    - Organ donation – transplantation
  - **CMV in the immunocompetent individual:**
    - Children – primary infection commonest in pre-schoolers; pre-school children are major reservoir of infection for adults; infected children excrete CMV in saliva + urine for a prolonged period
    - Adults – infection is usually asymptomatic and self-limiting; commonest clinical signs are: fever (for up to 2/52) + atypical mononucleosis
    - Intratrauterine infection:
      - Commonest cause of non-hereditary deafness related to congenital infection
      - May occur following primary maternal infection with viremia
      - Incidence of primary infection = 1/300 pregnancies
      - Incidence of fetal infection = 40% of cases of primary maternal infection (ie 1/750 pregnancies)
      - Most congenitally-infected infants appear normal at birth but in up to 40% of these the following sequelae occur: deafness + mild intellectual impairment
      - Diagnosis of congenital infection: amniocentesis at 19/40 (or at least 6/52 after suspected onset of maternal infection) – test for CMV DNA by PCR
    - **CMV in the immunodeficient individual:**
Reproductive and Obstetrics

- AIDS patients – retinitis (most common), colitis, oesophagitis, encephalitis
- Transplant patients – patients at greatest risk are CMV-negative recipients of CMV-positive organ transplants:
  - Pneumonitis (BM, lung transplant)
  - Hepatitis (liver transplant)
  - Reduced kidney function in renal transplant (eg rising Cr)
- CMV infection associated with blood transfusion:
  - Blood donors are not routinely screened for CMV antibody
  - CMV-negative blood or blood products should be given to premature infants <1500g at birth; CMV-neg recipients of CMV-neg transplants
- CMV infection associated with blood transfusion:
  - Blood donors are not routinely screened for CMV antibody
  - CMV-negative blood or blood products should be given to premature infants <1500g at birth; CMV-neg recipients of CMV-neg transplants

- Toxoplasma gondii:
  - Toxoplasmosis is caused by a protozoan parasite
  - Is a worldwide zoonosis
  - Cat family are principle hosts for t.gondii → infected oocysts are excreted in cat faeces (usually kittens) + may remain viable in moist soil for up to 18/12
  - Humans are intermediate hosts
  - Routes of transmission:
    - Ingestion of soil contaminated with oocysts
    - Ingestion of raw or undercooked meat containing tissue cysts (esp pork) – this is probably the most common route for human infection, but toxoplasmosis does occur in vegetarians
    - Blood transfusion
    - Organ transplant
    - Congenital transmission from mother to fetus
  - Toxoplasmosis in the immunocompetent individual:
    - Asymptomatic cervical lymphadenopathy, often unilateral (most common presentation)
    - Fever, myalgia
    - Acute pharyngitis
    - Maculopapular rash
    - Atypical mononucleosis on blood film. NB. Acute toxoplasmosis is usually a self-limiting illness + symptoms settle within a few months without treatment
  - Ocular toxoplasmosis:
    - Most cases in adolescents or adults result from re-activation of latent congenital infection
    - Must always be treated
    - Blurred vision, photophobia, visual field defects
    - Bilateral focal necrotising retinitis + yellow-white cotton patches surrounded by zone of hyperaemia
  - Toxoplasmosis in the immunodeficient individual:
    - May be acquired, but usually reactivation of latent congenital infection due to immunosuppression
    - Anti-toxoplasma chemotherapy is always indicated in immunodeficient pts
    - At risk groups are:
      - AIDS pts (most common)
      - Transplant pts
      - Leukaemia + lymphoma pts
    - Clinical syndromes:
      - In AIDS pts, CNS involvement is most common with solitary SOL on CT or MRI; necrotising encephalitis or meningoencephalitis
      - In transplant pts, clinical syndromes include myocarditis, pericarditis, pneumonitis, hepatitis, polymyositis
  - Congenital toxoplasmosis:
    - Prevention:
      - Antenatal screening not recommended as primary acquired maternal infection is uncommon; approx 75% of women of child-bearing age are susceptible (eg antibody neg); low levels of IgM (acute-phase) antibody can persist for years following primary infection
      - Avoid eating raw or undercooked meat
      - Wash vegetables + fruit thoroughly to remove soil
      - Wear gloves while disposing of cat litter + wash hands thoroughly afterwards
      - Wash hands thoroughly after gardening
    - Risk to fetus following primary maternal infection:
      - Overall incidence of fetal infection = 29%
      - In first trimester = 17%
In second + third trimesters = 42%

Complications of congenital infections:
- Spontaneous abortion, stillbirth, prem delivery
- Bilateral choroidoretinitis
- In severe cases may see maculopapular rash, lymphadenopathy, hepatosplenomegaly, microcephaly, hydrocephalus, cerebral calcification, epilepsy, blindness

- Tests of congenital infection = test amniotic fluid for toxoplasma DNA by PCR
- Tests of maternal infection = test for IgG + IgM toxoplasma antibodies in serum plus avidity tests
- Treatment of toxoplasmosis:
  - Pyrimethamine + folinic acid + clindamycin (for toxoplasmosis in neonate, ocular toxoplasmosis, immunocompromised pt)
  - Spiramycin (an analogue of erythromycin) – for treatment of maternal infection, continued to term

VZV:
- Chickenpox = primary VZV infection; shingles = recurrence of latent VZV infection
- Chickenpox:
  - Most cases occur in children under 13 yrs
  - Infection transmitted via infected nasopharyngeal secretions
  - Incubation = 14-15d
  - Period of infectivity = 2d before onset of vesicular rash until all vesicles have crusted + no new lesions
- Congenital chickenpox:
  - Incidence = 10-15%
  - Sequelae = shingles in first year of life (most common); 2-3% develop fetal varicella syndrome:
    - Skin scarring with dermatomal distribution
    - Ipsilateral limb hypoplasia
    - Eye + CNS lesions
- Perinatal chickenpox = maternal varicella developing 5d before delivery or up to 2d post-partum can result in severe varicella in the neonate with significant mortality
- Prevention of VZV infection in pregnancy:
  - Antenatal screening should be routine; >90% of women of child-bearing age are immune to VZV
  - NB. A hx of chickenpox provides reliable evidence of immunity
  - Sero-negative pregnant women should be offered zoster immune globulin (ZIG) within 2d of exposure to chickenpox
  - If maternal varicella occurs in the neonatal period, infant should be given ZIG after birth
  - Vaccinate all sero-negative women of child-bearing age who are not pregnant

Parvovirus B19:
- Clinical manifestations:
  - Erythema infectiosum (fifth disease) – slapped cheek disease
  - Erythema infectiosum occurs in epidemic waves, lasting 2-3 years + seen in primary school children
  - Most cases are asymptomatic – arthritis + arthralgia may occur in adult infection
- Other infections caused by parvovirus B19:
  - Transient aplastic crisis = may occur in pts with haemolytic disorders or disorders of ↑ erythropoiesis
  - Hydrops fetalis = caused by severe fetal anaemia + occurs 5/52 after maternal infection during pregnancy (1/3 of causes will resolve spontaneously; intrauterine transfusion improves clinical outcome)
- Prevention:
  - Routine antenatal screening is not recommended – approx 60% of women of child-bearing age are sero-neg for parvovirus B19; during epidemics in community, annual seroconversion rate ↑ 10-15%
  - If a pregnant woman has contact with a confirmed case, she should be tested for IgM + IgG antibodies
  - If maternal infection confirmed → fetus should be monitored for hydrops by US over 6-12/52 period

HSV:
- Congenital infection – intrauterine infection is rare
- Perinatal infection:
  - Primary genital herpes at term is an indication for C-section + treatment of infant with IV acyclovir
  - Women with recurrent genital herpes: C-section is not routinely recommended unless active genital lesions on the cervix are present at the onset of labour
Complications of Early Pregnancy

**Differential of Early Pain or Bleeding**

- 20% of women bleed in early pregnancy – it is **never** normal ⇒ investigate
- **Obstetric** causes:
  - 1. Miscarriage
  - 2. Ectopic
  - 3. Trophoblastic disease
- **Gynaecological causes**:
  - Period, STI, cervical (eg polyps, ectropion [endocervical columnar epithelium protrudes out through the external os of the cervix and onto the vaginal portion of cervix, undergoes squamous metaplasia, and transforms to stratified squamous epithelium], vaginitis, endometriosis, ovarian cyst (may be functional ⇒ irregular cycles), PID
- **Non-gynaecological**: UTI, GI (eg haemorrhoids)
- **Exam**:
  - CV, Resp, temp
  - Abdominal: tenderness/guarding/rebound
  - Pelvic exam:
    - Speculum: discharge, bleeding (coming from os? If so → uterine source), swabs, os
    - Bimanual: mass, endometriosis (⇒ fixed, retroverted uterus and utero-sacral nodularity on PR), cervical motion tenderness (⇒ ?PID)
- **Investigations**:
  - MSU
  - FBC, blood type + Rhesus
  - US
  - HCG

**Spontaneous Abortion/Miscarriage**

- = Loss of products of conception before the 20th week or weighing less than 400g
- 10 – 15% of recognised pregnancies. >75% in first trimester and due to fetal causes
- **Threatened** abortion:
  - Os is closed + may be bleeding from this. Fetus is viable (still has heart beat). No pelvic tenderness
  - Slight bleeding/spotting after a period of amenorrhoea. Minimal pain
  - Seen in 1/7 pregnancies. Uterus right size for dates. 80% will settle; 20% miscarry. Associated with preterm delivery
  - US + follow up with serum βHCG and/or further scanning 7-14 days
  - Bed-rest or supportive treatment with progestogens or βHCG have not been shown to offer any benefit
- **Incomplete/inevitable abortion**:
  - Cervix is dilating, more pain, heavier bleeding. May see products of conception protruding through os
  - Lower abdominal pain/contractions followed by heavy bleeding
  - US: heterogenicity
  - Management:
    - POC can be removed with sponge forceps to prevent cervical vasovagal shock (vasovagal caused by cervical stimulation)
    - Minimise bleeding by administering syntocin infusion
    - *Expectant* management – can take up to 8 weeks
    - Medical management – misoprostol (prostaglandin analogue; causes uterine contractions) administered orally or vaginally
    - Surgical evacuation if vital signs unstable
- **Complete abortion**:
  - Products of conception (fetus, placenta + membranes) expelled, bleeding stopped, cervix closed (don’t confuse with threatened), uterus small for dates
  - Variable amount of pain and bleeding. Uterus firm and contracted more than expected for period of amenorrhoea
  - If previous US has not confirmed intrauterine pregnancy should be managed as ‘pregnancy of unknown location’ with serum hCG levels followed until dx confirmed
  - Managed conservatively
- **Septic abortion**:
  - Usually due to infective complication of spontaneous incomplete miscarriage
- History of incomplete miscarriage
- Fever > 38°C, tachycardia, general malaise or abdominal pain, marked pelvic tenderness, purulent bloodstained vaginal discharge
- E.coli, staph, neisseria, chlamydia, strep etc
- Rarely release of endotoxins can lead to DIC and ARF
- Management – resuscitation, appropriate micro work-up, antibiotics and uterus evacuation

- Blighted ovum:
  - Anembryonic pregnancy – gestational sac develops without ovum
  - Presentation and management similar to missed miscarriage
  - Diagnosis based on USS findings of gestational sac diameter >20mm but no evidence of yolk sac or embryo

- Missed/delayed abortion:
  - Fetus dead but not expelled
  - Failure to expel products of conception after death of embryo or foetus
  - May have been vaginal spotting or brownish discharge
  - Regression of earlier signs and symptoms of pregnancy
  - Clinical exam: uterus smaller than expected for dates; cervix closed
  - Confirmed by 2 US scans (<12/40) 7 days apart
  - Management:
    - GA 13 weeks: may be expectant – products are expelled over next few days – 30% avoid any intervention
    - Medical – more successful with earlier stage miscarriage
      - Mifepristone – oral anti-progesterone stat, followed 36-48 hrs later by
      - Gemeprost – vaginal prostaglandin
      - Misoprostol – prostaglandin (oral or vaginal) causes cervical relaxation and uterine contractions
    - Surgical
      - Suction evacuation preferred in 1st trimester – misoprostol initially for cervical priming
      - 2nd trimester: medical methods possibly followed by uterine curettage

- Don’t forget requirement for anti-D prophylaxis in Rh-ve unsensitised women after miscarriage (including threatened)

- Causes:
  - None found – most common
  - Chromosomal abnormalities ~ 25%
  - Hormonal imbalance: eg failure of corpus luteum to produce enough progesterone
  - Maternal illness, abnormalities of the uterus (eg cervical incompetence), immunological factors, teratogenic drugs, infection, antiphospholipid syndrome

- Recurrent miscarriage = loss of 3 or more consecutive pregnancies, occurs in < 1%

- Risk factors:
  - Maternal age >35 (risk increases with increasing age)
  - Previous miscarriage or termination
  - Relative sub-fertility, assisted conception
  - Low pre-pregnancy maternal weight
  - Regular or heavy alcohol use
  - Stress
  - High paternal age or changing partners
  - Heavy bleeding
  - Low foetal HR (<85bpm)
  - Abnormal sized yolk sac
  - Small gestational size for age or small difference of mean sac diameter(MSD) and CRL

- Decreased risk: previous live birth, Nausea, Vitamin supplements, Diet – fresh fruit and veges daily

Ectopic Pregnancy

- = Any implantation outside the uterine cavity. > 95% in the fallopian tube

- 0.5 – 1 % of pregnancies. Fatal if untreated. Most common cause of death in 1st trimester

- Risk factors – anything slowing ovum’s path to the uterus:
  - Salpingitis (eg PID)
  - Surgery
  - Previous ectopic (recurrence in 10 – 20%)
  - Endometriosis
Reproductive and Obstetrics

- IUCD
- Assisted fertility

**Presentation:**
- Abdominal pain (often unilateral) or bleeding in any sexually active woman
- Usually around 8 weeks amenorrhoea, but may not have missed a period
- Can present with haemorrhagic shock: acute rupture – sudden severe abdominal pain and shock
- Shoulder tip pain due to blood in the peritoneum irritating the diaphragm (uncommon)
- Diarrhoea, painful defecation
- Cervical excitation (cervical motion tenderness)

**Examination:**
- Generalised or localised abdominal discomfort with or without signs of peritoneal irritation
- Unilateral adnexal tenderness
- Cervical excitation
- Slightly enlarged uterus
- Uncommonly adnexal mass

**Diagnosis:**
- βHCG – LOW for gestational age and rises slower than normal (normal doubling time is 2 days)
- Quantitative βHCG: at 1500-2000 should see sac on trans-vaginal US, at 6000 should see sac on abdominal US
- US can visualise in 2% of cases – key finding is empty uterus
- Laparoscopy is gold standard

**Possibilities to consider:**
- Multiple pregnancies takes few extra days to visualise gestational sac
- Heterotrophic pregnancy (concurrent uterine and ectopic) – spontaneous incidence of 1/14000 pregnancies, 1-3% with assisted conception

**Treatment:**
- Expectant – spontaneous resolution, only used when low or declining hCG
- Medical – IM methotrexate procedure of choice if:
  - Patient stable
  - Diagnosis of ectopic certain & unruptured
  - βHCG <10,000, ectopic <3.5cm, no foetal cardiac activity
  - Reliable patient follow-up
  - No contraindications to methotrexate
- Surgical – absolutely indicated if ruptured ectopic or haemodynamically unstable:
  - Laparotomy – unstable patient or unsuitable for laparoscopy (e.g. adhesions, obesity)
  - Laparoscopy – advantages over open surgery in experienced hands, shorter recovery time, lower risk of adhesions, haemoperitoneum not contraindication if patient stable

**Gestational Trophoblastic Disease**

<table>
<thead>
<tr>
<th>Partial Hydatidiform Mole</th>
<th>Complete Hydatidiform Mole</th>
<th>Choriocarcinoma</th>
</tr>
</thead>
<tbody>
<tr>
<td>Triplid 69 XXX, 69 XXY (ie fertilised by 2 sperm)</td>
<td>46 XX, (46XY)</td>
<td>46</td>
</tr>
<tr>
<td>Normal and dilated villi – some initially have a fetus</td>
<td>Dilated villi with trophoblast proliferation. No fetus</td>
<td>No villi. Atypical proliferating trophoblast</td>
</tr>
<tr>
<td>Little invasive potential</td>
<td>10% invasive, Choriocarcinoma 5% (ie 5% malignant)</td>
<td>Most have metastasised at diagnosis. 80% survival</td>
</tr>
</tbody>
</table>

- Proliferative abnormalities of trophoblast (placental cells = trophoblast)
- Aka hydatidiform mole (= molar pregnancy) can continue to grow and bury itself into surrounding organs
- Epidemiology: Occurs in 1.54/1000 pregnancies, 80% benign, 5% metastatic and cure rate >90%
- The tumour may completely or partially replace the placenta
- Spermatozoon enters an ovum that has lost its nucleus, or in which two sperms enter the ovum
- In over 90% of complete moles, only paternal genes are found; in partial moles, there are 2 sets of paternal genes + 1 of maternal
- Thought to be defective maternal immune response to trophoblast invasion → embryo starves, dies + is absorbed, whereas the trophoblast continues to thrive and sometimes invade
- Complete:
  - No foetus
  - Consists of hydropic hyperplastic villi
  - Derived from fertilisation of anucleated ovum, paternal origin only

Reproductive and Obstetrics 621
Either duplication of haploid sperm by meiosis (90%, homozygous 46XX)
Or dispermic fertilisation (10%, heterozygous 46XX or 46XY)

Partial:
- Foetus may coexist with focal trophoblastic proliferation
- Derives from maternal and paternal origin
- Results from dispermic fertilisation or failure of 1st meiotic division (triploid – 69 XXY, 69 XXX, 69 XYY)

Choriocarcinoma:
- Malignant invasion by trophoblastic cells – can arise years after a pregnancy
- Incidence 1 in 20,000-40,000 in western world
- See disordered growth of cytotrophoblast and syncytiotrophoblast arising within 2 years of antecedent pregnancy
- Invades myometrium
- Spreads predominantly by vascular route
- Pulmonary metastases present in 70% by diagnosis
- Risk 1000 times greater after hydatidiform mole than term pregnancy
- Management:
  - Based on prognostic score
  - Biologic behaviour more important than anatomic staging
  - Divided into low, medium or high risk
  - Chemotherapy by single, combination agents or intensive combination therapy respectively
  - Good prognosis with chemotherapy: 90-95%

Risk factors:
- Age < 15 yrs or > 35 yrs
- South East Asian or Middle Eastern origin
- Previous molar pregnancy

Presentation:
- Uterus large for dates in 50%
- No fetal heart sounds
- Vaginal bleeding +/- passage of grape-like villus
- Exaggerated pregnancy symptoms – hyperemesis, thyrotoxicosis, possibly early onset pre-eclampsia
- Very high levels of HCG
- Ground glass/speckled appearance on US and no fetus

Dx:
- USS: Classic ‘snow-storm’ pattern (complete) due to hydropic villi, or a vesicular pattern
- B-hCG (usually abnormally HIGH - better for use in follow up)
- CXR, CT, MRI for metastatic disease
- Baseline FBC, U&Es, Cr, LFTs, TFTs, bHCG, CXR
- Histopathology gold standard

Foetus may coexist with mole, if doubt about viability of coexisting pregnancy repeat USS before any intervention

Hyperemesis Gravidarum
- Rare (1 in 1000)
- ↑ Risk if young and primip, multiple pregnancy
- Presents with inability to keep food or drink down, hypovolaemia, polyneuritis (↓Vit B), liver and renal failure, ketonuria
- Admit to hospital. Rehydrate, exclude UTI, twins, and hydatidiform mole
Cardiovascular Changes & Disease in Pregnancy

**Cardiovascular Changes During Pregnancy**

- ↑ maternal HR from 4 weeks to 20% of pre-pregnancy values by time of late pregnancy
- ↑ blood volume from 6 weeks to 45-50% non-pregnant values in early 3rd trimester
- ↑ plasma volume leading to “physiological anaemia of pregnancy”
- ↑ cardiac output by 30-50% during pregnancy, reaches max mid-gestation
- ↓ TPR (20-30%), diastolic blood pressure falls (10-20%)
- Positional changes of gravid uterus in 3rd trimester → venocaval compression → CO reduced by as much as 25%
- Multiple births increase risks (33% increase in blood volume in twin pregnancy)
- Fetal circulation: the fetal PaO2 is ~40mmHg. However, the higher O2 binding affinity of fetal haemoglobin allows for 80-90% O2 saturation even at this lower partial pressure of oxygen. Small changes to maternal oxygenation can cause much larger changes in the fetus due the steep O2 binding curve of fetal haemoglobin at partial pressures <40mmHg
- Changes intrapartum:
  - Contraction → autotransfusion of 300-500ml back into systemic circulation
  - ↑ sympathetic drive in response to pain and anxiety → further ↑ HR and BP
  - CO increases by as much as 34% during contractions, 12% between contractions
- Changes postpartum:
  - Venocaval compression is relieved → redistribution of blood volume and subsequent ↑ CO of 60-80% followed by rapid ↓1hr post delivery
  - Common clinical findings in pregnancy: ↑pulse volume, ↑JVP pressure waves, ↑heart size (apex beat displaced by approx 1 cm), loud first heart sound, 3rd heart sound, ejection systolic murmur up to grade 3/6 in 90% women, peripheral oedema

**Non-Cardiac Changes in Pregnancy**

- Haematological:
  - ↑ thrombin formation → predisposes to VTE, CVA, ?MI (dissection), thrombus on prosthetic valves
- Connective tissue:
  - Change in levels of relaxin
  - This leads to ↓ collagen efficacy → risk of dissection in Marfan’s/bicuspid AV etc

**Cardiovascular Disease in Pregnancy**

- CVD is an important cause of maternal mortality
- Most will have a normal pregnancy however
- Largely due to change in haemodynamic state: ↑ in blood volume, fluctuations in cardiac output, ↓ TPR and hypercoagulable state.
- Tolerated by healthy women but can lead to de-compensation in pre-existing heart disease.
- High risk times: end of 2nd trimester, labour, immediate post-partum
- Causes maternal deaths (UK 1997-99): HD = thromboembolism
- Cardiac deaths – 30% congenital, 15% ischaemic, 56% acquired HD (cardiomyopathy, myocarditis)
- Recognition of HD in pregnancy can be difficult as many signs and symptoms of normal pregnancy mimic HD
- Normal cardiovascular symptoms and signs in pregnancy:

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Signs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dyspnoea - common, 50% complain of breathlessness by 20 weeks gestation, 75% by 31 weeks. Of concern if severe enough to restrict daily activities.</td>
<td>Bounding/collapsing pulse – can mimic AR</td>
</tr>
<tr>
<td>Orthopnoea - due to gravid uterus pressing on diaphragm</td>
<td>Tachycardia</td>
</tr>
<tr>
<td>Palpitations - common, due to ↑ HR and ↑ awareness of heart beat, study showed no correlation between arrhythmias &amp; sx</td>
<td>Ectopics</td>
</tr>
<tr>
<td>Dizziness/Syncope - due to vena cava obstruction → supine hypotension syndrome</td>
<td>Peripheral oedema</td>
</tr>
<tr>
<td></td>
<td>Distended jugular veins</td>
</tr>
<tr>
<td></td>
<td>Diffuse, brisk, displaced apex - &gt; 2cm consider abnormal</td>
</tr>
<tr>
<td></td>
<td>Loud 1st heart sound</td>
</tr>
<tr>
<td></td>
<td>3rd heart sound (84%)</td>
</tr>
<tr>
<td></td>
<td>Ejection systolic murmur (96%) grade 1-2/6, LLSE or Pulmonary area - concerning if diastolic, pansystolic, late systolic, grade 3/6 or above ESM or assoc. ejection click.</td>
</tr>
<tr>
<td></td>
<td>Continuous murmur (venous hum, mammary soufflé)</td>
</tr>
</tbody>
</table>

- Investigations:
- X-ray if strong clinical suspicion (radiation dose low, risk to foetus low with proper shielding)
- ECG
- Echo – excellent tool, no risk to foetus. Small pericardial effusions present in 44% pregnant women

- Chest X-ray and electrocardiographic findings in normal pregnancy.

<table>
<thead>
<tr>
<th>Chest X-ray</th>
<th>Electrocardiogram</th>
</tr>
</thead>
<tbody>
<tr>
<td>Straightened left heart border</td>
<td>Leftward shift of QRS axis</td>
</tr>
<tr>
<td>Increased cardiothoracic ratio</td>
<td>Small Q wave, inverted</td>
</tr>
<tr>
<td>Increased pulmonary vascular markings</td>
<td>T wave in lead III</td>
</tr>
<tr>
<td>Small pleural effusions (early postpartum period)</td>
<td>ST segment and T wave changes</td>
</tr>
<tr>
<td></td>
<td>Atrial/ventricular ectopics</td>
</tr>
</tbody>
</table>

**Low Risk HD in Pregnancy**
- Uncompensated L → R shunt (eg small ASD/VSD)
- Repaired lesion with no residual dysfunction
- Bicuspid AV without stenosis
- Mild-moderate PS
- Valvular regurgitation with normal function

**Intermediate Risk HD in Pregnancy**
- Some congenital HD
- Some acquired HD (eg rheumatic HD, CAD, cardiomyopathies)
- Arrhythmias
- Pre-eclampsia
- Peripartum cardiomyopathy

**High Risk HD in Pregnancy**
- Significant AS/MS
- Marfan’s especially with *aortic root dilatation*
- Large ASD/VSD
- PHTN (eisenmenger’s/idiopathic)
- R → L shunt (↑ predisposition to *paradoxical emboli* – eg DVT → CVA)
- Symptomatic HD
- HF

**Specific Diseases**
- Valve disease in pregnancy:
  - ↑ blood volume + ↑CO → fixed stenotic outflow lesions are poorly tolerated
  - ↓TPR → regurgitant lesions tolerated well
  - Additional demands at delivery → may require diuretics peripartum; consider AB prophylaxis (esp in rheumatic HD)
- Rheumatic HD – in pregnancy MS most common lesion. 5% maternal mortality. 51% of those with MS in pregnancy developed complication mainly in 3rd trimester or post-partum. A/w AF. Treat medically – standard rx. Failure to respond → percutaneous balloon valvotomy. Risk of complications low compared to surgery. MR and AR better tolerated due to ↓ decreased afterload (↓TPR).
- Congenital HD – even post-surgery may still cause problems. Those complicated by cyanosis, pulmonary hypertension or severe LV outflow obstruction are likely to lead to complications. ↑ risk of congenital heart disease in offspring. ↑ risk of congenital heart disease in offspring.
- MV prolapse - most common cardiac problem in pregnancy. Mostly well tolerated.
- Infective endocarditis – rare complication, mortality 10-30%. Prophylactic antibiotics during delivery controversial, only in high risk women (prosthetic valve, previous endocarditis)
- Ischaemic HD – increasing with ↑ age and co-morbidities of mothers. MI in pregnancy a/w high mortality (25-50%)
- Peripartum cardiomyopathy – unknown cause, occurs in pregnancy in women **without** prior history of heart disease. Incidence 1/3000. RF = multiparity, old, multiple pregnancy, pregnancies complicated by HTN. Defined as development of HF in last month of pregnancy or within 5 months of delivery, absence of identifiable cause, absence of prior HD, LV dysfunction on echo. Clinical course variable from refractory HF to full recovery. Standard therapy for HF should be initiated except **ACE-I should only be used post-partum (teratogenic, cause RF in foetus)**. Use heparin for anti-coagulation ante-partum due to risk of VTE. Mortality 25-50%. Those
Reproductive and Obstetrics

who recover usually do so within 6 months of delivery. Those with persistent LV dysfunction mortality is 85% over 5 years.

- Prosthetic heart valves:
  - Factors affecting pregnancy outcome include *type of valve and anticoagulation therapy*
  - Bioprosthetic valves wear out faster and may require re-operation in young women
  - There is no evidence they wear out faster in pregnant vs non-pregnant women
  - Are associated with good pregnancy outcomes, requiring less anti-coagulation than mechanical valves
  - Warfarin is teratogenic especially between weeks 6-12 of gestation. Heparin can be substituted
  - Anti-coagulation vital especially for mechanical valves and as *pregnancy is a hypercoagulable state*
  - LMWH has more predictable effect and better side-effect profile and appear to be safe for the foetus than UFH although there is some unresolved concern over potential teratogenic effects.

- Aortic dissection:
  - Pregnancy is associated with an ↑ risk of aortic dissection (due to ↑ haemodynamic shear stress and possible hormonal induced changes of the vascular wall) especially in those with predisposing risk factors e.g. Marfan’s, Ehlers-Danlos, co-arteration of the aorta and bicuspid aortic valve
  - Occurs more often in 3rd trimester. Suspect in any pregnant woman presenting with severe chest, back or abdominal pain
  - Ix include chest XR (lack of mediastinal widening does not rule out dissection), TOE, MRI
  - Consider *prophylactic β-blocker*. Pregnancy is not advised if aortic root diameter exceed 4cm.

- Arrhythmias – uncommon in pregnancy but pre-existing arrhythmias may be aggravated and new arrhythmias may appear in pregnancy. Usually benign. Tachyarrhythmias are *usually associated with structural HD* – treatment same as non-pregnant. Direct cardioversion can be performed in pregnancy. *Digoxin, quinidine, procainamide and adenosine relatively safe for mother and foetus*. B-blockers useful but evidence atenolol in 1st trimester assoc with IUGR. No problems with ICDs

Management of Pregnant Women with HD

- Women with HD require thorough evaluation and counselling before and during pregnancy → refer early
- Regular review
- High-risk periods (greatest CV demand) when cardiac decompensation is more likely to occur include:
  - The end of the second trimester (~ 28/40)
  - During labour
  - Immediate postpartum period
- Monitor medications:
  - ACEi contraindicated
  - β-blockers, hydralazine, methyldopa sweet
- Pregnancy contra-indicated in Eisenmenger’s, pulmonary hypertension, Marfan’s with aortic root dilatation.
- Consider prophylactic ASA/heparin/O2
- Early hospitalisation +/- bed rest may be needed
- Multidisciplinary care is essential for successful maternal and fetal outcomes.

Respiratory Problems in Pregnancy

Summary

- The pregnant patient is at risk of several pregnancy-specific respiratory complications, including amniotic fluid embolism, tocolytic-associated pulmonary oedema and pulmonary oedema complicating pre-eclampsia
- In addition, the pregnant state increases the risk of other respiratory complications, particularly pulmonary embolism and gastric acid aspiration
- Community-acquired pneumonia occurs in pregnant women at a similar incidence to the non-pregnant population, but the risk of varicella pneumonitis is increased. AIDS-related pulmonary infections should always be considered in this sexually active population.
- Management of the pregnant patient with pulmonary disease must take into account the anatomic and physiological changes affecting the respiratory system in pregnancy. Although management is similar to that in the non-pregnant patient, welfare of the fetus must be considered

Respiratory Physiology in Pregnancy

- The hormonal changes in pregnancy affect the URT
- Oestrogen is probably responsible for many of these effects
- The anatomy of the thoracic cage is altered by both the *enlarging uterus* as well as from *hormonal effects* → ligamentous laxity
The diaphragm is displaced upwards, but the potential loss of lung capacity is largely offset by an ↑ in the anteroposterior and transverse diameters and widening of the subcostal angle.

*Diaphragmatic function remains normal.* In the pregnant pt near term, the max transdiaphragmatic and inspiratory pressures that can be generated are similar to values generated by non-pregnant patients.

Changes to the chest wall return to normal within 6/12

**Effect of pregnancy on respiratory physiology**

<table>
<thead>
<tr>
<th>Anatomical changes</th>
<th>Physiological changes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Airway</td>
<td>Oedema, friability, rhinitis</td>
</tr>
<tr>
<td>Thorax</td>
<td>Widened diameters, widened subcostal angle, elevated diaphragm</td>
</tr>
<tr>
<td>Abdomen</td>
<td>Enlarged uterus, ↓ chest wall compliance</td>
</tr>
<tr>
<td>Cardiovascular</td>
<td>↑ LV mass, ↑ blood volume</td>
</tr>
</tbody>
</table>

**Respiratory Issues during Labour and Delivery**

- In active labour, hyperventilation ↑, and tachypnoea due to pain or anxiety may result in a more marked respiratory alkalosis
- A superimposed metabolic alkalosis can be produced by vomiting and volume depletion
- Alkalosis may ↓ fetal oxygenation by ↓ uterine blood flow
- In contrast, pain & anxiety may lead to rapid shallow breathing in some patients, resulting in alveolar hypoventilation, atelectasis, and mild hypoxaemia
- **Dyspnoea of pregnancy is usually an isolated symptom** and hx and examination do not reveal evidence of organic disease

**Pregnancy Specific Respiratory Disorders**

- Physiologic dyspnoea of pregnancy:
  - 60% of pregnant woman experience exertional dyspnoea, and 20% experience dyspnoea at rest.
  - Due to hyperventilation stimulated by high levels of progesterone, and impairment of breathing by the expanding uterus.
  - Physiological dyspnoea does not interfere with daily activities. Must differentiate it from pathologic causes of dyspnoea.
- Amniotic fluid embolism:
  - Occurs in 1:8000 to 1:80000 births. 10-80% mortality.
  - *Aminiotic fluid and cells enter the systemic circulation and block the pulmonary vessels,* resulting in pulmonary vasospasm, pulmonary hypertension and left ventricular failure.
  - Occurs as a *result of labour and delivery,* or as a result of uterine manipulation, or trauma. Can also occur postpartum.
  - Symptoms: sudden onset of dyspnoea, hypoxaemia, cardiovascular collapse, rarely DIC and fetal distress.
  - No specific treatment. Resuscitation and supportive management.
- Pre-eclampsia and pulmonary oedema:
  - 3% of women with preeclampsia develop pulmonary oedema during pregnancy, often as a result of aggressive fluid replacement for dehydration (which is common in women with preeclampsia).
  - Symptoms are of acute respiratory distress in a woman with preeclampsia.
  - Treatment: restrict fluid, supplemental oxygen, diuresis.
- Venous thromboembolism in pregnancy:
  - Leading cause of morbidity in pregnancy, leading cause of non obstetric maternal mortality.
  - Pregnancy increases risk of VTE to 5 times the risk in non pregnant women.
  - Risk factors in pregnancy:
    - Increased venous capacitance and decreased lower limb venous return due to compression by uterus lead to increased venous stasis.
    - Increased clotting factors in pregnancy.
  - Risk is further increased if: caesarean section, increased maternal age, prolonged bed rest, haemorrhage, sepsis, multiparity, obesity, inherited thrombophilias.
  - VTE difficult to diagnose - leg discomfort and swelling are common in pregnancy.
  - Venography and ultrasound to diagnose.
Pulmonary embolism in pregnancy:
- Hard to diagnose - dyspnoea and tachypnoea common in pregnancy.
- Diagnose with: compression ultrasonography, VQ scan, pulmonary angiography. These investigations involve minimal amounts of radiation and are reasonably safe in pregnancy.
- Treat with unfractionated heparin, continued throughout the rest of pregnancy, and then switch to warfarin from birth until 6 weeks post partum. Do not use warfarin in pregnancy (increased risk of fetal and neonatal haemorrhage, placental abruption).
- Recurrence rate of 4-15% in subsequent pregnancies.
- VTE prophylaxis required in pregnancy if woman had VTE in previous pregnancy, or if woman is in known hypercoagulable state. Use LMWH or unfractionated heparin continued for duration of pregnancy.

Pneumonia:
- Most frequent cause of non-obstetric infection in pregnancy, 3rd most frequent cause of indirect obstetric death.
- Pneumonia during pregnancy associated with preterm labour, fetal complications, adverse maternal outcome.
- Clinical features and causative organisms similar to those for non-pregnant women.
- Treatment also similar to that for non-pregnant women. See list of antibiotics safe in pregnancy (below).

<table>
<thead>
<tr>
<th>Bug</th>
<th>Drug</th>
</tr>
</thead>
<tbody>
<tr>
<td>Streptococcus pneumonia</td>
<td>Ampicillin/amoxicillin/cephalosporin</td>
</tr>
<tr>
<td>Mycoplasma pneumonia</td>
<td>Erythromycin/clarithromycin/azithromycin</td>
</tr>
<tr>
<td>Legionella pneumonia</td>
<td>Erythromycin/clarithromycin/azithromycin</td>
</tr>
<tr>
<td>Staphylococcus aureus</td>
<td>Flucloxacillin</td>
</tr>
<tr>
<td>Haemophilus influenza</td>
<td>Ampicillin/amoxicillin/cephalosporin</td>
</tr>
<tr>
<td>Chlamydia psittaci</td>
<td>Erythromycin</td>
</tr>
</tbody>
</table>

Tuberculosis:
- Should be aggressively treated in pregnancy.
- TB in pregnancy usually treated with isoniazid and rifampicin. Carries a low risk of adverse fetal effects.
- Dyspnoea is a common complaint in women with otherwise normal pregnancies.
- This symptom occurs in 15% of women in the first trimester, 50% by 19 week’s gestation and 75% by 31 weeks.
- A number of mechanisms have been proposed, but the most likely explanation is that this represents a normal perception of the increased minute ventilation accompanying pregnancy.

Existing Respiratory Conditions in Pregnancy

Asthma in pregnancy:
- Commonest respiratory disease encountered in pregnancy.
- In pregnancy, 1/3 of women find their asthma improves, 1/3 find it stays the same, and 1/3 find that it deteriorates.
- 10% of pregnant women with asthma experience an exacerbation of asthma during delivery or labour.
- Infant outcome is worse with increasing severity of asthma (IUGR, increased prenatal mortality), aggressive management of asthma is needed in pregnancy.
- Advice:
  - Avoid and control asthma triggers
  - Smoking cessation
  - GORD is a common trigger of asthma in pregnant women. Advise small meals, raising head of the bed, and treatment of GORD with H2 antagonists.
- Medications for asthma in pregnancy similar to those for non pregnant women. See list of drugs safe in pregnancy (below). Risk of medications is less than risk of inadequate asthma control.
- Aggressive management of asthma exacerbations required. Maintain O2 sats of >95% during exacerbations of asthma in order to maintain fetal oxygenation.

Cystic fibrosis:
- Close medical supervision during pregnancy is essential.
- Physiotherapy: postural drainage + percussion (harder to do adequately as pregnancy progresses), deep breathing on direct coughing and forced expiration manoeuvres, positive expiratory pressure masks, exercise.
- Treat infection: for staph. aureus and H. Influenza.
- Pseudomonas aeruginosa – regular nebulised colomycin to reduce frequency of exacerbations. PO: ciprofloxacin.
- Burkholderia cepacia – 2 weeks of ceftazidime or meropenem, in combination with an aminoglycoside. Avoid cotrimoxazole due to theoretical folate antagonism.
- **Counselling CF women** – risk of child inheriting CF, shortened life expectancy of CF patients affecting bringing up their children
- **Effect of CF:**
  - Risk of developing complications is dependent on lung function.
  - Frequency of hospitalisation, need for IV antibiotic and supplemental feeding are not significantly increased in pregnancy compared to non-pregnant CF patients.

- **Idiopathic pulmonary fibrosis:**
  - Little info available on effect on pregnancy. Authors recommend O₂ supplementation in patients who had exercise induced desaturations ≤ 94%

- **Sarcoidosis:**
  - Patients with inactive sarcoid experience no change during pregnancy.
  - Those with active disease – **condition improves**.
  - Those with chronic disease – remains stable
  - Prone to exacerbation during postpartum period, may require steroids.

### ARDS

- The pregnant pt is at **risk of developing ARDS from obstetric complications** as well as being at ↑ risk of developing various non-obstetric conditions
- Obstetric complications such as amniotic fluid embolism, chorioamnionitis, trophoblastic embolism, and placental abruption may result in acute lung injury and ARDS
- Pregnancy predisposes to other pulmonary insults which can cause ARDS, including gastric aspiration, pneumonia, air embolism and massive haemorrhage
- The diagnosis of ARDS is made by the presence of hypoxaemia with radiological evidence of diffuse pulmonary infiltrates, in the absence of cardiac failure

#### Evaluation of Respiratory Distress

<table>
<thead>
<tr>
<th>Disorder</th>
<th>Distinguishing features</th>
<th>CXR</th>
<th>Treatment</th>
</tr>
</thead>
</table>
| Amniotic fluid embolism          | Mechanism: Cellular contents or humoral factors in amniotic fluid produce acute pulmonary HTN & acute LV dysfunction  
See cardiorespiratory collapse, seizures, DIC | Normal/pulmonary oedema                  | Resuscitative and supportive measures             |
| Pre-eclampsia                     | Mechanism: In general, the pre-eclamptic woman is volume depleted, and pulmonary oedema most commonly occurs in the early postpartum period, associated with aggressive intrapartum fluid replacement  
See hypertension, proteinuria | Pulmonary oedema                         | Fluid restriction, administration of supplemental O₂ and diuresis |
| Tocolytic pulmonary oedema        | Mechanism: β-adrenergic agonists are used to inhibit uterine contractions in preterm labour.  
Complication of these which is unique to the pregnant state is the development of PO | Pulmonary oedema                         | Discontinue β-agonist                             |
| Aspiration pneumonitis            | History of vomiting, aspiration                                                         | Focal or diffuse infiltrates              |                                                    |
| Peripartum cardiomyopathy         | Gradual onset, cardiac gallop                                                           | Cardiomegaly, pulmonary oedema            |                                                    |
| Venous thromboembolism            | Sudden onset, chest pain                                                                | Normal/atelectasis/effusion              |                                                    |
| Pneumothorax/mediastinum          | Occurs during delivery, subcutaneous emphysema                                          | Pneumothorax/mediastinum                 |                                                    |
| Air embolism                      | Sudden hypotension, cardiac murmur                                                      | Normal/pulmonary oedema                  |                                                    |
| Asthma                            | Prior history, wheezing, diurnal variation                                              | Normal, hyperinflated                    | As per standard rx                                 |
| Pneumonia                         | Cough, fever, localised crackles                                                       | Consolidation                            | As per standard rx (avoid tetracyclines +         |

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<table>
<thead>
<tr>
<th>Valvular cardiac disease</th>
<th>Elevated JVP*, bilateral chest crackles, heart murmur</th>
<th>Pulmonary oedema</th>
</tr>
</thead>
</table>

Key Points

- **1. Physiological changes**: reduced FRC; hyperventilation with compensated respiratory alkalosis; ↑ oxygen consumption
- **2. Dyspnoea of pregnancy**: common benign complaint; normal history and physical examination; does not interfere with daily activities; non-progressive
- **3. Diagnosis of respiratory disease**: consider pregnancy-specific diseases; conditions predisposed to by pregnancy; and conditions not affected by the pregnant state
- **4. Management**: similar to management of the non-pregnant patient with respiratory disease; ensure optimal oxygenation; consider fetus in radiological investigations, although risk is low; consider fetus in pharmacological therapy

Respiratory Pharmacology in Pregnancy

- Err on the side of safety. Assume all drugs have an unknown effect on the fetus until proven otherwise.
- Drug classes commonly used to treat pulmonary diseases:
  - Beta agonists – OK in pregnancy. Little systemic absorption, no ill effects found on the fetus.
  - Ipratropium bromide: OK in pregnancy. No ill effects found on fetus.
  - Antihistamines and decongestants: *Not proven safe in pregnancy*. Brompheniramine (an anti-histamine) has been associated with congenital abnormalities.
  - Corticosteroids: Studies have found that systemic steroids have been associated with a small decrease in birth weight (~200gms). *Inhaled corticosteroids have been found to have no ill effects on the fetus.*
  - Common antibiotics: Penicillin, cephalosporins and erythromycin have all been shown to be safe to use in pregnancy.
  - Methylxanthines (e.g. Theophylline) - OK in pregnancy. Crosses placenta, but research has shown no ill effects on fetus.
- **Relatively contraindicated drugs in pregnancy**: sulphonamides, trimethoprim, aminoglycosides, nitrofurantoin, anti-tuberculosis drugs, tetracyclines, quinolones.
- Many respiratory investigations employ the use of ionizing radiation. Ionizing radiation in high doses has been associated with multiple ill effects on the fetus, including growth retardation, CNS effects, microcephaly, eye malformations, and childhood leukaemia.

Gestational Diabetes Mellitus (GDM)

- Definition: GDM is defined as “carbohydrate intolerance of variable severity with onset or first recognition during pregnancy”
- Occurs in 5% of pregnancies in NZ
- **Risk factors**: Gliccosuria, age > 30 years, obesity, family history of diabetes, past history of GDM or glucose intolerance, previous adverse pregnancy outcome (stillbirth, miscarriage) and belonging to a high risk ethnic group (Maori, PI, Asian), previous large baby
- For most it consists of mild glucose intolerance manifest during the 2nd or 3rd trimester and normalising following delivery

Aetiology

- Pregnancy is characterized by insulin resistance and hyperinsulinemia, thus it may predispose some women to develop diabetes. The resistance stems from placental secretion of diabetogenic hormones including growth hormone, corticotropin releasing hormone, placental lactogen, and progesterone, as well as increased maternal adipose deposition, decreased exercise, and increased caloric intake. These and other endocrinologic and metabolic changes ensure that the fetus has an ample supply of fuel and...
nutrients at all times. Gestational diabetes occurs when pancreatic function is not sufficient to overcome the insulin resistance created by changes in diabetogenic hormones during pregnancy

- ↑human placental lactogen + ↑ maternal adiposity (HPL, increases through pregnancy from placenta) → ↑insulin resistance
- Hyperglycaemia manifests only when B-cells are unable to ↑ insulin production to match the insulin resistance
- May unmask sub-clinical T2DM. May be genetic predisposition for this to occur
- Is also an ↑ need for insulin during pregnancy → for glucose storage

Consequences
- GDM is associated with increased perinatal morbidity:
  - 1. Macrosomia (>4000g or 90th centile): symmetrical or asymmetrical. GDM/DM babies are asymmetrically big (big shoulders and abdomen relative to head)
  - 2. Shoulder dystocia (due to macrosomia)
  - 3. Neonatal hypoglycaemia + polycythemia
  - 4. Hyperbilirubinaemia, RDS
- GDM is associated with increased intrauterine death
- GDM is associated with increased maternal complications:
  - 1. Is a strong risk factor for the development of diabetes later in life (~50%)
  - 2. Preeclampsia
  - 3. Polyhydramnios
  - 4. C-section

Screening
- Is usually asymptomatic (ie no polyuria and thirst). Risk factors have low predictive power ⇒ universal screening usual
- It is recommended ALL pregnant women be screened
- Glucose challenge:
  - The recommended screening test for GDM
  - Performed at 26-28/40
  - 50g glucose load followed by BG at 1hr (non-fasting)
  - If > 7.8mmol/L at 1hr → confirmatory test
- Confirmatory test → GTT:
  - If screening test positive → 75 g oral glucose tolerance test (fasting)
  - Venous plasma glucose level at 0 hours of ≥ 5.5 mmol/L and/or at 2 hours of ≥ 9.0 mmol/L → GDM
- Screening notes: If clinical suspicion high, diagnostic OGTT indicated, irrespective of the stage of pregnancy. If OGTT gives normal results early, repeat at 26 and 30 weeks’ gestation

<table>
<thead>
<tr>
<th>Indication</th>
<th>Optimal gestation for testing</th>
<th>Test</th>
<th>Diagnostic criteria — venous plasma glucose level (mmol/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical suspicion of GDM</td>
<td>Any time</td>
<td>75 g OGTT (fasting)</td>
<td>0 hours &gt; 5.5, 2 hours &gt; 9.0 (NZ)</td>
</tr>
<tr>
<td>Screening</td>
<td>26–28 weeks</td>
<td>50g glucose load (morning non-fasting)</td>
<td>1 hour &gt; 7.8</td>
</tr>
<tr>
<td>Confirmation of diagnosis after a positive screening test</td>
<td>26–30 weeks</td>
<td>75 g OGTT (fasting)</td>
<td>0 hours &gt; 5.5, 2 hours &gt; 9.0 (NZ)</td>
</tr>
</tbody>
</table>

OGTT = oral glucose tolerance test.
Aus = cut-off for Australia; NZ = cut-off for New Zealand (see text).

Management
- MDT approach: review every 1-2/52 from 30/40
- Education, diet, moderate exercise, insulin therapy (NB insulin doesn’t cross the placenta)
Oral hypoglycaemic agents have no role in GDM (not approved for use in pregnancy [metformin used in Wellington though!]).

Monitoring:
- Self monitoring optimal – 6 x daily
- Preprandial blood glucose level <5.5 mmol/L
- 2 hour postprandial <6.5 mmol/L
- HbA1c < 6% (check every 4 weeks)

Fetal surveillance:
- Ultrasound at 34 weeks (check fetal growth and polyhydramnios)
- CTG routinely started at 36 weeks

Delivery:
- At 38-40/40
- During labour, good glycaemic control needs to be maintained while avoiding hypoglycaemia (have glucose infusion ready)
- Maternal blood glucose level should be monitored for 24 hours postpartum

Neonate:
- Monitor BG
- Observe for RDS

Follow up:
- Diabetic counselling (due to increased risk of developing permanent diabetes)
- OGTT at 6-8 weeks postpartum to exclude permanent diabetes. Repeat OGTTs every 2 years.

Pre-Existing Diabetes
- If T2DM, weight loss prior to conception is advised
- Need to conceive when HbA1C < 8
- Even if tightly controlled, 4 – 5% risk of congenital abnormalities (2x general population)
  - Most common are neural tube and heart defects
- ↑ risk of complications for the mother:
  - Check for retinopathy at least twice during pregnancy (pre-existing retinopathy may worsen)
  - Get baseline renal function and ECG/Echo if cardiac problems (pre-existing nephropathy may worsen)
- Usual insulin injections have shorter action control harder. In early pregnancy, insulin requirements may reduce. Later they usually increase.
- Usually induced before term

Hypertension in Pregnancy
- NB. Measure BP sitting in pregnancy due to aortocaval compression

Normal Changes in Blood Pressure
- Physiology:
  - ↑O2 consumption from 300 to 350 ml per minute
  - ↑CO from 5 to 6.5 - 7 litres per minute due to ↑Stroke volume (10%) and ↑HR (15 bpm)
  - Peripheral resistance falls (due to hormonal changes)
  - ↓PCO2 to 31 mm Hg to increase gradient for shifting CO2 from fetus
  - ↑Blood volume by 40% from early pregnancy to delivery
  - ↑Ventilation
  - ↑Glomerular filtration →↑urination
- During first and second trimesters, BP (especially diastolic) falls by 10 - 20 mmHg, return to booking BP by 3rd trimester (partly due to hypotension →↑aldosterone)
- Venous distensibility + ↑venous pressure predispose to varicose veins

Hypertension in Pregnancy
- SBP > 140mmHg or DBP > 90mmHg
- Classified as:
  - 1. Gestational HTN: HTN after 20/40, no other multisystem features as cf pre-eclampsia (eg proteinuria)
  - 2. Pre-eclampsia
  - 3. Chronic HTN (essential or secondary)
  - 4. Pre-eclampsia superimposed on chronic HTN
**Essential Hypertension**

- Present **before** pregnancy and commoner in *older multips*
- If high blood pressure **before** 20 weeks, probably pre-existing hypertension
- Aim to keep BP < 140/90
- Treat with nifedipine, hydralazine, methyldopa
- 5 x more likely to develop pre-eclampsia than normotensive women
- Watch for ‘white-coat’ hypertension

### Pre-Eclampsia

- = Pregnancy-induced hypertension with proteinuria +/- oedema
- = Toxaemia
- = Pre-eclampsic toxaemia (PET)
- = *Gestational Hypertension*
- 2% of pregnancies
- Signs:
  - > 20 weeks pregnant
  - **Oedema, proteinuria, ↑BP** (↑systolic by 20 - 25 or ↑diastolic by 15 over booking BP)
- If < 20 weeks then ?hydatidiform mole
- Symptoms:
  - Is generally **asymptomatic** ⇒ **requires screening**
  - Headache & visual disturbances (due to oedema) can occur as can upper abdo pain (due to stretching of liver capsule)
- **May recur** in a subsequent pregnancy
- Normally returns to normal 3/12 post-delivery
- Risk factors:
  - Primiparity (as first time a female is exposed to the male “foreign body”)
  - *New partner*
  - Previous or family history of pre-eclampsia or eclampsia
  - Overweight
  - < 20 years (ie low sperm exposure) or > 35 years
  - *Multiple pregnancy* (or anything else that ↑placenta size)
  - Renal disease, essential hypertension, diabetes
  - IVF
  - Autoimmune disease (eg SLE, anti-phospholipid syndrome)
- Presentations:
  - In ‘normal’ pregnancy (ie low risk) – PET is usually mild and late (eg from 37 weeks)
  - In ‘abnormal’ pregnancy, may begin from as early as 20 weeks and be severe
- Pathogenesis:
  - Preeclampsia is a disorder characterised by widespread vascular endothelial malfunction and vasospasm
  - Mechanisms not certain. Genetic, nutritional, and environmental factors might play a part as well as:
    - Maternal immunologic intolerance (maternal-fetal immune maladaptation)
    - Abnormal placental implantation/poor trophoblast invasion (Abnormal vascularisation of the placental decidua by the syncytiotrophoblast during the secondary invasion (~ 28 weeks))
    - Leads to oxidative stress → toxins release → widespread vascular endothelium activation (present in many tissue, hence widespread organ involvement) → vascular endothelium becomes more sensitive to vasopressors → ↑TPR + BP → ↓perfusion of fetus + IUGR
- Organ effects:
  - Cardiovascular: ↑TPR + BP
  - **Haematological**: haemoconcentration + TCP + endothelial activation + DIC
  - **HELLP syndrome**: haemolysis, ↑LFTs, low platelets
  - **Renal**: ↓GFR due to proliferation of endothelial cells obstructing the capillaries + proteinuria
  - **Lungs**: pulmonary oedema
  - **Neuro**: meningeal irritation
- Effects on fetus:
  - **Asymmetric IUGR** (brain preferentially preserved)
  - If untreated → symmetric growth retardation  (if this occurs on its own then pre-existing fetal abnormality)
  - ↓Fetal movements, fetal respiratory effort and ↓amniotic fluid
• **Serious signs** (→ Urgent admission):
  - **Signs of ↑ICP**: headaches, vomiting, hyperreflexia, bilateral clonus
  - **Headache**, stomach pain, vomiting, ↑HR (i.e., mimics viral illness)
  - Sustained vasoconstriction → ischaemia (e.g., visual changes, brain) and ↑clotting/DIC. Also effects liver (RUQ pain), kidneys
  - Placental abruption
  - Placental ischaemia

• **Diagnosis**:
  - SBP > 140 or DBP > 90 after 20/40 **and** one of the following:
    - Proteinuria: > 300mg/24h or 30mg/mmol PCR
    - Renal insufficiency: Cr > 0.09mmol/L or oliguria
    - ↑ALT
    - Severe epigastric/RUQ pain
    - Neurological problems: convulsions (eclampsia), ankle clonus, HA, hyperreflexia
    - Haematological disturbance: TCP, DIC, haemolysis
    - Pulmonary oedema
    - IUGR

• **Examination**:
  - BP
  - **Abdominal exam** (for liver tenderness)
  - **Chest exam** (pulmonary oedema)
  - **Ophthalmology**

• **Assessment**:
  - Baby: **CTG** and **US**
  - Mum:
    - BP
    - Most important of the following are platelets and uric acid
    - **MSU**
    - **FBC**:
      - Either ↑Hb (haemoconcentration secondary to oedema) or ↓Hb (haemolysis secondary to DIC)
      - ↓Platelets – adhering to damaged capillary endothelium
    - **LFTs**: ↑AST/ALT (not ALP – that’s produced by the placenta). NB exclude acute fatty liver of pregnancy
    - **Cr + Uric Acid**: ↑ due to ↓renal flow. If bad then 24 hour urine to check for oliguria/renal failure
    - **Coagulation**: ↓fibrinogen due to DIC

• **Treatment**:
  - **Low dose aspirin**: pregnancy runs closer to term (controversial)
  - **Mild**: monitor BP and fetus; rest up (but not bed rest). If problems and > 37/40 then induce
  - **Moderate**: (e.g., BP of 140/90 but stable):
    - **Labetalol** (want β2 activity without any β1 activity). Contraindicated in asthma
    - **Methyldopa** (causes depression etc but safe for the fetus)
    - **Nifedipine** (other Ca blockers cause fetal malformations)
  - **Severe**: Hydralazine IV (↓BP). Aspirin (blocks thromboxane production → preferentially make prostacyclin), antihypertensives, anticonvulsant prophylaxis (Magnesium sulphate). Have to stabilise before delivery
  - **Delivery** is the only cure (although > half of fits occur post partum). Antihypertensives only mask the disease. Diuretics contra-indicated. May have serious illness with only mild proteinuria (1+). Usually resolves over 10 days.
  - Deliver now if ↓platelets, signs of renal failure, unstable BP etc (i.e., signs of serious disease), or if at term (>37 weeks)

**Eclampsia**

- 1 in 3000 pregnancies
- Major cause of maternal (due to intracerebral haemorrhage) and fetal (due to maternal hypoxia during seizure) morbidity/mortality
- Is unpredictable. **BP is not a good marker** of disease
- Generalised seizures (eclampsia) – treat with **Magnesium sulphate** (better than diazepam)
- May need to deliver baby
- Death from stroke (most common), liver, kidney or heart failure
Other Complications of Later Pregnancy

- Key complications: preterm labour, pre-eclampsia and small babies

Shock in Pregnancy

- Hypovolemic:
  - Bleeding before 20/40: miscarriage (complete, incomplete, septic); ectopic; GTD
  - Bleeding after 20/40: placenta praevia; placental abruption; uterine rupture

- Distributive:
  - Inverted uterus in 3rd stage of labour (shock without haemorrhage)
  - Amniotic fluid embolism (anaphylactic type reaction: SOB, hypotension, DIC; seen in 1st stage of labour or after labour)
  - Septicaemia

- Cardiogenic:
  - PE
  - Decompensated heart disease

Management:

- ABC
- Get help
- Large bore IVL
- Blood for tests, cross-match
- Give colloid to keep SBP > 100
- CPR, if >20/40 pregnant, need to move uterus left to stop compression of the IVC; breaths & compressions faster than normal
- Delivery or D & C often necessary
- Watch for signs of renal failure & Sheehan syndrome (pituitary ischaemia)

Antepartum Haemorrhage (APH)/Placental Abruption/Placenta Praevia

- APH = Any bleeding from the genital tract between 20th week (some definitions 24/40) and delivery

- Differential diagnosis:
  - Placenta praevia:
    - Implantation of the placenta in the lower uterine segment near or over the internal os.
    - Graded 1 to 4 (worst)
    - Suspect in any woman > 24/40 with painless vaginal bleeding
    - Risk factors: prior c-section (uterine scar), grand multiparity (>5), multiple birth, maternal age >35, tobacco/cocaine use, fibroid uterus (ie anything that causes scarring or reduces places for embryo to attach)
  
  - Placental abruption:
    - Premature separation of normally implanted placenta from the uterine wall
    - Often caused by the rupture of maternal vessels in the decidua basalis, where it interfaces with the anchoring villi in the placenta
    - Results in haematoma formation & bleeding can often be concealed
    - Peaks at 24 – 26 weeks gestation
    - Risk recurring in subsequent pregnancy = 10x
    - Risk factors: ↑maternal age, multiparity, maternal shock, poor nutrition, gestational diabetes, ↑BP, smoking, anything that causes maternal vasoconstriction (trauma, cocaine, etc)
    - Dx is mainly clinical (US is poorly sensitive)
    - If fetus alive & at least 34/40 → deliver
    - If fetus alive & <34/40 → delay delivery if mother stable, give steroids for baby’s lungs, monitor
    - If fetus dead → deliver
  
- Onset of premature labour
- Bleeding from other parts of the genital tract (eg cervical polyps, vaginitis, vulval varicosities)
- Fetal: Vasa praevia: Bleeding from an abnormal fetal vessel attached to the membranes over the internal os. Need ROM for this to occur. Mother will not be shocked

- Clinical differences between praevia and abruption:

<table>
<thead>
<tr>
<th></th>
<th>Placenta praevia</th>
<th>Placental abruption</th>
</tr>
</thead>
<tbody>
<tr>
<td>Presentation</td>
<td>Shock in proportion to visible blood loss</td>
<td>Shock out of proportion to visible blood loss (concealed)</td>
</tr>
<tr>
<td>Painless</td>
<td>Painless</td>
<td>Poorly localised abdominal pain</td>
</tr>
</tbody>
</table>
Exam
Bright red bleeding
No contractions, uterus well relaxed
Fetus easy to palpate with good heart sounds
Recurrent

Dark red bleeding and clots
Uterus tense and tender
May have no fetal heart sound detectable
Possible DIC

Other

• Assessment:
  ➢ ABCs
  ➢ History: previous bleeds, initiating factors, eg trauma, colitis
  ➢ ALWAYS ultrasound: exclude placenta praevia (detects 95 – 98% of cases) and major abruption with placental separation.
  ➢ NO vaginal exam until praevia excluded (can → severe haemorrhage)
  ➢ APT test to distinguish fetal from maternal blood
  ➢ If major blood loss, treat for shock → transfuse, give O2
  ➢ Give steroids
  ➢ If fetus alive, consider c-section before labour
  ➢ If fetus dead, induce

• Treatment:
  ➢ If Rhesus negative and no antibodies yet, give Anti-D within 72 hours
  ➢ Placenta praevia: If substantial, hospitalise till delivery, Caesar at 38 weeks
  ➢ Placental abruption: Hospitalise. Serious risk of PPH, also acute renal failure, pituitary necrosis, etc.
    Monitor retro-placental clot by serial ultrasound

Rhesus Haemolytic Disease

• Aetiology: if Rhesus –ve mother is ‘contaminated’ by blood from a Rhesus +ve baby ⇒ anti-D IgG antibodies (isooimmunisation)
• Later in the pregnancy, or in a following pregnancy, IgG can cross the placenta causing Erythroblastosis Fetalis (⇒ stiff oedematous lungs and hydrops – widespread oedema)
• Test for anti-D antibodies in all Rhesus –ve mothers at booking and in 2nd trimester. If elevated then monitor carefully
• Anti-D immunoglobulin given prophylactically to Rh –ve mothers:
  ➢ = IgG anti-D (anti-RhD) antibodies that bind to, and lead to the destruction of, fetal Rh D positive red blood cells that have passed from the fetal circulation to the maternal circulation. Therefore, in a Rhesus negative mother it can prevent sensitization of the maternal immune system to Rh D antigens, which can cause rhesus disease in the current or in subsequent pregnancies
  ➢ Within 72 hours after incident (eg amnio, threatened miscarriage, spontaneous abortion, any risk of trans-placental haemorrhage – TPH, etc)
  ➢ After birth if baby Rh +ve or group not known
  ➢ This prevents ‘iso-immunisation’ – gobbles up antigen before mothers immune system generates antibodies
  ➢ Don’t give anti-D if mother already producing Anti-D

Premature Labour

• = Labour (ie painful, regular contractions with cervical change) < 37 weeks
• 8% of babies, 85% of neonatal deaths
• Over-diagnosed – over 80% diagnosed will deliver at term without treatment. Hard to diagnose – regular uterine contractions are normal, cervical changes in labour can be subtle
• Braxton-Hicks contractions are common from 30 weeks but are not painful
• History: Is it true labour: check nature of contractions, urinary frequency (?UTI), backache, spotting or a change in vaginal discharge (normal in 3rd trimester – lots, white, non-smelling)
• Exam/ix:
  ➢ Maternal temperature
  ➢ Speculum: rule out ruptured membranes: see below
  ➢ CTG
  ➢ Investigations: temperature, BP, pulse, SFH, view cervix for clots etc (do NOT view cervix if risk of praevia – do US first), ?infection screen, US, MSU, fetal welfare
• Risks:
  ➢ Strongest association is previous preterm birth (↑4 times risk)
  ➢ Previous mid-trimester abortions (2 or more) – not 1st trimester spontaneous abortions
• Aetiology:
  - Spontaneous: 40%
  - **Multiple pregnancy**: 10%, ↑10 times risk
  - Maternal or fetal conditions (25%)
  - Infection
  - **Preterm premature rupture of membranes** (PPROM = rupture of membranes before labour commences and preterm)
  - APH (abruptio placentae, placenta praevia)
  - > 28 weeks, 80 – 90% survival
  - > 32 weeks, similar survival as term babies but complications

• Management:
  - Consider tocolysis (inhibition of uterine contractions → inhibiting labour):
    o Allows time for steroids to work and for transfer to neonatal unit, doesn’t actually improve morbidity/mortality
    o **Oral Nifedipine** (Ca channel blocker)
    o Indomethacin
    o β-agonists – Ritodrine and Salbutamol (risk of pulmonary oedema)
    o MgSO4
    o ?Not if PPROM. Can →↑risk of infection
  - **Steroids**: dexamethasone and betamethasone (*crosses placenta, prednisone doesn’t*) - 2 shots 12 hours apart. Always give first even if close to delivery → *maturation of lungs if between 24 and 34 weeks* (*↑surfactant production* → *↓fetal distress syndrome*) and neonatal better BP control post delivery
  - **Antibiotics**: consider if ROM, GBS etc: amoxycillin
  - **Delivery**: If < 26 weeks then vaginal delivery. C-section more likely if multiple pregnancy or breech.

**Premature Rupture of Membranes**

• = Rupture of membranes before labour is established. Normally rupture of membranes follows establishment of labour
• Check: have they really ruptured? Look for pooled liquor in posterior fornix → take swab from posterior fornix & leave it to dry on slide → amniotic fluid dries in a fern pattern (*ferning*)
• Do US for liquor volume and fetal well-being
• Risk of preterm labour + intrauterine infection
• Management:
  - Admit and monitor
  - Swabs for infection (a cause of PROM)
  - *Check for signs of infection*: fever, maternal or fetal tachycardia, ↑WBC
  - After 24 hours (time varies) commence prophylactic antibiotics
  - Low threshold for induction

**Symphysis Pubis Dysfunction**

• Excessive movement of the pubic symphysis as well as associated pain, possibly because of a misalignment of the pelvis. AKA pelvic girdle pain
• Thought to affect up to one in four pregnant women to varying degrees, with 7% of sufferers continuing to experience serious symptoms postpartum
• The main symptom is usually *pain or discomfort in the pelvic region*, centred over the symph
• Sufferers may walk with a *characteristic waddling gait* and have difficulty climbing stairs, problems with leg abduction and adduction, pain when carrying out weight bearing activities, difficulties carrying out everyday activities, and difficulties standing
• Diagnosis: is usually made from the symptoms alone
• The mainstays of currently accepted treatments are the use of elbow *crutches*, pelvic support devices and prescribed pain relief. The vast majority of problems will resolve spontaneously after delivery

**Cardiotocography**

• = Fetal heart rate monitoring
• **DRC BRAVADO** =
  - *Define Risk* (see indications for CTG, antenatal problems, gestation, etc)
  - *Contractions* (in 10 mins)
- **Baseline Rate** (should be **110-160**, excluding acc/dec, over 5-10min period)
- **Variability** (from the baseline: difference b/w peak + trough, should be **5-25min**, assessed over 40min)
- **Accelerations** (15bpm or more above baseline, lasting 15s; **should see 2 in 20 minutes**)
- **Decelerations** (should be **absent or early**: 15bpm or more below baseline, lasting 15s; **early**: early in contraction + return to baseline by end of contraction; **late**: mid-late in contraction + extend > 20s after contraction; **prolonged**: >90s; **variable**)
- **Overall** (normal or not)

### Indications for CTG

- **Antenatal** risk factors, increasing the risk of fetal compromise including:
  - Abnormal Doppler umbilical artery velocimetry
  - Suspected or confirmed intrauterine growth restriction
  - Oligohydramnios or polyhydramnios
  - Prolonged pregnancy >**42 weeks** gestation
  - **Multiple** pregnancy
  - **Breech** presentation
  - Antepartum **haemorrhage**
  - Prolonged rupture of membranes (>24 hours)
  - Known fetal abnormality which requires monitoring
  - Prior uterine scar / caesarean section
  - Pre-eclampsia
  - **Diabetes** (on insulin or poorly controlled or with fetal macrosomia)
  - Other current or previous obstetric or medical conditions which constitute a significant risk of fetal compromise

- **Intrapartum** risk factors, including:
  - **Induction** of labour with prostaglandin / oxytocin
  - Abnormal auscultation or CTG
  - **Oxytocin** augmentation
  - Epidural analgesia
  - Abnormal vaginal **bleeding** in labour
  - Maternal pyrexia
  - **Meconium** or blood stained liquor
  - Absent liquor following amniotomy
  - Active **first stage of labour** >12 hours (i.e. regular uterine activity cervix 4cm dilated)
  - Active **second stage** (i.e. pushing) >1 hour where delivery is not imminent
  - **Preterm** labour less than 37 completed weeks

### Classification of CTGs

- **Normal antenatal/intrapartum CTG trace:**
  - The normal antenatal CTG is associated with a low probability of fetal compromise and has the following features:
    - **Baseline** fetal heart rate (FHR) is between **110-160 bpm**
    - **Variability** of FHR is between **5-25 bpm**
    - **Decelerations** are **absent or early**
    - **Accelerations** x2 within **20 minutes**. The significance of the presence or absence of accelerations in intrapartum CTG is unclear. Therefore, **exclude accelerations during intrapartum interpretation**

<table>
<thead>
<tr>
<th>Features of Intrapartum Fetal Heart Rate (FHR)</th>
<th>Reassuring</th>
<th>Non-reassuring</th>
<th>Abnormal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline (bpm)</td>
<td>110-160</td>
<td>100-109, 161-170</td>
<td>&lt; 100, &gt; 170</td>
</tr>
<tr>
<td>Variability (bpm)</td>
<td>5-25 bpm</td>
<td>3-5 bpm for &gt;40 minutes (NB: may be a sleep phase) +25 bpm for &gt;40 minutes</td>
<td>Absent &lt;3 bpm, Sinusoidal pattern</td>
</tr>
<tr>
<td>Decelerations</td>
<td>None</td>
<td>Early decelerations, Variable decelerations</td>
<td>Complicated variable decelerations, Prolonged decelerations &gt; 3 minutes, Late decelerations</td>
</tr>
<tr>
<td>Accelerations</td>
<td>2 present in 20 minutes</td>
<td>Do not consider the absence of accelerations in intrapartum interpretation as being abnormal</td>
<td></td>
</tr>
</tbody>
</table>

- **Non-reassuring CTG trace** is where **ONE** of the following features is present:
  - The following features are **unlikely** to be associated with significant fetal compromise **when occurring in isolation**.
The presence of two or more features is considered abnormal as these may be associated with fetal compromise and require further action:

- Baseline FHR is between 100-109 bpm or between 161-170 bpm
- Variability of FHR is reduced (3-5 bpm for >40 minutes)
- Decelerations are variable without complicating features
- Do not consider the absence of accelerations in intrapartum interpretation as abnormal.

Abnormal CTG trace is where:

- The following features are very likely to be associated with significant fetal compromise and require further action:
  - Two of the features described in non-reassuring CTG trace are present, OR
  - Baseline FHR is <100 bpm or >170 bpm
  - Variability is absent or <3 bpm
  - Variability is sinusoidal
  - Decelerations are prolonged for >3 minutes / late / have complicated variables

Decelerations:

- Early = head compression (= cushing)
- Late = placental insufficiency + distress
- Variable = cord compression

Process

- Preparation:
  - Determine indication for fetal monitoring (refer to indications listed above)
  - Discuss fetal monitoring with the woman and obtain permission to commence
  - Perform abdominal examination to determine lie and presentation
  - Give the woman the opportunity to empty her bladder
  - The woman should be in an upright or lateral position (not supine)
  - Check the accurate date and time has been set on the CTG machine, and paper speed is set at 1cm per minute
  - CTGs must be labelled with the mother’s name, NHI number and date / time of commencement
  - Maternal heart rate must be recorded on the CTG at commencement of the CTG in order to differentiate between maternal and fetal heart rates

- Interpretation and documentation:
  - On all occasions when a CTG is performed there must be documentation of all features in the patient record. A ‘CTG sticker’ should be placed on the Progress Notes.
  - For women receiving continuous electronic fetal monitoring (EFM) the CTG should be reviewed at least every 15 to 30 minutes. Interpretation and response to findings must be documented on an hourly basis.
  - Any abnormalities documented in the patient record and reported to:
    - The senior midwife in birth suite, and / or
    - The registrar rostered to birth suite, and / or
    - The consultant obstetrician rostered to birth suite

In Labour

- Early decelerations (ie with a contraction) are probably normal (due to pressure on the head →↓HR - Cushings type reflex). Late decelerations (following a contraction) are a sign of fetal hypoxia. “Shouldering” (brief ↑HR either side of a deceleration) may signal cord compression

- Early hypoxia is indicated by a mild tachycardia, reduced variability and consistent late decelerations. 80% sensitivity (ie 1 in 5 unnecessary interventions). A not normal but not abnormal trace has a 20 – 50% sensitivity for hypoxia

- A poor CTG is an indicator only. May do scalp sample to confirm (checks for acidosis: pH < 7.2 or base excess > -12 getting bad ⇒ deliver now by the safest means). Would act now on a bad trace if not in labour or prolonged bradycardia < 80

- Red herrings:
  - Check maternal BP. Hypotensive mother → poor trace. Eg following epidural insertion, IVC compression (change position)
  - Hyperstimulation: contractions too long or fast → turn down syntocinon

Labour

- See also Obstetric Anaesthesia, page 870
- Definition = cervical dilatation or effacement in the presence of regular, painful uterine contractions:
1. Regular contractions (usually 3 in 10 minutes, lasting 40 – 50 seconds)

2. Cervical change:
   - More anterior
   - Effaced: depth of ‘rim’ normally 2 cm, 50% effaced = 1 cm
   - Dilated (but less than 3cm)
   - Soft (hard = like forehead, normal = like nose, soft = like chin)

3. +/- Show (mucus plug) or ROM (rupture of membranes)
   - 80% of all pregnancies last 38 - 42 weeks. 10% are preterm. 10% beyond the start of the 43rd week (although biggest cause is inability to reliably date conception)

How does it start:
   - **Uterine preparation**: ↑distension, ↑gap junctions in smooth muscle, ↑oxytocin receptors
   - **Cervical ripening**: PGE breaks down collagen + effect of Braxton-Hicks contractions
   - **Fetus**: ?vasopressin released in response to transient hypoxia, ?other hormones

Stages of labour:
   - **Latent**:
     - Initial stages of effacement + dilatation with regular contractions (as per the above)
     - Normal latent phase lasts 20hrs for a nullip; 15hrs for multip
   - **Active**:
     - 1st stage continued: from 3cm to fully dilated (1.2cm/hr for nullips; 1.5cm/hr for multips)
     - 2nd stage: passage of baby:
       - Pushing happens here
       - Primips: 30 minutes to 3 hours (median duration: 50 minutes)
       - Multips: 5 – 30 minutes (median duration: 20 minutes)
   - **3rd stage**: passage of placenta

**Bishop’s Score**
- Pre-labour scoring system based on vaginal examination to determine likelihood of induction
- Based on:
  - Dilatation
  - Effacement
  - Cervical consistency
  - Cervical position
  - Fetal station
- Mnemonic: Call PEDS For Parturition = Cervical Position, Effacement, Dilation, Softness; Fetal Station
- 13 highest score; **5 or less = labour unlikely to start without induction**; 9 or more = labour likely to start spontaneously

**Examination**
- **Mother**:
  - **General** – patient state:
    - Pallor – conjunctiva, tongue, nailbed
    - BP (hypo → ?blood loss, hyper → ?pre-eclampsia): sitting, correct cuff size, manometer at heart level, pulse
    - Oedema (Extravascular extracellular fluid accumulation. + up to knees ++ up to hips +++ abdominal wall ++++ ascites/anasarca)
    - Temperature (eg infection if prolonged period post-rupture)
- **Foetal position**: by abdominal inspection and palpation. 2/3rds of babies head first with back on the left. Descent – what portion of the head is below the pelvis (eg 3/5ths)
- **Fundal height**
- **Foetal welfare**:
  - CTG for 20 minutes (but incidence of fetal distress in early labour is low. Continuous monitoring → ↑interventions)
  - Intermittent auscultation every 15 – 30 minutes following a contraction. Approx every 5 minutes in 2nd stage.

**Clinical Management of Labour**
- **Partogram**:
  - Records BP, pulse, temperature
- Records cervical dilatation, descent (Friedman’s curve)
- Records fluids, meds
- **Monitoring**: fetal + tocometer: continuous (CTG) or intermittent
- Cervical examination:
  - Is cervix anterior or posterior
  - Dilatation
  - Cervical length/effacement
  - Consistency
  - Indications:
    - Timed to check progress (2-4hrs)
    - If any change in fetal heart rate
    - If evidence of slowing of labour
    - If giving analgesia
  - Should be done by a **single** examiner → consistency
- Pain relief in labour:
  - None
  - Entenox
  - Epidural (can cause hypotension, urinary retention, spinal block, harder to push)
  - Narcotics: pethidine (can cause fetal distress)
  - TENS machine (electrical impulses)

**Fetal Position, Examination and Definitions**

- **Quickening**: sensation of fetal movements felt at 16-18 weeks in multigravidas and 18-20 weeks in a primigravida
- **Lightening**:
  - = *Baby dropping*. →↓SFH (ie fundal height), development of lower segment of the uterus, descent of fetal head into pelvis
  - Subjective sensation of the fetus “dropping” in to the pelvis. Felt **around 34 weeks gestation**.
  - 1st pregnancy: 2 – 3 weeks before
  - 2nd pregnancy: may not be till 2nd stage of labour – uterus has lost some of its tone – doesn’t push baby down so well
- **Fetal lie**: relation of fetal spine to mother’s spine:
  - 1. **Longitudinal** (cephalic or breech)
  - 2. Transverse
  - 3. **Oblique** (unstable lie)
- **Fetal presentation**: portion of the fetus in the birth canal/lying over the pelvic inlet:
  - 1. **Cephalic** (96%): vertex, sinciput, brow, face
  - 2. **Breech** (3%): Frank (extended – ‘foot in mouth’), Complete (knees and hips flexed), Incomplete (footling). Only worry after 36 weeks – it can turn fairly easily before then
  - 3. **Shoulder**: transverse or oblique (1%)

**Malpresentation**:

- **Brow presentation** is caused by partial extension of the fetal head so that the occiput is higher than the sinciput
On abdominal examination, more than half the fetal head is above the symphysis pubis and the occiput is palpable at a higher level than the sinciput.

On vaginal examination, the anterior fontanelle and the orbits are felt.

- **Face presentation** is caused by hyper-extension of the fetal head so that neither the occiput nor the sinciput are palpable on vaginal examination
  - On abdominal examination, a groove may be felt between the occiput and the back.
  - On vaginal examination, the face is palpated, the examiner’s finger enters the mouth easily and the bony jaws are felt.

- **Compound presentation** occurs when an arm prolapses alongside the presenting part. Both the prolapsed arm and the fetal head present in the pelvis simultaneously.

- **Presenting part:**
  - The most dependent part of the fetus lying nearest the cervix. During vaginal examination it is the area with which the finger makes contact first (can be umbilical cord, head, etc).

- **Fetal attitude:**
  - “posture” of the fetus, eg extended neck
  - Relation of fetal parts to each other eg flexion. The typical fetal attitude in the uterus is flexion, with the head bent in front of the chest, the arms and legs folded in front of the body, and the back curved slightly forward.

- **Denominator:**
  - Arbitrary chosen point on presenting part of fetus used in describing position
  - Cephalic – occiput
  - Breech – sacrum
  - Face – mentum

- **Fetal position:** Relation of denominator to the maternal pelvic quadrants:
  - 3 sets of terms are used to describe position
    - 1. The denominator (occiput, mentum, or sacrum)
    - 2. Right or left, depending on which side of the maternal pelvis the denominator is in
    - 3. Anterior, posterior or transverse, according to whether the denominator is in the front, back or side of the pelvis
  - For example:
    - LOA = left occiput anterior (face down, 8 o’clock) – most common position
    - LOT = left occiput transverse
    - OA = occiput anterior (6 o’clock)
    - LOP = left occiput posterior (face up)
Caput succedaneum:
- Swelling of the fetal scalp immediately over the cervical os
- Fetal scalp edema: 0 to 3+
- Skull bones felt 1+
- Skull bones just felt 2+
- Skull bones not felt 3+

Moulding:
- Degree of overlap of fetal skull bones.
- + Bones just meet – easily separable
- ++ Overlap – separable
- +++ Overlap – inseparable
- Parieto-parietal 3+
- Occipito-parietal 3+
- Maximum of 6+
- May ↓BPD (biparietal parameter) by 0.5 – 1.0 cm

Striae gravidarum: (stretch marks of pregnancy) silvery streaks across abdominal wall from stress to the skin and results in the collagen and elastin breaking down.

Linea nigra (dark line): Normal discoloration in pregnancy due to increased production of pigment melanin

Engagement:
- Measured abdominally using fingers as measuring tools (each finger is a fifth; measured in fifths above pelvic brim)
- When the widest diameter of the presenting part has passed through the inlet ie BPD (greatest transverse diameter) in cephalic or intertrochanteric in breech
- Floating → Dipping → Engaged
- Descent of the fetal head into the pelvis is checked by abdominal examination when the head is imagined in segments of one fifth
- Engagement: when the maximum diameter of the fetal head has entered the pelvis → corresponds with only 2/5 of the head being palpable through the abdomen

Station:
- Is the relationship of the presenting part to an imaginary line drawn between the ischial spines. The location of the presenting part at the level of the spines indicates that the station is zero. Above that is – up to 5 and below is + to 5
- Measured vaginally
- Engagement of fetal head (see below). In (a) maximum diameter of head is above inlet of pelvis and head is not engaged; in (b) engagement has taken place (maximum diameter of head is below inlet of pelvis); in (c) head is not engaged; in (d) when mother sits up on her elbows, the head sinks in, an indication that the head will engage when labour starts
Crowning: encirclement of largest diameter of the fetal head by the vulvar ring/distension of the vulva with thinning of the perineum by the largest diameter of the head

Adequate sized pelvis has:
- Wide pubic angle (skeleton can fit a fist)
- > 10 cm between ischial spines
- Can’t reach sacral prominence (top of sacrum) on vaginal exam

Meconium:
- Fetal gut contents. 3 Grades:
  - 1 – Flecks of meconium in clear liquor
  - 2 – Thin uniformly stained
  - 3 – Thick green/pea-soup/sludge

Term/Dates:
- Term: 37-41 completed weeks
- Dates: EDD/40 weeks/280 days
- Post-dates: Beyond 40 weeks (unsure of LMP/late scan)
- Post-term: Beyond 41 weeks (sure of LMP/early scan)

Parity/Gravidity:
- Gravidity – number of times a woman has conceived
- Parity – number of pregnancies that attained viability. In New Zealand ≥ 20 weeks gestation or ≥400 grams

Ruptured membranes:
- = water broken
- Doesn’t necessarily mean in labour, most will over next few days
- Consider induction at around 24hrs due to infection risk (esp GBS)

Naegele’s rule:
- Rule for calculating an expected delivery date
- Add 7 days + 9 months to the FIRST day of the last menstrual period

Delivery of the Baby

Stages of labour:
- Stage 1: cervical effacement and dilation
  - Begins with painful uterine contractions of sufficient frequency, intensity, and duration to bring about effacement (thinning/flattening) + dilatation
  - Ends with complete cervical dilatation (10cm)
  - Signs of full dilatation:
    - 2nd show
    - Gaping of anus
    - Perineal bulge
    - Slowing of contractions
    - Mother’s attitude changes + becomes panicky
    - Need to bear down
  - Friedman curve – plot on a partogram:
    - Records cervical dilatation & fetal descent
    - Latent phase (cervical softening). 20 hours in nullip, 14 hours in multip
    - Active Phase: Acceleration phase and deceleration phase (= transition). Cervix dilates 1.0 – 1.2 cm/hr (Primiparous), 1.5 cm/hour (multiparous) to a maximum of 10cm dilated
➤ **Stage 2:** delivery of the baby
  ○ **Begins** at 10 cm dilated
  ○ **Ends** with delivery of the baby
  ○ 2 hours in primip, 45 minutes – 1 hour in multip.
  ○ **Cardinal movements:**

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  ○ **EDFIEREE**
  ○ **Engagement:** time when BPD passes through the pelvic inlet. **Abdominally, 2/5 is palpable.** If engaged, you know the pelvic inlet is big enough
  ○ **Descent:** descent through the vaginal canal and extension of fetal body.
  ○ **Flexion** of neck to reduce the diameter of presentation
  ○ **Internal rotation.** When head reaches pelvic floor: head rotates from 8 o’clock to 6 o’clock (ie anteriorly). Usually descent through pelvis transverse, then need to rotate face downwards
Extension: once head reaches vulva, occiput in direct contact with symphysis → crowning. Ritgen Manoeuvre – upward pressure on chin through perineum from below, downward pressure on occiput (stop anterior tear)

Restitution: once the head has been delivered, the occiput goes back to original position (transverse; this is restitution – return to normal position) – now realigned again with shoulder.

- Check for nuchal cord (around neck)
- Clear nasopharynx

External Rotation: rotate along the AP diameter of the pelvis, head rotates so that face looks directly at maternal thigh. Must happen before shoulders can be delivered

Expulsion: anterior shoulder, followed by posterior shoulder.

- Double clamp and cut cord, with baby below the level of the placenta if possible or if prem.
- Episiotomy: NOT routine. In NZ do them medio-lateral at time of Crowning. 1st degree = superficial, 4th degree = deep, including rectal sphincter and mucosa

Stage 3: separation and expulsion of the placenta

- Begins following birth of baby
- Ends with delivery of placenta + membranes
- Signs of placental separation: uterus becomes globular, sudden rush of blood, uterus rises, cord lengthens
- OK to wait if no heavy bleeding. Gentle traction on cord with supra-pubic pressure (stops uterus coming down) or fundal massage and maternal bearing down without traction
- Passive delivery of placenta = no intervention
- Active delivery of placenta:
  - Especially if risk of PPH (↓ PPH; seen in big baby/twins/previous PPH/anything that makes the uterus big eg polyhydramnios). See Postpartum Haemorrhage (PPH), page 654
  - Give 5 – 10 units Syntocinon (IV if risk of PPH, IM otherwise) when shoulder delivers then apply pressure on fundus to prevent inversion of uterus and pull on the cord (= controlled cord traction)
  - If PPH then IV infusion following bolus (T½ of Syntocinon is 3 – 5 minutes)
  - Complications of Syntocinon: hyperstimulation (→↑fetal hypoxia), uterine rupture, water intoxication (Syntocinon is like ADH), uterine muscle fatigue (→post-delivery uterine atony →↑risk of PPH)

- Can manually deliver if heavy bleeding (place hand into uterus and separate) – if no haemorrhage then wait for anaesthesia
- Then inspection, repair, rectal exam

Cord prolapse: Cord comes through cervix before head. C-section usually indicated. In meantime try to control pressure on cord – don’t push it back up. Risk if transverse lie

Pain Relief:
- Inhalation agent (eg nitrous oxide)
- Epidural: complications – hypotension, urinary retention, total spinal block, prolonged expulsive effort
- TENS
- Narcotics eg pethidine: action lasts 3hrs and can cause fetal respiratory distress – don’t give if delivery expected within 3hrs
- See also Obstetric Anaesthesia, page 870

Mechanics of Labour

1. Power: Contractions:
   - At outset: 1 every 15-30min
   - Mid-labour: slow onset, climax at 30-40s, last 60-90s
   - Successful contractions are regular, coordinated, strong

2. Passage (birth canal):
   - Least important factor (generally doesn’t impact birth)
   - Ligaments soften to facilitate a successful birth

3. Passenger:
   - Size, presentation, lie, attitude, position

Abnormal Labour

- Dystocia = difficult labour
- = Labour does not progress normally. Due to problems with:
1. **Power** – eg ineffective uterine contractions (frequency, duration, coordination, strength), or hyperactive (eg spasm)

2. **Passage** – disproportion between the size of the pelvis and the fetus (eg scarred cervix), and soft tissues must ripen + dilate. Most 2.5-4kg babies come out fine

3. **Passenger** – abnormal lie, presentation, position or structure of the fetus (NB. Biggest diameter of baby’s head = 9.5cm)

4. **Psyche** – excessively anxious or sedated mother (but if sedatives can ↓contractions then probably not true labour), conduction anaesthesia (ie epidural) may weaken lower uterine contractions and therefore not assist head rotation and flexion

- Risks to foetus in distress:
  - Hypoxia +/- ischaemia
  - Trauma
  - Meconium aspiration (meconium = first stool. Abnormal to find it in amniotic fluid).

- Types:
  - **Protracted** labour – takes longer than normal
  - **Arrested** labour – progresses normally then stops. During active stage, progress = *either* further dilation or further descent
  - Can happen at any stage

- **Causes of failure to progress:**
  - 1. **Prolonged latent phase** (>20hrs for nullip; >14hrs for multip)
  - 2. **Primary dysfunctional labour**: never enters active phase. Associated with primagravids, OP or deflexed neck, post maturity and unripe cervix
  - 3. **Secondary arrest**: enters active phase then stops. *No change in dilatation for 2hrs; no change in descent for 1hr.* More likely than primary dysfunctional labour to be associated with absolute cephalo-pelvic disproportion
  - 4. **Cervical dystocia**: Primary (rare) or secondary (eg following cone biopsy)

- **Evaluation:**
  - Palpate or monitor uterine contractions
  - Perform cervical exam (and check history)
  - Determine lie/position of fetus
  - Review medication

- **Indications for emergency CS:**
  - Failure to progress
  - Fetal distress

- **Treatment:**
  - Hypertonic contractions – pain medication, Syntocinon
  - Hypotonic contractions – Syntocinon, AROM (artificial rupture of membranes)

- **Interventions in 1st stage of labour:**
  - 1. Wait
  - 2. Amniotomy (break the waters)
  - 3. Oxytocin
  - 4. CS
  - 5. Active management of labour

- **Interventions in the 2nd stage of labour:**
  - 1. Augmentation of powers
  - 2. Maternal posture
  - 3. Manual rotation
  - 4. Instrumentation delivery
  - 5. Episiotomy
  - 6. CS

### Abnormal Presentations

- **Breech:**
  - More prone to abnormal labour
  - The frequency of breech presentation falls as pregnancy advances. *Most babies spontaneously turn to become cephalic by 37/40*
  - If baby is still breech at 37/40, **external cephalic version** can be trialled
  - C-section if < 1000 gm (body comes through at 7 – 8 cm dilated and head gets stuck = "entrapped of after-coming head) or > 3600 or 4000 gm. C-section becoming
more routine for any breech

- **Face** (rather than occiput first):
  - Occurs with complete extension. Mentum (chin) anterior can be delivered vaginally
  - **Don’t** use forceps and Syntocinon

- **Brow**:
  - *Incomplete flexion* (midway between face and vertex)
  - Converts to either face or occiput – **can’t** deliver as brow

- **Occiput transverse**:
  - Head can’t flex and rotate from transverse to occiput anterior. Gets stuck at iliac spines
  - Risk factors include pelvis shape (wide and squashed = platypoid)
  - Rotate manually or with forceps, or C-section

- **Occiput posterior** (i.e. face up):
  - 5 – 10 %, prolonged second stage, painful labour (lots of back pain), bigger tears and episiotomies
  - Treatment: continued observation, forceps +/- rotation, or CS

- **Abnormal fetal structure**:
  - Macrosomia
  - Hydrocephalus
  - Hydrops Fetalis: total body oedema eg due to heart failure secondary to Rh-isoimmunisation
  - Meningocele (a neural tube defect)

- **Pelvic abnormalities**:
  - Inlet: failure to descend/engage (failure to descend prior to labour in a nullip is a bad sign)
  - Mid: smaller capacity than inlet, often associated with OT/OP
  - Outlet: rare in the absence of contracted mid-pelvis
Obstructed Labour

- Obstructed labor is an important cause of maternal morbidity and mortality, especially in developing countries – said to cause 8% of maternal death worldwide
- Obstruction may be caused by absolute fetopelvic disproportion or unfavourable orientation. Rarely pelvic tumours or scarring
- Immediate causes of maternal death from this obstructed labour are ruptured uterus, complications of C-section, postpartum haemorrhage and postpartum sepsis
- Interventions to prevent the adverse effects of obstructed labour include:
  - Predicting obstructed labour:
    - Maternal height and shoe size (height below 150cm and shoe size below 4 used to predict cephalopelvic disproportion) – limited value
    - X-ray pelvimetry – insufficiently predictive
    - Estimation of fetal weight – not effective for predicting
  - Preventing obstructed labour:
    - Preventing unwanted pregnancy – education and access to family planning is very important in the prevention of maternal death from all causes
    - Early induction of labour (to limit fetal growth) – not effective
    - External cephalic version at term for breech/transverse lie – at term but not before term (= >37/40) = effective for reducing breech presentation and C-section
  - Promoting efficient first-stage labour:
    - Companionship during birth – more likely to have spontaneous vaginal birth
    - Fluid intake – starvation is bad, women should receive adequate fluids
    - Routine early amniotomy during labour – should be reserved for women with abnormal labour progress
    - Augmenting slow labour with amniotomy and uterotonic drugs – no more beneficial than conservative management in mild delays of progress of labour
    - Misoprostol for labour induction or augmentation – low dosages is a life-saving drug in low-income countries (only option for labour induction with an unripe cervix); large doses can be dangerous
    - Posture to correct foetal malposition – lateral/posterior position of fetal presenting part is less likely to persist after women spend 10 min on hands and knees – more research justified
    - Posture during 1st and 2nd stage labour – uterine efficiency greater in lateral rather than dorsal position and upright postures associated with improved progress of active phase of labour → women should be encouraged to give birth in the position they find most comfortable
  - Diagnosing obstructed labour:
    - Partogram (labour graph) – evaluates progress of first stage of labour by plotting cervical dilatation and descent of head; concept could be developed for screening for referral from primary to secondary level care
  - Managing prolonged labour and facilitating delivery:
    - Vaginal cleansing to reduce risk of sepsis after prolonged labour – studies showed significant reduction in postpartum fever/endometritis when vagina lavaged or wiped with dilute chlorhexidine during labour
    - Vaginal lubrication – not yet adequately investigated
    - Selective episiotomy – episiotomy should be avoided except when essential to achieve delivery
    - Assisted vaginal delivery – ventouse is better than forceps
    - McRoberts position for shoulder dystocia:
      - Mother supine with hips + knees flexed = straightens pelvic angle
      - Decrease risk of trauma + increase maternal uterine force
    - Zavanelli manoeuvre for shoulder dystocia or breech presentation
Replacement of partially born fetus and then C-section

- C-section: If ruptured uterus
- **Symphysiotomy** (division of pubic symph) – when C-section is not available or unsafe this may be lifesaving for mother and baby (rapidly performed, simpler, requires minimal equipment etc.)

- For these strategies above to be effectively implemented women need to utilise and access health services as soon as problems occur during labour – services need to be culturally acceptable to women

**Shoulder Dystocia**

- **HELPER:**
  - Call for Help
  - Episiotomy
  - Legs up [McRoberts position]
  - Pressure subapublically [not on fundus]
  - Enter vagina for shoulder rotation
  - Reach for posterior shoulder and deliver posterior shoulder/ Return head into vagina
  - [Zavanelli maneuver] for C-section/ Rupture clavicle or pubic symphisis

- **Shoulder dystocia:**
  - Failure of delivery of the fetal shoulder(s), whether they are the anterior, posterior, or both fetal shoulders.
  - As the fetus descends through the birth canal, the shoulders must twist to allow them to pass smoothly out. If either the fetal shoulders are too wide, or the mother’s pelvis is too narrow, the fetus is unable to twist, and the shoulders remain in an antero-posterior alignment. This may result in the anterior shoulder being obstructed behind the symphysis pubis, impeding delivery. This leads to shoulder dystocia. If the sacral promontory also obstructs the posterior shoulder, bilateral (and more difficult) shoulder dystocia occurs.

- Shoulder dystocia is uncommon, occurring in 0.2-3% of pregnancies. When it does occur however, it can result in significant fetal and maternal harm, including:
  - **Neonatal brachial plexus injury** due to stretching of brachial nerves. Most cases resolve before discharge from hospital, but some injuries are permanent eg Erb’s palsy
  - **Neonatal hypoxic ischemic encephalopathy** and/or death, due to prolonged compression of the umbilical cord in the birth canal.
  - Neonatal clavicle fracture, directly, or as a result of intervention to release the fetus.
  - Neonatal fracture of the humerus, which occurs as a result of maneuvers performed to free the baby.
  - Extensive **maternal perineal lacerations** and extension of episiotomy as baby is forced through.
  - Maternal postpartum haemorrhage.

- Antenatal risk factors for shoulder dystocia include (in descending order of importance):
  - History of shoulder dystocia in prior vaginal delivery
  - Fetal macrosomia (large baby)
  - Maternal diabetes or impaired glucose tolerance
  - Excessive weight gain (>35lb) during pregnancy
  - Maternal obesity
  - Post-term pregnancy

- Intrapartum risk factors include:
  - Precipitous (rapid) 2nd stage of labour
  - Operative vaginal delivery (ventouse, forceps, or both)
  - Prolonged second stage:
    - Without regional anesthesia (>2 h for nulliparous patients, or >1 h for multiparous patients)
    - With regional anesthesia (>3 h for nulliparous patient, >2 h for others)
  - Induction of labour for impending macrosomia

- In spite of these risk factors, shoulder dystocia is impossible to predict in a specific patient. The reason for this is that the condition is caused by a dynamic or evolving mechanical event.

- A diagnosis of shoulder dystocia is based mainly on clinical judgement, and the decision is often subjective. Signs include:
  - Failure of shoulder delivery after downward traction.
  - Failure of shoulder delivery within 60 seconds of head delivery.
  - Increased traction needed to deliver the baby's shoulders
One important sign is the **turtle sign**, where the baby’s head, after initially protruding out of the introitus after head delivery, subsequently withdraws partly back into the introitus like a turtle going back into it’s shell.

- **Maneuvers for alleviation of shoulder dystocia** (in order that they should be attempted:
  - McRoberts maneuver: This involves hyperflexing the mother’s legs tightly to her abdomen. This widens the pelvis, and flattens the lumbar spine. If this maneuver does not succeed, an assistant applies pressure on the lower abdomen (suprapubic pressure) to disimpact the anterior shoulder, and the delivered head is also gently pulled. The technique is effective in about 42% of cases.
  - Rubin maneuver: Insertion of one hand anteriorly to access posterior aspect of anterior fetal shoulder. Pressure by the fingers can sometimes rotate the fetal trunk into the (wider) oblique plane.
  - Wood’s screw maneuver: The fetus is rotated 180 degrees so that the anterior shoulder faces posterior and the posterior shoulder faces anteriorly.
  - Jacquemier’s maneuver: Delivery of the posterior shoulder first, in which the forearm and hand are identified in the birth canal, and gently pulled. This can be effective, but may cause neonatal fracture of the humerus.
  - Episiotomy
  - Gaskin maneuver: This involves moving the mother to an all fours position with the back arched, widening the pelvic outlet.

- If all the above fails, more drastic measures can be used including:
  - Zavanelli’s maneuver, which involves pushing the fetal head back in conjunction with performing a caesarean section.
  - Intentional fetal clavicular fracture, which reduces the diameter of the shoulder girdle that requires to pass through the birth canal.
  - Maternal **symphysiotomy**, which makes the opening of the birth canal laxer by breaking the connective tissue between the two pubis bones, facilitating the passage of the shoulders.
  - Abdominal rescue, where a hysterectomy facilitates vaginal delivery of the impacted shoulder.

**Post-Term Labour**
- ≥42/40
- Risk factors:
  - Nulliparity
  - Previous post-term pregnancy
  - Obesity
  - Diabetes
- Risks of post-term pregnancy:
  - Perinatal mortality doubles (seen as soon as 41/40)
  - Higher incidence of macrosomia
  - Maternal: ↑ labour abnormalities (3rd & 4th degree tears), ↑ CS

**Induction of Labour**
- Prediction of likelihood for normal labour: Bishop’s score
- Reasons for induction:
  - ≥42/40
  - Pre-eclampsia
  - ↓ growth, ↓ FM
  - Diabetes
  - PROM
- Contraindications:
  - 1. Prior classical CS
  - 2. Active herpes
  - 3. Umbilical cord prolapse
  - 4. Transverse lie
  - 5. Placenta praevia
- Methods of induction:
  - 1. Stretch & sweep (membrane stripping): stretch the cervix & sweep the finger around, not AROM
  - 2. Prostaglandins on the cervix (ripen cervix; beware in multips → can lead to hyperstimulation of uterus + once applied, cannot remove)
  - 3. Artificial rupture of membranes (amniotomy)
  - 4. Oxytocin drip
5. **Breast stimulation** (natural oxytocin)
   - Amniotomy + oxytocin more effective than in isolation

### Complications:
- **Tachysystole**: abnormal/excessive uterine contractions; uterine rupture
- **Hyponatremia**: with oxytocin: is a similar structure to ADH → water retention
- Hypotension: with rapid oxytocin injection
- Failure of induction

#### Forceps
- To provide traction, rotation or both to the fetal head
- **Indications**: delay in second stage, fetal distress, malposition, poor maternal effort, etc
- **Types**: outlet, mid or low – depends on the station of the fetal head and degree of rotation
- Should **never be used when fetal head is not at least at 0 station** (2/5 felt abdominally above symph) as you don’t know if the head will fit through
- **Requirements**: cephalic presentation, known position (ie LOA), contractions present (mum needs to push at same time), ROM, fully dilated otherwise cervical tear (→ ↑ bleeding and possible future cervical incompetence), empty bladder and adequate anaesthesia
- **Complications**:
  - Maternal: vaginal, cervical or uterine laceration, bleeding, bladder or bowel injury, often episiotomy
  - Fetal: bruising, scalp, skull, eye or brain injury

#### Ventouse/Vacuum
- Suction applied over posterior fontanelle
- Cf. Forceps:
  - Less space necessary, often leads to spontaneous flexion/rotation, don’t need to know exact fetal position
  - Will pop off if too much pressure → less risk of trauma to mum or baby
- Contraindicated in preterm delivery due to ↑ risk of fetal scalp/head injury
- Complications = lacerations (to mum + baby), cephalohaematoma

#### Syntocinin
- Given as IV infusion
- T1/2 = 3-5min
- **Complications**:
  - Hyperstimulation → uterine rupture, uterine muscle fatigue
  - Post-delivery uterine atony

#### Caesarean Section
- **Types** (refers to uterine not skin incision):
  1. **Lower segment transverse**: ↓ risk of uterine rupture in subsequent pregnancy (<1%)
  2. **Classical**: vertical incision in upper segment of the uterus. 5 – 6 % risk of rupture in subsequent pregnancy. ↑ Bleeding, infection, ileus
  3. **Low vertical**: vertical incision in the lower segment – treat as classical
- **Indications for classical**: preterm breech, fibroids, anterior placenta praevia, transverse lie with back down
- **Risks to mother**:
  1. 4 – 6 times greater than for vaginal delivery
  2. **Anaesthetic risk for mother**. Especially aspiration (slow digestion → usually something in the stomach). Give antacid and Maxalonal (↓ acidity if aspirates and ↓ vomiting). Give 02 to mum → ↓ fetal hypoxia. Group and hold. Usually use spinal or epidural anaesthetic (although → vasodilation → ↓ BP → ↑ fetal distress)
  3. Infection
  4. Bleed (placenta gets 500mls of blood a minute at term). May → hysterectomy.
  5. DVT (pregnant, surgery and immobile) → PE (most common cause of maternal death)
- **Future obstetric complications**:
  - ↑ Risk of caesarean section next time. Can normally trial labour and 70% will progress normally. 1% uterine rupture (↑ ↑ ↑ pain, hypotensive). **Can’t be induced if previous Caesar** – strong contractions against a closed cervix → ↑ risk of rupture
Risk of placenta growing in the scar next time. May → placenta accreta (abnormal adherence to uterus which →↑risk of PPH)

- Indications:
  - Placental: praevia, abruption, vasa praevia
  - Fetal: disease (eg hydrops), malpresentation, distress, cord prolapse
  - Maternal: eclampsia, severe PET, active HSV, cardiac disease, cervical cancer, prior uterine surgery, obstruction (eg fibroids, ovarian tumours)
- Herpes Simplex Virus: Caesarean indicated if current genital outbreak at delivery. Only approx 1% of babies infected but approx 50% mortality if infected

**Perinatal Asphyxia**

- **Asphyxia:** cessation of gas exchange → hypoxia and hypercarbia. Can occur in utero, intra-partum or postnatally.
- **Fetal distress:** fetus demonstrates one or more clinical indicators of hypoxia (eg early passage of meconium and HR changes on CTG)
- **Hypoxic-ischaemic encephalopathy (HIE):** clinical manifestation in the neonate of a previous hypoxic-ischaemic insult. Need for resuscitation (or not) at birth does not necessarily correlate with HIE later on:

<table>
<thead>
<tr>
<th>Grade</th>
<th>Features</th>
<th>Mortality</th>
<th>Neurologic Sequelae in survivors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild</td>
<td>Irritability, poor sucking, hypotonia</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>Moderate</td>
<td>Convulsions, lethargy, poor feeding,</td>
<td>5%</td>
<td>21%</td>
</tr>
<tr>
<td></td>
<td>abnormal tone</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Severe</td>
<td>Comatose, seizures, ventilated</td>
<td>75%</td>
<td>100%</td>
</tr>
</tbody>
</table>

- Cerebral Palsy, see Cerebral Palsy
- Systemic effects of hypoxia:
  - Brain: hypoxic ischaemic encephalopathy (all are potentially reversible except for this one)
  - Kidney: renal failure
  - CV: hypotension
  - Liver: coagulopathy
  - Respiratory: meconium aspiration, pulmonary hypertension
  - Gut: ischaemia

**Postnatal Assessment**

- See Examination of the Newborn, page 915
- In the delivery room:
  - 1. Dry off and keep warm
  - 2. Achievement of normal adaptation
  - 3. Apgars (HRITC)
  - 4. Does there need to be a cord pH?
  - 5. Does the placenta need to go for histology?
  - 6. Initial check
  - 7. Vitamin K
  - 8. First feed
- In the first week:
  - Cardiac status - murmur, failure, femorals
  - Jaundice
  - Skin sepsis
  - Umbilical cord
  - Weight loss (should be < 10%)  

**Resuscitation of the Newborn**

- At level A below, if meconium and not breathing and floppy → suction trachea +/- oropharynx under direct vision
Changes with first breath: fluid pushed from airway and alveoli → ↓ resistance in pulmonary vascular bed → ↑ P in left side of heart → functional closure of FO + DA

- Do not attempt intubation in the newborn unless skilled. The worst thing to do is intubate the stomach and not realise it. Can happily bag-mask for an hour or so
- ABC: A & B much more important than C in a newborn (and child), therefore get to C last (ie do RTC: resp, tone, colour before getting to HR)

Initial actions:
1. Start the clock
2. Dry babe and keep them warm
3. Assess (do you need help: call):
   - Breathing: tilt head + jaw thrust if necessary
   - Tone
   - Colour
4. Inflation breaths:
   - 5 breaths using Neopuff (5cm H20 P of PEEP) and E-C grip
   - Sustained for up to 2-3 seconds
   - Up to 30-40cm H20 P (positive inspiratory pressure: PIP)
5. Reassess:
   - HRTC (HR, resps, tone, colour)
6. Prior to compressions, check:
   - Chest rising and falling with breaths
   - Check airway and breathing
   - Compressions are useless until the chest is being inflated

7. Compressions:
   - If HR < 60 at this stage
   - Compress to 1/3 of the diameter of the chest (either two thumbs or 2 fingers)
   - 3:1 for 30s then reassess: HRTC

Postpartum Complications

- Maternal mortality used to be mainly due to PPH and puerperal fever, now PE is the biggest cause

Definitions of Perinatal and Maternal Mortality

- Perinatal mortality = death of a fetus after 20th week or > 500 gm through to the time of delivery + death in first week
  - Born dead = late fetal death
  - Death in first week = early neonatal death
  - Perinatal mortality rate (PMR) = (LFD + ENND)/1000 live births. In NZ is 6 – 8 per 1,000. Varies from region to region

Reasons for perinatal death:
  - Hypoxia (eg placenta separated, maternal hypertension)
  - Prematurity
  - Congenital abnormality (eg heart defect, spina bifida)
  - Trauma (eg difficult birth)

Maternal death:
  - Death associated with pregnancy or trophoblastic disease up to 3 months after the event (required to be reported to Medical Officer of Health)
  - Causes:
    - Obstetric causes – 70%. Includes DVT/PE, hypertension, anaesthetic death, haemorrhage
    - Associated medical deaths (eg asthma, heart disease)
    - Associated malignancy (eg breast cancer)
    - Suicide/homicide

Postpartum Haemorrhage (PPH)

- PPH = excessive vaginal blood loss after childbirth causing signs or symptoms
- Clinical findings in obstetric haemorrhage:

<table>
<thead>
<tr>
<th>Volume loss</th>
<th>SBP</th>
<th>S &amp; S</th>
<th>Degree of shock</th>
</tr>
</thead>
<tbody>
<tr>
<td>500-1000ml</td>
<td>Normal</td>
<td>Palpitations, tachycardia, dizzy</td>
<td>Compensated</td>
</tr>
<tr>
<td>1000-1500ml</td>
<td>Slight fall (80-100mmHg)</td>
<td>Weak, tachy, sweating</td>
<td>Mild</td>
</tr>
<tr>
<td>1500-2000ml</td>
<td>Moderate fall (70-80mmHg)</td>
<td>Restless, pallor, oliguria</td>
<td>Moderate</td>
</tr>
<tr>
<td>2000-3000ml</td>
<td>Marked fall (50-70mmHg)</td>
<td>Collapse, anuria, air hunger</td>
<td>Severe</td>
</tr>
</tbody>
</table>

Primary PPH:
  - = Loss of > 500 ml < 24 hours after delivery
  - Limitations: estimating loss is difficult and loss may be concealed
  - Causes (the 4Ts):
    - Tone:
      - Uterine atony (80-90%).
      - Failure of myometrium to contract + constrict blood vessels
      - Causes: anything that causes large uterus – twins, polyhydramnios, macrosomia; relaxants (nifedipine, Mg, NSAIDs); rapid/prolonged labour; oxytocics; fibroids
    - Tissue:
      - Obstructed uterine contraction/retractions: fibroids, retained placenta
      - Placental abnormality: placenta accreta (placenta attaches too deep into uterus), placenta praevia
      - Excessive cord traction
      - Retained blood: uterine distension + prevents effective contraction
    - Trauma:
Reproductive and Obstetrics

- Uterine surgery: CS, hysteroscopy etc
- Prolonged or vigorous labour: especially if oxytocin/PG used
- Damage to genital tract: spontaneous or instrumentation
- Cervical laceration: forceps
  - Thrombin:
    - Acquired TCP: HELLP (haemolysis, elevated LFTs, low platelets), DIC, abruptio placentae, sepsis
    - Pre-existing TCP
    - Anticoagulants

- Management:
  - RESUSCITATE mother. Test bloods for coagulopathy
  - ECG, BP, O2 Sats, UO
  - Can treat expectantly (watch and wait) or active intervention
  - Expectant/physiological management:
    - No oxytocics
    - Cord not cut until pulsation ceases + no clamp applied other than umbilical clamp
    - No cord traction
    - Deliver spontaneously using gravity or nipple stimulation
  - Active management:
    - AKA active management of third stage of labour (AMTSL)
    - ↓ PPH by 50-60%
    - Give IM/IV oxytocics (ie syntocinin; or misoprostol [PG]) with or immediately after birth of bubs
    - Early cord clamp (↓ risk of PPH)
    - Controlled cord traction after placental separation
  - Management of the 4Ts:
    - Tone: uterine massage; if uterus feels boggy, give oxytocin
    - Tissue: if RPOC plan for manual extraction
    - Trauma: direct pressure on site of bleeding, pack uterine cavity, resus
    - Thrombin: FBC + coag profile, transfusion
  - Deliver placenta and inspect for completeness (may be missing portion)
  - Surgical management: laparotomy, uterine artery ligation, ovarian artery ligation, hysterectomy, embolization
  - Inspect genital tract for trauma. Eg vaginal lacerations, ruptured uterus
  - If bleeding continues ⇒ uterine atony. IM prostaglandins + other procedures

- Secondary PPH:
  - = Loss of any volume of blood > 24 hours and < 6 weeks post delivery. Usually 1 – 2 weeks after
  - Causes:
    - Uterine infection
    - Retained placenta/clot, often infected
    - Missed trauma
  - Antenatal risk factors:
    - Age >35, smoking, BMI >30, parity >5, macrosomia, >42/40
    - Pre-eclampsia
    - Abnormal placentation or accessory lobes on placenta
  - Intrapartum RF:
    - Induction or prolonged labour
    - Epidural or CS or episiotomy
    - Rapid labour
  - Diagnosis: Ultrasound +/- signs of infection: fever, tender uterus, offensive lochia (discharge after delivery)
  - Management: curettage with US guidance + antibiotics (Broad spectrum + anaerobic cover)

- Pharmacology:
  - Syntocinon: action lasts 20 – 30 minutes, causes hypotension, H2O retention, contraindicated in CV disease (eg pre-eclampsia). Used for labour induction or augmentation
  - Ergot alkaloids (eg Ergometrine). For PPH. Causes hypertension and vomiting. Contraindicated in hypertension.
  - Prostaglandin F2a. IM for PPH. Contraindicated in Asthma, CV disease

- Sequelae:
  - Massive bleed → shock and death
  - Puerperal anaemia and morbidity
- **Sheehan’s syndrome**: ischaemia of anterior lobe of pituitary → pan-pituitary insufficiency
  - Thrombosis + embolism
  - Septicaemia/infection
  - Fear of further pregnancies
- **Prophylaxis**:
  - Active management of 3\(^{rd}\) stage
  - Elective C-section if placenta praevia
  - 50% risk next time, reduces to 20% if active management
  - If at risk, then have active management of 3\(^{rd}\) stage labour, have wide bore cannula in place and specialist backup available

**Puerperal Fever**

- **Puerperium**:
  - = Time in which reproductive organs return to their pre-pregnant state – usually **6 weeks after delivery**
  - Uterus involutes from 1 kg to 100 gm. Pelvic organ by ≈10 days
  - **Lochia** = postpartum vaginal discharge: red for day 1 – 3 → yellow next 10 days → white until 6 weeks (rubra → serosa → alba)
- Puerperal fever = temperature of at least 38 C on any 2 of the first 10 days after abortion or delivery, exclusive of the first 24 hours
- **Incidence**:
  - ~ 6%
  - After vaginal delivery: 1 – 3 %
  - After Caesarean: ~10%
- **Pathogenesis**: assume infection until proven otherwise. Can deteriorate quickly – need rapid assessment
- **Sources**:
  - Clots, retained placenta, etc can facilitate growth
  - Generally an ascending infection
  - Lower genital tract (eg anaerobes)
  - Bowel: E. Coli and G –ive
  - Attendants: staph and haemolytic strep
  - Environment or partner
- **Risk factors**:
  - Caesarean delivery
  - Premature rupture of membranes
  - Frequent cervical examination
  - Internal foetal monitoring
  - Pre-existing pelvic infection including bacterial vaginosis
  - Diabetes
  - Nutritional status
  - Obesity
- **Severity is related to**:
  - Bacterial factors: virulence, resistance, etc
  - Host: general health, immune status
  - Pregnancy related: duration of labour post-ROM, invasive examinations
- **Causes**:
  - **Endometritis** (uterine infection):
    - Most common cause (50%), more common after NVD
    - Fever, uterine tenderness on abdominal palpation, foul-smelling lochia (post-partum vaginal discharge)
    - Treat aggressively to avoid abscesses
    - Can proceed to peritonitis, septicaemia, etc
    - Prophylaxis during CS can ↓ incidence
  - **Mastitis**: usually occurs 2 – 3 weeks postpartum & is associated with cellulitis over the affected area. S aureus is common therefore Rx with fluclox. Continue BF
  - **UTI**: ↑ risk from catheterisations, operative vaginal delivery
  - **Thrombophlebitis**:
    - 1% of women present with painful tender varicose veins. Look for DVT symptoms
    - Mechanism: Hypercoagulation + stasis of uterine/ovarian veins. Progression of pelvic infection.
    - Symptoms: Flank/lower abdo pain, constant. Ileus can occur.
Reproductive and Obstetrics

Signs: PE, palpable pelvic veins, tachycardia out of proportion to fever
- Treat with anticoagulation (LMWH)
- Wound and episiotomy infections: r/o nec fasc
- Respiratory tract infection, atelectasis, epidural abscess: can complicate anaesthesia

- History:
  - Urinary symptoms
  - Erythema and drainage from wound
  - Respiratory symptoms (cough, pleuritic chest pain, or dyspnoea)
  - Fever and chills
  - Abdominal pain
  - Foul-smelling lochia
  - Painful, tender, swollen legs
  - Breast engorgement in cases of mastitis

- Exam:
  - Top-to-toe assessment
  - Especially wound sites

- Investigations:
  - FBC
  - Urinalysis
  - Urine culture, blood culture, wound culture
  - High vaginal swabs
  - US + maybe CT/MR

- Management:
  - General: fluids, correct anaemia, pain relief
  - Antibiotics: start empirical treatment immediately
    - CCDHB protocol is IV Cefuroxime + Metronidazole
    - Clindamycin + gentamicin used elsewhere

Postnatal Depression
- Signs of clinical depression at 4-6wk need postnatal assessment (early detection essential to prevent severe depression)
- Seen in around 10-20%
- DSM-IV: (weight loss, forgetfulness, impaired concentration are relatively normal postnatal)
  - Low mood
  - Tearfulness
  - Lack of drive/enjoyment
  - Feelings uselessness/hopelessness
  - Emotionally detached
  - Body symptoms – wound pain, headache, back pain
- Risk factors: genetic, hx depression, current life stressors, lack social support, marital dissatisfaction, hx postnatal depression
- Antenatal depression is best predictor of postnatal depression
- Antenatal depression:
  - Similar risks to postnatal, associated with alcohol/drug abuse, IUGR, preterm, C-section, ADHD
  - Severe psychomotor retardation, early wakening, suicidal ideas require psychiatric intervention
- Diagnosis: underdiagnosed – 50% unrecognised, only ~10% get treatment
  - >2/52 persistent depressive symptoms/functional impairment + >4 symptoms
  - Commonly use self-reporting scales
- DDx:
  - Postnatal blues (self-limiting, ~85% experience)
  - Puerperal psychosis – psychiatric emergency
- Treatment:
  - Responds well to treatment, usually only psychological counselling and social interventions. Recovery 2/3 in first year, 90% by 2 years.
  - Some severe cases need pharmacological treatment (aim for lower sedation).
  - Can get neonatal withdrawal syndrome in antenatal depression and malformations from first trimester SSRI use.
• No known effective primary prevention (causes highly heterogeneous biopsychosocial/cultural factors). Secondary prevention – postnatal psychological checks best approach.
• **Paternal:** 5-24% in early postnatal period, closely related to maternal depression. Also unemployment, hx mental illness, young.
• **Infant effects:**
  - Stress during pregnancy correlates to preterm delivery/Low BW
  - Postnatal depression can adversely affect emotional, behavioural, cognitive development of infant. It is a **predictor of negative parenting behaviour**
• **The psychoneuroimmunology of PND:**
  - The **innate immune system** and the **hypothalamic-pituitary-adrenal** (HPA) axis remain in flux in the postpartum period and may be the cause of postpartum depression (PPD) as dysfunction in either system can lead to depression in non-pregnant women. Cortisol secretion in response to stress usually suppresses innate immune pro-inflammatory cytokines (TNF-α, IFN, IL-1,2,6) while stimulating transcription of anti-inflammatory cytokines(IL-4 & -10). In contrast, pro-inflammatory cytokines downregulate HPA axis mediators.
  - Maternal anti-inflammatory cytokines predominate to maintain immunosuppression during pregnancy. Immediately postpartum, pro-inflammatory cytokines predominate in response to perineal tissue damage, uterine ischaemia, pain, exertion and emotional stress. This usually dampsens after one week. When this response is exaggerated for months, this may cause **Systemic Inflammatory Response Syndrome** (SIRS; anti-inflammatory cytokines immunosuppress during pregnancy but immediately postpartum, pro-inflammatory cytokines kick in; this usually ↓ over the first week, when exaggerated however, this is SIRS) which **includes depression and thus could result in PPD.** Exact mechanisms not entirely understood.
  - Maternal CRH, ACTH and cortisol increase dramatically during pregnancy with an abrupt drop and central axis suppression within three days postpartum. It is proposed that HPA axis function is not adequately suppressed in PPD. **HPA dysfunction has been linked with depression, attachment disorder of infancy, anorexia nervosa and chronic fatigue.**
  - The combination of HPA axis dysfunction and SIRS postpartum may cause PPD yet further study is required.

**Other Postpartum Complications**
• **Postpartum thyroiditis:** has a hyperthyroid followed by a hypothyroid phase. Treat **symptomatically** (ie β-blocker for hyperthyroid phase)

**Six-Week Check**
• Looking for problems that may not have been present at birth (ie don’t check for imperforate anus, they’d be dead by now!)
• The main aim of the 6 week check is to:
  - **Detect abnormalities in the baby** that may have become clinically detectable since birth
  - Explain the advantages of immunisation for the baby and **offer immunisation**
  - Check the psychological and physical well-being of the mother
  - Promote breast feeding and healthy attachment

**Checks for Baby**
• General well-being including **sleeping** and **feeding**
• Physical:
  - **Growth:** check serial measurements in the Child Development Book
  - **Head and neck:**
    - Palpate fontanelles
    - Palpate neck – goitre, SCM mass, brachial cyst
    - Choanal atresia
    - Suckle, cleft palate
    - Red eye reflex – congenital cataracts
  - **Chest**
    - Inspection – RR <60, respiratory distress
    - Heart: Auscultate for murmurs, look for pallor, dyspnoea with feeds, FTT (1% affected, VSD in 30% of these)
    - Auscultation
  - **Abdomen**
Pelvis
- Femoral pulses
- Hip dislocation: unstable hips may not present until after birth. 0.4%, girls = 5 * boys. Need to treat before they begin to walk. Investigate with US and Xray. Treat with Pavlik harness

Genitals: Check boys for undescended testes (cryptorchidism) — 2%, especially if premature, spontaneous descent unlikely beyond 3 months, surgery at 9 – 12 months. See See also Male Genitourinary, page 337
- Undescended Testis, page 973

- LL: talipes
- Neuro: tone, posture, primitive reflexes

Developmental milestones:
- GM: lift head while prone
- FM: fix and follow gaze 180 degrees
- Language: coo in response to voice, quiets
- Social: smile spontaneously
- Sight (do they follow an object, smile at a face, etc): at risk if premature or birth asphyxia
- Hearing (startles with loud noise, etc): at risk if family history, rubella, CMV, toxoplasmosis, <1500 gm, severe asphyxia
- The mother is likely to be aware of the presence of absence of these

Checks for Mum

- History:
  - Use SMOCS judiciously (especially PBDIS)
  - General well-being
  - Signs of post-natal depression or adjustment disorder: poor sleep or appetite, feeling ‘low’, anxious or guilty, thoughts of harming herself or the baby. Complete a screening survey such as the Edinburgh Postnatal Depression Questionnaire (10 questions, past 7 days). See Perinatal and Postpartum Mood Disorders, page 717
    - 1. Able to laugh, see funny side of things
    - 2. Look forward with enjoyment to things
    - 3. I blame myself unnecessarily for things
    - 4. Anxious, worry for no reason
    - 5. Scared, panicky for no reason
    - 6. Things getting on top of you
    - 7. Insomnia
    - 8. Felt sad, miserable
    - 9. Crying with unhappiness
    - 10. Self harm feelings
  - Breastfeeding: Is this going well?
  - Bowel and urine continence – encourage pelvic floor exercises
  - Perineum/wound: pain, dyspareunia, etc
  - Discharge: Lochia: rubra → serosa → alba
  - Contraception
  - Incontinence
  - Review of pregnancy and child-birth experience

Exam:
- BP
- Weight: loss of 60% of weight gained during pregnancy
- Examine breasts for infection or cracked nipples
- Abdominal exam: involution of the uterus – should be at or approach pre-pregnant size
- Pelvic exam: healing of laceration or episiotomy, lochia assessed, size and tenderness of uterus
- Cervical smear if not up-to-date
- Check of other complications that may have arisen in pregnancy: BP, diabetes, anaemia, UTIs, etc

Immunisation
- 6-week imms due:
  - Infranix hexa
    - Diptheria
    - Tetanus
Reproductive and Obstetrics

- Pertussis
- Polio
- HBV
- Haemophilus influenzae type b
  - Prevenar
  - Streptococcus pneumoniae

Education

- SUDI: smoking, non-breastfeeding, prone sleeping, co-sleeping
- Stop smoking
- Talk about safety at home, car seats etc
- Dental hygiene: milk or water only in a bottle
- Weight loss, nutrition: weight loss happens slowly → still breastfeeding so need ↑ intake. ↑Ca + Fe intake
- Avoid ETOH, limit caffeine whilst BF

Contraceptive advice:

- Low levels of sexual interest common
- Return of fertility is variable. If not breastfeeding ovulation can occur as soon as 28 days
- Lactational amenorrhoea method: Complete breast feeding provides 98% protection (if BF every 4h during day + q6h at night) for the first 6 months (provided they continue to have amenorrhoea). Normally start contraception at 3 months
- POP: Start in early puerperium. Very effective in conjunction with breast-feeding. Start CoC when feeding frequency has ↓ by half, when solid food started or with first bleed (whichever first). Amount transferred to baby over 2 years = 1 tablet’s worth
- COC: alters quantity and quality of milk therefore contraindicated if BF. If not breast feeding start on day 21 (↓thrombosis risk and won’t have ovulated yet)
- IUCD: Best inserted within 10 minutes of placenta delivery, minimizes risk of expulsion (1/20 risk) or from 4/52 postpartum
- Sterilisation: wait a while – may change their mind
- Natural family planning: problematic due to variable effect of lactation on periods

BF: exclusive until 6/12, wean until 2 years:

- Regular sucking:
  - Most effective method of maintaining lactation
  - Prolactin and milk ejection reflex initiated frequently preventing abnormal distension of alveoli
  - Distension: milk engorges alveoli yet no let-down reflex, alveoli unable to secrete efficiently and suckling avoided with pain
  - Impaired inhibition of dopamine, reduction in milk secretion
- Improving BF establishment:
  - Baby given to mother to caress and suckle soon after birth
  - Baby fed on demand
  - No other nutrition is available to baby
  - Be kind to mum.
- Engorgement:
  - Takes time for milk supply to adjust to demand, end lactation
  - Electric pump, 48h bromocriptine
  - Appropriate sized bra
- Cracked nipples: aggressive suckling, empty manually instead
- Milk stasis:
  - Engorged alveoli exerts pressure on duct, milk seeps into surrounding tissue – non-infectious inflammation
  - Treat with more regular feeding, finishing manually
- Acute Mastitis:
  - Infant nasopharyngeal Staph/Strep, usually 1/52 PP
  - Fever, tender, red, firm area on breast
  - Manage: Flucloxicillin, continue suckle if no pain nor pus (abscess), incision and drainage

Issues for Follow-Up

- Gestational HTN
  - HTN arising after 20/40 without any pre-eclampsia features
  - Resolves by 3/12 PP
• **Pre-eclampsia**
  - As above + proteinuria > 300mg/24h, urine protein:creatinine 30mg/mmol
  - Eclampsia ‘like lightening’ convulsions, coma
  - Monitor BP, antihypertensive regime

• **Rubella**
  - Congenital rubella syndrome, live attenuated virus
  - Immunization if non-immune at antenatal check

• **Gestational Diabetes**
  - 50% chance of developing type II diabetes mellitus, important to detect early to minimize future disease impact
  - 50% chance in next pregnancy
  - Fasting glucose
  - GTT – normal, repeat fasting glucose every 3 years, if abnormal, repeat yearly
  - Lifestyle changes
  - Refined carbohydrates, fibre
  - Avoid obesity, exercise, smoking
  - Annual HTN check

• **Stress incontinence:**
  - Common antenatal complaint and 30% new mothers continue having problems at 6/52 PP, especially instrumental births (forceps)
  - Reassurance: mostly improves at 6/12
  - Pads if necessary
  - Pelvic Floor Exercises
    - Contract and hold 10s
    - Relax, repeat
    - TV, couch, driving, urinating

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**Breast**

**Key Exam Information**

- Breast cancer occurs in 1 in 8 to 1 in 12 women in NZ
  - Infiltrating ductal carcinoma: 75%
  - Infiltrating lobular carcinoma: 10%
  - Others make up the rest. NB. Inflammatory breast cancer is bad news (ie worst prognosis)

- It is the leading cause of death in 18-44 year old women
- Breastscreening Aotearoa undertakes mammography for 45 – 69 year old women every other year (although ca incidence ↑ above age 69 but cost-benefit issues)
- If a lump can be felt it warrants referral
- Triple assessment:
  - Clinical: hx and exam
  - Radiological: US +/- mammography (generally if > 35)
  - Pathological:
    - FNA → cytology
    - Core bx (14g needle) → histology
    - Resection bx
- Treatment:
  - Wide local excision with RT
  - Mastectomy
  - Sentinel node bx +/- axillary node clearance
- Risk factors:
  - Female! (biggest RF)
  - Age (↑++ from age 45)
  - Hormones: nulliparity, 1st child >35, obesity, ETOH (↑ liver clearance of oestrogen)
  - FHx: only accounts for ~ 2% of cancers
- Fibroadenoma: round, smooth, common in ages 16-35, if big → remove
- Cysts: common, ↑ >35yrs, lots = fibrocystic change
- Breast pain: common, can be cyclical, can try evening primrose oil
- Mastitis:
Lactational: initial milk overproduction → squashed back into breast → chemical mastitis → secondarily infected with *staph aureus* → flucloxacillin → if no response ? abscess → US and aggressive treatment

Non-lactational: skin issues eg pimple or milk/nipple duct buildup (due to smoking) → abscesses

- **Gynaecomastia:**
  - 10% of guys: puberty (generally settles) and older age
  - Secondary: drugs, hyperthyroidism, paraneoplastic syndromes (lung ca: do CXR; testicular cancer; hepatocellular cancer), liver disease, cannabis, testicular atrophy

- **Nipple discharge:** normal colour is khaki green, blood is abnormal

- **Breast examination:**
  - **7 – 10 days** after the beginning of menses
  - Adequately expose breast, ? chaperon
  - **Inspection:**
    - While sitting on side of bed
    - Look for dimpling and nipple deformity with patient’s hands on her hips and then above her head
    - Size, symmetry, shape, scars, swellings, skin changes
  - **Palpation:**
    - Patient supine with hands behind her head
    - Use quadrant approach, in a radial pattern around the nipple (also examine nipple)
    - Distinguish glandular tissue from breast fat
    - Check for loss of pliability as well as for masses
    - Lymph nodes:
      - Axilla: checked for enlarged axillary lymph nodes – 1 – 2% of cancers present as axillary lumps
      - Supraclavicular
      - Cervical
    - Examine BOTH breasts
    - Characteristics of breast cancer: fixed, immobile, single, hard

- **Mammography interpretation:**
  - >50yrs: sensitivity 90%; <30: sensitivity 50%
  - Microcalcifications herald worse prognosis (ie more likely ca) than larger calcifications
  - MLO = mediolateral oblique: essentially a lateral, breast is squashed from side to side; tells you where lesion is in superior/inferior plane
  - CC = craniocaudal: squashed from top to bottom; tells you where lesion is in the lateral/medial plane

**Physiology & Anatomy**

- 3 – 4 days before menses, ↑oestrogen and progesterone → cell proliferation and water retention
- During pregnancy, cell proliferation ↑. Post-partum, prolactin → milk production.
- At menopause, breast involution due to replacement of glandular tissue by fibrosis and fat. Occurs with age

**Anatomy**

- Breast is between the 2nd and 6th intercostal spaces
- Superficial and deep fascia form a sandwich around the breast
- ~12 lobes
- Lobe = single lactiferous duct + its branches
- **Lobule/TDLU** = terminal duct + its branching ductules + glands
- **Basic functional unit** in the breast is the lobule = terminal ductal lobular unit (TDLU)
- TDLU consists of 10-100 acini, that drain into the terminal duct
- The terminal duct drains into larger ducts and finally into the main duct of the lobe (or segment), that drains into the nipple
- **Myoepithelial layer:** cell layer surrounding ductules; is the key diagnostic criteria for invasion when this layer is breached
- Blood supply from IMA, lateral thoracic, internal thoracic arteries
Breast History
- Previous lumps
- Pain
- Nipple discharge:
  - Is it blood stained
  - Is it unilateral or bilateral
  - Is there an associated lump
- Changes related to menstruation
- Parous state – breast feed?
- Last period
- Family History

Breast Exam
- 7 – 10 days after the beginning of menses
- Inspection: while standing, look for dimpling and nipple deformity with patient’s hands on her hips and then above her head
- Palpation:
  - Patient supine with hands behind her head
  - Distinguish glandular tissue from breast fat
  - Check for loss of pliability as well as for masses
  - Axilla: checked for enlarged axillary lymph nodes – 1 – 2% of cancers present as axillary lumps
- Characteristics of breast cancer: fixed, immobile, single, hard

Breast Investigations
- Clinician/surgeon: examination and history
- Pathologist: FNA (\( \rightarrow \) cytology) and core biopsy (\( \rightarrow \) histology)
- Radiologist: mammography and ultrasound. Clues on mammography:
  - Calcification:
    - Benign: very large, well rounded
    - Malignant: clusters, variable border, cast in a duct
  - Density

Breast in Pregnancy and Breastfeeding
- WHO recommendations: exclusive breastfeeding for up to 6 months and continuing breastfeeding into the second year alongside appropriate complementary feeding
- Changes during pregnancy:
- Oestrogen, progesterone, HPL (human placental lactogen), PRL and HCG → acinar cellular hyperplasia in early pregnancy, hypertrophy in later pregnancy, duct sprouting
- By end of pregnancy, breast is composed almost entirely of lobules separated by relatively scant amount of stroma
- Immediately after childbirth:
  - ↓Progesterone → milk production under the influence of PRL
  - Milk let down:
    - Sucking → ↑pulsatile oxytocin → myoepithelial cells squeezes milk down duct. Also due to neuroendocrine reflex (eg hearing baby cry). Sensitive to emotional stress
    - Sucking also stimulates PRL → continued milk production
- Advantages of breast feeding:
  - Infant: ↓infant mortality (two fold), ↓SUDI, bonding, cheap, portable, anti-infective properties (lysozyme, IgA, lactoferrine, etc), ↓ atopic disease, ↓ obesity, ↓ DM
  - Maternal: contraceptive, sucking promotes uterine contractions → ↓PPH, ↓pre-menopausal breast + ovarian cancer
  - Sufficient on its own until 4 – 6 months
  - See also Breast-feeding, page 919
- Contraindications: maternal HBsAg, CMV or HIV +ive, active breast HSV lesions, amiodarone
- Breast care:
  - Sore/cracked nipple prevention:
    - Poor position, poor hygiene, irritation (clothing, soap)
    - Treatment: shields, advice on position, break suction with finger, don’t use creams
  - Breast engorgement:
    - Supply > demand → enlarged breast → baby can’t latch on
    - Management: feed on demand, no other fluids for baby, express, paracetamol
  - Mastitis:
    - Cellulitis of interlobular connective tissue (mainly Staph Aureus)
    - Fever, tiredness, muscle aches and pains
    - Treatment: antibiotics (flucloxacillin), analgesics, regularly empty breast (continue feeding), massage lumps towards nipple when feeding
  - Abscess:
    - Secondary to mastitis, febrile and toxic, red and tender > 48 hours
    - Treatment: surgical drainage, antibiotics, antipyretics, analgesics, ?suppress lactation
  - Inverted or retracted nipples: gently pull out through pregnancy

**Pre-Term Milk**
- = milk made when baby is pre-term
- Contains:
  - ↑protein
  - ↑fat
  - ↑sodium
  - ↑chloride
  - ↑iron
  - ↓lactose
  - ↓calcium
  - ↓phosphate
- Advantages:
  - Increased tolerance of milk
  - Shorter gastric emptying time
  - Transition to full enteral feeds faster
  - Reduced risk and severity of NEC
  - Reduced risk of atopy
  - Improved neurodevelopmental outcome
  - Visual acuity/retinal maturational enhanced
  - Physiological stability greater during breastfeeding

**Colostrum**
- Small amounts. Average **7-14mls**
Higher protein, IgM, IgG and secretory IgA, Lactoferrin and Lyoymes plus macrophages, lymphocytes and neutrophils protect the newborn from infection. ↑ levels of the epidermal growth factor, stimulates cell growth. Has a laxative effect.

**Mature Milk**

- Contains:
  - Fat, protein, carbohydrates, water, vitamins, minerals, trace elements, hormones, enzymes, growth factors, immunological and protective factors
- **Variability of fat content in breastmilk:**
  - Fore-milk - lower content
  - Hind-milk - higher content
  - Fat content varies throughout the feed, the day and through different stages in lactation.
- Approximately **87% water in breastmilk** therefore babies do not need to be supplemented with water
- Minerals:
  - Levels of sodium, calcium, phosphorus and magnesium considered ideal for the term, breastfed baby.
  - May not be enough for the preterm baby, even though preterm breastmilk contains higher levels of these minerals. Because of the immaturity of their gastric and renal systems, particularly before 32 weeks, these may need supplementation
- Iron:
  - Full term babies have sufficient iron stores for 4-6 months and high levels of lactose and Vitamin C assist with absorption.
  - Preterm babies may require iron supplementation as they are unable to absorb iron effectively and may not contain sufficient amounts
- Immune factors:
  - Antibodies
  - Antiviral factors
  - Antibacterial factors
  - Antiparasitic activity.

**How Milk is Made**

- The rate of milk synthesis is related to the degree of emptiness of the breast. This is called **autocrine control**.
- As the alveolar lumen fills, compounds in the retained milk itself signal the secretory cells to slow down milk synthesis
- The **emptier the breast, the faster it tries to refill**. The rate of milk synthesis ranges from 11-58ml/hour/breast. Emptier breasts make milk quicker than full ones.
- Babies remove an average of **76% of available milk in a 24 hour period**

**Prolactin**

- Amount of prolactin released is related to the intensity of nipple stimulation.
- Although prolactin is necessary for milk secretion, plasma protein levels do not directly regulate milk synthesis and secretion.
- Prolactin is secreted episodically. Peaks 7-20 times a day. Higher levels at night when the least nursing occurs.
- Possibly has a relaxing effect.
- Can be affected by smoking and drinking.
- PRL inhibiting factor is released when baby not nursing + suckling inhibits this
- **PRL receptor theory = frequent feeds in early lactation → stimulates the development of prolactin receptors.**
  - Receptors per cell increases in early lactation and remains constant. Evidence shows that when a mother breastfeeding early and often, milk production is greater and the infant gains weight quicker and continues longer

**Latching**

- Baby close to mother and in alignment. Tummy to tummy.
- Baby’s mouth opposite mother’s nipple.
- Chin to the breast first.
- Breast presented with fingers well back from areola
- Shaped to fit baby’s mouth
- Baby’s mouth must be gaped before attaching to the breast
Baby Friendly Hospital Initiative

- BFHI is a global movement spearheaded by WHO and UNICEF that aims to give every baby the best care in life by creating a health care environment where breastfeeding is the norm.
- Requirements for accreditation:
  - To have 75% of mothers exclusively breastfeeding from birth to discharge
  - Meeting the requirements of the 10 steps to successful breastfeeding.
  - Meeting the requirements of the WHO Code of Marketing of breastmilk substitutes.
- Every facility providing maternity services and care for newborn infants should
  - 1. Have a written breastfeeding policy that is routinely communicated to all health care staff.
  - 2. Train all health care staff in skills necessary to implement this policy.
  - 3. Inform all pregnant women about the benefits and management of breastfeeding.
  - 4. Help mothers initiate breastfeeding within a half-hour of birth
  - 5. Show mothers how to breastfeed and how to maintain lactation even if they should be separated from their newborn infants.
  - 6. Give newborn infants no food or drink other than breastmilk, unless medically indicated.
  - 7. Practice rooming in. Allow mothers and infants to remain together 24 hours a day.
  - 8. Encourage breastfeeding on demand.
  - 9. Give no artificial teats or pacifiers to breastfeeding infants.
  - 10. Foster the establishment of breastfeeding support groups and refer mothers to them on discharge from the hospital or clinic

Breast Discharge

- Causes:
  - Causes of galactorrhoea:
    - Physiological
    - Drug related (eg dopamine)
    - Bronchogenic cancer
    - Prolactinoma
  - Duct ectasia (periductal mastitis) – most common cause in pre-menopausal women. Discharge may be serous, greenish or bloody
  - Carcinoma: usually associated with a palpable mass – cause in 10% over age 55. Cancer unlikely if discharge is coming from both nipples and/or multiple ducts. Cytologic examination has 50% sensitivity
- Management:
  - History and exam
  - Get mammogram, re-examine in 3 and 12 months, and repeat mammogram in 12 months
  - Sample to discharge to lab
  - Check serum PRL, especially if a pre-menopausal woman has irregular periods
- Pregnancy and discharge:
  - Epithelial hyperplasia may \rightarrow blood-stained discharge (usually normal)
  - Galactoceae: a milk filled cyst due to plugged duct
- Galactorrhoea:
  - Physiological: menarche/ menopause
  - Secondary to dopamine: chlorpromazine, haloperidol, metoclopramide, methyldopa
  - Prolactinoma: bronchogenic cancer or pituitary tumour

Developmental Problems

- Inverted nipples are common. If a previously normal nipple inverts \Rightarrow cancer until proven otherwise (although nipple retraction is more likely to be inflammatory than malignant)
- Virginal/ Adolescent Hypertrophy: very large breasts developing around puberty. Problem with stroma. Aetiology unknown
- Hypomastia: almost complete failure of breast development. May be unilateral
- Accessory nipples (don’t have lobular tissue underneath)

Breast Pathology

<table>
<thead>
<tr>
<th>Breast pathologies</th>
<th>Features</th>
<th>Macro</th>
<th>Micro</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fibroadenoma</td>
<td>Common + benign; 20-35yrs</td>
<td>Well circumscribed</td>
<td>1. Proliferation of ducts + stromal tissue 2. Originates from terminal duct lobular unit (TLDU)</td>
</tr>
<tr>
<td>Condition</td>
<td>Description</td>
<td>Patterns:</td>
<td>Components required for dx:</td>
</tr>
<tr>
<td>------------------------------------------------</td>
<td>------------------------------------------------------------------------------</td>
<td>---------------------------------------------------------------------------</td>
<td>--------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td><strong>Fibrocystic changes</strong></td>
<td>Firm, mobile mass</td>
<td>- Common + benign; 25-45 yrs</td>
<td>1. Cysts</td>
</tr>
<tr>
<td></td>
<td>In older women, mamm calcifications</td>
<td>- Can mimic cancer</td>
<td>2. Apocrine metaplasia</td>
</tr>
<tr>
<td></td>
<td>Increases in size in preg, decrease w age</td>
<td>- Often bilateral + hormonal cyclical changes seen</td>
<td>3. Fibrosis</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Mainly TDLU affected</td>
<td>4. Calcification</td>
</tr>
<tr>
<td></td>
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<td></td>
<td>5. Adenosis (increase in size + number of glands)</td>
</tr>
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<td></td>
<td></td>
<td></td>
<td>6. Chronic inflammation</td>
</tr>
<tr>
<td></td>
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<td></td>
<td>7. +/- epithelial hyperplasia (↑ risk of ca if present, no ↑ risk if not)</td>
</tr>
<tr>
<td><strong>Ductal carcinoma in-situ</strong></td>
<td>Precursor lesion</td>
<td></td>
<td>1. Holes seen where calcifications were</td>
</tr>
<tr>
<td></td>
<td>Limited to ducts + lobules by BM + myoepithelial cells</td>
<td></td>
<td>2. Proliferation of malignant cells, usually confined to a single duct system</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>3. Grades: low, intermediate, high</td>
</tr>
<tr>
<td><strong>Paget’s disease</strong></td>
<td>Crust, scale, erythema over nipple</td>
<td></td>
<td>1. Lobules extended by uniform, small round cells with round nuclei</td>
</tr>
<tr>
<td></td>
<td>Malignant cells extend from DCIS in duct to the nipple</td>
<td></td>
<td>2. Can extend into ducts</td>
</tr>
<tr>
<td><strong>Lobular carcinoma in-situ</strong></td>
<td>Usually incidental</td>
<td></td>
<td>1. Invasion of myoepithelial layer</td>
</tr>
<tr>
<td></td>
<td>Frequently multicentric and bilateral</td>
<td></td>
<td>2. Loss of normal tissue arch</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>3. Necrosis in high grade</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>4. Mitoses + other cytological features of malignancy</td>
</tr>
<tr>
<td><strong>Invasive ductal carcinoma</strong></td>
<td>Graded according to:</td>
<td></td>
<td>1. Small, uniform cells growing in Indian file (single file)</td>
</tr>
<tr>
<td></td>
<td>1. Tubule/gland formation</td>
<td></td>
<td>2. Lack of cohesiveness (no e-cadherin)</td>
</tr>
<tr>
<td></td>
<td>2. Nuclei</td>
<td></td>
<td>3. No gland formation</td>
</tr>
<tr>
<td></td>
<td>3. Mitoses</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Invasive lobular carcinoma</strong></td>
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<td></td>
<td></td>
</tr>
<tr>
<td><strong>Intraductal papilloma</strong></td>
<td>Benign</td>
<td></td>
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</tr>
<tr>
<td><strong>Acute mastitis</strong></td>
<td>Breast-feeding complication</td>
<td></td>
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</tr>
<tr>
<td></td>
<td>Development of cracks in skin of nipple allowing staph + strep to invade breast tissue</td>
<td></td>
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</tr>
</tbody>
</table>
Inflammatory Breast Disease

- Acute Mastitis and breast abscess:
  - Usually occurs in early lactation
  - Usually staph aureus (abscess), less often strep (cellulitis)

- Fat Necrosis:
  - A solid mass caused by injury (e.g., seat belt injury)
  - Necrotic fat cells surrounded by an inflammatory infiltrate, with later calcification and scarring. Can mimic carcinoma

- Duct ectasia
  - Uncommon cause of a breast mass. Usually older woman, tender and nipple retraction
  - Pathogenesis: Dilation of larger ducts with secretions → loss of epithelium → ulceration → blood or serous discharge → infection → periductal mastitis (abscess + fibrosis) → nipple retraction
  - Histology: Chronic inflammation and fibrosis around ducts loaded with lipid and macrophage rich material
  - Cause unknown. Correlated with smoking
  - → Preductal mastitis: periareolar inflammation, abscess formation, unilateral, single duct, etc

- Plasma cell mastitis: Rare cause of a breast mass. Probably the same as duct ectasia but with ↑ plasma cells

A tumour can block lymphatics causing inflammation ⇒ cancer is always a differential

Fibrocystic Disease

- A ‘catch-all’ category for gross and micro cysts
- Don’t call it mammary dysplasia
- Commonest disease of the breast
- Cause obscure – unopposed oestrogen a known factor. Women on combined pill get less fibrocystic disease

- Classification by size:
  - Gross cysts: very easy to diagnose on US. 40s. Drain with FNA
  - Micro cysts: usually 30’s and 40’s. May have cyclical pain. Resolves after menopause
  - Galactocele – milk filled cyst, usually with lactation

- 5 components (either separately or together):
  - Cysts:
    - Dilated ducts containing cloudy serous fluid (sometimes bloody or infected)
    - All breasts contain microcysts during childbearing years. Abnormal when > ~ 2mm
    - Histology: epithelium may be flattened, cuboidal, columnar, piled up or show apocrine metaplasia. Surrounding stroma likely to be fibrous
  - Fibrosis:
    - Dense collagenisation distorting/compressing epithelial structures
    - Most common in upper outer quadrants, patient’s in 30s
  - Sclerosing adenosis:
    - Usually a tender lump in the upper outer quadrant, patient around 40
    - Benign proliferation of small ductules in a fibrous stroma, but histologically circumscribed
    - Lining cells proliferate to fill the ducts
    - Increased risk of cancer with florid (2*) and atypical (4*) hyperplasia
    - Mimics cancer both clinically and microscopically
  - Apocrine Metaplasia: Benign metaplastic change to tall cells with eosinophilic cytoplasm resembling those of secretory glands (e.g., lactation, sweat, etc)
  - Duct (and sometimes lobular) epithelial hyperplasia

Generally Benign Breast Tumours

Fibroadenoma

- Most common benign breast tumour – no malignant potential
- Hypertrophy of a lobule, compressed by stroma (⇒ sharply circumscribed), hard and very mobile – up to 2 – 3 cm diameter.
- Common in 16 – 24 years. Rapid growth for 6 months, 1/3 will regress.
- Diagnosis by FNA if < 25 years, surgical enucleation if > 35 years
- Histology: ↑ fibrous tissue surrounding normal ducts that are often crushed flat. Risk of subsequent cancer = 2.17
- Cytology: cells clump together (cohesive) compared with malignancy which are normally non-cohesive
- Giant fibroadenoma: Variant:
Two peaks of incidence: 14 – 18 years and 40 – 50 years
Large: 5 – 10 cm
Typically oriental and black races
Diagnosis: FNA
Treatment: surgical enucleation (no excision margin)

**Phyllodes Tumour**
- Rare but ‘worrisome’ mixture of stromal and epithelial cells
- 30 – 50 years
- Shiny skin + vascular markings
- Wide spectrum from benign to frankly malignant. Grow rapidly
- Diagnosis: FNA + core biopsy. Cleft into the tumour on US is characteristic
- Treatment: excision with 1 cm margin
- Recur locally

**Papilloma**
- < 1 cm epithelial proliferation in a major duct just below the nipple
- Can → bloody discharge and/or nipple retraction
- 1 in 100 is a papillary carcinoma

**Breast Cancer**

**Breast Tumours**
- Carcinoma (epithelial origin):
  - Ductal (in situ or invasive)
  - Lobular (in situ or invasive)
- Intralobular:
  - Fibroadenoma
  - **Phyllodes** (tumour growing from periductal stromal cells, has leaf-like processes)
- Interlobular (stromal):
  - Lipoma
  - Angiosarcoma

**Summary from 2008 BMJ Review**
- Breast cancer mortality is falling in the Western world as a result of advances in treatment, but it remains a leading cause of death owing to the high and increasing incidence
- Several risk factors may present opportunities to lower risk, such as prolonged use of combined hormone replacement therapy and lifestyle factors
- Tamoxifen or raloxifene taken for five years prevents a third of breast cancers, but with no evidence of a reduction in deaths from breast cancer
- For women at high risk of breast cancer, screening with MRI is significantly more sensitive than mammography
- Advances in surgery continue to decrease morbidity through use of sentinel lymph node biopsy and oncoplastic surgery
- Adjuvant radiotherapy for many women can now be given over shorter periods, with similar efficacy and side effects
- Adjuvant systemic therapy has substantially reduced breast cancer mortality
- For oestrogen receptor positive cancers, aromatase inhibitors are more effective than tamoxifen in postmenopausal women
- Chemotherapy substantially improves the survival of selected patients
- Commercially available molecular tests may further refine selection of patients for chemotherapy, and validation studies are under way

**Pathology**
- **Clinical features**: upper outer quadrant most common; spread to ipsilateral axillary LNs
- **Types**: invasive ductal + invasive lobular carcinoma (also mucinous, medullary, papillary, tubular)
- Hereditary BC: ~12% of women have FHx; of all inherited BC ~ 85% is ass w BRCA1 or BRCA2
- Prognoisis:
  - Staging is key – mets/LN involvement most important
  - **Type, grade, stage** all play a part though
Receptor status of the tumour (eg HER2) also important

Hormone receptors:
- Presence of oes + prog −R correlate well with response to chemo (can treat with tamoxifen)
- Presence of −R determined by different stains
- HER2/neu (c-erbB-2): oncogene that encodes human epidermal GF receptor; this can be overexpressed in some cancers; detected using FISH
- HER2 positive tumours have a poorer prognosis than HER2 negative tumours
- Herceptin = trastuzumab – monoclonal Ab against HER2/neu receptor

BRCA1/BRCA2:
- If normal, these genes protect against breast + ovarian ca
- If abnormal, 50-85% risk for BC; 10-60% risk for ovarian ca; increased risk for prostate ca in men

Epidemiology
- ~2300 cases/yr; ~650 deaths
- Commonest cause of cancer death in women
- 10% life time incidence (usually over 70)
- Maori rate similar to non-Maori
- 75% diagnosed with breast cancer are over 50. Uncommon under 40. Mean age of diagnosis is 60 – 65. Younger if genetic risk
- If > 70 years, more likely to be indolent and hormone responsive. If < 35 then large and aggressive
- Survival:

<table>
<thead>
<tr>
<th>Stage</th>
<th>5-year survival (%)</th>
<th>10-year survival (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>80</td>
<td>65</td>
</tr>
<tr>
<td>II</td>
<td>75</td>
<td>55</td>
</tr>
<tr>
<td>III</td>
<td>55</td>
<td>40</td>
</tr>
<tr>
<td>IV</td>
<td>10</td>
<td>5</td>
</tr>
</tbody>
</table>

Risk Factors
- Major risks:
  - Woman (100 * men)
  - Age
  - Previous breast cancer, also previous (or family) history of endometrial, prostate, or ovarian cancer
  - Genetic predisposition (eg BRCA1 or 2 account for 5% of breast cancers)
  - Epithelial hyperplasia (fibrocystic breast disease)
  - Family History:
    - FDR 2-3x risk
    - Most with family history don’t develop it, most who get it won’t have a family history
    - Risk is above population risk for only 1% of female population
    - 4% have a moderate increase in risk if:
      - A mother, sister or father developed breast cancer before 50, or in both breasts
      - More than one close relative on the same side of the family who had breast or ovarian cancer (geneticist said only genetic if 3 or more affected relatives – it is so common have to have a high incidence in family before suspecting a family loading)
- Minor risks:
  - Oestrogen exposure:
    - Slight increase for OCP and Depo-Provera (only while taking it – and usually young so less of an issue)
    - Longer duration between menarche and menopause
    - First child beyond 35 or no children
  - Not having lactated (never breastfed) → slight ↑risk of premenopausal cancer
  - Obesity
  - HRT for more than 5 years increases risk by about 30%. Risk disappears within 5 years of stopping
  - Caucasian
  - Radiation, environmental hazards
- Not risk factors:
  - Smoking
  - Small (now disproven?) relationship with low fat, high fibre diet

Symptoms
- Presenting symptoms:
Painless mass: 66%
- Painful mass: 11%
- Nipple discharge: 9%
- Usual presentation is a dominant, painless mass
- New lump or thickening
- Change in breast shape or size
- Puckering or dimpling of the skin
- Change in a nipple
- Lumpiness in one breast soon after period ends
- Pain in the breast that is unusual

**Investigations**
- History and clinical exam
- Mammogram:
  - Not sensitive < age 35
  - Calcifications: low risk are coarse or rounded, high risk are clustered or branching
  - Shadows: malignant are less circumscribed
- Ultrasound
- FNA → Cytology
- Core or hook wire biopsy

**Pathogenesis**
- Most tumours occur in the epithelial component lining the ducts and lobules. Epithelial hyperplasia (1 – 2 times risk) → Atypical hyperplasia – proliferation and atypia of ductal or lobular epithelium. Risk of subsequent cancer = 4 times.
- Tumour cells secrete cytokines → fibrosis → lump. Easier to detect in an older woman (↑ fat and ↓ intra-lobular fibrosis)
- All breast cancers are different. Tumour growth rates vary considerably. On average takes 9 years to reach 1 cm.
- Death is from metastases which can occur at any time
- Spreads to lymph nodes via lymphatics and directly to distant sites via blood stream – not via lymph nodes. 
- Lots of implicated genes. Those in familial breast cancer include:
  - **BRAC1:**
    - Autosomal dominant (but recessive at the level of the cell): if carrier then 65 – 75% risk (ie high penetrance)
    - A tumour suppressor gene, expressed in breast, ovary, thymus, testis
    - Accounts for 40 – 50% of familial breast cancer
  - **BRAC2:**
    - Associated with male breast cancer, not ovarian
    - 10% of inherited breast cancer

**Classification of Breast Cancer**
- Classification:
  - **In-situ**
  - **Infiltrative (invasive)**

<table>
<thead>
<tr>
<th>Ductal</th>
<th>Intraductal carcinoma</th>
<th>Infiltrating ductal carcinoma:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>• No special type (NOS)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Medullary carcinoma</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Mucinous carcinoma</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Tubular carcinoma</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Metaplastic</td>
</tr>
<tr>
<td>Lobular</td>
<td>Non-infiltrating (in situ) lobular carcinoma</td>
<td>Infiltrating lobular carcinoma</td>
</tr>
</tbody>
</table>

- Most cancers are intraductal
- Plus Paget's Disease of the Nipple
- Non-infiltrating/in-situ breast cancer: Does not metastasise but recurrence is a problem. Can become infiltrative and then metastasise
  - Intraductal carcinoma (20 – 30%):
Comedocarcinoma: solid intraductal proliferation, central necrosis, microcalcifications on mammogram.
- Classified by nuclear grade (low, intermediate and high) and the presence or absence of necrosis.
- Can eventually become invasive: removal → cure.

- Paget’s disease (a type of ductal carcinoma in situ): lesion of the nipple caused by malignant cells arising from ducts and invading the nipple epithelium. Looks inflamed (early on can look like eczema). Most often an underlying duct carcinoma.

- Lobular carcinoma in situ:
  - Usually an incidental finding on biopsy affecting terminal ductules
  - Proliferation of terminal ductules and acini
  - 1% per year risk of invasive carcinoma in same or opposite breast – removal isn’t necessarily cure.

- Invasive/infiltrating breast cancer:
  - Main risk factor: ↑ age

- Infiltrative ductal carcinoma (65 – 80%):
  - No special type: Most common. Grossly stellate or multinodular and very hard. Histologically compressed ductules in a very desmoplastic stroma
  - Medullary: Big, bulky and soft, plentiful lymphocytes, better prognosis than other types
  - Tubular Carcinoma: well-formed glands, best prognosis

- Infiltrative lobular carcinoma:
  - Histological: Indian files around ducts, small cells
  - Often bilateral

- Features of invasive cancers:
  - Usually dominant mass
  - Usually painless
  - In time fixed to deep fascia → immobile
  - Orange peel appearance: blocked lymphatics → oedema + suspensory ligaments contract → distorted shape
  - Also nipple retraction, ulceration of overlying skin
  - Majority arise in the outer quadrants – particularly the upper, outer quadrant

- On mammography:
  - Infiltrative edge: not well demarcated
  - ↑ Density compared with adipose tissue
  - Micro-calcifications: small clustered areas of necrosis

**Prognosis**

- Stage: axillary metastases most important, also size. Cancers found on mammography or by self-examination are smaller ⇒ better prognosis
- Grade
- Oestrogen receptor sensitivity: if positive then better – more differentiated and Tamoxifen → regression

**Treatment of Breast Cancer**

- Can’t cure metastases ⇒ aim of treatment is local control
- Options:
  - Two options (similar long-term survival):
    - Removal of the lump + radiation therapy (significant ↓ in local recurrence)
    - Mastectomy (or radical mastectomy) + reconstruction
  - +/- Radiotherapy (planned to limit dose to the heart, lung or opposite breast
  - +/- Tamoxifen (anti-oestrogen)
- Surgery:

<table>
<thead>
<tr>
<th>Mastectomy</th>
<th>Breast Conservative</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient preference</td>
<td>Patient preference</td>
</tr>
<tr>
<td>Large tumour or Large tumour/breast ratio</td>
<td>Small tumour or small tumour/breast ratio</td>
</tr>
<tr>
<td>Multiple tumours</td>
<td>Single tumour</td>
</tr>
<tr>
<td>+ive margins</td>
<td>Focal microcalcification</td>
</tr>
<tr>
<td>Previous breast RT</td>
<td>-ive margins</td>
</tr>
<tr>
<td>Pregnancy, etc, etc</td>
<td></td>
</tr>
</tbody>
</table>
Most common metastasis is in the bone. Bisphosphonates \(\rightarrow\) slow osteolysis

Risk factors for recurrence in breast cancer (\(\Rightarrow\) consider adjuvant chemo):
- Axillary node status (strongest predictor)
- Tumour size (> 1 cm)
- Histological tumour type and grade

Adjuvant Chemotherapy:
- Approx 25 – 30% ↓risk of recurrence, 15 – 20% ↓risk of death. Improves long term survival in node positive and node negative disease
- 4 to 6 courses over 3 – 6 months optimal
- 2 agents better than one: eg
  - AC: Adriamycin (an anthracycline) and Cyclophosphamide. ‘Gold standard’.
  - Adriamycin causes vomiting and wasn’t used so much until 5HT3 antagonists were available
  - CMF: Cyclophosphamide, Methotrexate and Fluorouracil (another ‘Gold Standard’)

Hormone Therapy:
- Aim: prevent breast cancer cells from receiving stimulation from oestrogen
- Only is oestrogen receptor sensitive
- Oestrogen deprivation:
  - Block oestrogen receptor: eg Tamoxifen – antagonist. Taken for 5 years. Side-effects:
    - Largely well tolerated
    - 1 in 3 have post menopausal flushes, vaginal dryness/discharge
    - Initial nausea, weight gain
    - Rare retinopathy
    - Agonist in the uterus \(\rightarrow\) ↑endometrium \(\rightarrow\) ↑risk of endometrial carcinoma (1 in 1000, usually curable)
  - PE/DVT (1 – 2 %)
  - Suppress synthesis: aromatase inhibitors (work in adipose tissue, eg in post menopausal women), LHRH agonist (pre-menopausal, switches off the ovary)
  - Destroy ovaries (surgery or RT)
- Leads to ↓recurrent, ↓40% incidence of contralateral breast cancer (although absolute risk low)

Breast Screening
- A Cochrane review concluded that mammographic screening reduces the risk of dying of breast cancer by about 15%, at the expense of a 30% increase in diagnosis
- Of proven benefit in reducing mortality in women over 50: benefits under 50 unclear
- 2 yearly screening after 50 reduces chances of dying from breast cancer by about 1/3. Reduces a one in 42 chance to one in 60
- In NZ is free from 50 – 64
- Mammograms less reliable in under 50s: denser breast tissue. Higher false positives \(\rightarrow\) unnecessary investigations. Sensitivity for < 50 years is 50% - 60%, for > 50 years is 80+%. 5 – 10 % screened sent for further investigations. Positive predicative yield is 8.5% (high false positive rate)
- Further investigations: ultrasound, FNA, biopsy
- Of 1000 screened, 70 to 120 will be positive, 10 to 30 will proceed as far as open biopsy, and 5 to 10 will have cancer
- Mammogram less accurate if on HRT
- Interval cancers: fast growing cancers appearing between mammograms – never ignore a lump
- Application of screening criteria (see Criteria for Screening Programmes, page 1031):
  - It is an important health problem – with a significant incidence. It is preventable
  - A screening test is available: a two yearly double view double read mammography (double reading increases cancer detection by 15% compared with single reading and reduces recall rate)
  - The screening test is available, acceptable (83% a little uncomfortable only), reasonable sensitivity, but low PPV
  - Natural history is well understood, and there is a detectable pre-symptomatic stage
  - Screening leads to interventions that increase the quality of life: relative risk reduction 10 – 30% for women in the 50 – 65 age group. However, lots of unnecessary interventions, and for a majority (>70%) whose cancer is diagnosed, the outcome is unchanged (but will live with 2 years extra knowledge of condition)
  - Is there an appropriate infrastructure to provide screening and follow-up? There have been pilot studies
  - Is it cost effective: Needs at least 70% screening coverage to be cost effective.
Sexual Health

Background

Epidemiology

- Most STIs seen in 16-25 y/o
- C. trachomatis most common bug
- MAP more commonly infected
- Around 140 neonatal chlamydia cases in NZ/yr, ~6 gonorrhoea
- Syphilis on the ↑ by 200% since ’04 + is a marker for HIC transmission behaviours
- Genital herpes (HSV) ↑ 17% over last 5 years (?↑ oral sex)
- HPV ↓ 14.4% over last 5 years (vaccine)

Sexual History Taking

- Purpose of sexual history is to determine:
  1. Whether or not there has been a risk of exposure to an STI including HIV
  2. If it is an appropriate time to take tests (window period – genital tests are not taken unless at least 14 days has elapsed from unprotected sex, unless symptomatic. For blood tests wait 3 months)
  3. Who else had been at risk and may need testing/treating

- Approach:
  1. “Going to ask personal questions – want to be able to offer right tests and care”
  2. Ask why they’ve come
  3. Use patient’s language
  4. Don’t make assumptions about anyone
  5. Lot’s of reassurance: STI’s are common, confidentiality, support relationship issues – let them decide, continue at a later date
  6. Not interested in their orientation but what they do

- Questions:
  1. Are you sexually active?
  2. Partners in the last 6 months – male or female?
  3. Protected or unprotected sex?
  4. What type of sex? Anal (receptive/insertive), oral, vaginal?
  5. Ever paid for sex?
  6. Travelled overseas + had sex?
  7. Ever had an STI? Been tested for one?
  8. Any itching/rashes/sores/discharge/fever/dysuria?
  9. Alcohol and drug history
  10. Do you suspect that you may be at risk from HIV or other STI?
  11. Need to ask about sexual abuse – won’t volunteer it: Ever had sex when you didn’t want to, any unwanted touching/non-consenting sex?
  12. Do you suspect you might be at risk of HIV/or STI?

Exam

Female

- 1. Inspection: pubic lice, genital warts, ulcers, blisters, scabies
- 2. Palpation: inguinal lymph nodes
- 3. Vaginal examination with speculum
- 4. Bimanual examination of pelvis if indicated

Male

- Examination of external genitalia
- Palpation of inguinal nodes
- Palpation of scrotal sac and testes

Tests

Blood Tests

- Hepatitis B (Ag and Ab)
- Syphilis: EIA/RPR/TPHA
- HIV Ab if appropriate with counselling and consent. Always attend for results. Have pretest discussion
- Hep C if appropriate (hx of IVDU/blood transfusion pre ‘80)

**Female**
- Routine swabs for STI testing – should be done with every woman, especially those under 25 yrs, pregnant or those at risk of STIs:
  - 1. *Endocervical* swab for *gonorrhoea* (Amies bacterial culture swab)
  - 2. *Endocervical* swab for *chlamydia* (NA amplification test: PCR; better than urine test)
  - 3. *High vaginal* swab for *BV, candidiasis + trichomonas* (Amies bacterial culture swab)
  - +/- *smear* if required
  - +/- first pass urine for chlamydia – useful if also has urinary symptoms
  - Self-collected vaginal swab for chlamydia only useful for opportunistic asymptomatic screening or if refuses exam, not appropriate otherwise

**Male**
- 1. *Urethral* swab for *gonorrhoea*
- 2. *First pass urine* (ie not MSU) for *chlamydia*
- +/- *gram stain* of urethral discharge if appropriate
- +/- *anal swab* for gonorrhoea if appropriate
- +/- *throat swab* for gonorrhoea if appropriate

**Sexually Transmitted Infections (STIs)**

**Notifiable STIs**
- Syphilis
- Gonorrhoea
- Chancroid (bacteria; rare in NZ; painful ulcers on the genitals and painful swollen lymph glands)
- LGV (lymphogranuloma venereum caused by a Chlamydia strain; small genital or rectal lesion, which can ulcerate + LAN)
- Must inform MoH, can get medical officer of health involved if won’t inform partner
- NB. HIV is NOT a notifiable disease!

**Types and Incubation**
- Chlamydia (7 – 21 days) ⇒ don’t test till 14 days after contact (unless symptomatic)
- Gonorrhoea (range 1 – 14 days, commonly 2 – 5 days)
- Trichomonas (5 – 28 days)
- Herpes Simplex Virus (2 days onwards – maybe years)
- Human Papilloma Virus (3 – 8 months, up to a year, vertical transmission possible)
- Human Immunodeficiency Virus (HIV) – (seroconversion illness 2 – 6 weeks after exposure, HIV antibodies almost always present after 3 months. Mean time to developing AIDS defining illness 9 – 12 years)
- Hepatitis B (1 – 6 months)
- Syphilis (9 – 90 days)
- Non-specific urethritis
- Pediculosis Pubis: Public Lice (mature lice – immediate, eggs – 2 weeks to mature, larvae – 1 week to mature)
- Scabies (3 – 30 days, 6 weeks for itch to develop)
- Hepatitis C and A may be sexually transmitted
- Not necessarily sexually transmitted:
  - Normal anatomical variants
  - BV ⇒ sexually associated but not an STI, due to commensals
  - Dermatoses
  - Candidacies (commensals)
  - Molluscum contagiosum (3 weeks – months)
  - Urinary tract infections
  - Prostatitis
  - Vulval disorders

**Vaginal Discharge**
- Cervical secretions in women not on the pill, and which change during the cycle, are part of normal discharge. Mucus is clear or clear/white. Some inflammatory cells are normal in the latter half of a cycle
- Desquamating vaginal cells with healthy lactobacilli are major part of normal discharge – pH < 4.5
- Key history questions:
  - Colour
  - Odour
  - Itch
- Differential:
  - 1. Thrush (Candidiasis): thick, creamy, lumpy, very itchy, not smelly
  - 2. Trichomoniasis: greeny yellow frothy discharge, fishy smell, moderate itch
  - 3. Bacterial Vaginosis: thin, grey homogenous d/c, odorous, itchy
  - 4. Chlamydia: asymptomatic or discharge
  - 5. Atrophic vaginitis: brown, spotty discharge (from bruising), pain, no itch. Treatment: oestrogen cream or HRT

<table>
<thead>
<tr>
<th></th>
<th>Bacterial Vaginosis</th>
<th>Trichomoniasis</th>
<th>Candidiasis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prominent symptoms</td>
<td>Discharge, odour</td>
<td>Discharge, vulval irritation, fishy</td>
<td>Itch</td>
</tr>
<tr>
<td>Classical signs</td>
<td>No vulvitis or vaginitis</td>
<td>Vulvitis, vaginitis, strawberry cervix</td>
<td>Vulvitis, vaginitis – fissured and sore</td>
</tr>
<tr>
<td>Classical discharge</td>
<td>Greyish-white, thin, may be frothy</td>
<td>Green/yellow, watery, pools in posterior fornix, may be frothy</td>
<td>White, flocculent, thrush plaques</td>
</tr>
<tr>
<td>Risk factors</td>
<td></td>
<td></td>
<td>Pregnancy, antibiotics, steroids, diabetes</td>
</tr>
<tr>
<td>Vaginal pH</td>
<td>pH &gt; 4.5 (often 5.0 – 6.0)</td>
<td>pH &gt; 4.5 (often 6.0 – 7.0)</td>
<td>pH &lt; 4.5 (often 3.0)</td>
</tr>
<tr>
<td>KOH test (amine/Whiff test)</td>
<td>Positive</td>
<td>Weakly positive</td>
<td>Negative</td>
</tr>
<tr>
<td>Wet mount preparation</td>
<td>Clue cells present (vaginal cells covered by anaerobes &amp; Gardnerella vaginalis), Replacement of lactobacilli with small coccobacilli (Gardnerella) or motile curved rods (Mobilinus). Few pus cells</td>
<td>Trichomonads (motile flagellate), pus cells</td>
<td>Yeast cells (blastospores)</td>
</tr>
<tr>
<td>Gram stained smear</td>
<td>Clue cells: G-ive curved rods. G variable coccobacilli.</td>
<td>Pus cells: acidride orange stain</td>
<td>Most common cause of discharge</td>
</tr>
<tr>
<td>Treatment</td>
<td>Anti-anaerobe: oral metronidazole</td>
<td>Oral: doxycycline (remember 7 day rule)</td>
<td>Clotrimazole pessary</td>
</tr>
</tbody>
</table>

### Gonorrhea vs Chlamydia

<table>
<thead>
<tr>
<th></th>
<th>Gonorrhoea</th>
<th>Chlamydia</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Bug</strong></td>
<td>Gram negative intracellular diplococci</td>
<td>Gram negative rods or cocci</td>
</tr>
<tr>
<td><strong>Incubation</strong></td>
<td>1-10d</td>
<td>7-21d</td>
</tr>
<tr>
<td><strong>Preferred site</strong></td>
<td>Columnar cells of urethra, endo-cervix, rectum, pharynx, conjunctiva</td>
<td></td>
</tr>
<tr>
<td><strong>Transmission risk</strong></td>
<td>90% M-F with 1 sexual episode</td>
<td>20% M-F per episode of sex</td>
</tr>
<tr>
<td><strong>Symptoms</strong></td>
<td>Males: 95% symptomatic Femaless: often asymptomatic</td>
<td>Males: 30% asymptomatic Females: 70% asymptomatic</td>
</tr>
<tr>
<td></td>
<td>Yellowy odorous d/c + erythema + dysuria (urethra/cervix)</td>
<td>Clear milky d/c in males, mucopurulent d/c in females</td>
</tr>
<tr>
<td><strong>Tests</strong></td>
<td>Male: urethral swab; Female: endocervical swab Culture: intracellular gram negative inclusions</td>
<td>Male: first void; Females: endocervical swab PCR</td>
</tr>
<tr>
<td><strong>Treatment</strong></td>
<td>Ceftriaxone</td>
<td>Azithromycin</td>
</tr>
</tbody>
</table>
NB. 30% co-infection

*Neisseria Gonorrhoeae*

- **Description:** G–ve diplococci
- **Symptoms:**
  - Male: 90% symptomatic. *Discharge & dysuria* (razor blade pain). 30% also have chlamydia
  - Female: only 20% symptomatic – can have vaginal discharge or pelvic pain. Pick up with opportunistic/selective screening if under 25, multiple partners, changed partner in last 6 months, IUCD, etc
  - Rectal and pharyngeal: often asymptomatic
- **Diagnosis:** gram stain microscopy if symptomatic or contact, or culture on chocolate agar
- **Advice:** no sex until minimum of 3 days since treatment completed
- **Treatment:**
  - Ceftriaxone 250mg imi stat if sensitivities not known (often given as 500mg dose)
  - Ciprofloxacin 500 mgs (a quinolone) stat if sensitivities known (use Ceftriaxone if pregnant)
  - Co-infection possible with chlamydia therefore all regimens should empirically treat for chlamydia (azithromycin 1g stat)
- **Contact tracing** required. Treat partners
- **Test for cure at 14 days** (legal requirement)
- **Complications:** See Pelvic Inflammatory Disease *(PID)*, page 677

*Chlamydia Trachomatis*

- **Description:** obligate intracellular bacteria, STIs are types D – K. Highest in 20 – 24 year age group
- **Symptoms:**
  - Urethritis, unexplained cystitis, mucopurulent cervicitis, pelvic pain, irregular bleeding
  - 80% of females and 50% of males have no symptoms. Suspect and test if sexual contacts have it, if patients asks for STI tests, patients under 25 with new/multiple partners
  - Up to 30% associated with concurrent *N* Gonorrhoea infection
- **Diagnosis:**
  - Female: swab from affected area, including from endocervix. Rotate 6 – 10 times. Urine test alone not sufficient. Most common site of single infection is cervix (ie urine is clear)
  - Male: first pass urine test
  - PCR test easier sampling (urine test)
  - Opportunistic detection has been shown to reduce rates of PID and ectopic pregnancy
- **Advice:**
  - Abstain until treated – if not use condoms
  - **Contact trace** (arbitrary look back at 3-6 months)
- **Treatment:**
  - 1. *Azithromycin* 1g stat dose is first drug of choice (use this in pregnancy, breastfeeding)
  - 2. Doxycycline 100mg bd for 7d (*not* in pregnant/breastfeeding women)
  - Known positive and partners: *Azithromycin* 1 g stat orally – directly observed treatment
  - In *pregnancy:* *erythromycin* ethylsuccinate 800mg qid for 7 days – must be treated to prevent amnionitis and premature rupture of membranes
  - In PID: Doxycycline/erythromycin for 14 days and ornidazole 500 mgs bd for 7 days, plus consider gonorrhoea in which case penicillin/ciprofloxacin in addition
  - Test of cure in 3 weeks if non-compliance or re-infection suspected. Urine test is adequate for males and females
  - Test high risk patients only for cure
  - If reinfection, then ?untreated partner
- **Complications:**
  - Neonatal: conjunctivitis, pneumonitis 2 – 4 weeks later
  - See Pelvic Inflammatory Disease *(PID)*, page 677

*Herpes Simplex Virus (Type 2)*

- See Herpes Simplex Virus *(HSV)*, page 818

*Pelvic Inflammatory Disease (PID)*

- Inflammation of endometrium, fallopian tubes, pelvic peritoneum → spreads from bacterial infection of neck of cervix
• Bilateral
• Acute febrile illness
• Left untreated → permanent scarring + adhesions, chronic pain + infertility
• Mostly caused by chlamydia or gonorrhoea
• 1-4% assoc with IUDs → actinomyces
• 1/3 cases TB
• Risks: risk factors for STDs, history of salpingitis, IUD
• Most likely in young sexually active F
• Symptoms:
  ➢ Lower abdominal pain
  ➢ Metorrhagia – acyclical bleeding
  ➢ Post coital bleeding
  ➢ Vaginal discharge
  ➢ Deep dyspareunia
  ➢ Fever
  ➢ May be signs of peritoneal irritation
• Investigations:
  ➢ Gram stain: gram –ve diplococci GC
  ➢ Cervical culture
  ➢ USS
  ➢ Laparoscopy
• Diagnosis:
  ➢ Cervical motion tenderness
  ➢ Laparoscopy needed for definitive diagnosis
  ➢ Bloods: FBC, blood cultures, Hep B, hep C, syphilis, HIV
  ➢ Cervical swabs
  ➢ Pap smear
  ➢ USS
  ➢ MSU
  ➢ Must have: lower abdo pain + temp > 38, ↑ WBC, cervical discharge, pelvic abscess, positive culture for gonorrhoea or chlamydia, high risk partner
• Consequences of untreated PID: chronic pelvic pain, abscess, peritonitis, adhesions, ectopic pregnancy 7x risk, infertility, bacteraemia.
• Treatment:
  ➢ Treat with polymicrobial cover
  ➢ Outpatient care:
    o Typical findings
    o Mild disease
    o Tolerates oral abs
    o Ceftriaxone 250mg IM + doxycycline 100mg bid for 14 days
  ➢ Inpatient care:
    o Atypical infection
    o Pelvic abscess
    o Moderate/severe illness
    o Pregnant
    o Clindamycin 900mg + gentamicin + doxycycline for 14days
    o If failure = surgery
  ➢ Remove IUD
  ➢ Reportable disease: treat partners

Reiter’s Syndrome*
• Triad of arthritis (big joints – hot, red swollen, bilateral), urethritis and conjunctivitis
• 10:1 are males, usually 25 – 35 years
• Often (not always) caused by chlamydia (an immunological reaction, HLA B27+ more susceptible)
• Treatment: treat residual infection, if any
• See Reiter’s Syndrome, page 437

Genital Warts
• Can get anal warts without anal intercourse
External warts usually benign (types 6 & 11 – not oncogenic)

Treatment:
- Destructive: Condyline, liquid nitrogen – high recurrence rate
- Imiquimod – topical cream, up-regulates immune system, expensive ($150 per month), 19% recurrence, requires treatment for 8 – 12 weeks

A vaccine is at stage 3 trials

Non-Sexually Transmitted Genital Skin Lesions

- Not all skin lesions on the genitals and surrounding areas are due to STDs
- Normal anatomical variants:
  - Pearly penile papules: small papillae around the corona of the penis
  - Sebaceous cysts of the penis, labia minora and scrotum
  - Normal papillae in the vaginal vestibule: can be mistaken for warts
- Dermatoses:
  - Contact dermatitis: soaps, deodorants, etc
  - Psoriasis: especially head and corona of the penis. Red, scaly plaques. Not itchy. Look for it elsewhere
  - Reiter’s Syndrome: urethritis, conjunctivitis, arthritis in addition to skin lesion
  - Lichen Planus: itchy plaques on the penis
- Infections (not necessarily sexually acquired):
  - Seborrhoeic dermatitis: a fungus, red, sharply defined area covered with honey coloured scales
  - Candidiasis: red, irritating, itchy rash. Treat with Clotrimazole (Canesten)
  - Dermatophyte infections (tinea) are common. Characteristic spreading edge, itchy
  - Folliculitis: small pustule around a hair follicle
  - Scabies: red, itchy nodules – may not resolve despite treatment. Treat with malathion 0.5%
  - Erythrasma: scaly, flat, brown, pigmented rash, not itchy. Caused by corynebacterium
  - Molluscum contagiosum: may be sexually acquired. Small, pearly umbiliated lesions on the thigh and buttocks

HIV

- See AIDS, page 495
- Assessment of risk: “I have a quick checklist of questions which I go through with all my pts, some may not apply to you but they are routine questions”
  - Establish risk contacts within a 3/12 window
  - Discuss the significance of negative results in relation to “window period” (~ 5% will take 12/52 to test positive), newer tests give positive results by 4-6/52
- Confidentiality can be preserved – coding of lab test forms
- Assess support systems + coping skills
- Informed consent must be obtained prior to testing
- Routine testing in pregnancy: we test as we can prevent transmission (or ↓ risk), not every knows their risk factors (partners), is a very (but not 100%) accurate test, results over phone or face to face, can refuse
- Significance of a positive test:
  - Needs confirmatory test if possible before discussion with pts (Western blot)
  - Do you know the difference between HIV + AIDS? (if you picked up HIV yesterday, today your test would be negative; takes ~ 6-12/52 to become positive; a positive test doesn’t mean you have AIDS; takes ~ 10 years or more to develop AIDS)
  - If you were positive, who would you tell? What would happen with sex? How would you tell your partner?
  - NB. Results are confidential
Exam Tips & Acronyms/Mnemonics

Acronyms & Mnemonics

- HPC: SOS: severity/impact on functioning, onset (what brought this on?), support
- Mental state examination: ASEPTIC
- Suicide risk factors: SAD PERSONS (sex, age, depression, previous attempt, ethanol/other substance abuse/ethnicity, rational thinking impaired/psychosis, social support lacking, organised plan, no spouse, sickness: psych and medical)
- Depression diagnosis: SAD SPACE Guidelines: sleep, appetite, depression, suicide, psychomotor agitation, anhedonia, concentration, energy/fatigue, guilt/worthlessness
- Alcohol dependence questions: CAGE (felt need to cut down, annoyed by criticism, felt guilty, eye opener)
- Delirium aetiology: I WATCH DEATH (infection/infarction, withdrawal, acute metabolic, trauma, CNS pathology eg tumour, hypoxia, dehydration, endocrine, acute vascular, toxins, heavy metals)
- MMSE: ORARL: orientation (person; time: d/month/yr; place: current location, city, country), registration (name 3 objects), attention and calculation (serial 7s), recall, language and drawing (no ifs etc)
- Reversible causes of dementia: DEMENTIA (drugs, eye/ears, metabolic, emotions [psych conditions], nutritional, tumour/trauma, infection, alcohol)
- Manic symptoms: DIG FAST (distractability, irritability, grandiosity, flight of ideas, activities ↑, speech ↑/sleep, thoughtlessness: sex/spending etc)
- Lithium SE: the 4 T’s: tremor, thyroid (hypo), terrible renal disease, teratogen
- Schizophrenia symptoms: PINC (positive symptoms, insight lacking, negative symptoms, cognition impaired/catatonic or disorganised behaviours)
- Dementia symptoms: MAD CAP (memory, aphasia, disorientation, cognition, apraxia/agnosia, personality)
- General anxiety disorder symptoms: RIMS FC (restlessness, irritability, muscle tension, sleep disturbance, fatigue, concentration)
- Delirium diagnosis: GCCPFAS (good cooks can pan fry and sauté: GMC, consciousness, cognition [globally impaired], perception, fluctuating, attention, short/sundowning [worse at night])
- Antipsychotic SEs: CAGE MEN (CV: QT + orthostatic hypo, Anti-Ch, Gynaecomastia [PRL], EPS [+ TD, dystonia, akathisia, PS], Metabolic syndrome, Erectile dysfunction, Neuroleptic malignant syndrome)
- Dependence criteria: WTF CULT (withdrawal, tolerance, forfeit things, continued use despite, unsuccessful attempts, larger amounts or longer time, time spent recovering/obtaining/using)
- SSRI SEs: FINISH SA (fat, insomnia, nausea, increased anxiety, sexual dysfunction, headache, sweating, ↓ appetite)
- PTSD: RID FAN HACS (recurrent intrusive distressing thoughts with flashbacks, nightmares and avoidance and hyperarousal symptoms [↓ sleep, anger, ↓ concentration, hypervigilance])
- Personality disorders: TB RP ISAC (pattern of thinking and behaviour that is rigid and pervasive, manifest by impulsivity or social impairment, or affect or cognitions)
- Thought content - "DROPS"
  - Depersonalisation/derealisation/delusions
  - Recurrent themes
  - Obsessions (± compulsions)
  - Phobias
  - Suicidal thoughts
- Anorexia Nervosa = FAB 15
  - Fear of wt gain
  - Amenorrhoea (FTT in prepubescent children)
  - Body image disorder
  - 15% below minimum ideal body weight
- Organic causes of anxiety to be ruled out for GAD ddx = CHOPES
  - Cardiac failure or arrhythmia
  - Hyperthyroid, hypoglycaemia, hypercapnia
- Other psychiatric disease
- Pneumonia (apparently!)
- Encephalitis, seizures
- Substance abuse

- Neuroleptic malignant syndrome symptoms and signs = TRACTA
  - Temperature ↑
  - Rigid muscles
  - Autonomic instability
  - CK ↑
  - Tremor
  - Altered level of consciousness

- Suicide risk factors = TIP OFF
  - Thought of hurting yourself or about suicide?
  - Intentions.... do you want to die or is it more that you need to express how bad things are?
  - Plan and means to succeed?
  - Other attempts in the past – how did you feel, what did you want to happen?
  - Factors
    - Positive = support, not living alone, have plans for the next few days
    - Negative = alcohol, agitated, other mental illness, lives alone, no support
  - Freakin’ crazy (delusions ++ suicide risk)

**Diagnosis**
- Of any disorder: impairment in social or occupational or relational functioning and or clinically significant distress
- Diagnosis is not better accounted for by another diagnosis, substance abuse, GMC etc
- Need to do hx, exam, lx, formulation
- Need to discuss dx with pt (and maybe colleagues for 2nd opinion)

**DDx**
- Other psychiatric diagnoses
- Axis 2 diagnoses!
- GMC: especially thyroid
- Alcohol and drugs

**Aetiology**
- Bio (eg familial, NT) psycho (eg personality traits etc) social approach
- Genes vs environment (eg drugs, psychosocial stressors, head injury etc etc)
- Personality: innate temperament + quality of early relationships + early life experiences

**Treatment of Psychiatric Illness**
- EM DR B.S. FRED:
  - Establish therapeutic alliance and shared understanding
  - MDT approach
  - Diagnosis: hx + exam + ix + DDx + consider ETOH and drugs + GMC + discuss with pt
  - Risks: determine, ?MHA, ?CATT
  - Biopsychosocial approach: drugs, psychotherapy, social interventions
  - Self-help: diet, exercise, sleep, hobbies, relaxation, ↓↓A & D
  - Formulation/Follow-up: response and drug SE
  - Referral/Recovery emphasis
  - Emergency contacts
  - Drugs: R/B/SE/why, how, what, when, start low, go slow

- Families should be involved:
  - Can encourage compliance
  - Can recognise early signs of serious treatment side effects
  - Can recognise impending symptoms of relapse
Mental Health in New Zealand

Epidemiology

- Prevalence
  - Severe mental illness: 3%
  - Chronic and/or disabling: 5%
  - Mild and/or transient: 19%
  - No mental health problems: 73% - includes up to 25% who don’t meet diagnostic criteria, but face disability in function. Source: Wilson 1997

- NZ Spending:
  - Mental illness: 8%
  - All other Illness: 92%

- Youth Problems in NZ
  - 17% have had a major depressive episode
  - 10% alcohol dependence
  - 11% social phobias
  - 3% attempted suicide

- Disorders commonly presenting in primary care:
  - Depressed mood
  - Anxiety
  - Unexplained physical symptoms
  - Cognitive disturbance
  - Substance Abuse
  - Sleep disturbance
  - Sexual dysfunction
  - Weight change or abnormal eating
  - Psychotic symptoms

- International (World Bank) – Disability Life Years Lost
  - Mental Illness: 17%
  - All other illness: 83%

- Christchurch psychiatric epidemiology study, adults from 18 – 64:

<table>
<thead>
<tr>
<th></th>
<th>Total Population</th>
<th>Male</th>
<th>Female</th>
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</thead>
<tbody>
<tr>
<td>Affective Disorders</td>
<td>9.4%</td>
<td>6.3%</td>
<td>12.4%</td>
</tr>
<tr>
<td>Substance Abuse</td>
<td>9.1%</td>
<td>15.4%</td>
<td>3.0%</td>
</tr>
<tr>
<td>Schizophrenia</td>
<td>0.2 (underestimates)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anxiety</td>
<td>8.4%</td>
<td>5%</td>
<td>12%</td>
</tr>
</tbody>
</table>

Maori Mental Health

- Reference: Trends in Maori Mental Health 1984 - 1993, Ministry of Maori Development
- Maori admission rates compared with Pakeha: females similar, Maori males 2 times pakeha
- Maori readmission rates have grown faster than non-Maori. Maori males 2 times more likely to be readmitted
- By specific diagnoses:
  - Maori drug and alcohol first admission rates rising relative to non-Maori
  - Maori admission rates for schizophrenia are similar to pakeha, readmission rates are higher
- Maori more likely to be referred to mental health services by welfare or law agencies than by a doctor (opposite for Pakeha)
- Maori more likely to be compulsorily admitted
- Issues:
  - Maori view of mental health and illness vs. Western psychiatric paradigm
  - Specifically Maori services
  - Maori workforce development
- Issues in treating a Maori patient:
  - Uncertain identity and alienation from society → distrust of practitioner
  - Must use interventions that enhance a Maori sense of well-being. Whanau must be basic unit of service delivery. Therapeutic alliance is with whole family, not just patient
  - Complexity of problems → lots of agencies involved in care (eg illness, substance use, poverty)
Aetiology of Psychiatric Disorders

- The 4 p’s (3 really, as the last is for protective factors): predisposing, precipitating, perpetuating, protective

**Predisposing Factors**

- Determine a person’s vulnerability to psychological distress. Causes include:
  - **Genetic endowment** (e.g., strong genetic component in psychosis)
  - **Environment in utero** → minor damage to CNS
  - **Personality: innate temperament/quality of early relationships/early life experiences**: combination of genetic, uterine development, childhood experiences (physical, psychological, social), adolescence.
    Particular personalities are prone to certain disorders. Eg early obsessional traits may → obsessive-compulsive disorders

**Precipitating Factors**

- Factors that occur shortly before the onset of the disorders and are likely to have caused it. Eg:
  - **Biological**: hypothyroidism, drugs, drugs of abuse, head injury, other injury
  - **Psychological**: eg loss of self-esteem owing to relationship or financial catastrophe
  - **Social**: eg moving house, changing job, family disturbance

**Perpetuating Factors**

- Factors that prolong the course of the disorder: eg secondary demoralisation, personality traits, GMC etc

**Protective Factors**

- Factors protective against psychological distress eg close family relationships, adaptive coping strategies, job etc
- Those strengths that have allowed the pt to continue functioning despite adverse experiences

**Psychiatric Aspects of Physical Illness**

- The most common psychiatric illnesses in physical illness are mood disorders and acute organic mental disorders
- Occur in one of three ways:
  - 1. Psychological distress can precipitate mental illness
  - 2. Physical distress can cause psychological ill-health (as can the medicines for physical disease)
  - 3. Physical and psychological disorders may exist simultaneously and independently (especially in the elderly)
- Pain: a common medical symptom. Can cause (eg head, neck, lower back, abdomen, genitalia) or arise from psychological disturbance (eg facial pain – antidepressant therapy can be effective).

**Psychiatric Issues for Patients with Chronic Physical Illnesses**

- Studies have provided evidence of a strong link between mental illness, mental health, and physical health, especially as it relates to chronic disease occurrence, course, and treatment
- Depression has been shown to affect the occurrence, treatment, and outcome of several chronic diseases and conditions, including heart disease, diabetes, hypertension, cancer, and obesity
- Depression is more common in ALL disease groups than in the general population
- **Anxiety** is more common in people with heart disease, stroke and cancer than in the general population
- Depression commonly develops after a stroke, especially after a stroke affecting the left hemisphere of the brain
- Approximately 1 in 6 persons who have experienced an MI suffer from major depression, and at least twice that many experience significant depressive symptoms
- Among cancer patients judged terminally ill, 53% met psychiatric diagnostic criteria, with delirium being the most frequently diagnosed disorder
- In addition, 21% cancer patients are reported to be depressed
- The presence of physical conditions is a risk factor for suicidal behavior even in the absence of mental disorder. Epilepsy was the physical condition most strongly associated with the suicidal outcomes. Physical conditions were especially predictive of suicidality if they occurred early in life. As the number of physical conditions increased, the risk of suicidal outcomes also increased
Psychiatric History

Summary

- Observation is key!
- Suicide assessment:
  - **Predisposing** factors: family history of suicide, psych illness, or alcohol & drug, personality, childhood and developmental difficulties, suicide exposure, other illness, environment (eg living alone, isolated), age and sex
  - **Precipitating** factors (short-term risk factors): major/stressful life event, current mood, thoughts about the future, mental state (eg psychosis, judgement, impulsivity), alcohol and drug use, current plans, expectations of outcome, availability and lethality of method
  - **Protective** factors: cognitive flexibility, strong social supports, hopefulness, treatment of disorders, responsibility for children
- For screening for psychiatric illness in teenagers see SHEADSSSS Risk Assessment, page 1009

In a Nutshell

- **Setup**: room for safety
- **Introduction** and **CONFIDENTIALITY** (everything we talk about is between you, me and the team looking after you)
- **PC**: what sorts of problems are troubling you/were troubling you when you came into hospital? **What do you think is going on?**
- **HPC**: SOS:
  - What’s been going on?
  - Severity: impact on life/function
  - Onset: what brought this on? What do you think is going on?
  - Supports: do you have anyone you talk to about all this?
- Systems enquiry: CAMP SAND:
  - **Cognitive** (any problems with your memory? or your thinking? Do you know where you are? Time? Person?);
  - **Anxiety** (do you have lots of things that you’re worried about? Is that par for the course for you, would you describe yourself as a worrier? Do you ever feel really panicky? feelings of apprehension, worry, fear, do you avoid things because of these? Feelings of of impending doom/death, thoughts that keep coming to mind, find yourself doing things over and over like checking/cleaning, any fears?);
  - **Mood** (how would you describe your mood over the past few weeks?);
  - **Psychotic symptoms** (any unusual thoughts, preoccupations that others find strange? any visions, sensations, thoughts that are unusual or that others don’t experience? Are your thoughts all your own? Do you know what other people are thinking? Do other people know what you are thinking? Do you feel like you’re being watched/followed? See messages on TV/radio);
  - **Suicide** (have you had thoughts of hurting yourself? Or suicide? Any plans or the means to actually go through with it? Have you ever tried anything in the past? What stopped you? Or thoughts about harming others?)
  - **Alcohol and drugs**
  - **Neurophysiological** (SAD SPACE Guidelines)
  - **Development** (any problems during birth? How was your childhood/school/family life/relationships/law/religion/sex?)
- **Past psychiatric history**: Have you had any psychiatric treatment before? Is the present illness like the previous one? Any problems in the past with A & D?
- **PMHx**
- **Meds/allergies**
- **FHx**:
  - Who’s in your family? Get on well with them? Any problems?
  - Any family problems with breakdown, admission to psychiatric hospital, on medications etc?
- **SHx & personal history**:
  - Tell me a bit about your childhood and background? What are the important things you remember?
  - Do you know of any problems with your birth? Any problems during childhood/adolescence/adulthood?
  - Sexual, marital, children, friendship, law, religion etc
- **Mental state**: ASEPTIC
Formulation: “Why does this pt suffer from this problem at this point in time?”. Predisposing, precipitating, perpetuating, protective factors taking a biopsychosocial approach

History

Safety: ABCDE: assistance available, be prepared/alert/aware, chairs in correct position/chaperone, dangerous objects removed, exits accessible

Confidentiality is important – mention it
➢ But it is not between the pt and the student – b/w the pt and the team, else can run into issues eg with suicide confessions

Follow up on what the pt says: they may say, “I’ve been feeling a bit down lately”, ask them what they mean by that; listen for the clues/cues from the pt

This will include the patient’s narrative, and is therefore subject to revision and embellishment according to the state of mind of the individual and the relationship with the interviewer. The patient may adjust the history according to the interviewer’s hypothesis and values. History taking is therefore collaborative and therapeutic. It is helping to construct the illness story

Explain purpose of interview, that it will take some time, note taking, etc

Introduce each new topic with open-ended questions

Summarise at the end, ask if there’s anything else the pt wants to add

Clear conclusion and follow-up plan

Identifying Data

➢ Name, date of interview, age, sex, race, country of birth, occupation, date of hospital admission, marital status

➢ Use as opportunity to put the patient at ease, build rapport

Reasons For and Circumstances of Referral/Admission

➢ Who made the referral, why now, what expectations

List of Presenting Symptoms and Their Duration

➢ List each symptom and duration, use patient’s own words

➢ Is the situation acute or chronic

Suggested questions:
➢ What sort of problems are troubling you/were troubling you when you came to hospital?
➢ What have been the main difficulties?

History of Current Illness

➢ Need to know the patient’s story: patient’s situation and preceding/precipitating events

➢ Narrative account of development of symptoms

➢ Include medication and compliance

Suggested questions:
➢ When did you last feel well?
➢ What are the worst worries in your life?

➢ Onset, course and progression, precipitating, perpetuating factors, effects on everyday life, treatments so far, previous episodes

Systematic Enquiry

➢ Should screen for all these in every patient

➢ Anxiety Symptoms:
➢ See History Taking in Anxiety Disorders, page 701
➢ ASK: Feelings of apprehension or fear, panic, excessive worrying or avoidance

➢ Mood Symptoms:
➢ ASK: “how would you describe your mood?” Symptoms of depression or mania, such as depressed or elevated mood, psychomotor changes, socially indiscreet behaviour
➢ Refers to long-term/sustained emotional state (ie over last week/months) and is subjective experience of the patient
➢ Prevailing mood at the time: quality (eg depressed, sad, angry, irritable, happy, elated, suspicious, perplexed, anhedonia), intensity (ask about extremes), reactivity, duration (when was it last normal)
➢ Persisting or fluctuating; if so what pattern
➢ Aggravating or relieving factors
➢ Associated symptoms
- **Patient’s attribution of mood**

- **Psychotic symptoms:**
  - Thought disorder, delusions or hallucinations

  - Thought disorder = abnormalities in the thinking process – evidenced by disorganised speech, thinking or behaviour
  - Delusions:
    - Fixed, false belief held with conviction, without evidence and are culturally inconsistent
    - Fixedness is key, resisting coercion to change, and preoccupying
  - Hallucinations = abnormal perceptual phenomena in the absence of external stimuli. Ask about visions, sensations, noises that are unusual or not shared by others

- **Suicidibility** or other dangerous behaviour: See Suicide Assessment and Management, page 693
  - *ASK:* “ever had thoughts about ending it all?” “ever had thoughts about harming others?”
  - *If yes:* “gosh, things have obviously been really hard for you, can you tell me some more about what’s been going on for you?”

- **Cognitive functioning:** See Cognition, page 690
  - *ASK:* memory loss, full name, where they are, time, etc

- **Neurophysiological changes:**
  - Measure severity of primary process
  - *ASK:* changed sleep, energy/motivation, concentration, appetite/weight (look for a 5% change over several weeks), sex
  - Sleep: initial, middle, terminal phases, how much in total, is it restful

- **Alcohol or drug use:**
  - Present or past
  - Smoking, alcohol, illicit drugs, sleeping tablets/tranquillisers

- **Stressors**

- **Medications and Compliance**

- **Impulse-Control Screen**: Screen for gambling (comorbidity of gambling with other psycyh symptoms is common)

### Past Psychiatric History

- Dates, duration, diagnoses, treatment, response to treatment and outcome

- Suggested questions:
  - *Have you had any psychiatric treatment before?*
  - *Is the present illness like the previous one?*

### Previous Medical History and Medications

- Past serious illnesses, disabilities, current illnesses and medication

### Family History

- **Parents and siblings**: age, state of health (mental & physical), occupations, situation, personalities, relationship to patient. May help to draw up a family tree

- Get idea of family atmosphere during childhood: personalities of parents and relationships have lasting influence on subsequent relationships. How much care did you get from each parent? How controlling/protective were they?

- Ask about grandparents, and parents up-bringing

- *ASK:* who is in the family? Which are the most important relationships? Has anyone in the family been treated for nerves, had a breakdown, been admitted to a psych hospital, committed or attempted suicide, had an A & D problem?

- Categorise under:
  - Structure of family
  - Description of key people
  - Description of important relationships
  - Family roles
  - Family history of psychiatric illness or alcohol abuse
Social & Personal History

- Important events and influences in patient’s life
- Start open ended: Tell me a bit about your childhood and background? What are the important things you remember?
- Birth: difficulties, parents situation at time
- Childhood: family situation, illnesses, injury, nervous symptoms (eg enuresis/bedwetting, fears, phobias, how did they feel going to school, etc). Did you ever have any unpleasant experiences – did anyone ever harm you, hurt you, interfere with you sexually?
- School: primary to tertiary. Academic, sporting, relationships with peers and teachers
- Employment: types of jobs, reason for leaving, work performance & satisfaction, relationships at work
- Sexual: age at puberty, sexual orientation, sexual experience (current and past), sexual satisfaction, contraception, sexual abuse, unpleasant or distressing sexual experiences. Introduce when talking about adolescence. Aim is to establish abnormalities or concerns about sexual functioning or relationships
- Marital: duration of courtship, age at marriage, age, occupation and health of spouse, marital relationship and problems
- Children: pregnancies, ages and names of children, health, personalities, schooling, occupations, difficulties in relationship with parent
- Friendships: long-standing friends and confidences
- Current living situation and finances
- Difficulties with law
- Leisure activities and interests
- Religion: upbringing, beliefs and practices, changes in religious belief (important to ask, won’t volunteer)

Premorbid Personality

- Patient’s opinions and interviewer’s impressions of premorbid personality
- Personality = enduring characteristics, so requires evaluation over time

Patient’s Attribution of Illness

- What the patient thinks is the cause of the illness
- Possibly include under ‘insight’ in mental state exam

Mental State

- Insert Mental State Exam write-up here (See Mental State Examination, page 688)
- ASEPTIC

Formulation

- Core of the psychiatric assessment: why did this person become ill in this way at this time?
- Opinion about what explains the presentation and what treatment may work
- Manner in which patient’s problems are unique. Not a summary of problems but the crucial factors, based on a theoretical knowledge of the aetiology of psychiatric illness. The linkages/connections between different aspects should add something new – all the raw material should have been presented before
- Should cover the 4 Ps: predisposing factors, precipitating factors, perpetuating factors, protective factors
- Conceptualise by filling in this table:

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<thead>
<tr>
<th></th>
<th>Predisposing</th>
<th>Precipitating</th>
<th>Perpetuating</th>
<th>Protective</th>
</tr>
</thead>
<tbody>
<tr>
<td>Biological</td>
<td></td>
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</tr>
<tr>
<td>Psychological</td>
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</tr>
<tr>
<td>Psychosocial</td>
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</table>

- Suggested outline (one paragraph per bullet):
  - Paragraph 1: Describe problem
  - Paragraph 2: Why is this patient at risk of a psychiatric illness, using bio-psycho-social framework
  - Paragraph 3: Describe triggers to presentation
  - Paragraph 4: Describe relevant prognostic factors, positive and negative
  - Paragraph 5: Balanced assessment of risks: especially of suicide and violent behaviour

Diagnosis and Differential Diagnosis

- Manner in which patient’s problems are similar to others (cf formulation which emphasises uniqueness)
- Usually presented using DSM-IV or ICD-10. (See DSM-IV-TR Classification, page 696)
- In differential diagnosis: **concisely state evidence for and against** each possible diagnosis in order of probability – only include evidence that discriminates between diagnoses
• Don’t forget general medical conditions if there is sufficient evidence

Management Plan
• **Safety**: how will the risks identified be contained or minimised. Is the patient consenting or committed?
• **Medical**: any medical conditions requiring attention
• **Diagnosis**: is it clear? If not, what needs to be done?
• **Psychiatric Management**: can be divided into management of target symptoms and management aimed at underlying disease. Can be considered under bio-psycho-social headings. Divide into timeframes – now, the next day or two, longer term
• Always mention family in plan: information and support for them, their role in helping the patient, assistance with the significant stresses the family may face, etc
• Consider using this approach:

<table>
<thead>
<tr>
<th>Biological</th>
<th>Psychological</th>
<th>Social</th>
</tr>
</thead>
<tbody>
<tr>
<td>Short term</td>
<td>Eg change antipsychotic to</td>
<td>Eg support pt + family + educate about schizophrenia etc</td>
</tr>
<tr>
<td>Medium term</td>
<td>Eg monitor response to...</td>
<td>Eg support group, family therapy</td>
</tr>
<tr>
<td>Long term</td>
<td>Eg pt finding confiding relationship</td>
<td>Eg pt finding confiding relationship</td>
</tr>
</tbody>
</table>

Experience Interviewing the Patient
• Difficulties interviewing the patient, reactions/emotions evoked by patient, how you dealt with these

Mental State Examination
• Like a physical examination
• This is NOT an assessment of cognitive function (the mini-mental state is about cognitive function, but is just part of a description of mental state)
• 7 headings: **ASEPTIC**:
  - Appearance + behaviour
  - Speech
  - Emotion (mood and affect)
  - Perception
  - Thoughts
  - Insight
  - Cognition

Appearance and Behaviour
• **General appearance**: age, physique, hair, make-up, tattoos, scars, clothing (self neglect, incongruous dress, weight loss)
• Facial expression: suggestion of depression, anxiety, physical disorder (eg parkinsonian syndrome)
• Posture
• Abnormal movements:
  - Mood
  - Involuntary movements (tics, dystonia [an unpleasant spasm of muscle groups], akathisia [restless legs], tardive dyskinesia [involuntary movements of the tongue, lips, face, trunk, and extremities that occur in patients treated with long-term dopaminergic antagonist medications], parkinsonism)
  - **Psychomotor agitation** (eg how long to answer a question)
• Level of consciousness
• **Attentiveness**: distractability, internal preoccupations
• Social behaviour: overfamiliar, disinhibited, withdrawn, preoccupied, co-operative or not, bizarre behaviour

Speech
• **Rate** – fast/slow
• **Amount/quantity** – a lot/little
  - Pressure = ↑ quantity and rate of speech, difficult to interrupt
  - Poverty of speech = ↓ quantity of speech
  - Mutism
• **Volume** – loud/soft
• **Tone** – monotone/normal
• **Spontaneity**, Continuity, Articulation, Prosody, **Pressure**
Thinking

- The content is described under “Thoughts”
- Ability for speech: dysarthria, dysphonia, dysphasia

**Thinking**

- Thinking is a goal directed flow of ideas, symbols and associations initiated by a problem or task and leading towards a reality-oriented conclusion
- Form of thought disorder = Formal thought disorder *(cannot form logical, structured thought)*, see below
- Thought form/process:
  - May be best demonstrated by direct quote (ie write verbatim what they say to demonstrate abnormal thought form)
  - Is there a linear, logical connection between ideas or not – from an opening statement through to a goal
  - Then define type of thought process, eg:
    - Circumstantiality
    - Loosening of association/word salad
    - Flight of ideas (ie mania)
    - Derailment
    - Tangential (talks at great length but never gets to the point)
    - Interpenetration of themes (rapid change to something completely different)
    - Poverty of thought
    - Neologisms
    - Blocking/thought block (stops mid thought)
- Thought content = “DROPS”
  - Depersonalisation/derealisation/delusions
  - Recurrent themes
  - Obsessions (± compulsions)
  - Phobias
  - Suicidal thoughts
- Thought content:
  - Depersonalisation: *feeling detached from oneself*, feeling unreal (often with anxiety)
  - Derealisation: *feelings of unreality of the external world*
  - Spectrum: ideas → concerns → preoccupations → overvalued ideas → obsessions → delusion. Note different levels of conviction:
    - Over-valued idea: I think it but accept that others don’t
    - Preoccupations
    - Obsessional: I know it’s not true but I can’t get it out of my head
    - Delusional: I think that, and everyone else thinks that, and I don’t believe them if they say they don’t
    - Phobias
    - Suicidal and homicidal ideation: see Suicide Assessment and Management, page 693
- Obsessional phenomena:
  - Obsessional thoughts: “any thoughts keep coming repeatedly into mind, even when you are trying to get rid of them?”
  - Compulsive rituals: “do you ever have to repeat actions over and over which most people would only do once?”

**Mood and Affect**

- Mood:
  - “How would you describe your mood over the past few weeks (ie in terms of happiness or sadness)?”
  - The patient’s subjective description, what they report
  - Pervasive and sustained emotion (eg over at least 2 weeks)
  - Verbatim recording (record word for word): depth, intensity, duration, fluctuations
  - NB sad = specifically down about something in particular; depressed mood = pervasively down about everything
  - Ask:
    - How they see themselves, how they see the world, how they see the future
    - Sense of hope or hopelessness
    - When was your mood last normal?
    - Anything make it better or worse?
    - Vegetative symptoms (hypothalamic, physiological): appetite, sleep, libido, constipation, energy
Psychological Medicine

- **Anhedonia** (lack of enjoyment for life)
- Temper, agitation, irritability
- Feelings of worthlessness
- **Suicide**: see below

➤ Might be easier to move onto questions about suicide: “have you ever thought that you would be better off being dead?” not “I ask all my pts this...”

➤ Mood descriptors:
  - Mania, hypomania
  - Euthymia, hyperthymia, hypothyymia
  - Depression
  - Alexithymia (unable to understand, process or describe emotions)
  - Dysthymia

- Affect:
  ➤ **Refers to the objective appearance of emotions observed during the interview**: anger, anxiety, elation, irritability, depressed, etc
  ➤ **Reactive**, euthymic, dysthymic etc
  ➤ **Quality, intensity** (heightened, normal, blunt, flat), **stability, range**
  ➤ Variations: labile, restricted, blunted, flattened, inappropriate, fluctuating
  ➤ Appropriateness: *congruous* with thinking or not

**Perception**
- Hallucinations, illusions, and sensory distortions
- **Sensory distortion**: things look big, small or distorted
- **Illusions**:
  ➤ Misrepresentation of external environment – transformation without perception
  ➤ **Misperceptions of real objects** eg the curtain moved, there must be a person behind it

- **Hallucinations**:
  ➤ ASK: about visions, sensations, noises that are unusual or not shared by other people
  ➤ **External perception without any external stimulus**. Hearing voices inside your head is not a hallucination – they should hear them as coming from outside their head
  ➤ Can be auditory, visual, olfactory, tactile or taste
  ➤ If auditory, clarify characteristics: sounds or voices, one or more voices, **talk to you or to each other**, give commands, **do you recognise them, believe them**. Can be **second person** (”what are you doing, silly fool”) or **3rd person**: “look at him; what a fool”

- **Delusions**:
  ➤ ASK: about any unusual concerns, thoughts? thoughts that others find strange?
  ➤ Evaluating delusions: Describe unusual statement, experience or event, decide if it is false, is there any cultural determination, classify it
  ➤ Explore delusions thoroughly to determine if they are indeed delusions rather than perhaps just an overvalued thought (see thought content below)
  ➤ Passivity phenomena/control:
    - **Thought insertion**: reports ‘alien’ thoughts. Are your thoughts all your own?
    - **Thought broadcast**: thoughts transmitted to other people. Do other people know your thoughts?
    - **Thoughts spoken aloud**: feels as if thoughts are audible to others. Can other people hear what you’re thinking?
    - **Thought echo**: involuntary repetition of thoughts
    - **Thought withdrawal**
  ➤ Delusional mood
  ➤ Delusional perception: perception + delusional interpretation
  ➤ Paranoid delusions: Is anyone trying to harm you?
  ➤ Referential delusions: have you noticed anything (eg on TV) that refers to you
  ➤ Grandiose delusions, sexual delusions
  ➤ Delusions of guilt, hypochondriasis, nihilism
  ➤ Delusions of misidentification and misrepresentation: refers to the belief that people have been replaced by impostors

**Cognition**
- See also Mental State Exam175, page 180
- Briefly:
Psychological Medicine

- Level of consciousness
- Orientation: time, place, person
- Attention + concentration: serial sevens, day or month of the year backwards
- Memory
- MMSE

- Is defined by how we assess it!
- Can test with Mental Status tests, etc
- Observe alertness, attention and concentration (serial sevens, spell ‘world’ backwards, days or months backwards), orientation (time, place and person), memory, executive function, localised functions
- Testing memory: short term – recollection at 5 minutes, recent memory – events over past several days (adapt to patient’s interests), remote memory – personal events, birth date, sequence of events [NB – this classification is really an artefact – it doesn’t correlate with how memory works]
- Language: word finding, comprehension, reading, writing
- Calculation: needed for getting change, paying bills
- Visuospatial: dressing, finding way around, neglect, problem for driving
- Visual perception: can’t recognise what they see
- Personality change: usually exaggerates or ameliorates premorbid state: motivation, spontaneity, persistence, care, social conduct, quality of relationship, aggression
- Problem solving ability
- Consider in the context of ADLs and Instrumental ADLs (eg using phone)
- If confused may need to interview an informant
- Patient will usually water down symptoms

Insight and Judgement

- Awareness of their own mental condition, do they recognise the reasons for their difficulties
- Full, partial, limited, grossly impaired
- Base around 4 questions:
  - Are they aware of the phenomena others have observed
  - If so, do they recognise them as abnormal
  - If so, do they consider they are caused by mental illness
  - If so, do they need treatment
- Judgement:
  - Estimate the patient’s judgment based on the history or on an imaginary scenario. To elicit responses that evaluate a patient’s judgment adequately, ask the following question. “What would you do if you smelled smoke in a crowded theater?” (good response is “call 111” or “get help”; poor response is “do nothing” or “light a cigarette”)

RCH MSE

- Background
  - MSE is a systematic appraisal of the appearance, behaviour, mental functioning and overall demeanor of a person. In some ways it reflects a “snapshot” of a person’s psychological functioning at a given point in time.
  - A MSE is an important component of the assessment of a patient.
  - Most of us intuitively perform many parts of a MSE every time we interact with or observe others.
  - Observations of person’s mental state are important in determining a person’s capacity to function, and whether psychiatric follow-up is required.
  - Judgements about mental state should always consider the developmental level of the person and age-appropriateness of the noted behaviour(s).
  - If there is any indication of current suicidal or homicidal ideation the person must be referred for risk assessment by a qualified mental health clinician.
- Appearance:
  - A person’s appearance can provide useful clues into their quality of self-care, lifestyle and daily living skills.
    - distinctive features
    - clothing
    - grooming
    - hygiene
- Behaviour:
As well as noting what a person is actually doing during the examination, attention should also be paid to behaviours typically described as non-verbal communication. These can reveal much about a person’s emotional state and attitude.
  - facial expression
  - body language and gestures
  - posture
  - eye contact
  - response to the assessment itself
  - rapport and social engagement
  - level of arousal (e.g. calm, agitated)
  - anxious or aggressive behaviour
  - psychomotor activity and movement (e.g. hyperactivity, hypoactivity)
  - unusual features (e.g. tremors, or slowed, repetitive, or involuntary movements)

- Mood and affect:
  - It can be useful to conceptualise the relationship between emotional affect and mood as being similar to that between the weather (affect) and the season/climate (mood). Affect refers to immediate expressions of emotion, while mood refers to emotional experience over a more prolonged period of time.
  - **Affect:**
    - range (e.g. restricted, blunted, flat, expansive)
    - appropriateness (e.g. appropriate, inappropriate, incongruous)
    - stability (e.g. stable, labile)
  - **Mood:**
    - happiness (e.g. ecstatic, elevated, lowered, depressed)
    - irritability (e.g. explosive, irritable, calm)
    - stability

- Speech:
  - Speech can be a particularly revealing feature of a person’s presentation and should be described behaviourally as well as considering its content (see also section on Thoughts). Unusual speech is sometimes associated with mood and anxiety problems, schizophrenia, and organic pathology.
    - speech rate (e.g. rapid, pressured, reduced tempo)
    - volume (e.g. loud, normal, soft)
    - tonality (e.g. monotonous, tremulous)
    - quantity (e.g. minimal, voluble)
    - ease of conversation

- Cognition:
  - This refers to a person’s current capacity to process information and is important because it is often sensitive (though in young people usually secondary) to mental health problems.
    - level of consciousness (e.g. alert, drowsy, intoxicated, stuporous)
    - orientation to reality (often expressed in regard to time/place/person - e.g. awareness of the time/day/date, where they are, ability to provide personal details)
    - memory functioning (including immediate or short-term memory, and memory for recent and remote information or events)
    - literacy and arithmetic skills
    - visuospatial processing (e.g. copying a diagram, drawing a bicycle)
    - attention and concentration (e.g. observations about level of distractibility, or performance on a mentally effortful task – e.g. counting backwards by 7’s from 100)
    - general knowledge
    - language (e.g. naming objects, following instructions)
    - ability to deal with abstract concepts (e.g. describing conceptual similarity between two things).

- Thoughts:
  - A person’s thinking is generally evaluated according to their thought content or nature, and thought form or process.
    - **Content:**
      - delusions (rigidly held false beliefs not consistent with the person’s background)
      - overvalued ideas (unreasonable belief, e.g. a person with anorexia believing they are overweight)
      - preoccupations
      - depressive thoughts
      - self-harm, suicidal, aggressive or homicidal ideation
- **Obsessions** (preoccupying and repetitive thoughts about a feared or catastrophic outcome, often indicated by associated compulsive behaviour)
  - Anxiety (generalised, i.e. heightened anxiety with no specific referent; or specific, e.g. phobias)
    - **Process:**
      - Thought process refers to the formation and coherence of thoughts and is inferred very much through the person’s speech and expression of ideas.
      - highly irrelevant comments (loose associations or derailment)
      - frequent changes of topic (flight of ideas or tangential thinking)
      - excessive vagueness (circumstantial thinking)
      - nonsense words (or word salad)
      - pressured or halted speech (thought racing or blocking)
- **Perception:**
  - Screening for perceptual disturbance is critical for detecting serious mental health problems like psychosis (this is relatively rare in young people, though peak onset is between 19 and 22 years), cases of severe anxiety, and mood disorders. It is also important in trauma or substance abuse. Perceptual disturbances are typically marked and may be disturbing or frightening.
    - **Dissociative symptoms:**
      - derealisation (feeling that the world or one’s surroundings are not real)
      - depersonalisation (feeling detached from oneself)
    - **Illusions:**
      - the person perceives things as different to usual, but accepts that they are not real, or that
      - things are perceived differently by others
    - **Hallucinations:**
      - probably the most widely known form of perceptual disturbance
      - hallucinations are indistinguishable by the sufferer from reality
      - can affect all sensory modalities, although auditory hallucinations are the most common
      - in children it is common to experience self-talk or commentary as an internal “voice”
      - command hallucinations (voices telling the person to do something) should be investigated
      - important to note the degree of fear and/or distress associated with the hallucinations
- **Insight & Judgement:**
  - Insight and judgement is particularly important in triaging psychiatric presentations and making decisions about safety.
    - **Insight:**
      - acknowledgement of a possible mental health problem
      - understanding of possible treatment options and ability to comply with these
      - ability to identify potentially pathological events (e.g. hallucinations, suicidal impulses)
    - **Judgement:**
      - refers to a person’s problem-solving ability in a more general sense
      - can be evaluated by exploring recent decision-making or by posing a practical dilemma (e.g. what should you do if you see smoke coming out of a house?)

**Suicide Assessment and Management**

- **Always** screen all psychiatric patients for suicide
- **Definitions:**
  - **Attempted suicide:** self-inflicted harm intended to cause death
  - **Parasuicide:** act intended to communicate distress NOT intended to cause death (more common than attempted suicide)
  - **Self-mutilation:** self-inflicted injury, which is often ritualistic or repetitive, and is neither intended to cause death nor to appear that way

**Suicide History**

- **Overview:**
  - Establish and maintain rapport → engage with the pt!
  - Evaluate for:
    - TIP OFF
    - Suicidal thinking
    - Suicidal intent
    - Suicidal plans/previous attempt?
    - Organised plan?
- **Future** orientation: plans for future etc
- **Freakin'** crazy: delusions, hallucinations etc
- Relevant mental status: including mood, drugs/alcohol, labile, impulsiveness, insight, etc

- Assessment of risk factors

- **Ideation questions:**
  - Have you ever considered harming yourself/wanted to end your life?
  - Do you see a future for yourself?
  - Do you think a lot about death?
  - What specifically have you thought about this? When did you start thinking this way?
  - Have you talked to anyone about this?
  - **Do you think that you actually want to die** – or do you want others to realise how bad things are for you?
  - Have you thought of a plan to kill yourself?
  - Do you have the means?
  - What has stopped you so far?
  - Have you thought about the effect your death would have on family and friends?
  - How do you feel about accepting help?
  - How does talking about this make you feel?
  - If can’t ask the question directly, then ‘what do you think about suicide’, ‘what would you do if it got that bad’, ‘how bad does it get… have you ever felt so bad that you wanted to end your life’
  - Have you thought of **hurting anyone else**?

- **Past Suicide attempt(s):**
  - **What** did you do?
  - When did you start thinking about suicide? **Why** did you think that?
  - **When** did you plan to do something? (ie was it **impulsive or planned**)
  - When did you start to action the plan? What triggered that (what was the final straw)?
  - Did you leave a note/say goodbye/wind up your affairs?
  - **What stopped you** going through with it?
  - How did you get to be in hospital?
  - Are you surprised to be alive? (ie did they genuinely think it was going to kill them)
  - Has anything changed in the things that made you try?
  - What did you feel about getting help?

- **Screen for symptoms (use CAMP SAND):**
  - **Depression:**
    - Have you been feeling down in the dumps/very sad?
    - Have you lost interest/ability to enjoy yourself?
  - **Anxiety/panic:**
    - Have you been feeling very tense or anxious?
    - Have you been worrying a lot about things?
    - Do you ever get overwhelming anxiety/dread that something awful is going to happen?
  - **Psychosis:**
    - Have you had any thoughts that are unusual for you and that other people would find unusual?
    - Have you had the feeling that people are talking about you/have it in for you?
    - Have you heard any unusual voices/experiences?
  - Ask about:
    - Changes in sleep, appetite, weight, energy, concentration
    - Severity: how are you coping at work etc
    - Stressors: has **anything happened recently** to trigger these problems?
  - Background psychiatric hx, PMHx, meds, **alcohol and drugs**, FHx, personal history

**Examination**
- Ensure mental status examination done
- Physical examination is essential:
  - Look for physical stigmata and sequelae of presenting suicide attempt
  - Signs of alcohol or BZD withdrawal
  - Evidence of undisclosed OD
  - Scarring from previous attemps/self-mutilation

**Investigation**
- Ix specific to the self-harm attempt
• Therapeutic drug levels where appropriate
• Blood alcohol level
• Urine drug screen

Assessment of Risk

• SAD PERSONS (sex, age, depression, previous attempt, ethanol/other substance abuse/ethnicity, rational thinking impaired/psychosis, social support lacking, organised plan, no spouse, sickness: psych and medical)

• Predisposing Risk Factors:
  ➢ Present from birth or soon after:
    o Sex: Female more likely to try, male more likely to succeed
    o Genetic or congenital factors
    o Family History of suicide, psychiatric illness or substance abuse
    o Personality Traits (eg impulsiveness, perfectionism, hopelessness, low self esteem)
  ➢ Risk Factors developed later in life:
    o Suicide exposure
    o Psychiatric diagnosis: depression, substance abuse (esp. age 40 – 60) and schizophrenia show strongest correlation
    o Other illness
    o Previous suicidal intents: include factors listed above, type and frequency of ideation, etc
    o Environmental factors: separated, living alone, elderly, isolated, unemployed
    o High risk situations: eg young males

• Protective Factors: decrease risk:
  ➢ Cognitive flexibility
  ➢ Strong social supports
  ➢ Hopefulness
  ➢ Treatment of disorders
  ➢ Responsibility for children
  ➢ Are there other things that would stop them?

• Precipitating Factors: short term risk factors:
  ➢ Humiliating/precipitating life event: job loss, move, separation, death, interpersonal problems
  ➢ Post partum
  ➢ Recent discharge from a psychiatric hospital: a high risk time
  ➢ Current mood: depression increases risk significantly
  ➢ Thoughts and expectations about the future. Very important to assessing overall risk. Is the future hopeless? If they have nothing to live for, suicide is easier
  ➢ Mental State: mood, psychosis (→ impaired judgement, voices may tell them to do it, paranoia), judgement, impulsivity (be aware of effect of alcohol if person is sober when interviewed: when you drink, how do you feel afterwards)
  ➢ Current plan: detail, lethality (not how lethal it actually would be, but what did patient think would happen), fantasies (eg have they thought about other’s reactions to their death), expectations of outcome (eg do they want to be found?) Availability of method

High Risk

• Within the next 72hrs if:
  ➢ Recent serious attempt (ie method was potentially lethal/violent/well-planned/interrupted by chance) OR
  ➢ Remains fixed on wish to die or refuses treatment OR
  ➢ The presence of acute agitation due to depression, anxiety or psychosis OR
  ➢ Patient has had thoughts about suicide and intends to act on them OR
  ➢ If the patient is uncooperative and the assessment was incomplete OR
  ➢ If the following are present: psych illness, significant stress, history of impulsivity or violence, family history of suicide

Low Risk

• Within the next 72hrs if:
  ➢ 1. The pt attempted suicide that was clearly non-lethal, readily discovered or discussed and the pt has no intent to repeat the attempt. The pt can identify this as a cry for help and willingly accepts treatment
  ➢ 2. The pt has suicidal thoughts but no intention of acting on them and actively seeks appropriate help with a specific problem seen as the root cause of the suicidal thoughts
  ➢ 3. Other significant psychopathology have been excluded (eg depression, psychosis)
4. The patient does not have longstanding personality problems
5. The pt has a supportive social network
6. The pt is cooperative with the assessment and follow-up plans

**Influence of Community Standards and Norms on Suicide**

- **Individualism**: you’re a failure if you can’t make it on your own
- **Copy cat** syndrome
- Expectations of achievement → individuals set high expectations and fail
- Community encourages the use of weapons
- Community **demeans the poor** → see themselves as unimportant
- Community encourages external locus of control → can’t change anything ⇒ fatalism
- Community encourages/condones suicide in certain circumstances
- People with certain conditions alienated, eg psych illness
- **Minority culture alienated** by enforced dominance of the dominant group’s beliefs and values (hegemony) → alienation

**Management of Current Suicide Risk**

- For a high risk:
  - Emergency assessment (eg CAT team) followed by regular nursing assessment
  - Pt should not be allowed to leave hospital until this has been completed
  - If the pt refuses, you should contact the mental health crisis team and arrange to start mental health act proceedings → you can ask a registered nurse to complete Section of the MHA, which allows the pt to be detained for up to 6 hours for the purpose of a psych assessment. You need to complete a supporting medical assessment and to fill in the appropriate forms
  - Make sure the pt is not left unattended: get a nursing “special”
- For low risk:
  - Pts may be **discharged after discussion** with the crisis team/psychiatrist on call
  - They should receive mental health **follow up on the next working day**
- Further actions:
  - **Plan the next few days**: especially if a weekend, or they have poor social supports. Should be detailed, and given to the patient on paper to take home. Should include contact with other people and things the patient enjoys
  - Ensure **family member/responsible friend is available** explain to this person what has happened and that the pt is now safe but requires extra support until further professional assistance has been arranged. Tell them how to contact the MH crisis team
  - Encourage use of informal supports: whom can they talk to. If there is nobody, why do they feel like this?
  - Use **other services**: Lifeline, Youthline, Samaritans, community organisations, support groups, sports/hobby groups etc
  - Offer **follow-up**: opportunity to reassess patient, and provide further support
  - Consider **referral** to specialist care: Community Psychiatric Nurse, social worker, psychiatrist, psychologist, CATT
- Afterwards:
  - Liaise with other professionals
  - Discuss with another team member to review your risk assessment and management plan
  - **Be aware of your own response**: patients like these can cause considerable concern or evoke a strong emotional response

**Interviewing Aggressive Patients**

- Understanding why they are aggressive is important:
  - Poor anger control
  - Inappropriately managed
  - Overwhelmingly afraid
  - Most clients are afraid/confused by their own feelings
- Aggressive patients often try to change the ‘rules’ of the relationship between professional and client by trying to dominate. The interviewer must maintain the boundaries. If ‘rules’ are broken (eg threats, etc) → terminate the interview
- Interviewing tips:
  - Is it wise to interview them at all?
  - Get as much information about their history and current state before you start
Patient’s home most difficult environment
Ensure you and the client have direct access to a door
Appear confident!
Ensure there are no missiles (tea cups, ash trays)
Don’t sit eyeball to eyeball. Have the client in a low, soft chair
Have someone else sit in
Remain aware of client’s body language
Negotiate breaks with the client – take a walk in the corridor

Responses:
Set limits: “I can’t help you if you keep shouting”
Demanding patients: “Perhaps I need to know a bit more before I decide to…”
Reflection: “I can see that made you very angry”
“I just want to understand about what has made you so upset”

Evaluation:
Diagnose psychiatric disorder and assess mental state – especially paranoid states, command hallucinations, intoxicated, delirium, manic, depressed
History of violence, abuse, neglect
Who are intended victims
Emotional stressors
Quality of self control
External constraints on behaviour
Physical exam: old and new injuries

Sedation: if drug sedation is necessary:
Haloperidol 2.5 – 5 mg PO/IV and Clonazepam 2 mg PO/IM. Effect takes up to 20 – 30 minutes. Repeat at 30 minute intervals to maximum of 3 doses
If you forcibly restrain or medicate someone, should initiate Mental Health Act (otherwise it constitutes common assault)

DSM-IV-TR Classification
Published 1994, replaces Diagnostic and Statistical Manual of Mental Disorders III and III-R
TR = text revision
Allows us to be on the same page, guides treatment, gives pts a name for what they’re going through, for research purposes

Multiaxial Approach
The DSM-IV organizes each psychiatric diagnosis into five dimensions (axes) relating to different aspects of disorder or disability:
Axis 1: Clinical disorders eg major depression, adjustment disorder, schizophrenic disorder. Basis in medical model
Axis 2: Personality disorder or traits and mental retardation/intellectual disabilities. More blurred distinction between person and pathology
Axis 3: General medical conditions (physical disorders and conditions)
Axis 4: Psychosocial and environmental problems (eg severity of psychosocial stressors, problems with primary support group, social environment, educational, occupational, housing, economic, access to health care system)
Axis 5: Global assessment of functioning (eg in the previous year; 100 = perfect function, 0 = no functioning)
Axis I refers broadly to the principal disorder that needs immediate attention; e.g., a major depressive episode, an exacerbation of schizophrenia, or a flare-up of panic disorder. It is usually (though not always) the Axis I disorder that brings the person “through the office door.”
Axis II, we indicate the personality disorder that may be shaping the current response to the Axis I problem (or can be the reason for presenting). Axis II also indicates any developmental disorders, such as mental retardation or a learning disability that may be predisposing the person to the Axis I problem. For example, someone with severe mental retardation or a paranoid personality disorder may be more likely to be “bowled over” by a major life stressor, and succumb to a major depressive episode.
Axis III lists any medical or neurological problems that may be relevant to the individual’s current or past psychiatric problems; for example, someone with severe asthma may experience respiratory symptoms that are easily confused with a panic attack, or indeed, which may precipitate a panic attack.
- Axis IV codes the major *psychosocial stressors* the individual has faced recently; e.g., recent divorce, death of spouse, job loss, etc.
- Axis V codes the "level of function" the individual has attained at the time of assessment, and, in some cases, is used to indicate the highest level of function in the past year. This is coded on a 0-100 scale, with 100 being nearly "perfect" functioning.

### Diagnostic Classes

<table>
<thead>
<tr>
<th>Major Diagnostic Class</th>
<th>Examples of Disorders</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Disorders usually first diagnosed in infancy, childhood or adolescence</strong></td>
<td>Mental retardation, Specific Learning Disorders, Pervasive Developmental (eg Autistic), Attention Deficit and Disruptive Behaviour, Tic, Conduct Disorder</td>
<td></td>
</tr>
<tr>
<td><strong>Delirium, Dementia and Amnestic and Other Cognitive Disorders</strong></td>
<td>Delirium (eg due to GMC, substance intoxication or withdrawal), Dementia (eg due to Alzheimer’s, Vascular, HIV, Head Trauma, CID, Parkinson’s, Huntington’s). See Dementia, page 731 and Delirium, page 736</td>
<td>Some with specifiers for uncomplicated, with delirium, with delusions, with depressed mood</td>
</tr>
<tr>
<td><strong>Mental Disorders due to a General Medical Condition (GMC) not elsewhere classified</strong></td>
<td>Catatonic disorder or personality change due to …</td>
<td>Most of diagnostic classes have a category ‘due to a GMC’ where the symptoms fit that class – eg Mood Disorder due to a GMC</td>
</tr>
<tr>
<td><strong>Substance Related Disorders</strong></td>
<td>For most substances there are [Substance] Use and [Substance] Induced (including psychotic, mood, anxiety etc)</td>
<td>Specifiers include: with/without physiological dependence, full/partial/sustained/early remission, with onset during intoxication/withdrawal</td>
</tr>
<tr>
<td><strong>Schizophrenia and Other Psychotic Disorders</strong></td>
<td>Schizophrenia, Schizophreniform, Schizoaffective, Delusional, Brief Psychotic</td>
<td>Specifiers for Schizophrenia include paranoid, disorganized, catatonic, undifferentiated and residual types</td>
</tr>
<tr>
<td><strong>Mood Disorders</strong></td>
<td><strong>Depressive</strong> (Major Depressive Disorder – single episode and recurrent – and Dysthymic), <strong>Bipolar</strong> (Bipolar I &amp; II, Cyclothymic), Cyclothymia, Dysthymia</td>
<td>Some have specifiers for severity, psychotic, remission specifiers, chronic, with catatonic/melanchoic/atypical features, with post-partum onset, with seasonal pattern/rapid cycling</td>
</tr>
<tr>
<td><strong>Anxiety Disorders</strong></td>
<td>Panic (with/without agoraphobia), Agoraphobia (without panic), Specific Phobia, Social Phobia, Obsessive-Compulsive, Post Traumatic Stress, Acute Stress, Generalised Anxiety</td>
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</tr>
<tr>
<td><strong>Somatoform Disorders</strong></td>
<td>Somatization, Undifferentiated Somatoform, Conversion, Pain, Hypochondriasis, Body Dysmorphic, Somatoform</td>
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<tr>
<td><strong>Factitious Disorders</strong></td>
<td>Factitious Disorder with predominantly psychological/physical signs</td>
<td>Patients intentionally produce signs of medical or mental disorders and misrepresent their histories and symptoms. Have compulsive quality – but behaviours are purposeful and deliberate</td>
</tr>
<tr>
<td><strong>Dissociative Disorders</strong></td>
<td>Dissociative Amnesia, Fugue, Identity Disorder, Depersonalisation</td>
<td>Patient feels lack of unity in state of consciousness, confusion regarding their identity or multiple identities. Fugue = short-term amnesia</td>
</tr>
<tr>
<td><strong>Sexual and Gender Identity Disorders</strong></td>
<td>Sexual Dysfunctions (of desire, arousal, orgasmic, pain), Paraphilias (eg paedophilia), Gender Identity</td>
<td></td>
</tr>
<tr>
<td><strong>Eating Disorders</strong></td>
<td>Anorexia Nervosa (restricting or binge/purging type), Bulimia Nervosa (purging type, non-purging type)</td>
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<tr>
<td><strong>Sleep Disorders</strong></td>
<td>Primary Sleep (eg dyssomnias and parasomnias) and related to another mental disorder</td>
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<tr>
<td>Impulse-Control Disorders Not Elsewhere Specified</td>
<td>Eg Kleptomania, Pyromania, Pathological Gambling, Intermittent Explosive Disorder</td>
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<td>--------------------------------------------------</td>
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<tr>
<td>Adjustment Disorder</td>
<td>With depressed mood, anxiety, mixed, disturbance of conduct/emotions</td>
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<td></td>
<td>Where symptoms appear within 3/12 of an identifiable stressor. Should not meet criteria for another axis I or II disorder, &amp; excludes bereavement. <strong>A short-term maladaptive reaction to a stressor</strong> (ie impairs social/occupational function or causes distress).</td>
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</tbody>
</table>

| Personality Disorders                            | Paranoid, Schizoid, Schizotypal, Antisocial, Borderline, Narcissistic, Histrionic, Dependent, Avoidant, OCD. See Personality Disorders, page 760 |

| Other Conditions that may be a focus of clinical attention | Psychological factors affecting medical condition (eg mental disorder/personality traits/ maladaptive health behaviours affecting medical condition), medication-induced movement disorders, relational problems, problems related to abuse or neglect, Non-compliance, Malingering, Bereavement |

**Using DSM Diagnoses**

- In DSM III-R, “Delirium, Dementia and Amnestic and Other Cognitive Disorders”, “Mental Disorders Due to a General Medical Condition” and “Substance-Related Disorders” were grouped under the single heading “Organic Mental Syndromes and Disorders”. “Organic mental disorder” is no longer used as it implies other disorders don’t have a biological basis
- Qualifiers on Diagnostic codes:
  - Severity and course specifiers: **mild, moderate, severe**, in **partial remission**, in **full remission, prior history of** (ie have had full recovery)
  - Principal diagnosis/Reason for visit: if more than one diagnosis, which one was the principle one leading to admission/contact. Difficult to determine in dual diagnosis (substance related + non-substance related). Multiple diagnoses can be reported in multiaxial fashion
  - Provisional: when strong assumption that criteria will be meet, but insufficient evidence currently available
- Not-otherwise specified used when:
  - Symptoms below clinical threshold or there is an atypical or mixed presentation
  - Symptom pattern is not included in DSM IV
  - When there is **uncertainty about aetiology**: eg whether it is due to a general medical condition, is substance induced or is primary
  - There is incomplete or inconsistent information
- **Frequently used criteria** – to exclude or suggest differential diagnoses:
  - Criteria have never been/are not meet for...
  - Does not occur exclusively during the course of...
  - Not due to the direct physiological effects or a substance of a general medical condition – ie these have had to have been considered and ruled out
  - Not better accounted for by...
- These criteria establish a hierarchy:
  - Disorders due to a general medical condition or substance-induced disorder pre-empts diagnoses of primary disorder with the same symptoms (eg Cocaine-induced mood disorder pre-empts Major Depressive Disorder)
  - A more pervasive disorder pre-empts diagnosis of a less pervasive disorder with a subset of the symptoms of the more pervasive disorder (eg Less pervasive disorder will have ‘Criteria have not been meet for [the more pervasive disorder]’)
  - When there are very difficult diagnostic boundaries, use ‘not better accounted for’ to permit use of clinical judgement

**Adjustment Disorder**

- Differs from an anxiety disorder which lacks the presence of a stressor, or post-traumatic stress disorder and acute stress disorder, which usually are associated with a more intense stressor
Stressors
- Generally an event of a serious, unusual nature that an individual or group of individuals experience
- The stressors that cause adjustment disorders may be grossly traumatic or relatively minor, like loss of a girlfriend/boyfriend, a poor report card, or moving to a new neighborhood

DSM-IV Criteria
- The development of emotional or behavioural symptoms in response to an identifiable stressor(s) occurring within three months of the onset of the stressor(s).
- These symptoms or behaviors are clinically significant as evidenced by either of the following:
  - Marked distress that is in excess of what would be expected from exposure to the stressor
  - Significant impairment in social or occupational (academic) functioning
- The stress-related disturbance does not meet the criteria for another specific Axis I disorder and is not merely an exacerbation of a preexisting Axis I or Axis II disorder.
- The symptoms do not represent Bereavement.
- Once the stressor (or its consequences) has terminated, the symptoms do not persist for more than an additional six months.

Treatment
- Counseling, psychotherapy, crisis intervention, family therapy, and group treatment are often used to encourage the verbalization of fears, anxiety, rage, helplessness, and hopelessness.
- Sometimes small doses of antidepressants and anxiolytics are also used

Anxiety Disorders
- Disorders in which anxiety is a characteristic feature or the avoidance of anxiety seems to motivate abnormal behaviour

Introduction
- Anxiety is usually normal, useful and protective. We learn to fear normal anxiety. Yerkes Dobson Curve (1908): moderate levels of anxiety can improve performance, but performance improvement plateaus and then falls with ↑ anxiety.
- Only when anxiety begins to interfere with social or occupational functioning is it considered abnormal
- Anxiety becomes debilitating if severe
- 4 clusters of responses:
  - Physiological: autonomic nervous system arousal, ↓ sleep
  - Cognitive/thoughts: perception of danger, threat, loss, hypervigilance
  - Affective/emotion: nervousness, fear, ↓ concentration
  - Behavioural: fight or flight
- Anxiety disorders lead to:
  - Overactivation of cognitions about personal danger
  - Underestimation of ability to cope
- Differential Diagnoses:
  - Exclude anxiety due to substance intoxication or withdrawal, or due to delirium
  - Physical conditions that cause or exacerbate anxiety (hyperthyroidism, hyperventilation – eg asthma, pheochromocytoma, drug withdrawal, etc)
- Becomes a disorder when it causes significant distress or interferes with social or occupational functioning

Anxiety
- 1. An emotional state with the subjectively experienced quality of fear
- 2. An unpleasant emotion that may be accompanied by a feeling of impending death
- 3. A feeling directed towards the future, perceiving threat of some kind
- 4. There may be no recognisable threat or is out of proportion to the emotion it provokes
- 5. May be subjective bodily discomfort and bodily disturbance

Physiological Aspects of Anxiety
- Exactly the same as when going for a run
- Cardiac function: ↑ basal rate, ↓ deceleration after stress, ↑ awareness of heart function
- Electrodermal response: ↑ skin conductance etc
- Peripheral blood flow: ↑ vasodilation, ↓ renal and splanchnic flow
- NT abnormalities: ↑ adrenaline/NA, ↑ central NA + 5HT activity

**History Taking in Anxiety Disorders**

- Introductory Questions:
  - Are there currently things in your life that are causing distress/worry?
  - Are there things that have happened in the past that you can’t stop thinking about?
  - How is your general health?
  - Any one else in your family had similar problems?
  - Most anxiety is part of a mixed anxiety/depression → importance of full psychiatric assessment

- General Anxiety:
  - Would you describe yourself as a worrier? Do you worry about things that others don’t worry about?
  - Do you sometimes make mountains out of molehills?
  - Do you ever find it hard to make decisions?

- Panic:
  - Have you ever felt your heart pounding, felt frightened/afraid – what do you think was the cause?
  - Ever felt like a disaster was about to happen to you?
  - Do they occur when other people wouldn’t feel afraid?
  - Do you avoid going out?

- Phobias/Avoidance:
  - Is there anything you would avoid if you could? What happens if you are unexpectedly faced with that object/situation?
  - Do you have worries/fears that prevent you from doing things you would like – or that others can do without difficulty?
  - Are you only worried if others will see you?
  - Are you worried/anxious in other settings?

- Obsessions and Compulsions:
  - Obsessive thoughts: Any thoughts that keep coming repeatedly into mind, even when you’re trying to get rid of them?
  - Compulsive rituals:
    - Do you ever have to repeat actions over and over which most people would only do once?
    - Do you ever find yourself having to do things over and over again to get them just right?
    - Do you find yourself spending a lot of time doing things like cleaning or checking that everything is safe?
    - What happens if you are interrupted when doing these things?

- Trauma:
  - Do you still have recurrent memories of an upsetting event?
  - Do you have nightmares, have trouble sleeping, or feel jumpy?
  - Are there things that remind you of the event? Do you avoid these?
  - How has the trauma changed the way you feel about the future, about what you enjoy?

**Panic Disorder (With or Without Agoraphobia)**

- Panic = periodic, discrete bouts of panic symptoms that occur abruptly and peak within 10 minutes
- Prevalence = 2%
- Panic disorder is characterized by the spontaneous and unexpected occurrence of panic attacks, the frequency of which can vary from several attacks per day to only a few attacks per year. Panic attacks can occur in other anxiety disorders but occur without discernible predictable precipitant in panic disorder

**Panic Attack**

- Psychological symptoms:
  - Sudden, unpredictable attacks of intense fear or terror
  - Feelings of impending doom
  - Fear of losing control or dying
  - Derealisation (world feels unreal), depersonalisation (feels detached from the world)

- Physical symptoms:
  - CVS: palpitations, CP, sweating
  - Resp: SOB
  - GIT: nausea, choking
  - Neuro: trembling, faintness, dizziness, parasthesiae, trembling/shaking

- May have limited symptom attacks
• Can happen either way: physical symptoms whilst exercising \(\rightarrow\) PA or PA occurs spontaneously
• Found across anxiety disorders and in non-anxious population

**Assessment**

• What do you think is going on?
• Enquire about the panic attacks themselves (from a systems based approach)
• Rule out medical causes:
  - CV: CP, SOB, orthopnoea etc
  - Thyroid: lost weight, heat intolerance
  - Seizure: LOC, epilepsy hx
• Ask about substance use
• Ask about excessive caffeine intake

**Panic Disorder**

• **Recurrent and unexpected panic attacks.** Situational-bound panic attacks are characteristic of social or specific phobias, although situationally-predisposed panic attacks are frequent in Panic Disorder
• **Normal bodily sensations misinterpreted.** Catastrophic misinterpretation of bodily sensations/mental events (eg has palpitations \(\rightarrow\) think they’re having a heart attack).
• High **anticipatory anxiety**: persistent worry about having additional attacks
• **Hyper-vigilance** for feared sensations (always on the look out)

**Aetiology**

• **Genetic**: evidence supports some anxiety disorders may be inherited
• Physiological: lactate-induced panic
• NTs: NA, SHT and GABA receptors may be involved in anxiety disorders; SHT depletion \(\uparrow\) susceptibility to panic
• Cognitive and behavioural causal factors: the cognitive theory of panic:
  - Perceived control and safety
  - Anxiety sensitivity as a vulnerability factor for panic
  - Safety behaviours and the persistence of panic
  - Cognitive biases and the maintenance of panic

**Agoraphobia**

• = ‘Fear of fear’; fear of having a panic attack; fear of the market place
• = Fear of situation where escape may be difficult or embarrassing in the event of a panic attack; an unrealistic and intense fear of being away from home or other protected places
• **Avoid or endure with dread** situations associated with panic attacks and feared bodily sensations
• Characteristically involve clusters of situations including being outside the home, being in a crowd, on a bridge, in a car, train or bus
• But fear is **NOT** of the situation (eg being in a crowd), rather of **having a panic attack in that situation**
• Can occur with or without a history of panic disorder
• In Panic disorder, the more agoraphobic avoidance there is, the worse the prognosis
• Differentiating from Social Phobia: in panic disorder, they **fear evaluation of what panic causes them to do** (difficulty breathing, dizziness, weakness in limbs). In Social phobia, they **fear evaluation of what they do or say regardless of panic** (blushing, sweating, trembling)

**Diagnostic Criteria**

* DSM-IV criteria for panic disorder states that: panic attacks must be associated with more than 1 month of subsequent persistent worry about:
  - Having another attack
  - Consequences of the attack
  - Significant behavioural changes related to the attack
• Panic attack is defined as having 4 of the following 13 symptoms that develop abruptly and peak within 10 minutes from onset
• These cannot be due to substance use, other medical or other psychological diagnoses:
  - Palpitations, pounding heart, or accelerated heart rate
  - Sweating
  - Trembling or shaking
  - Sense of shortness of breath or smothering
Psychological Medicine

- Feeling of choking
- Chest pain or discomfort
- Nausea or abdominal distress
- Feeling dizzy, unsteady, lightheaded, or faint
- **Derealization** (world is unreal) or **depersonalization** (feeling detached from oneself)
- Fear of losing control or going crazy
- Fear of dying
- Numbness or tingling sensations
- Chills or hot flushes

**Treatment**

- **Bio:**
  - SSRIs (low dose to start but may need higher dose than depression eg 60mg)
  - Tricyclics or MAOIs
  - Benzos should be avoided where possible but can be used as a single dose or very intermittently as can be highly effective in aborting a panic attack
- Psycho: CBT
- Social: education, family support re triggers etc

**Specific Phobia**

- Persistent and irrational fear and avoidance of a specific object or situation
- Leads to avoidance or intense anxiety on exposure to feared stimulus
- Exposure to the phobic stimulus → immediate anxiety response which may take the form of a situationally bound or situationally predisposed panic attack
- Fear recognised as excessive
- **Disruptive to functioning** such that there is **marked distress about having the phobia** (important – who cares about a snake phobia in NZ)
- > 6/12 duration
- Common: 10-11%
- **20-40% heritability** for phobias (also GAD and PTSD)
- Can also be anxious about fear reaction
- Usually related to **animals** (mice, snakes, spiders), **natural environment** (earthquakes), **blood**, injection or injury; **specific situations** (eg clausrophobia, heights)
- Develop due to:
  - Direct conditioning through personal experience
  - Verbal or vicarious transmission (eg develop shark phobia after watching Jaws)
- Treatment:
  - Graded exposure
  - Cognitive restructuring
  - Physiological control: relaxation and medication (short-term only)

**Social Phobia**

- Fear they will do or say something embarrassing or humiliating. Also fear visible anxiety symptoms
- Fear of negative evaluation of performance in social situations.
- Probability and cost of negative evaluation is over-estimated and the **person recognises that the fear is excessive/unreasonable**
- Early onset
- >6/12 duration
- **Leads to avoidance** of social gatherings, public travel, etc
- Interferes with functioning (social, occupational, relational)
- Epidemiology: 6 month prevalence is 2 per 100, more females, onset in teens through to 35 → social isolation
- Aetiology:
  - Interaction of **psychosocial and biological causal factors** ie conditioned response, genetics
  - Learned behaviour
  - Genetic and temperamental factors
  - Perceptions of uncontrollability

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*Psychological Medicine* 703
Generalised Anxiety Disorder

- Worry about worry: a meta-worry!
- Excessive and persistent worry about a number of areas of life including family, health, job, finances, etc
- Worrying is the dominant source of discomfort: spend half an average day worrying – most recognise they worry excessively about minor things but can’t control it
- At least six-month duration, chronic fluctuating course
- Epidemiology: 2 – 8 % of the population, onset 20 – 40 years, male = female
- Symptoms:
  - Restlessness, feeling on edge, difficulty concentrating, mind going blank
  - Irritability, muscle tension
  - Sleep disturbance (esp difficulty getting back to sleep after waking, anticipatory thoughts while awake)
- Co-morbidity/differential: mood disorders, adjustment disorder (clearly identifiable stressor), panic attacks, socially anxious, low self-esteem, avoidant or dependent personality disorder

Aetiology

- Psychosocial causal factors:
  - The psychoanalytic viewpoint
  - Classical conditioning (If a stimulus that results in an emotional response is repeated alongside another stimulus which does not cause an emotional response, eventually the second stimulus will result in the same emotional response. Classical Conditioning is thus ‘learning by association’) to many stimuli
  - The role of unpredictable and uncontrollable events
  - A sense of mastery: immunising against anxiety
- Biological causal factors:
  - Genetic factors
  - A functional deficiency of GABA
  - Cluster C personality traits

DSM-IV Criteria

- Excessive anxiety and worry about a number of events or activities, occurring more days than not for at least six months that are out of proportion to the likelihood or impact of feared events.
- The worry is pervasive and difficult to control.
- The anxiety and worry are associated with three (or more) of the following six symptoms (with at least some symptoms present for more days than not for the past six months):
  - Restlessness or feeling keyed up or on edge
  - Irritability
  - Muscle tension
  - Sleep disturbance (difficulty falling or staying asleep, or restless unsatisfying sleep)
  - Being easily fatigued
  - Difficulty concentrating or mind going blank
- The anxiety, worry, or physical symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.

Treatment

- Education and counselling
- Psychological therapy: CBT → anxiety management and relaxation; training: relaxation, breathing control, structured problem solving, gradual confrontation of fears
- Bio: SSRIs, often higher doses than depression
- Avoid sedatives: they will love them but will become dependent on them and underlying problems won’t be fixed
- Specialist referral if symptoms persist for a further 3 months

Obsessive Compulsive Disorder

- People experience either obsessions, compulsions or both.
  - Obsessions are (recurring intrusive distressing uncontrollable thoughts) recurrent thoughts, impulses or images which are intrusive, inappropriate and cause marked anxiety and distress. The person recognises these as irrational
Compulsions are (things you have to do repeatedly to ↓ anxiety) repetitive, often ritualised behaviours whose behaviour serves to diminish anxiety caused by obsessions e.g. hand-washing, ordering, checking or mental acts e.g. counting or repeating words
- Obsessions can lead to compulsive behaviours
- Upsetting and intrusive obsessional thoughts that are difficult to control (e.g. fear of contamination), leading to compulsive rituals (although can have rituals in the absence of obvious obsessions)
- Common compulsions: cleaning, checking, counting
- Lifetime prevalence = 1%; age of onset = adolescence; see co-morbidity with other disorders

**Signs and Symptoms**
- Examples of **obsessions**:
  - Concern for order and constancy
  - Concerns about doing something wrong, **having to get it right**
  - Cleanliness
  - Forbidden sexual thought
  - Obsessional slowness
- Examples of **compulsions**:
  - Handwashing
  - Checking
  - Collecting
  - Repeating behaviours
  - Arranging things
  - Cleaning

**Aetiology**
- **Psychosocial** causal factors:
  - The psychoanalytic viewpoint
  - Behavioural viewpoint
  - The role of memory
  - Attempting to suppress obsessive thoughts
- **Biological** causal factors:
  - **Genetic**: may play a role
  - Brain damage e.g. trauma
  - **Serotonin abnormality** (does respond to high dose SSRIs)

**Diagnostic Criteria**
- **Either** obsessions or compulsions:
  - **Obsessions** as defined by (1), (2), (3) and (4):
    - 1. **Recurrent and persistent thoughts, impulses, or images** that are experienced, at some time during the disturbance, as **intrusive** and **inappropriate** and that cause marked **anxiety** or **distress**
    - 2. The thoughts, impulses or images are not simply excessive worries about real-life problems
    - 3. The person **attempts to ignore or suppress such thoughts**, impulses, or images, or to neutralize them with some other thought or action
    - 4. The person **recognizes** that the obsessional thoughts, impulses or images are a **product of his or her own mind** (not imposed from without as in thought insertion)
  - **Compulsions** as defined by (1) and (2):
    - 1. **Repetitive behaviors** (e.g., hand washing, ordering, checking) or **mental acts** (e.g., praying, counting, repeating words silently) that the **person feels driven to perform in response to an obsession**, or according to rules that must be applied rigidly
    - 2. The **behaviours or mental acts are aimed at preventing or reducing distress or preventing some dreaded event** or situation; however, these behaviors or mental acts either are not connected in a realistic way with what they are designed to neutralize or prevent or are clearly excessive
- At some point during the course of the disorder, the person has recognized that the obsessions or compulsions are **excessive** or **unreasonable**. Note: this does not apply to children.
- The obsessions or compulsions cause marked distress, are **time consuming** (take more than one hour a day), or **significantly interfere with the person's normal** routine, occupational (or academic) **functioning**, or usual social activities or relationships.
- If another Axis I disorder is present, the content of the obsessions or compulsions is not restricted to it (e.g., preoccupation with food in the presence of an eating disorder; hair pulling in the presence of trichotillomania;
concern with appearance in the presence of body dysmorphic disorder; preoccupation with drugs in the presence of a substance use disorder; preoccupation with having a serious illness in the presence of hypochondriasis; preoccupation with sexual urges or fantasies in the presence of a paraphilia; or guilty ruminations in the presence of major depressive disorder).

- The disturbance is not due to the direct physiological effects of a substance (e.g., a drug of abuse, a medication) or a general medical condition.

**Treatment**

- High dose SSRIs and longer course yields moderate effects
- Hard to treat with CBT and antianxietytics
- Consider antidepressants
- Some evidence of effectiveness of low dose risperidone (?may be delusional component)

**Post Traumatic Stress Disorder (PTSD)**

- = Long lasting anxiety or memories about a severe traumatic event, including nightmares, flashbacks, anxiety, avoidance of reminders
- Lifetime incidence 9% in NZ
- 3rd only to depression and substance abuse disorders in young adults and more common in young people
- Types of traumatic stressors: earthquakes, floods, fires, war, crimes of violence, accidents
- Co-morbid diagnoses: alcoholism, depression, generalised anxiety, panic attacks

**Symptoms**

- RID FAN HACS (recurrent intrusive distressing thoughts with flashbacks and avoidance and hyperarousal symptoms [↓sleep, anger, ↓ concentration, hypervigilance])
- Intrusive:
  - Distressing recollections
  - Dreams
  - Flashbacks
  - Psychological and physiological trigger reactions
- Avoidance:
  - Avoid thoughts, feelings or discussions
  - Avoid activities, places
  - Memory blocks
  - Numbing of emotions
  - Anhedonia
  - Alexithymia (emotions unknown)
- Hyperarousal symptoms:
  - Sleep disturbance
  - Anger problems
  - Concentration problems
  - “On guard” hypervigilance → constantly looking out for symptoms

**Diagnostic Criteria**

- Actual or threatened severely traumatic event (threat of death, serious injury, witnessing trauma to others, learning about violent death of loved one) where the response was intense fear, helplessness or horror
- Event is persistently re-experienced: recollections, dreams, distress to cues of an aspect of the event
- Persistent avoidance of stimuli associated with the trauma (triggers) and numbing of general responsiveness (eg ↓interest in activities, detachment, etc)
- Persistent symptoms of increased arousal (eg difficulty sleeping, irritability, ↓ concentration, hypervigilance)
- Duration of > 1 month
- Causes significant distress or impairment in social/occupational function

**Types**

- Acute: duration of symptoms > 1/12 < 3/12
- Chronic: duration of symptoms > 3/12
- Delayed onset: onset > 6 months after stressor
- Differential: OCD, Acute stress disorder (resolves within 4 weeks), adjustment disorder, psychotic disorders, malingering
Co-morbid Diagnoses
- Alcoholism
- Depression
- Generalised anxiety
- Panic attacks

Treatment
- Psychotherapy:
  - CBT and group therapy and EMDR (eye movement desensitisation and reprocessing; focus on an image related to trauma)
  - Individualised
  - Only when the pt is not in crisis
  - Exploration of trauma memories
  - Explore ways in which to manage these memories with coping strategies
- Pharmacotherapy: SSRIs and occasionally low dose BZDs long-term

Acute Stress Disorder
- Distinguished from PTSD by duration < 1 month (i.e. short term reaction)
- Includes avoidance, fear of being alone, muscle tension, disbelief, problems with sleep, concentration and memory, guilt, self-doubt

Other Anxiety Disorders
- Anxiety disorder due to a GMC: eg hyperthyroidism, hypoglycaemia, CHF, pneumonia, B12 deficiency, encephalitis
- Substance-induced anxiety disorder: during intoxication or withdrawal eg amphetamines, caffeine, cocaine, marijuana, meds, heavy metals, CO, CO2
- Anxiety disorder NOS

Treatment of Anxiety Disorders
- Confronting the feared stimulus is essential for all of the treatment approaches but anxiolytic drugs may lessen the effectiveness of exposure therapies

Behavioural Approaches
- Confront with relaxation: systematic desensitisation
- Confront with tension: blood and injection phobias
- Social skills training

Cognitive Behavioural Therapy (CBT)
- Effective for most anxiety disorders
- Cognitive restructuring is not effective with specific phobias; some effectiveness for social phobia if combined with social skills training
- Response more long lived than for drug treatment
- Includes:
  - Breathing retraining (slow, abdominal breathing exercises)
  - Cognitive restructuring (Detailed self-monitoring of emotions and associated cognitions is used to identify specific beliefs, appraisals and assumptions. Relevant cognitions are categorized into types of errors, such as overestimations of risk of negative events, or catastrophizing of meaning of events)
  - Relaxation, graded exposure, desensitisation
- Panic disorder:
  - Conceptualise panic disorder as an acquired fear of bodily sensations, particularly sensations associated with autonomic arousal, in individuals with certain psychological and biological predispositions for the disorder
- Individuals for whom CBT works best are generally highly motivated and value a problem-solving approach: requires that the patient learns the skills of self-observation and of becoming a personal scientist, learns cognitive and behavioural coping skills, and learns to repeatedly practice the skills in anxiety-provoking contexts outside of the therapy setting
- The central focus of CBT is teaching patients a set of cognitive and somatic coping skills to effectively manage their anxiety as they conduct repeated exposure to feared situations and sensations
Psychodynamic Psychotherapy
- Symptoms result from mental processes outside conscious awareness. Aim is to elucidate these
- Identify and alter core conflicts

Drug Treatment
- Antidepressants:
  - Panic disorder:
    - SSRIs are the first-line treatment, often higher doses than depression eg 60mg
    - Suppression of panic attacks may occur after 4 – 6 weeks. Minimum treatment usually 6 months.
  - Social phobia: May be useful (moclobemide [MAOI], paroxetine [SSRI])
  - OCD:
    - Clomipramine (a TCA) and SSRIs may be a useful adjunct to CBT
    - Help minimize compulsions and manage the depression often associated with OCD
  - PTSD: SSRIs
  - GAD: SSRIs, often higher doses than for depression
- Benzodiazepines:
  - May be useful for the short term or acute treatment of acute stress reactions
  - Due to tolerance and dependence, these are not useful for long-term use
- Betablockers: Useful for the treatment of social phobia when performance anxiety is the main problem.
  These prevent noticeable symptoms (eg blushing or shaking), which are typically interpreted catastrophically
  by individuals. However, these drugs are not useful if the anxiety is more generalized

Benzodiazepines
- Mode of action: enhanced GABA mediated inhibition throughout the CNS
- GABA (gamma-aminobutyric acid) increases membrane Cl- permeability → hyperpolarisation
- Binding affinity important in governing duration and degree of effect, in addition to elimination and dosage.

<table>
<thead>
<tr>
<th>Hypnotics</th>
<th>T½</th>
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<tr>
<td>Ultra-short acting</td>
<td>Midazolam 1.5 – 2.5</td>
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<tr>
<td>Sleep sustainers</td>
<td>Zopiclone 4 – 6</td>
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<td></td>
<td>Temazepam 6 – 9</td>
</tr>
<tr>
<td>Others</td>
<td>Lorazepam 9 – 12</td>
</tr>
<tr>
<td></td>
<td>Naxitrazepam 25 – 35</td>
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<tr>
<td></td>
<td>Flunitrazepam 15 – 35</td>
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</tbody>
</table>

Anxiolytics
| Diazepam 32 | Active metabolite T½ is 40 – 200 hours |
| Chlor Diazepam 12 | Same metabolite as Diazepam |
| Lorazepam 12 | Pronounced withdrawal |
| Oxazepam 8 | Slow absorption |
| Alprazolam 14 | Panic disorders, antidepressant effects in anxiety states |
| Clonazepam | Useful anticonvulsant activity |

- Key pharmacodynamic differences:
  - Chlor Diazepam and Diazepam: shorter elimination time than their active metabolites. Doses of benzos
    with active metabolites should be reduced in the elderly, especially if ↓renal function
  - Midazolam: often used as premed for procedures and GA – relaxes and amnesia
  - Zopiclone (Imovane): differs from BDZs and barbiturates, but has same actions (sedation, anticonvulsant,
    anti-aggressive and muscle relaxant). Binds to BDZ binding sites. Peak plasma conc. in 1 hour, T½ of 4
    hours. At higher doses: hangover effect, memory disturbance, rebound insomnia, interaction with alcohol
- Metabolism:
  - Eg: diazepam →temazepam →oxazepam
  - Inactive conjugates excreted
- Adverse Effects:
  - Daytime sedation: with long acting BDZs where slow elimination leads to accumulation of drug and active
    metabolites
  - Daytime agitation/irritability: with ultra short acting BDZs (triazolam, midazolam), especially in those with
    anxiety
Psychomotor functional impairment: beware if driving or operating machinery
Amnesia: with short acting BDZs
Physical dependence: All BDZs are addictive
CNS effects of BDZs all exacerbated by alcohol
Broken sleep patterns are particularly common after withdrawal of hypnotics
Discontinuation of long-term use must be gradual (2 – 3 months) never abrupt. Withdrawal similar to hyperadrenergic state – anxiety, tremor, ataxia, confusion, insomnia, nausea, seizures (especially with lorazepam). Withdrawal syndrome can be prolonged (ie months). Treating withdrawal: change to diazepam (greater dose flexibility), reduce dose by 10% every 2 – 4 weeks. Use counselling and relaxation
Lorazepam as a hypnotic where insomnia is a complication of anxiety – but never just as a hypnotic
See Treatment of Insomnia, page 859

**Differentiating Anxiety and Depressive Symptoms**

- **Coexistence** of anxiety and depressive symptoms is **common**:
  - Depressive symptoms occur **secondarily** especially in panic disorder, agoraphobia and OCD. If anxiety disorders go untreated → demoralised and progressive restrictions on function → depression
  - Anxiousness and irritability are seen in the majority of depressed patients, panic attacks may occur

- Differentiating:
  - GAD/Panic disorder don’t usually have full range of **vegetative symptoms**
  - Anxious patients have trouble getting to sleep, **depressed wake early**
  - Anxious patients don’t lose the capacity to **enjoy things or be cheered up**
  - Asking which symptoms came first can be helpful

<table>
<thead>
<tr>
<th>More common in anxiety</th>
<th>More common in depression</th>
<th>Common to both</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Bodily</strong></td>
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<tr>
<td>Difficulty falling asleep</td>
<td>Early waking, oversleeping</td>
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<td><strong>Feelings</strong></td>
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<tr>
<td>Helplessness</td>
<td>Sadness, despair</td>
<td>Irritability</td>
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<tr>
<td>“Stressed out/keyed up”</td>
<td>Guilt, hopelessness</td>
<td>Feelings of doom, anxious</td>
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<td>Apprehension</td>
<td>Lack of motivation</td>
<td>Dependent</td>
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<td></td>
<td>Lack of pleasure, flatness</td>
<td>Loss of enjoyment</td>
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<tr>
<td></td>
<td>↓Interest in normal activities, apathy</td>
<td>Tearful</td>
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<td>Rapid mood swings</td>
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<tr>
<td><strong>Thoughts</strong></td>
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<tr>
<td>Expecting the worst Catastrophic thinking</td>
<td>Slowed speech, thought processes, response times</td>
<td>Difficulty with concentration</td>
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<td>Suicidal thoughts</td>
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<td>Indecision</td>
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<td><strong>Behaviour</strong></td>
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<td>Phobic avoidance of feared situations</td>
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<td>Easily startled</td>
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<td>Dissatisfaction with life</td>
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<td>Anxiety reducing rituals</td>
<td>Decreased socialising</td>
<td>Derealisation</td>
</tr>
<tr>
<td>Hyperventilation</td>
<td></td>
<td>Depersonalisation</td>
</tr>
</tbody>
</table>

**Mood Disorders**

**Mood Disorders and Suicide**

- Risk of suicide in those with depressive disorder is **30 times** the normal population
- **10-15%** of pts who have had a **severe depressive illness** will eventually commit **suicide**
- Highest risk period is 1-2 years after hospitalisation
- 90% of completed suicides suffered with depression at some time
- About **20-50%** of those with **BAD** will make a suicide attempt at some time

**DSM IV Diagnostic Categories**

- Major depression
- Dysthymia
- Cyclothymia
- Depressive disorder NOS
• Bipolar disorder
• Bipolar disorder NOS
• Mood disorder secondary to medical condition
• Substance induced mood disorder
• Adjustment disorder (separate classification)

Depressive Disorders

Diagnosis of Major Depressive Disorder/Episode (MDE)

• Depression diagnosis: SAD SPACE Guidelines: sleep, appetite, depression, suicide, psychomotor agitation, anhedonia, concentration, energy/fatigue, guilt/worthlessness

• DSM IV criteria:
  ➢ 5 or more of the following present during the same 2-week period and represent a change from previous functioning
  ➢ At least one symptom must be depressed mood or loss of interest/pleasure
  ➢ [NB exclude symptoms clearly related to a general medication condition, delusions or hallucinations]
  ➢ Note duration and persistence of each symptom, and compare to normal:
    o 1. **Depressed mood**, most of the day, nearly every day (either self report or observed by others)
    o 2. Markedly **diminished interest or pleasure** in all, or all most all, activities (exclude grief reaction)
    o 3. Significant **weight** loss/gain or ↓/↑ in **appetite** (exclude cancer, Tb, hypothyroid)
    o 4. **Insomnia/hypersonomnia** nearly every day (exclude sleep apnoea): classically early morning wakenings
    o 5. **Psychomotor agitation or retardation** (excessive repetitious and pointless motor activity that is associated with feelings of tension. Needs to be observable, not just felt). Eg have you been fidgety/restless or felt 'stuck in the mud' or in slow motion?
    o 6. **Fatigue** or loss of energy nearly every day
    o 7. Feelings of **worthlessness** or excessive or inappropriate **guilt** nearly every day. Eg how do you feel about yourself, have you blamed yourself for things, do you feel guilty?
    o 8. Diminished ability to think or **concentrate**, or indecisiveness, nearly every day
    o 9. Recurrent thoughts of death, **suicidal ideation** without a plan, an attempt or a plan
  ➢ Symptoms do not meet criteria for a mixed episode
  ➢ Symptoms cause significant distress or impairment in social and occupational functioning.
  ➢ Exclude depression if symptoms:
    o Are due to physical illness, medication or street drugs
    o Occur within 2 months of significant bereavement (except if marked impairment, morbid preoccupation with worthlessness, suicidal ideation, psychotic symptoms or psychomotor retardation). **Key difference between grief and depression is whether they themselves feel worthless or not**

• Severity determined by:
  ➢ Number of symptoms as per above
  ➢ Impact on functioning

• Also review risk factors and CAMP SAND:
  ➢ **Prior history** of major depressive episode or suicide attempt. Previous episode → 50% lifetime risk of recurrence
  ➢ **Family history** of mood disorder or suicide attempts. If no family history then lifetime risk 10 – 20%. If heavy genetic loading this may double the risk (very polygenic)
  ➢ Chronic or severe **physical illness** (may → demoralisation and hopelessness)
  ➢ Concurrent **substance abuse**
  ➢ **Recent stressful life events and lack of social support** (stress should not be used to ‘explain away’ symptoms, stress may precipitate a major depressive episode)
    ➢ Childhood trauma, abuse, parental conflict or deficient parental care
    ➢ Recent childbirth or other family changes (eg divorce, children leaving home)
    ➢ Responsibilities for caring for others (eg elderly relatives)

• Differentials:
  ➢ **Substance abuse**
  ➢ Other psychiatric disorders, eg anxiety, eating and adjustment disorders, personality disorders, somatization
  ➢ Dementia in older people (a key differential is memory)
  ➢ General medical conditions and medication. Drugs affecting mood:
Steroids: on 20 mg 1.3% get depression, on 80mg 20% get depression
Lipid soluble β blocker
New drug affecting P450 metabolism and ↑ plasma conc. of existing drug

Grief reaction: Depressive symptoms common during periods of grief. Usually begins within 2 – 3 weeks of bereavement and usually resolves without treatment – although supportive counselling/practical help may be indicated

- In children and adolescents, feelings of guilt, emptiness, self-dislike and failure are common – but are underreported by parents, who may instead report a decline in behaviour or academic performance
- Can use questionnaires: e.g. GHQ (General Health Questionnaire) or CES-D – useful either for screening or in borderline situations – gives something to discuss with patient
- Little point in trying to separate exogenous from endogenous depression (often a chicken & egg situation). It’s usually multifactorial – regardless of cause may well need a multi-factorial approach to management

Subgroups

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>Essential Features</th>
<th>Implications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Psychotic Depression</td>
<td>Hallucinations and/or delusions</td>
<td>More likely to become bipolar than non-psychotic types (esp under 25s). May be misdiagnosed as schizophrenia</td>
</tr>
<tr>
<td>Melancholic Depression</td>
<td>Anhedonia AND depressed mood</td>
<td>Indicative of more severe depression. More likely in older patients. May be misdiagnosed as dementia if cognitive impairment or psychomotor retardation are prominent</td>
</tr>
<tr>
<td>Atypical Depression</td>
<td>Various: overeating, oversleeping, weight gain, mood still reactive to events, anxiety symptoms, heaviness in arms &amp; legs ('leaden paralysis')</td>
<td>Common in younger people. May be misdiagnosed as a personality disorder. Poor response to treatment</td>
</tr>
<tr>
<td>Postpartum Depression</td>
<td>See page 713</td>
<td></td>
</tr>
<tr>
<td>Postpartum Psychosis</td>
<td>See page 713</td>
<td></td>
</tr>
<tr>
<td>Seasonal Affective Disorder</td>
<td>Typically onset in autumn and remits in spring, Summer episodes may also occur</td>
<td>Recurrent</td>
</tr>
<tr>
<td>Catatonic Depression</td>
<td>Disturbances of motor behaviour</td>
<td></td>
</tr>
</tbody>
</table>

Epidemiology and Aetiology

- **70% of women and 40% of men** have experienced clinically significant depressive symptoms by the age of 65
- Depressive symptoms are common: 13-20% point prevalence
- Mean age = 27
- More common in:
  - Women (Female: Male is 2:1)
  - Lower SES/unemployed/welfare
  - Divorced/separated
  - MAP
  - Urbanised areas (? ↑ stressors)
  - ?? Smoking
  - Homosexuality/people who are ostracised/bullied/excluded
- ↓ risk in:
  - Lowest rates in married and never divorced
  - Never married
- Vulnerability factors from various studies:
  - Gene x environment factors/stress
  - Loss of mother before age 11; excess life events prior to onset of depression; lack of supportive relationship; 3 or more children < 14 at home; not working outside home
  - Quality of maternal attachment (related to sensitivity of HPA axis)
  - Physical abuse/neglect/no praise
  - Parental loss/parental style/attachment disorders/deprivation/childhood abuse
- Variety of theories:
  - Biological (eg neurotransmitter dysfunction):
    - Monoamine hypothesis: abnormality in a monoamine NT system at one or more sites in the brain
    - SHT: antidepressant ↑ levels of SHT
  - Neuroendocrine:
HPA axis: in 50% of pts with mod-severe depression, cortisol is ↑ with loss of circadian rhythm

Thyroid function: T4 often normal but T3 may be ↓; blunted TSH response to TRH

Kindling-sensitisation hypothesis of mood disorders:
- Repeated exposure to stress and or neurochemical changes during depressed episode sensitises brain regions responsible for affect and reward

Freud: unresolved early childhood events resurrected by similar events in later life

Beck: Cognitive triad: people feel helpless → hopeless → worthless. Selective abstraction – extrapolate from one event to everything. Treatment: Uncover underlying schema. Then challenge faulty thinking (is it always that bad?), challenge automatic thoughts

Predisposing Factors & Precipitating Factors
- Definite genetic link
- Prevalence in FDR: 15% (vs 5%) → ask FHx!
- MZ:DZ = 54%:24%
- Personality:
  - The most relevant personality traits are obsessional traits and readiness to develop anxiety
  - Neuroticism as assessed on the Eysenck Personality Questionnaire may predispose to major depression
  - Low self-esteem
- Precipitating Factors:
  - Recent life events (70% of depressive episodes are preceded by life events)

Assessment
- Cultural issues:
  - Different cultures have different views on the cause and treatment of depression.
  - Appreciating the cultural perception of the individual → better therapeutic relationship and ↑ effectiveness of intervention.
  - Consider referral to culturally appropriate service.
  - Cultural issues may affect the way the interview is conducted. Eg if Maori, establish initial rapport before asking name and personal information, don’t make eye contact when discussing sensitive information, a family member speaking on a patient’s behalf is not being dominating, etc
- Assessment of severity: Use the number of DSM IV criteria met or severity rating scales. Allows classification into mild, moderate and severe. Can be used to monitor progression of treatment and relapse
- Assess duration: (> 6 months, > 24 months)
- Refer to specialist services when:
  - There is serious risk of suicide (or harm to others, especially younger children)
  - The child is under the age of 13 years
  - There are psychotic symptoms or bipolar disorder (depressed phase)
  - The diagnosis is unclear and needs further evaluation
  - Melancholic features are so severe that they are unable to look after themselves and have inadequate community support
  - There are complex problems (eg poor relationship, another psychiatric disorder)
  - Considering enhancing antidepressants with mood stabilisers (eg lithium)
  - Failure to respond to recommended treatment within 12 weeks

Treatment of Depressive Disorders

Principles of Treatment of Major Depressive Disorder
- Fundamental to treatment is:
  - Establishing positive therapeutic relationship
  - Developing shared understanding of problems
- General treatment principles:
  - Discuss diagnosis
  - Establish rapport
  - Manage risk (ie are the high risk for suicide)
  - If drugs: discuss side-effects, start low, go slow
  - Monitor for response cf remission
  - Vegetative symptoms tend to improve first, cognitive symptoms take longer
- Safety: suicide risks common (lifetime risk 25 – 50%). Higher in delusional Major Depressive Episode. Consider safety of others, especially if psychotic beliefs or Postpartum Depression
Use a biopsychosocial approach

Monitoring treatment in primary care:
- Check for treatment response, side effects, and alteration in stressors or supports
- If severe, monitor twice weekly by consultation and phone, if mild then weekly
- Assess response in week 6

**Biological Treatments of MDD**
- **Drug treatment**: See Antidepressant and Mood Stabilising Medication, page 722

**Psychological Treatments of MDD**
- Indicated if:
  - Person with mild to moderate chooses this as first line
  - If partial response to drugs at week 6 or 12 and residual symptoms are largely psychological
  - There are continuing issues/cognitive beliefs that ↑ the risk of relapse
  - Not as sole treatment in severe, psychotic or melancholic depression
- Promoting change: behaviour, thoughts, emotion
- Different therapies (CBT + IPT most effective):
  - **Cognitive behavioural therapy** (See Cognitive Behavioural Therapy (CBT), page 766)
  - Interpersonal therapy:
    - Exploration of the origins of depression in terms of interpersonal losses
    - Disputes and transitions, social isolation, deficits in social skills
    - Effective in acute treatment of depression, particularly for vocational and social sequelae
  - Psychodynamic therapy
  - Problem solving therapy (See Problem Solving Therapy 768)
  - Hypnotherapy
  - Psychoanalysis
  - Transactional analysis
  - Marital or family therapy

**Social and Other Treatments of MDD**
- **Lifestyle changes** that have been shown to be effective (THESE ARE KEY):
  - Stress management: relaxation techniques
  - ↓ alcohol and drugs
  - Good sleep patterns
  - A balanced diet
  - Physical exercise
- Minimise adverse life events eg financial hardship, housing difficulties
- Role of family, friends and self help groups important in maintaining a supportive environment
- **Education** (over time):
  - Depression is an illness not a weakness.
  - Treatment is effective and recovery is normal and expected.
  - Recurrence is possible so compliance is important. However, sometimes there is only partial remission between episodes.
  - Recognition of warning signs and seeking early treatment will reduce severity
- **Electroconvulsive Therapy** (ECT): see Electroconvulsive Therapy

**Antidepressant and Mood Stabilising Medication**
- The most suitable antidepressant for first-line treatment of moderate or severe depression is a **SSRI**, starting at 20 mg
- Antidepressants are associated with a 50 to 60 percent response rate among patients with major depression in primary care
- The major classes used to treat depression are considered “first generation” (MAOIs and TCAs) and “second generation” (SSRIs, SNRIs)
- SSRIs are first choice in primary care and have similar response to TCAs with fewer side effects and less danger with overdose. MAOIs should be restricted to patients who do not respond to other treatments
- Side effects are minimized by starting at low doses. Therapeutic doses may need to be decreased in the elderly. Antidepressants are usually taken in the MORNING to avoid sleep disturbance.
An initial therapeutic response typically occurs within two to six weeks of antidepressant therapy (may be side effects in this period, important to push through these). No response to antidepressant therapy at 8 weeks – switch to another antidepressant.

Partial responders may benefit from augmentation (with bupropion) or change to another antidepressant

Duration: at least 6-9 mths after a first episode of depression. When discontinued, should be tapered over two to four weeks.

Maintenance therapy (>2y) should be given to patients with >3 episodes, dysthymia and major depression

Drug treatment has similar outcomes as psychological or combination treatment (BMJ 2000, 320: 27-30)

Indications for Antidepressant Use

- Generally not indicated for mild disorder until monitoring, lifestyle changes and psychological therapies have been attempted
- Indicated for mild disorder when there is a history of severe episodes or in dysthymic disorder which is persistent and disabling
- For moderate, TCA or SSRIs are equally indicated: depending on contraindications and toleration of side effects:
  - SSRIs where severe heart disease, significant anticholinergic problems, and where alertness is important
  - Amitriptyline and imipramine cause the most postural hypotension and AntiACH effects of the older TCAs. **Good where sleep disturbance is a major symptom**
- For severe with melancholic features, TCAs at sufficient dose if side effects can be tolerated. Otherwise SSRIs (caution in pregnancy – risks not fully known)
- If psychotic, use atypical antipsychotics or consider ECT
- For moderate and severe, continue for at least 9 months. If more than one recent episode, consider continuing for up to 3 years
- During pregnancy: More experience with TCAs (ie more confident effects on fetus will be minimal) although SSRIs still recommended as first-line
- Maintenance therapy at full therapeutic dose should be considered if high risk of relapse
- Li in relapsing bipolar and as possible adjunct in relapsing unipolar depression

Mode of Action of Antidepressants

- Increase concentration of noradrenergic or serotonin neurotransmitters in the synaptic cleft.
- Leads to adaptive changes eg downregulation of post synaptic β and 5HT2A receptors (hence therapeutic delay)
- Older agents also had antimuscarinic and antihistaminic activity

Starting and Stopping

- Onset of effect can take 2 or so weeks, with full effect possibly not for 4 – 8 weeks
- Side effects, if any, likely to kick in before onset of effect
- Dose-escalation is a trade-off between desire to reach therapeutic plasma levels as soon as possible while avoiding side-effects
- Rapid cessation of any antidepressant can cause a withdrawal syndrome from a few days resolving in about 4 weeks. Taper off treatment. (Less risk with SSRIs due to longer T½)

SSRIs

- = Selective Serotonin Re-uptake inhibitors
- Action: Initially inhibit 5HT re-uptake. Long term, normalise 5HT1A and 5HT2 receptor density
- Pharmacokinetics: Well absorbed. Fluoxetine: active metabolite with T½ of 7 – 10 days. Others, T½ of Use: Therapeutic delay of 3 – 4 weeks. Can be given once a day MANE
- About 24 hours, inactive metabolites
- Examples: Fluoxetine/Prozac, Paroxetine/Arapax, Citalopram (popular in the UK, not subsidised in NZ)
- Dose: 20mg (for all; can ↑ to a max of 80mg for fluoxetine)
- Use in pregnancy – Category C:
  - Fluoxetine use should be considered during pregnancy only if the potential benefit justifies the potential risk to the foetus, taking into account the risks of untreated depression
  - Fluoxetine may increase risks of congenital anomalies, persistent pulmonary hypertension, neonatal behavioural syndrome, and pre-term birth
- Use in breastfeeding:
  - Is excreted in breast milk
All of the antidepressants cross in the breast milk to some degree varying from < 2% (Sertraline and paroxetine) to 6% with fluoxetine, but these are below the guide of 10% and are generally considered safe when breastfeeding.

**SSRI Side effects:**
- **Common:**
  - Nausea 23%, diarrhoea 15%, headaches, nervousness/anxiety (early in treatment, Fluoxetine more stimulant than Paroxetine) and insomnia 25%
  - Sexual dysfunction is common (erectile dysfunction, ↓ arousal and orgasm [in women too])
  - Weight loss 4%
- **Less common:**
  - Postural hypotension uncommon, but can be significant
  - Sweating, constipation, weight loss, EPS (akathisia, dystonias, tardive dyskinesia), hyponatraemia
- **Less affinity for aminergic receptors than TCA**
- **Lack of cardiac toxicity in overdose (significantly less than TCAs)** – no effect on QTc
- **May precipitate serotonin syndrome:** fever, tremor, myoclonic jerks, seizures, diarrhoea, hyper-reflexia. Can be fatal. NEVER prescribe MAOIs and SSRIs
- **Care in variety of medical conditions**
- **Withdrawal of SSRIs:** Withdraw slowly
  - GI: nausea, vomiting, diarrhoea, loss of appetites, abdominal pain, abdominal distress
  - General somatic distress: lethargy, flu-like symptoms
  - Sleep disturbance: insomnia, abnormal dreams including nightmares and decreased need for sleep
  - Affective symptoms: irritability, anxiety symptoms, agitation
  - Problems with balance: dizziness, vertigo, light-headedness, ataxia
  - Sensory abnormalities: paraesthesia, numbness, blurred vision/diplopia, visual lag
- **Interactions of SSRIs:**
  - Cytochrome P450 inhibition is a major risk factor: 2D6, 3A4, 2C – depending on drug type (eg Sertraline, Fluoxetine, Paroxetine)
  - 2D6: 10% Caucasians lack it
    - Inhibited by Fluoxetine, Sertraline and Paroxetine
    - TCAs plasma levels/effects ↑ by 50 – 400%
    - Haloperidol levels may be increased (Fluoxetine most potent at this)
  - 2C:
    - Phenytion (up to 3 fold ↑)
    - Tolbutamide (hypoglycaemia with Sertraline)
    - Warfarin (↑ INRs on sertraline and paroxetine)
    - Diazepam (sedation with fluoxetine)
  - 3A4: involves many drugs, including triazolam, carbamazepine, erythromycin, terfenadine, midazolam. Potential for multiple interactions
- **Nefazodone:** An SSRA + 5HT2 antagonist. Not really an SSRI but similar action. Side-effects similar to TCAs: nausea, dry mouth, dizziness, constipation, blurred vision
- **St John’s Wort** (Hypericum): inhibits re-uptake of 5HT, noradrenaline and dopamine. In correct dose is as effective as imipramine and significantly better than placebo. Adverse effects include nausea, but no antimuscarinic effects. With SSRI can cause mild serotonin syndrome. Mild enzyme inducer → ↑ metabolism of warfarin, and others

**Tricyclic Antidepressants**
- **Examples:** Amitriptyline, Imipramine, Doxepin, Nortriptyline (least orthostatic hypotension), Dothiepin, Clomipramine
- **Action:** Inhibit reuptake (therefore ↑ [ ]) of serotonin, noradrenaline or both plus DA, and BLOCK anti-Ach, anti-α1, anti-H1
- **Use:**
  - Clinical response takes 10 – 14 days. Start with low dose and increase gradually.
  - Relapse common ⇒ continue for 6 months
  - Not in acute MI. Care if suicidal (overdose risk), mania, and variety of medical conditions
- **Pharmacokinetics:**
  - Very low Vd ⇒ dialysis for overdose ineffective
  - Long T½ ⇒ once a day dose possible, but may split dose to reduce the dose dependent anti Ach effects
  - Well absorbed. Extensive 1st pass metabolism to active metabolites.
  - Individual variability in metabolism ⇒ difficulty setting dose.
Protein bound and large Vd.
Long T½ (15 – 30 hours), prolonged in elderly. Can be given once daily, but high peak plasma levels →↑side effects

**Side effects of TCAs:**
- Inhibit reuptake of:
  - 5HT → anorexia, nausea, vomiting
  - NA → tremors, tachycardia, erectile and ejaculatory dysfunction, insomnia
  - DA → less significant
- Block:
  - Ach → dry mouth, urinary retention, blurred vision, constipation, tachycardia
  - Alpha 1 → postural hypotension (persistent in elderly). Delay in ejaculation and erectile dysfunction
  - H1 → sedation, weight gain
- Other: Possible convulsions, ataxia, manic reactions, respiratory depression, bundle branch block, delirium. **Arrhythmias/arrest in overdose**
- There are marked differences in side-effect profile between people and between drugs

**Withdrawal of TCAs:**
- GI: nausea, vomiting, abdominal cramps, diarrhoea
- General somatic distress: lethargy, flu-like symptoms, headache
- Sleep disturbance: insomnia, abnormal dreams including nightmares
- Affective symptoms: anxiety, agitation, low mood
- Less commonly: movement disorders, mania, hypomania, arrhythmias, tachycardia, ventricular ectopic beats

**TCA Drug interactions:**
- Alcohol potentiates sedation
- Potentiation of antimuscarinic drugs, adrenaline, noradrenaline and pseudoephedrine
- Anticholinergics: worsening of dry mouth, tachycardia, constipation, urinary retention, blurred vision, narrow angle glaucoma
- Antihistamines, alcohol, anxiolytics: sedation (especially bad if driving)
- Anaesthetics: arrhythmias and hypotension
- Diuretics: postural hypotension
- Antihypertensives: increased hypotensive effect
- MAOIs: CNS excitation (look like they’re thyrotoxic) and hypo-hypertension
- SSRIs: Fluoxetine inhibits TCAD plasma levels/side effects

**Tricyclic Overdose:**
- Gastric lavage up to 18 hours post ingestion, charcoal, support respiration
- Symptoms:
  - Anticholinergic signs: rapid pulse, dilated pupils
  - Cardiac: hypotension (<1 blocking effect), arrhythmia (PR and QRS intervals)
  - Neurological: CNS, seizures, sedation, extrapyramidal syndromes
  - Respiratory: depressed CNS
  - Other: ileus and urinary retention
- Sodium bicarbonate if life threatening arrhythmias, lignocaine for ventricular rhythms, magnesium.
  Beware use of physostigmine

**Other Antidepressants**
- Bupropion (NE & DA reuptake inhibition)
- Trazadone (5HT2, alpha-ANT)
- **Venlafaxine** and Duloxetine (NE & SHT reuptake blockers: SNRIs)
- Mirtazapine (presynaptic alpha 2 ANT and 5HT2 and 5HT3 ANT)

**MAOIs (Monoamine Oxidase Inhibitors)**
- Action:
  - Inhibits MAO, which breaks down SHT and noradrenaline intracellularly. Isoenzymes in gut and liver (type A) and brain (type B) all inhibited
  - MAO-A (intestine, placenta): selectively oxidises NA, Ad and SHT
  - MAO-B (platelets): oxidises phenylethylamine
  - Tyramine and Dopamine are substrates for both forms
- Types:
- Standard MAOIs are irreversible. Eg Tranyl-cypromine, Phenelzine inhibit MAO-A. **Selegiline** (deprenyl) irreversibly inhibits MAO-B
- **Reversible** inhibitor of MAO - A (RIMA), eg **Moclobemide**. Similar efficacy to TCAs and SSRIs. Given 3 times a day

- **Use:**
  - MAOIs rare as first line treatment. Use moclobemide instead
  - Therapeutic delay for about a month

- **Pharmacokinetics:**
  - MAOIs: Well absorbed. Pharmacokinetics of little importance as kinetics depends on irreversible inhibition
  - RIMAs: Well absorbed. Wears off quicker than MAOIs. Fairly extensive 1st pass metabolism. 50% protein bound. Large Vd. T½ is 2 hours

- MAOI side effects. MAO inhibition →↑ catecholamine levels:
  - Postural hypertension, urinary hesitancy, dry mouth, blurred vision
  - Impotency and anorgasmia 20%
  - Hepatotoxicity
  - Carpal tunnel like syndrome
  - CNS: agitation, anxiety, hypomania, headache, tremor,
  - Other: weight gain, insomnia.
  - Contraindicated/caution in variety of medical conditions

- Food interaction: tyramine rich foods:
  - Foods include avocado, aged cheddar, yoghurt, meat, red wine, chocolate, yeast extracts, some beers, vegemite, pickled herrings, chicken liver.
  - Tyramine a precursor to dopamine and nor-adrenaline. Normally tyramine metabolised in gut by MAO.
  - If inhibited →↑plasma conc. →↑noradrenaline →hypertensive crisis, subarachnoid haemorrhage, etc.
  - Adrenaline breaks down to HMMA, which can be detect in the urine.
  - RIMAs have 10 times the capacity to metabolise tyramine (ie food much less of an issue)

- **Drug Interactions:**
  - Sympathomimetics, including indirectly acting sympathomimetics (eg in cough mixtures such as ephedrine): hypertension
  - Opiod analgesics: hypo/hypertension
  - Antihypertensives: loss of effect, exacerbation of hypertension
  - Anticholinergics: increased effects
  - SSRIs and pethidine: serotonergic syndrome (fever, sweating, convulsion, confusion)
  - L-Dopa: dopaminergic crisis
  - Potentiate oral hypoglycaemics (sulphonylureas)

- **MAOI Overdose:**
  - Symptoms: CNS hyperactivity, sweating, hyperthermia, tachycardia, hyperventilation, muscle rigidity +/- dystonic facial and limb movements
  - Treatment: α and β blockers, chlorpromazine + supportive management

**Perinatal and Postpartum Mood Disorders**

- **13-20%** of women suffer from depression either **during** pregnancy or in **PN** period
- High relapse rate on stopping medication

**Postnatal Disorders**

<table>
<thead>
<tr>
<th>Disorder</th>
<th>Frequency</th>
<th>Symptoms</th>
<th>Course</th>
<th>Risks &amp; Treatment</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>Postpartum Blues</td>
<td>70 – 80%</td>
<td><strong>Tearfulness, anxiety,</strong></td>
<td>3 – 4 days post</td>
<td>Treatment: <strong>support,</strong></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>irritability, poor</strong></td>
<td>partum and can</td>
<td><strong>reassurance, monitor.</strong></td>
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<tr>
<td></td>
<td></td>
<td><strong>concentration, euphoria</strong></td>
<td>last up to a few</td>
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<td></td>
<td></td>
<td></td>
<td>weeks. <strong>Early</strong></td>
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*Psychological Medicine*
Postpartum Depression 10 – 15% Common symptoms: anxiety, irritable, crying, lack of interest in baby, guilt, hard making decisions, hopeless, panic attacks, especially insomnia & fatigue, appetite change, palpitations, CP. Mood may fluctuate. Obsessional thoughts. Suicidal ideation, homicidal thoughts. Not before 3rd day. 80% onset within first 6 weeks. Peak at 6/52. Gradual onset – may not be apparent until 4th or 5th month. Duration 6 – 9 months (up to a year). Any time 30 – 50% chance of recurring in next postpartum period. May approach 100% if history of mood disorder and previous postpartum depression. Treat as for MDE

Postpartum or Puerperal Psychosis (No criteria in DSM-IV) 0.1 – 0.2% Severe, labile (unstable) mood. Obsessional thoughts (eg about baby’s health). Suicidal & homicidal ideation. Delusions (eg baby defective), suspicious, persecuted, confused. Sleep disturbance. Extreme anxiety and agitation Acute onset 1 – 6/52 post partum. Good prognosis. Duration 2 – 3 months. Early 30 – 50% chance of recurring in next postpartum period Treatment: Ensure safety. Antidepressant, Lithium, antipsychotic. Consider ECT early – safe and effective. Higher risk a/w BAD and schizoaffective disorder

- Highest vulnerability is in first 3/12 after delivery
- Screen (not a diagnostic test) at post-natal check up (6 weeks) using Edinburgh Postnatal Depression Scale (EPDS):
  - 10 item self-rated questionnaire for detection of postpartum depression, scored 0, 1, 2, or 3
  - A score of 12 or more on EPDS OR an affirmative answer on q 10 (suicidal thought) requires more thorough evaluation
- Rule out other causes of depression/DDx:
  - Hypothyroidism (more common post-partum)
  - Substance abuse
  - Recurrence of previous psychiatric illness
  - Initial presentation of a psychiatric illness (eg schizophrenia or anxiety disorders – postpartum period increases risk)
  - Adjustment disorder with depressed mood

Possible Aetiological Factors
- Possible, PND not caused by these things
- Stress of delivery, difficult pregnancy
- Lack of sleep
- Hormonal: levels of oestrogen, progesterone, cortisol and thyroid hormones drop sharply after birth
- Isolation, lack of support
- Internal conflicts about role as mother: motherhood idealised or devalued, very difficult adjustment in role, powerless, dependent, alone, may have had unrealistic expectations, etc
- May not have wanted to be pregnant, may now feel trapped in unhappy situation (eg relationship)
- Cultural factors: cultures vary in support offered (eg by extended family) to new mother, in pressures to return to work (variable maternity leave policies), differing attitudes to female children, etc.
- Considerable overlap in the risk factors for major depression, post-partum depression, inadequate parenting and child abuse

Treatment
- General measures:
  - Exercise
  - Family and friends
  - Sleep

Risk factors: PHx of PND, depression during pregnancy, PHx of depression/mood disorder/substance abuse. FHx, marital or financial stress, lack of self-confidence, lack of support, hx of severe PMS, underlying medical condition

- Psychological Medicine 718
Diet

- Bio: medication
- Psycho: counselling/psychotherapy
- Social: support groups (specifically for PND)

- Mild symptoms: counselling and group therapy
- Moderate to severe: meds + psychotherapy and psychosocial support + REFERRAL to specialist maternal MH service

Key for answering any exam question re treatment:
- Establish a therapeutic alliance! (write for any condition)
- Discuss diagnosis
- Talk about SE of drugs
- Start low and go slow
- Exclude risk factors
- Follow-up

Psychotropic Drugs in Pregnancy and Breastfeeding

- Little evidence about the safety of most psychotropic meds in pregnancy and BF
- For most meds there really is insufficient data about their use/safety during pregnancy
- Risks of psychotropic drugs in pregnancy:
  - Mostly safe (except valproate)
  - At conception and in the first trimester: small risk of major malformations and congenital birth defects
  - In the second and third trimester: labour, delivery and perinatal complications, neurobehavioural sequelae
- Risks of untreated psychiatric illness in pregnancy:
  - Suicidal behaviour
  - Poor self-care
  - Inadequate nutrition
  - Poor antenatal clinic attendance
  - Direct effects on the fetus
  - Impact on future attachment
- Principles:
  - Establish therapeutic alliance, discuss rationale, side effects, balancing risks and benefits, allow informed decision
  - Choose drugs with lower risk profiles for mother and fetus or infant
  - Start at lowest effective dose and slowly ↑, particularly important when risks might be dose related
  - Use monotherapy in preference to combo therapy
  - Use additional precautions for preterm, low birthweight or sick infants
  - When stopping a drug in a woman with a mental disorder who is planning a pregnancy, pregnant or BF, take into account the risk to the fetus or infant during the withdrawal period and the risk from not treating the disorder
- Check whether drugs enter breast milk (all antidepressants cross in the breast milk to some degree varying but these are below the guide of 10% and are generally considered safe when breastfeeding)

- First-line = SSRIs:
  - Start low, gradually ↑
  - Fluoxetine 10-60mg/d
  - Paroxetine 20-60mg/d
  - Citalopram 20-60mg/d
- If can’t tolerate SSRIs or no response then consider tricyclics
- If no luck, then try SNRIs such as venlafaxine
- ECT is effective for those with severe depression/psychosis

Sequela

- Long term effect of postnatal depression on child development:
  - Disturbances in mother-infant relationships (eg attachment)
  - Impaired cognitive and emotional development in later infancy
  - ↑ risk of longer-term behavioural and social development of the child
- These factors compounded by indices of socio-economic adversity, which are risk factors for these outcomes and for depression. So good initial diagnosis and treatment important
Dysthymia
- Essentially a chronic, lower grade depression which is rarely severe enough to fulfil the criteria for recurrent depressive disorder
- Epidemiology:
  - 3% prevalence
  - F > M
  - Unemployed and those with loss of close relative or chronic medical illness
- Diagnostic criteria:
  - Depressed mood for most of the day, for more days than not, for at least 2 years
  - Other depressive symptoms; 2 or more of:
    - Poor appetite or overeating
    - Insomnia or hypersomnia
    - Low energy or fatigue
    - Low self-esteem
    - Poor concentration
    - Feelings of hopelessness
  - But not a major depressive episode, no manic, hypomanic or psychotic features, no substance abuse or GMC
  - Symptoms cause clinically significant impairment in social, occupational or other important areas of functioning
- Differences from Major Depressive Disorder:
  - Difficult as differences in onset, duration, persistence and severity are not easy to retrospectively evaluate
  - Major depression often has a more marked contrast from normal. In dysthymic disorder, low mood is less easily distinguished from person’s normal function
  - If major depressive episode on top of existing dysthymic disorder, then may recover more quickly than normal from the major depression, but are at significantly higher risk of relapse with faster cycles
- Treatment:
  - Biological: Antidepressants (SSRIs) for up to three years together
  - Psychological: CBT or IPT
  - Social: Appropriate life skills training

Cyclothymia
- = Less severe mood disturbance with persistent instability (hypomania + depression) of mood, has a less chronic course than Dysthymia
- Epidemiology:
  - 3%
  - M = F
  - Common in relatives of pts with major affective disorders
- For at least 2 years, the presence of numerous periods with hypomanic symptoms and numerous periods with depressive symptoms
- 33% will develop bipolar affective disorder
- Rx: mood stabilisers maybe required

Seasonal Affective Disorder
- 4%; F > M
- Pathophysiology unknown, ?dysregulation of melatonin
- Clinical features:
  - Atypical depressive features: anxiety, irritability, ↑ fatigue, ↑ sleep, ↑ appetite + weight gain (CH craving)
  - Onset usually in autumn or winter
  - Mild hypomania often experienced in summer
- Treat with light therapy: 10000 lux from light box

Bipolar Affective Disorder (Manic-Depression)
- Affects 1% of the population (35,000 New Zealanders)
- Mean age of onset = 21 years; 90% of pts before 50 years; higher in urban areas
- Genetic predisposition:
  - No family history then risk is 1%
- FDR then risk is 10%
- MZ:DZ = 79%: 19% (ask FHx!)

### Symptoms:
- Manic symptoms (DIGFAST distractability, irritability, grandiosity, flight of ideas, activities ↑, speech ↑/sleep, thoughtlessness [spending/sex etc.]):
  - **Euphoria**: elevated mood or inappropriate reaction to external events for an extended period of time
  - **Inflated self-esteem or grandiosity**: believing/talking/acting as if considerably better at something or has special powers
  - **Irritability**: energized, angry, raging
  - **Flight of ideas/racing thoughts**: sped-up, tangential, circumstantial thoughts
  - **↑ speech**: dramatically amplified volume, *uninterruptable*, ↑ rate and or pressure
  - **↓ need for sleep**
  - Excessive involvement in pleasurable or dangerous activities
  - **↑ in goal-directed activity or psychomotor agitation**
  - DistraCtability

- **Depressive Phase**: same symptoms as for major depressive episode

### History questions for mania:
- How do you feel about yourself?
- Do you feel that you are special?
- Have you needed less sleep?
- How much have you been spending lately?

### Classifications of Bipolar Disorder:
- **Mixed Episode**: rapidly alternating mood – at least 1 week in which the criteria are met for a manic episode and a MDE nearly every day
- **Bipolar I**: one or more manic or mixed episodes, usually accompanied by MDEs
- **Bipolar II**: one or more MDEs accompanied by at least one hypomanic episode
- **Cyclothymia**: At least 2 years of numerous periods of hypomanic symptoms and depressive symptoms that don’t meet criteria for mania or MDE

### Co-morbid conditions:
- Alcohol and other substance abuse disorders
- Schizoaffective disorder
- Anxiety states
- PTSD/borderline PD

### Can be very stressful on relationships for family members

### Poor prognosis with:
- Poor treatment adherence
- Mixed affective states
- Rapid cycling
- Chronic depression
- Severe mania
- FHx of non-response
- Thyroid dysfunction
- Comorbid conditions

### Hypomanic Episode
- Mood is elevated or irritable to a degree that is definitely abnormal for the pt and is sustained for at least 4 consecutive days
- 3 or more of the following signs must be present, leading to some interference with personal functioning but NOT enough to cause marked impairment in social or occupational functioning in daily living:
  1. ↑ activity or physical restlessness
  2. ↑ talkativeness
  3. Difficulty in concentration or distractability
  4. ↓ need for sleep
  5. ↑ sexual energy
  6. Mild overspending, or other types of reckless or irresponsible behaviour
  7. ↑ sociability or overfamiliarity
- Hypomanic episodes are similar to manic episodes in that they have essentially the same symptoms, but differ in:
  - The length of time
- Impairment is not as severe
- May not be viewed by the individual as pathological
- Others however may be troubled by erratic behaviour

**Manic Episode**

- Mood must be **predominantly elevated, expansive or irritable**, and definitely abnormal for the pt
- The mood change must be prominent and lasts at least **1 week**
- The episode is **sufficiently severe** to cause **marked impairment** in social or occupational or relational functioning
- At least **three** of the following signs must be present:
  - 1. ↑ activity or physical restlessness
  - 2. ↑ talkativeness
  - 3. **Flight of ideas** or the subjective experience of thoughts racing
  - 4. Loss of normal **social inhibitions**, resulting in behaviour that is inappropriate to the circumstances
  - 5. ↓ need for **sleep**
  - 6. Inflated self-esteem or grandiosity
  - 7. **Distractability** or constant changes in activity or plans
  - 8. Behaviour that is **foolhardy or reckless** and whose risks the individual does not recognise eg spending spree, foolish enterprises, reckless driving
  - 9. Marked ↑ **sexual energy** or indiscretions

**Biological Treatments**

- **Mood stabilising** medication:
  - **Lithium** carbonate (requires regular blood tests. Can they get to the lab?):
    - SE: the 4 T’s: tremor, thyroid (hypo), terrible renal disease, teratogen
  - **Carbamazepine** (Tegretol)/**Sodium Valproate** (Epilim):
    - Use for Li resistance/intolerance
    - More effective at preventing mania than depression
  - **Lamotrigine**:
    - Mood stabiliser
    - More effective for depressive symptoms than for mania
  - All have similar efficacy, Lithium most common
- Atypical antipsychotic or tranquillising medication often added during early stages to reduce agitation and hyperactivity:
  - **Quetiapine and Olanzapine** for mania/hypomania and possibly as a mood stabiliser
  - **Risperidone** for mania
- Antidepressant medication can be used during depressive phase (although therapeutic delay a problem), and withdrawn gradually when it resolves. If used in isolation without a mood stabiliser, may precipitate a manic phase as the depression lifts
- Maintenance therapy should **continue indefinitely**

**Lithium**

- Indication: In bipolar, but also recurrent unipolar or treatment resistant depression
- In mania, takes **3-4 days for therapeutic effect** (ie not great for acute treatment of mania), with a **75% response rate**
- There are more controlled trials demonstrating the efficacy of Lithium monotherapy for treatment of acute mania (including patients with psychosis) than any other medication available, thus a good starting point.
- Beneficial effect in ↓ **suicide risk**
- Is evidence of loss of efficacy during prolonged treatment
- Useful as a mood stabiliser and antidepressant
- Pharmacokinetics:
  - Variable absorption. T½ is 18 hrs in young, 26 hours in elderly. **Excreted unchanged. 80% reabsorbed in proximal tubule**
  - Renal clearance of Li reduced by **diuretics, NSAIDs**, theophylline, caffeine, dehydration, low sodium
  - Clearance related to tubular sodium load. If ↑Na excretion (eg loop and thiazide diuretics) then ↓Li excretion.
  - ACE inhibitors → ↑Li levels
- Monitoring:
Narrow therapeutic range for maintenance treatment: 0.4 – 0.8 mmol/l
Therapeutic drug monitoring for Li is mandatory when: side effects, relapse of symptoms, serious illness (e.g. dehydration), dose adjustment
Check THYROID and RENAL FUNCTION before starting
Monitoring every three months should include Li levels, electrolytes, thyroid function (initially)
Monitor 12 hrs after immediate release, 5 hrs after slow release. Slow release preparations prevent peaks in plasma conc. (→ nausea, headache)

Side Effects:
- Minor symptoms such as tremor and nausea do not predict serious toxicity:
  - Tremor (especially elderly), nausea, loose bowel motions (especially if levels > 0.8 mmol/L)
  - Polyuria (especially when starting)
  - Weight gain: approx 4 kg
  - Pretibial oedema
  - Metallic taste
- Dose dependent adverse effects:
  - 1.5 – 3 mmol/l – ataxia, weakness, drowsiness, thirst, diarrhoea
  - 3 – 5 mmol/l – confusion, spasticity, convulsions, dehydration, coma, death
- Dose independent: hypothyroidism (reversible in early stages), nephrogenic diabetes insipidus, ECG changes & arrhythmias, acne, GI disturbance, weight gain, ↓ bone calcium
- Long term Li does not change GFR or lead to renal failure

Psychological Treatments
- Essential as for depression: CBT + IPT, but social rhythms therapy also
- Social rhythms therapy:
  - Those with BAD have a predisposition to circadian rhythm and sleep-wake cycle abnormalities that may cause a relapse
  - Life events (negative and positive) can also disrupt the person’s social rhythms that, in turn, impact on circadian rhythms and sleep-wake cycles and lead to relapse
  - SRT combines IPT or CBT with behavioural interventions to help pts regularise daily routines, diminish interpersonal problems and adhere to medications

Prognosis
- For Bipolar I pts, 50% achieved syndromal recovery (no longer meeting criteria for dx) within 6/52 and 98% at 2 years
- 72% achieved symptomatic recovery (no symptoms at all) and 43% functional recovery (occupation etc)
- Bipolar I is a recurrent and disabling illness: 90% who have one manic episode have another within 5 years, 90% have at least one hospitalisation
- Bipolar disorder is associated with high rates of substance abuse and suicide (18-25 x general population), 15% die by suicide

Psychotic Disorders
- Psychosis:
  - = Distortion, or loss of contact with, reality (e.g. delusions, hallucinations, thought disorder [thought disorder refers to abnormalities in the thinking process]) without change of consciousness (cf Delirium)
  - Refers to thought disorder; delusions; or hallucinations
  - Thought disorder refers to abnormalities in the thinking process
  - Ask about disorganised speech, thinking or behaviour
  - Delusions refer to abnormal beliefs that are held with conviction, are without evidence and are culturally inconsistent
  - Ask about unusual concerns, preoccupations or statements
  - Hallucinations are abnormal perceptual phenomena in the absence of external stimuli
  - Ask about visions, sensations, noises that are unusual/not shared by other people, or observations to suggest this
- See Mental State Examination, page 688, for definitions and history questions relating to psychosis
- Classification/Diagnostic hierarchy for psychosis:
  - Organic psychoses: Delirium, dementia, general medical conditions eg meningitis, brain tumours
- **Functional psychoses** (due to physiological [e.g. neurotransmitters] not anatomical changes): Mania, schizophrenia, depression
- Non-psychotic disorders: anxiety disorders, abnormal illness behaviours
- Personality disorders

**Types of Psychotic Disorder**
- **Brief Psychotic Episode**: symptoms have lasted **> 1 day but < 1 month**, and the patient has returned to pre-morbid functioning in that time. Uncommon. May develop in response to severe psychosocial stressor. More common in personality disorders (histrionic, narcissistic, paranoid, schizotypal, borderline)
- **Schizoaffective Disorder**: manic or depressive syndrome develops concurrently
- **Delusional Disorder**: non-bizarre delusions present for 1 month without any other symptoms of schizophrenia
- **Schizophreniform Disorder**: duration of **> 1 month but < 6 months** (may progress to schizophrenia)
- Schizophrenia

**Schizophrenia**
- Key features: positive symptoms, negative symptoms, deterioration in functioning over time (6/12)
- It is not a split personality (i.e. multiple personality disorder)

**Epidemiology**
- 1% (30,000) NZers have or have had schizophrenia
- Median age of presentation: males 19, female 24
- Higher in lower SES
- Higher in urban areas than rural areas (↑ stressors)
- Higher in immigrants

**DSM-IV Criteria**
- A. Characteristic symptoms: **2 or more** of the following, each present for a significant portion of time **during a 1/12 period**:
  - 1. Delusions
  - 2. Hallucinations
  - 3. Disorganised speech
  - 4. Grossly disorganised or catatonic behaviour
  - 5. **Negative symptoms** i.e. affective flattening, alogia, avolition, asociality etc
- B. Social/occupational dysfunction: For a significant portion of time since the onset of the disturbance, one or more **major areas of functioning** such as work, interpersonal relationships or self care are **markedly below** the level achieved prior to the onset
- C. Duration: Continuous signs of the disturbance persist for at least **6/12**. This 6/12 period must include **at least 1/12 of symptoms that meet criterion A** and may include periods of **prodromal or residual phase symptoms**
- D. Schizoaffective and mood disorder exclusion
- E. Substance/GMC excluded

**Symptoms**
- **PINC**: positive symptoms, insight lacking, negative symptoms, cognition impaired/catatonic or disorganised behaviours
- **Positive symptoms**:
  - **Hallucinations**: perception in the absence of external stimuli. Come from external space. Typically auditory 2nd (talking to you) or 3rd person (others talking about you) hallucinations (but can be visual [more common in organic psychosis], auditory, olfactory, gustatory, tactile)
  - Delusions: fixed false beliefs out of cultural context
  - **Thought disorder**: ‘loss of syntax’, non-linear. Different to confusion or incoherence. *Thought broadcasting, thought insertion, thought withdrawal* = thought alienation (thought stolen from mind)
  - **Bizarre and/or disorganised behaviour**: e.g. aggressive, disinhibited, violent (often in ‘self-defence’ if paranoid - rare but possible). Includes: **Catatonic behaviour**: if long term, untreated psychosis then may assume odd positions, waxy flexibility, totally unresponsive
- **Negative symptoms** (the 6 A’s):
  - **Deficiency of mental function** – Cognitive symptoms: difficulty concentrating, learning, hard to assemble thoughts. *Not a decline in intelligence. Will still remember*. Don’t try to pull the wool over their eyes
  - **Alogia**: poverty of speech or speech content
- **Affective flattening**: including reduced intensity of emotional response
- **Asociality**: ↓ ability to feel intimacy or to initiate or maintain social contacts
- **Avolition**: apathy, amotivation
- **Anhedonia**: don’t care about their lack of interest, cf depression where they want to enjoy themselves but can’t
- **Attentional impairment**: uninterested in the company of others, unresponsiveness, withdrawal
- **Impact of negative symptoms**: contribute to social dislocation, isolation, ↓ in ADLs, ↓ in functional ability
- **Course of negative symptoms**: often present at the outset but the earlier a psychotic illness is treated, the less likely is the development of negative symptoms over time
- **Can be primary** (due to the illness) or **secondary** (eg to positive psychotic symptoms; more withdrawn due to paranoid fears etc)

- **Prodrome** = gradual change prior to first episode of frank psychosis. Look for:
  - ↓Concentration, attention drive, motivation
  - Depression, anxiety
  - **Sleep** disturbance
  - Social withdrawal, suspiciousness
  - These are common in adolescence: you’re looking for marked change over previous function

- **Cognitive symptoms**:
  - Not a criteria but occurs commonly (85%)
  - Usually present **prior** to onset of illness
  - CI related to social and functional outcomes and a predictor of overall treatment response
  - Wide range of cognitive functions can be impaired in schizophrenia:
    - Memory
    - Attention
    - Motor speed
    - Verbal fluency
    - Executive functioning

- **“First rank” symptoms**:
  - Common in persons with schizophrenia but can occur in other psychotic illnesses and mania:
    - **Auditory** hallucinations: audible thoughts, 2 or more voices discussing the person in 3rd person and voices commenting on behaviour. *I am* (first-person singular). *You are* (second-person singular). He, she, one or it *is* (third-person singular)
    - Thought interference: thought **withdrawal**, thought **insertion** and thought **broadcasting** (thoughts are “broadcast” beyond the head so that other people can hear them)
    - Feelings, impulses or acts experienced as being under **external control**
    - Delusional perception

- **“Poor insight”** as a symptom: **anosognosia** → the lack of knowledge, or not knowing you do not know
  - The most common symptom of acute psychosis
  - Leads to confabulation, poor adherence etc

**Associated Problems & Other Symptoms**

- Suicide in **15%**
- **Lack of insight**, very common (→ non-compliant with medication)
- **Ideas of reference** (everyone is talking about you)
- **Substance abuse**: co-morbid problem, ?self medication
- **Depression** in schizophrenia: diagnosed as Depressive Disorder NOS
- Neurological symptoms: abnormalities in balance, proprioception, graphesthesia, disorder in smooth eye pursuit, decreased blinking
- EPS (extra-pyramidal side effects) in 20% of drug naïve people suffering from schizophrenia (⇒ it’s not always due to drugs)
- **Comorbidity** in schizophrenia:
  - **Anxiety** disorders
  - Depression
  - Substance use
  - Personality disorder
  - **Physical comorbidity** and higher non-psychiatric mortality (DM, CVD)
Subtypes
- Not very commonly used
- Paranoid: delusions and hallucinations
- Disorganised: disorganised speech, behaviour, flat/inappropriate affect
- Catatonic: motor immobility, excessive motor activity, negativism, stereotypies (repeated monotonous movements), echolalia, echopraxia
- Undifferentiated
- Residual

Aetiology
- Multi-factorial and poorly understood: don’t know about relative loadings for predisposing and precipitating factors
- Genetic:
  - One parent affected → 5% chance, two parents → 45% chance, sibling affected → 10% chance; MZ twins = 46%
  - Several candidate genes (dysbindin, neuregulin) identified → susceptibility
- Neurodevelopment:
  - Brain injury at birth and perinatal complications (eg low Apgar)
  - Born in winter and spring, ?viral influences
  - Insults at this age not causal – but some correlation
- Neuropathology of psychotic disorders:
  - Evidence for early neurodevelopmental anomalies
  - Evidence for progressive grey-matter loss involving medial temporal and prefrontal regions
  - Evidence of late neurodevelopmental (post pubertal) changes during early stages of psychosis
- Neurobiology of schizophrenia:
  - Dopamine hypothesis:
    - Schizophrenia results from ↑ levels of dopamine in the brain
    - Based on DA antagonists (eg atypical antipsychotics) are effective in the treatment of schizophrenia and dopaminergic agents exacerbate/can cause psychotic symptoms (L-Dopa)
  - Other NTs implicated: 5HT3, GABA
  - Anatomical abnormalities:
    - Enlargement of lateral ventricles
    - Smaller than normal total brain volume
    - Cortical atrophy
    - Widening of the third ventricle
    - Smaller hippocampus
  - PET & SPECT scans show hypofrontality: ↓ glucose utilisation in frontal lobes
  - Neurological symptoms: soft signs → balance issues, proprioception etc issues
- Social causation: eg Shift and Drift or Breeder theory to try and explain higher incidence in lower socio-economic groups
- Emotion theory (a lot of critical comment and high expectations from parents)
- Vulnerable personality: Cluster A personality traits: schizoid, schizotypal, paranoid
- Head injury
- Precipitating factors: life events, drug abuse, etc

Differential Diagnosis
- Psychiatric disorders: bipolar (manic phase), Major Depression with Psychotic Features, Brief psychotic disorder, schizophreniform disorder (shorter duration), schizoaffective disorder (+ mood disorder), delusional disorder, depersonalisation disorder
- Medical illness: temporal lobe epilepsy, brain tumour, trauma, infectious (syphilis, HIV), SLE
- Drugs: amphetamines, cocaine, cannabis, PCP (Angel dust), alcohol withdrawal, benzo withdrawal, barbiturate withdrawal

Course and Outcome
- Course: prodrome (insidious, problems in language, reading, cognitive abilities & behaviour) → active → residual
- Prognosis: 10% good outcome; 45% intermediate outcome; 45% bad outcome (10-15% suicide)
**Poor** prognostic indicators: FHx, insidious onset, early age, chronic duration, single, male, predominant negative features, structural brain abnormal etc

**Positive** prognostic factors: absence of FHx, normal pre-morbid personality/functioning, period between onset and treatment < 6/12, presence of precipitating factors, presence of affective symptoms, good response to treatment, onset of first episode after 30, female

~30% will experience persistent symptoms → historically = treatment-resistant schizophrenia, now termed incomplete recovery

- Factors contributing:
  - Pt factors: substance abuse, physical comorbidity
  - Illness factors: poor insight, intellectual disability, early or insidious onset, longer prodrome etc
  - Treatment/therapist factors: non-compliance, side-effects, wrong dose, drug interactions, inadequate rehab etc

**Assessment**

- **Establish rapport**: this will be the first encounter of a lifetime of encounters with MH services. Try to get off to a good start!
- Domains for assessment: home, employment/study, activities, drugs, sexuality, suicide
- Assess social situation, and family views and functioning

**Recovery from Psychotic Illness**

- 20%: no further episodes
- 10–15% die: suicide/early death
- 60% ongoing, 20% with serious disability

**Treatment of Psychosis**

- Any treatment for mental disorder: biological + psychological + social interventions
- Early intervention improves outcome, reduces disruption/trauma (‘collateral damage’), etc. Important given stage of life (adolescence) and the potential problems for subsequent social and occupational development etc
- MDT treatment programme involving health professionals, family members, support agencies, and cultural/community context
- Brain’s ability to process and interpret information is affected ⇒ think carefully about how information conveyed is received. Keep the facts simple, avoid distractions and pressure, ask one question at a time, give plenty of time to answer

**Hospitalisation**

- Safety to self or community
- To establish a dx
- Management of acute episode – use of mental health act
- Stabilisation of medication
- To manage comorbid conditions
- For carer respite
- Forensic reasons

**Psychological Treatment**

- Psychological: supportive, education, self-care skills. Social skills training and community integration skills → overcome withdrawal → significant ↓ in readmissions
- Psychoanalysis and exploratory therapies have limited value
- CBT (don’t try and memorise specifics, here more as an example of CBT):
  - The central notion of CBT is that the way in which people make sense of their environment (including psychotic experiences) influences their affect and behaviour. CBT posits that people with emotional disorders such as depression see themselves or the world around them in negative and distorted ways, which lead to distress and behaviour that serve to reinforce and maintain their negativity.
  - The agenda for each session is developed collaboratively but hallucinations and delusions are often high on the list. Patients often

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**Psychological Medicine**

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want to understand things better, feel more in control, or be able to use better coping skills.

- A feature of CBT for schizophrenia that distinguishes it from other types of psychosocial interventions is the importance it places on understanding the onset of psychotic symptoms using a stress vulnerability model. This model emphasizes the notion that we all have the capacity to experience psychotic symptoms if we are placed under sufficient stress. However, owing to our individual genetic, physiological, psychological, and social vulnerabilities, we vary in our vulnerability to a psychotic breakdown.

- Another feature of CBT for schizophrenia that helps distinguish it from other more traditional CBT approaches is the emphasis placed on normalizing psychotic experiences. Time is often spent looking at the prevalence of unusual experiences (e.g., voice hearing in the normal population) in order to eliminate catastrophic interpretations of what having these experiences may mean. Patients often also have very distressing beliefs about what it means to have the diagnosis of schizophrenia. Therefore, time is spent examining beliefs about the diagnostic label of schizophrenia to try to decatastrophize these thoughts by providing information about more optimistic views recently published concerning the long-term outcome of the illness.

- CBT work to improve adherence with medication arises out of these sessions attempting to understand the individual formulation of the patient’s schizophrenia. The patient’s view of taking antipsychotic medication should be carefully explored. In working with delusions, it is best to begin with more superficial techniques such as peripheral questioning to outline the main areas of delusional impact. From there, behavioural homework can be used to lead to the generation of alternative explanations. Affects such as fear and anger can be reduced in intensity and avoidance tackled in session or out of session with the help of a (good) case manager.

**Social Treatment**

- **Assertive** (to combat stigma) community care. Relapse prevention: understanding drugs, warning signs, prognosis, side effects
- **Education**, compliance
- **Hospitalise** for acute loss of functioning
- Outpatient treatment is rehabilitative
- Families should be involved:
  - Can encourage compliance
  - Can recognise early signs of serious treatment side effects
  - Can recognise impending symptoms of relapse

**Biological: Antipsychotic Medication**

- **Treat early**, immediately if psychotic, key issue with maintenance medication is compliance
- Neuroleptics (antipsychotic) or major tranquilisers
- May also use lithium, carbamazepine, antidepressants and benzodiazepines for psychosis
- Antipsychotic drugs are used for 4 primary purposes:
  - 1. To manage acute positive symptomatic disturbances
  - 2. To induce remission from positive symptom exacerbations
  - 3. For maintenance therapy
  - 4. To prevent relapses or new episodes of positive symptoms (ie prophylaxis)
- Reduced risk of relapse in schizophrenia, but 40% will still relapse within a year
- Two effects:
  - Reduces delusions and hallucinations (may take 1–2 weeks)
  - Tranquillising/calming effect (↓acute agitation, immediate effect)
- Mostly act on D2 receptors
- For first presentation, treat with **low dose and use atypicals** (↓side effects →↑compliance). Use adjunctive long acting benzodiazepine for first few weeks to sedate and ↓agitation
- Can be administered orally, IM, IV and some as **DEPOT** (but not yet for atypicals)
- Side effect: over sedation, extra-pyramidal, anti-cholinergic and hypotensive
- All relatively effective at reducing positive symptoms, but ‘atypicals’ better than ‘typicals’ at reducing negative symptoms (eg ↓motivation, interest, lack of emotional display, restricted speech)
- All have hepatic elimination
- Clinical practice recommendations:
  - **Atypicals** are the treatment of choice
  - **Clozapine** as soon as treatment resistance is evident (in practice, used if failed two other drugs)
➢ **Depots** (inject: forms a precipitate which slowly releases over time) for identified adherence problems and relapse with trials of oral antipsychotics

- Factors **increasing** treatment adherence:
  - Acceptance of illness
  - Perceptions of severity
  - Level of support
  - Family stability

- Factors **decreasing** treatment adherence:
  - Side effects
  - Poor symptom control
  - Complex regime
  - Substance abuse
  - Impaired judgement
  - Poor communication, dr-/pt relationship

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<td>Fluphenazine</td>
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<td>Flupenthixol</td>
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<tr>
<td></td>
<td>Thiothixene</td>
<td>+  +  +/−</td>
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<td>Risperidone</td>
<td>+/−  ++  +</td>
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- * = Available as depot

**Typical Antipsychotics**

- Mode of action:
  - Block dopamine (D2) receptors
  - Most also have low affinity for 5HT2 receptors
  - Varying amounts of:
    - Anticholinergic
    - Antihistamine and
    - Anti α1 effects

- D2 effects at:
  - *Mesolimbic/mesocortical tracts*: antipsychotic effects; negative symptoms
  - *Nigrostriatal tracts*: extrapyramidal (Parkinsonian) side effects; long-term → upregulation of receptors → tardive dyskinesia
  - *Hypothalamic-pituitary pathway*: ↑PRL; antihistamine effects → drowsy, weight gain

- **Alpha adrenergic** effects: ↓BP, drowsiness

- **Anticholinergic** effects: constipation, blurred vision, dry mouth, drowsy, urinary retention

- **Adverse Effects**:
  - **CAGE MEN**
  - **QTC PROLONGATION**
  - **Extrapyramidal Syndromes (EPS):**
    - Acute: Occur early in treatment – usually first two months.
    - 1. Dystonias (muscle cramps and spasms): treat with benztpmine parenterally
    - 2. Akathisia (restlessness, legs especially): treat with β blocker or benzodiazepine
    - 3. Parkinsonism (tremor, cogwheel rigidity, bradykinesia, mask like face) – may improve with time
    - Anticholinergics only indicated in those whose antipsychotic dose cannot be safely reduced. (= antiparkinsonian medication, eg antimuscarinic drugs such as Cogentin)

- **Tardive Dyskinesia:**
Late onset dyskinetic syndrome due to antipsychotic drug treatment. Usually months or years after treatment
Fairly common: 15 – 30%
Slow, repetitive involuntary movements of mouth/face, and maybe limbs and trunk: lip smacking, tongue protrusion. Disappear during sleep
Risk factors: old age, organic brain disease, negative symptoms, alcohol abuse
Irreversible in 50%
No established protocol for treatment: try dose reduction, lithium, or change to clozapine
Made worse by dopaminergic agonists and anticholinergics

Other effects:
- Sedation
- Anticholinergic effects (dry mouth, constipation, blurred vision, urinary hesitancy)
- α-blockade (postural hypotension, tachycardia, delayed ejaculation)
- Endocrine effects (↑PRL, marked weight gain, ↓libido, impotence, amenorrhoea)

Neuroleptic Malignant Syndrome:
- Rare (0.2 – 1%), potentially fatal (20% mortality)
- See: hyperthermia, rigidity, and impaired consciousness.
- Emergency treatment (cooling, fluids, etc)

Interactions:
- Potentiate sedation with hypnotics, alcohol, opioid analgesics
- FLUOXETINE increases risk of EPS

Atypicals
- These drugs target specific dopamine receptors and/or may block or inhibit reuptake of SHT
- Difference between typical and atypical antipsychotics is the ability of the atypicals to treat the negative symptoms of schizophrenia, also ↓risk of developing tardive dyskinesia
- SE: weight gain, sedation, hyperglycaemia, anticholinergic effects, less PRL elevation, QT PROLONGATION, some EPS, ↑lipids

Clozapine:
- Mode of action: numerous receptors: D1, D2, D4, 5HT2, blocks α-1, H1 and muscarinic receptors
- Effective in individuals not responsive to classical antipsychotics, effective for positive and negative symptoms, no extrapyramidal side effects, no impact on sexual or reproductive function.
- Side effects:
  - Weight gain (this is a common problem with atypicals)
  - Agranulocytosis/blood dyscrasias in 1-2% by 1 year, most in first 18 weeks → regular blood tests. In NZ, only available through a distribution system that ensures weekly/monthly blood testing before dispensing of the next supply
  - Sedation, tachycardia, constipation, and seizures (3% at highest dose)
  - Drowsiness and sedation
  - Orthostatic hypotension
  - Potent enzyme inhibitor: significant drug interaction potential
  - Serotonergic crisis with SSRIs
  - Hypersensitivity syndrome: PUO, arthritis, rash
  - Prolongation of QT
  - Myocarditis

Risperidone:
- Mode of action: binds to 5HT2 and D2 receptors, antagonises H and α-1 receptors
- Similar efficacy as other antipsychotics for positive symptoms. Effective for negative side effects and also affective symptoms (depression, anxiety).
- Some dose related extrapyramidal side effects. ↑PRL at high doses. Also insomnia, agitation, anxiety, headache

Olanzapine:
- Mode of action similar to clozapine. Like clozapine has minimal impact on PRL
- Similar efficacy to haloperidol, but more impact on negative symptoms
- Sedation, headache, dizziness, constipation, dry mouth, weight gain

Quetiapine
Ziprasidone
Aripiprazole (new partial DA agonist)
Dementia

- Cognitive impairment/brain failure:
  - = the diminished ability to think
  - Failure of a major organ system ie the brain
  - NOT a normal part of ageing
  - > 50% not identified
  - Need to use standardised MMSE

Dementia

- = progressive, non-reversible decline in intellectual/cognitive & emotional abilities with impairment in social/occupational functioning
- = chronic, generalised impairment of memory (key feature), intellect, and personality with no impairment of consciousness (cf delirium)
- Acquired
- Not a feature of normal ageing
- Characterised by:
  - A MAD CAP (attention/concentration, memory, aphasia, disorientation, cognition, apraxia/agnosia, personality)
  - Memory loss
  - Impairment in ADL (eg leaving oven on)
  - Disorientation
  - Difficulty learning
  - Loss of language skills; loss of judgement and planning
  - Personality changes
  - Can have perceptual changes and psychotic symptoms
- Cf the forgetfulness of old age:
  - Normal memory changes with ageing = age-associated memory impairment = late life forgetfulness cf (>24 in MMSE)
  - Will see mild cognitive impairment (MCI) = isolated memory impairment = cognitive impairment, not dementia (CIND)
  - Stable memory: remote memory, remembering gist of information
  - Changing memory (ie this is lost in age-associated memory impairment): new learning, depth of processing, recall of details of new info/events, nonverbal memory

Epidemiology:

- Prevalence doubles every 5 years between ages 60 and 90
- 1% of those between 60-64 up to 30-50% of those older than 85 years
- Approximately 60% of nursing home beds are occupied by pts with dementia
- AD accounts for most pts with dementia who are older than 55 (50-90%)

DSM-IV Criteria

- A. Development of multiple cognitive deficits including both:
  - 1. Memory impairment (either ability to learn or recall), and
  - 2. One of aphasia (language disturbance), apraxia (unable to carry out learned tasks), agnosia (impaired recognition despite intact sensory function), disturbance in executive functions/personality/social conduct
- B. Gradual onset and continuing decline
- C. Significant impairment in social or occupational functioning, and a decline on previous function
- D. Not due to other CNS, systemic or substance use conditions
- E. The deficits do not occur exclusively during the course of a delirium
- F. The disturbance is not better accounted for by another Axis I disorder

Causes of “Reversible” Dementia/Cognitive Decline

- 10% = “reversible”: is reversible cognitive decline rather than dementia (dementia is progressive)
- Causes:
  - DEMENTIA
  - Drugs
  - Emotional illness → psychiatric disorder
  - Metabolic and endocrine disorders
  - Eye and ear problems
Differentiating Delirium from Dementia

- Key factors:
  - Are the changes **abrupt** or over a long period?
  - Is the level of **consciousness** impaired?
  - Are there hallucinations?
  - Are there physical signs present?

**Folstein MMSE**

- Folstein Mini-Mental Status Examination (max 30, <26=concern, <24=further assessment)
  - **Orientation** (max 10)
    - What is today's date? _____
    - What is the year? _____
    - What is the month? _____
    - What day is today? _____
    - What season is it? _____
    - What building are we in? _____
    - What floor are we on? _____
    - What town are we in? _____
    - What province are we in? _____
    - What country are we in? _____
  - **Registration** (max 3)
    - "ball", "flag", "tree"; ask to repeat. First _____ repetition is score. Repeat until get right or 6 times.
  - **Attention & calculation** (max 5)
    - 100-7's for 5 subtractions _____ OR spell "world" backwards with 1 for each letter in exactly the right place
  - **Recall** (max 3)
    - 3 previous words (from Registration) _____
  - **Language** (max 9)
    - Name a watch and a pencil (2 points) _____
    - Repeat the following "no ifs, ands or buts" (1 point) _____
    - Follow a three stage command: "take the paper in your right hand, fold it in half and put it on the floor" (3 points)
    - Repeat and obey the following CLOSE YOUR EYES (1 point) _____
    - "Write a sentence"; **must have noun, verb and be sensible** (1 point) _____
    - Draw 2 intersecting pentagons each side 1". Must have 10 angles and intersect (1 point) _____
- Total Score _____/30

**DDx**

- If you scored low on MMSE, DDx = delirium, depression, ↓IQ, dementia etc

**Assessment**

- Three steps:
  - Recognise memory and cognitive impairment
  - **Diagnose** dementia
  - Determine cause
- General: age, absence of psychiatric history or co-existing physical illness
- General account from carer, including memory impairment, behaviour change, mood change, physical symptoms, disruption of ADLs, dangerous activity eg driving or leaving oven on
- Onset: insidious or acute
- Stepwise deterioration (suggests vascular), seizures
- **Fluctuation**, including early evening, **nocturnal worsening** ("sunsetting")
- Family history including Huntington’s
Clinical Course and Complications

- **Amnesia:**
  - Early: forget names, appointments, repetitive in conversation, some insight, leaving elements or taps on
  - Later: forget faces, recent events
  - Advanced: forget past, identity, relatives, no insight

- **Language:**
  - Early: difficulty word finding
  - Later: ↓articulateness, difficulty following conversation
  - Advanced: rambling, incoherent

- **Dyspraxia (difficulty sequencing tasks):** Difficulties with dressing, cooking → safety issues: wandering, kitchen/road safety
- All lead to → difficulties with ADLs, safety, caregiver stress, depression, elder abuse etc
- Other: depression (difficult to distinguish), psychosis, personality & behavioural change

Examination

- General: posture, gait, consciousness level, wandering, restlessness, feeding and dressing difficulties
- MMSE
- Neuro: focal signs, involuntary movements, pseudobulbar signs (swallowing, speech production), primitive reflexes

Investigation

- Cognitive Function: test with mini-mental state: **26 or above = normal**, 20 – 26 = mild, 11 – 20 = moderate, < 10 = severe
- FBC (macrocytosis) and LFTs: is it alcohol induced?
- Exclude: THYROID, space occupying lesion, B12 deficiency, AIDS, syphilis
- CT if focal neurological signs, new or odd psychiatric disorder, or age < 75 with shorter history. NB include temporal lobe orientated views, as atrophy of medial temporal lobe is one of the earliest CT findings in Alzheimer’s disease

Treatment

- First sort whether delirium vs dementia and reversible vs non-reversible
- Treatment of any cause found. Treatable causes include:
  - Benign brain tumour, especially subfrontal meningioma
  - Subdural haematoma
  - Wilson’s disease: akinetic rigid syndrome, bulbar palsy
  - Deficiency: B12, B6, B1
  - Hypothyroidism
  - Alcoholic dementia
  - Infection: HIV, syphilis
- **Improve functional ability:**
  - Relieve distressing symptoms (eg secondary incontinence)
  - Regular routines (diaries, reminders)
  - Establish competence and ENDURING POWER OF ATTORNEY early on (using PPPR act later on is more involved)
  - Assess ability to drive
  - Practical assistance (eg meals on wheels, rest home care, respite)
  - Support for the family (involvement in rehabilitations, information, etc)
- **Drugs:**
  - Cholinesterase inhibitors:
    - Hold off progression for a year or two? Better motivation, improvement in ADLs
    - 12 weeks before effect can be reliably assessed
    - Side effects: nausea, diarrhoea, vomiting, muscle cramps, fatigue, anorexia
    - Eg Rivastigmine (Exalon): titrate up monthly: 1.5 mg bd → 3.0 mg bd → 4.5 mg bd → bd 6.0 mg
    - Eg Donepezil (Aricept): 5mg od → 10 mg od after a month if necessary
    - Cautions: peptic ulcer disease, arrhythmias
    - Not currently funded and pretty expensive
  - Other drugs with possible benefit:
    - Antioxidants (eg vitamin E, gingko biloba etc)
NSAIDs
Oestrogen

Treatment for vascular dementia: control of blood pressure and aspirin

Alzheimer's

2/3 of dementia. Is a syndrome, not a single disease. F > M. Course 6 – 8 years (⇒ may die of something else first)

If < 65 then Alzheimer's disease, if > 65 then Senile dementia, Alzheimer's type

Clinical diagnosis. Diagnosis only certain at autopsy

Aetiology: genetic predisposition (mutation in B amyloid precursor protein [APP] on Ch21) + environmental triggers (Aluminium)

Risk factors: age, FHx (RR 4), apolipoprotein E4, female (2:1), head trauma, low education, systolic hypertension, Down's syndrome

Presentation:
- Marked impairment of memory: anterograde and retrograde (eg how old are you, are you married, what are your children’s names, etc)
- Aphasia with word finding defect early on
- Visuo-spatial problems: getting lost
- Loss of interest: hobbies, dealing with finances, new circumstances, etc

Gross pathology:
- Atrophy in frontal, parietal, occipital and temporal regions, with secondary widening of sulci and dilation of ventricles

Micro:
1. Neurofibrillary tangles: intracytoplasmic coiled filaments of the protein tau
2. Senile plaques: amyloid beta peptide surrounded by filamentous material. Motor and sensory cortex sparing. A few are normal. There are lots in Alzheimer’s
3. Amyloid angiopathy
Granulovacuolar degeneration: clear intraneuronal cytoplasmic vacuoles

Pathogenesis:
- ?Accumulation of amyloid beta protein, with failure to exocytose the protein
- Apoe4 allele is a marker for Alzheimer’s but is not yet recognised as a screening or diagnostic tool

Defuse Lewy Body Dementia

Lewy bodies = intracellular eosinophilic inclusions (proteins such as ubiquitin)
About 20%, second most common dementia
Overlap with Alzheimer’s and Parkinsonian Dementia

Characteristic features:
- Often associated Parkinsonian features (rigidity, tremor and bradykinesia) – less tremor but truncal rigidity
- Fluctuating cognitive function and level of consciousness
- Can see fluctuating attention and visual hallucinations (so like delirium)
- Frequent faints and falls
- Marked cholinergic neuronal loss → rapid progression
- Very sensitive to neuroleptics (= anti-psychotics). A small dose can → profound tranquilliser effect

Vascular Dementia

15 – 20%, third most common
Risk factors: age, previous history of CVD, CVA, high BP, high cholesterol, smoking, etc. M > F
Caused by discrete infarcts (ie multi-infarct dementia) but also small vessel disease (eg cerebral arteriolar sclerosis from chronic hypertension)

Characteristics:
- Stepwise decline
- Stigmata of stroke
- Abnormal neuro exam
- Often impaired attention and frontal features, emotional lability
- CT/MR show multiple small and some larger infarcts
- Multiple subcortical white matter injury → Binswanger disease (damage to association fibres)
Other Types of Dementia

- Pick’s disease = frontotemporal:
  - 5%
  - Much less common, but similarities with Alzheimer’s.
  - Differences are early onset of personality, behavioural changes and language impairment.
  - Atrophy of frontal and temporal lobes (ie clearly localised).
  - Microscopically, surviving neurons show ballooning degeneration (Pick’s cells) and Pick’s bodies (filamentous intracytoplasmic inclusions). No senile plaques or neurofibrillary tangles
- Alcoholic Dementia. 10%. See Pathological Effects of Alcohol on the Brain, page 753
- Rarer causes:
  - Creutzfeldt-Jakob Disease (CJD)
    - Fatal, rapidly progressive dementia with psychiatric and behavioural disturbances. Less than 1 per million per year, usually elderly
    - No helpful lab findings (including CSF)
    - Aetiology: abnormal neuronal protein coded by the PRNP gene. Prion causes conformational change from a α-helix to a β-sheet → chain reaction → neuronal death
    - Can be transferred via pituitary extracts, dural grafts, etc
    - 15% of cases familial
    - No macroscopic changes. Microscopically: spongiform encephalopathy – vacuoles in neurons and neuropil (ie extracellular) → neuronal loss and gliosis (marked astrogliosis)
  - Variant CJD (vCJD). Affected young adults, progressed more slowly, early behavioural changes. Spongiform changes plus plaques composed of prion protein. Caught from Bovine Spongiform Encephalopathy (BSE, Mad Cow Disease). Prions very difficult to inactivate (eg standard disinfectants, formalin, UV light don’t work)
  - Huntington’s Disease:
    - Prevalence: 7 per 100,000
    - Clinical: Choreaathetotic movements and progressive dementia from age 35 – 40. Depression, erratic behaviour, apathy, problems with speech and swallowing. Death in 15 years on average
    - Genetics: Autosomal dominant, short arm of chromosome 4
    - Gross: diffuse gyral atrophy, marked atrophy of caudate nucleus and putamen, dilation of ventricles
    - Micro: loss of neurons in atrophied areas, replaced by fibrillary gliosis
  - HIV & syphilis

Dementia Due to Head Trauma

- Presence of dementia directly due to head trauma
- Severity and type of cognitive or behavioural impairment depends on location and extent of injury
- Symptoms include aphasia, attention problems, irritability, anxiety, depression, apathy, aggression, other personality change
- Is usually non-progressive unless repeated head trauma (eg boxer). Progressive decline following single trauma suggests another problem (eg hydrocephalus or major depressive episode)

Management

- Fatigue and stress result from:
  - Poor concentration, impaired executive function and ↓memory due to injury
  - Sleep requirements increase, but patients try and do the same amount as before
  - No knowledge about what to expect (both patients and families)
- Fatigue + stress → frustration, anxiety and depression. So reduce factors leading to fatigue and stress
- Management focuses on:
  - Education
  - Proper assessment of cognitive deficits by a psychologist (eg cognitive testing = neuropsychological testing)
  - Support from informed family, friends and employers
  - Regular breaks/sleeps. Take things in small bites and structure day around these
  - Teach relaxation methods
  - Compensating for cognitive losses: structured day (↓ability to plan), lists, diaries
  - Continual reassurance
  - Medication:
• Use for depression if symptoms do not resolve with counselling and support. SSRIs have least side
effects. TCA if headaches, or sleep is a problem (side effects include daytime sedation and
↓cognitive function)
• Maybe Methylphenidate (Ritalin) - ↑ arousal to extend time possible to work

Prognosis
• Only 20 – 30% return to full function 1 – 2 years after a mild head injury
• Degree of cognitive difficulty in first month NOT a good prognostic indicator
• Need to consider PTSD as differential or co-existent diagnosis
• Good prognostic indicators: strong social support, early intervention by a specialist HI recovery service
• Bad prognostic indicators: persisting cognitive difficulties at 6 – 9 months

Delirium
• Global and transient disturbances of consciousness, attention, perception, thinking, memory, psychomotor
  behaviour, emotion and sleep/wake cycle
• = Acute Confusional State, transient cognitive impairment
• = acute form of brain failure and is a medical emergency
• Epidemiology:
  ➢ Rare in the community
  ➢ Common in hospital, especially in elderly, 20-30% of > 65 years olds admitted to medical wards
  ➢ Higher incidence in nursing homes
  ➢ 30% in open heart surgery; > 50% in hip #
  ➢ Significant mortality: approx 25% of elderly patient acquiring delirium in hospital die
• Will get poor history from the patient. Need informant
• Predisposing factors:
  ➢ The ageing brain: ↓ capacity for homeostatic regulation/resistance to stress/disease; changes in
    metabolism/response to drugs
  ➢ Underlying structural brain disease (eg atherosclerosis, Alzheimer’s)
  ➢ Chronic disease
  ➢ Impaired vision and hearing
• Pathophysiology:
  ➢ Thought to result from excessive NT release (Ach and DA) with widespread decline in cerebral metabolism
    and alterations in neurotransmission
  ➢ Other likely mechanisms: failure of cerebral oxidative mechanisms, CNS effects of lymphokines
  ➢ Functional rather than structural

Symptoms
• Rapid onset (potentially related to new illness/drug). Rarely lasts more than several weeks. Improves if pt
  doesn’t die
• Fluctuating cognition/consciousness (cf psychiatric illness, which does not present with impaired
  consciousness)
• Disturbance of ATTENTION, mood, arousal, self-awareness
  ➢ Global cognitive impairment
  ➢ Reversible
• Disorientation to time/place/person
• Marked abnormalities of attention and concentration
  ➢ Attention unfocused
  ➢ Less aware of surroundings
  ➢ Easily distractable
  ➢ Trouble with concentration and commands
  ➢ Thinking: disorganised, delusions, rambling incoherent speech
  ➢ Memory impairment
• Perceptual abnormalities: illusions and hallucinations (especially visual)
• Psychomotor behaviour: hyper/hypo active, purposeless
• Mood/emotions: labile, agitation, fear, anxiety
• Sleep-wake cycle: disrupted or even reversed
• Fluctuating : often agitated in evening (“sundowning”)
DSM-IV Criteria

- GCCPFAS (good cooks can pan fry and sauté: GMC, consciousness, cognition [globally impaired], perception, fluctuating, attention, short/sundowning [worse at night])
- A. Disturbance of consciousness
- B. Change in cognition or development of perceptual disturbance not accounted for by dementia
- C. Development over a short period of time (usually hrs to days); tends to fluctuate during the course of the day
- D. Evidence on hx, exam or lab findings that disturbance caused by direct physiological consequence of a GMC

Aetiology

- I WATCH DEATH:
  - INFECTION/infarctions – cerebral and non-cerebral: Especially chest and urinary tract, also sepsis, meningitis, encephalitis, AIDS, Hepatitis, etc
  - Withdrawal: alcohol, amphetamines, barbiturates, benzos, cocaine
  - Acute metabolic: hypoglycaemia, hyponatraemia, hypokalaemia, hyper/hypocalcaemia, acidosis, uraemia, porphyria
  - Trauma
  - CNS pathology: stroke, epilepsy, Parkinson’s, Huntington’s, MS, Tumour, normal pressure hydrocephalus (confusion, incontinence, gait disturbance)
  - Hypoxia/hypercapnia
  - Deficiencies/DEHYDRATION/drugs
  - Endocrine: Hyper/hypothyroidism, hyper/hypoPTH, Hyper/hypoadrenocorticolism, diabetes mellitus, phaeochromocytoma
  - Acute vascular/MI
  - Toxins – drugs: antiarrhythmics, antibiotics, anti-virals, anti-fungals, β-blockers, etc
  - Heavy metals: mercury etc

- Common causes: Often multi-factorial – a little bit of a number of things
  - Infection: UTI, pneumonia
  - Drug reactions
  - Hypoglycaemia
  - ↓O2 or ↑CO2

- Differential of acute confusion:
  - Psych illness: delirium, psychosis, dementia, depression
  - Drugs, illness, metabolic, trauma, hypoxia, poisoning/overdose, post-ictal, ↓thiamine

Types of Delirium

- Hyperactive (classical): least common
- Hypoactive: 1/3 of cases
- Mixed: ½ of cases
- Also: delirium tremens and BZD withdrawal

Assessment

- Hx: often need collateral
- Have a high index of suspicion
- Thorough physical exam paying attention to septic screen
- MMSE
- Monitor attention
- Ix:
  - Rule out potential causes as listed above
  - FBC, urinalysis, U & E, Cr, glu, LFTs, cardiac enzymes, TFTs, folic acid, B12, VDRL, drug screens
  - CXR, CT/MRI
  - ECG
  - Maybe LP/EEG

Risk Factors

- Multiple, severe or unstable medical problems
- Dementia or cognitive impairment
- Polypharmacy
Surgery
Metabolic disturbances
Advanced age (especially > 80 years)
Infection (especially UTI)
Fractures (especially hip)
Visual impairment
Fever or hypothermia
Psychoactive drug use

Management

First, recognise the delirium (it often isn’t). Careful and repeated assessment. Watch for confused/disoriented behaviour or inattention, especially at night

Treatment of underlying cause: may require history from care giver

Supportive care:
- Reorientation (a smoke and a cup of tea works wonders!)
- Reassurance of pt and family re transient nature
- Environment: consistent, comfortable and safe
- Attention to noise and light levels (not too much nor too little)
- Continuity of staffing
- Family member (or even an orderly) to sit with patient
- Familiar objects (eg family photos) in the room
- Stimulate during the day: get them dressed, false teeth in, glasses on, hearing aid in

Avoid restraints

Attention to nutrition and hydration

Manage: fluids, electrolytes, O2 etc

Target risk factors of cognitive impairment, sleep deprivation, immobility, visual and hearing impairment

Drugs: only if agitated, restless and self/others at risk
- Atypical antipsychotics: Quetiapine, olanzipine risperidone
- Lorazepam (short acting benzo) 0.5 – 2 mg q 15 – 20 min iv/im/sublingual/po for sleep only as can add to confusion during the day

Prognosis and Risks in Delirium

- 6-35% die in hospital; 1 year after discharge ~ 50%
- About 25% have accelerated cognitive decline
- Extends the length of hospitalisation → ↑ risk of nosocomial infections, falls
- ↑ risk of recurrent delirium
- ↑ rate of institutionalisation, pressure sores etc

Somatoform Disorders

- Presence of physical symptoms suggesting a GMC but are not explained by that condition, by substances or medications, or by another mental disorder (eg Panic Disorder)
- Must cause significant distress or impairment in social or occupational functioning
- Difficult to manage: need to check for physical conditions → constant testing → reinforces worry. If find something on tests this validates and reinforces the worry
- Processes contributing to symptoms and motivation for symptom production is unconscious → they don’t know it’s not real.
- Cultural, stress, developmental and self-esteem factors may contribute

<table>
<thead>
<tr>
<th>Disorder</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Somatization Disorder</td>
<td>Polysymptomatic, recurrent and chronic, 5-10% of primary population, often young female, system review profusely positive, key differentials: physical disease, depression</td>
</tr>
<tr>
<td>Conversion Disorder</td>
<td>Monosymptomatic, mostly acute, high prevalence, often young females, low education, excellent prognosis unless chronic, key differentials: depression, schizophrenia, neurological diseases. Weakness, paralysis, pseudoseizures, involuntary movements (eg, tremors), and sensory disturbances (eg, aphonia, deafness, blindness) are the most frequent complaints. Symptoms often enable patients to avoid an unpleasant situation at home or work, attract attention, or gain support from others (unconscious however)</td>
</tr>
</tbody>
</table>
**Hypochondriasis**

**Disease concern or preoccupation**, middle to older age, especially if previous physical disease, M = F, may be obsessional, course waxes and wanes, key differentials: depression, physical disease, personality or delusional disorder

**Body Dysmorphic Disorder**

**Obsessive pre-occupation with feelings of ugliness or concern with body defect**, rarer, adolescence or young adult, key differentials: delusional disorder, depression, somatization disorder

**Pain Disorder**

'**Simulated**' pain syndrome incompatible with known physiology or anatomy, female to male is 2:1, 4th or 5th decade, very common in pain populations, key differentials: depression, physical disease, malingering

---

**Somatization**

- Somatic symptoms with no physical cause found (+/- anxiety/depression)
- Aim of treatment is to reattribute the symptoms to relate them to psychological problems
- Approach to managing in a non-specialist practice setting:
  - **Feeling understood**:
    - Take full history, including pain during a typical day
    - Watch for emotional clues or links with stressors: “what are you thinking about when it hurts”
    - Ask about social/family factors
    - Explore health beliefs: “What do you think is wrong”
    - Focus exam
  - **Change the agenda**:
    - Feed back results
    - Acknowledge reality of pain
    - Reframe complaints: set them in the context of life events. “I’m struck by the fact that these pains started shortly after … and that you’ve been crying a lot… Do you think there might be a connection”
  - **Making the link**:
    - Make the link to life events clearer to the patient
    - Use negotiating style: “Do you think that’s possible… perhaps…”
    - Projection: “Has anyone else suffered from symptoms like these… Did your mother get headaches – what caused those”? May be easier to see the connection in others

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**Hypochondriasis**

- The core clinical feature of hypochondriasis is persistent preoccupation with having a serious medical illness despite appropriate medical evaluation and reassurance

**Diagnostic Criteria**

- A. Preoccupation with fears of having, or the idea that one has, a serious disease based on the person’s misinterpretation of bodily symptoms.
- B. The preoccupation persists despite appropriate medical evaluation and reassurance.
- C. The belief in Criterion A is **not of delusional intensity** (as in Delusional Disorder, Somatic Type) and is not restricted to a circumscribed concern about appearance (as in BDD).
- D. The preoccupation causes **clinically significant distress** or impairment in social, occupational, or other important areas of functioning.
- E. The duration of the disturbance is at least **6 months**.
- F. The preoccupation is not better accounted for by GAD, OCD, Panic Disorder, a Major Depressive Episode, Separation Anxiety, or another Somatoform Disorder.

---

**Disorders Due to a General Medical Condition**

- Psychiatric symptoms occur in a wide range of medical conditions
- Use surgical sieve (VITAMIN C & D)
- Neurological:
  - Degenerative: Parkinson’s, Huntington’s, Wilson’s → depression, dementia, psychosis
  - Epilepsy: 30 – 50 % have psychiatric illness at some stage, can be due to medication
  - Brain tumours: especially frontal lobe or limbic system
  - Head injury
  - Demyelinating disorders: eg MS
- Infectious:
  - Herpes simplex encephalitis → changed personality, psychosis
  - Rabies, syphilis, CJD, Kuru (in PNG)
Psychological Medicine

- HIV
- Autoimmune: Systemic lupus erythmatosus: eventually 50% have psych symptoms
- Endocrine:
  - Hyperthyroid → confusion, anxiety, agitated depression, manic, delusions, with weakness and muscle loss
  - Hypothyroid → if severe then hypomania, depression, hallucinations
  - Hypercalcaemia (due to PTH disorder) → delirium, changed personality, apathy, ↓cognitive function
  - Hypocalcaemia (due to PTH disorder) → delirium, changed personality, eventually tetany
  - Hypoadrenocorticism (Addison’s) → apathy, depression
  - Hyperadrenocorticism (Cushing’s) → agitated depression
  - Total pituitary failure → hypothyroid and hypoadrenocorticism
- Metabolic:
  - Hepatic encephalopathy → ↓memory, ↓LOC, changed personality
  - Uraemia encephalopathy: renal failure → ↓memory, ↓orientation, ↓LOC
  - Hypoglycaemia: agitation/restlessness
  - Ketoacidosis → easy fatigue
  - Acute intermittent porphyria → ↑ porphyrins (components of haemoglobin synthesis): acute colicky abdominal pain, motor polyneuropathy, psychosis, anxiety, insomnia, lability of mood, depression.
  - Barbiturates absolutely contraindicated. 0.2 – 0.5% psych patients have undiagnosed porphyria
- Nutritional:
  - Niacin deficiency
  - Thiamine deficiency
  - B12 deficiency → neuro degeneration → depression, irritability, moodiness
- Toxins:
  - Mercury: depression, irritability, psychosis, tremor, weakness
  - Lots of others
- Cancers Eg carcinoma of the pancreas
- Medication:
  - Mood disturbances from: stimulants, steroids, L-dopa, etc
  - A previous condition (eg major depressive disorder) can be triggered by medication with the capacity to cause depressive symptoms

**Substance Use Disorders**

**The Top 10 Things to Know About Addiction**

- 1. Addiction is fundamentally about compulsive behaviour
- 2. Compulsive drug seeking is initiated outside of consciousness. Addictive behaviour appears to involve processes outside of the sufferer’s personal consciousness by which cues are registered and acted upon by primitive regions of the brain before consciousness occurs
- 3. Addiction is about 50% heritable and complex environmental influences are involved
- 4. Most people with addictions who present for help have other psychiatric problems as well (axis 1 disorder ~ 74%)
- 5. Addiction is a chronic relapsing disorder in the majority of people who present for help
- 6. Different psychotherapies appear to produce similar treatment outcomes
- 7. ‘Come back when you’re motivated’ is no longer an acceptable therapeutic response
- 8. The more individualised and broad-based the treatment a person with addiction receives, the better the outcome
- 9. Epiphanies are hard to manufacture (ie a dramatic recovery experience)
- 10. Change takes time

**Diagnostic Criteria**

- Two types of disorder:
  - Substance use disorders: abuse and dependence
  - Substance induced disorders: secondary to substance use (eg withdrawal, psychosis, persisting dementia or amnestic disorders, etc). Require evidence of substance use and are not related to pre-existing problems
- Abuse vs. dependence:
  - Abuse implies use is causing job, social, legal or physical problems or impairing function in some way
  - Dependence (a step worse) requires signs of withdrawal and tolerance
Used to be a definition for ‘the addictive personality type’: but research has shown no consistent correlation with the proposed criteria.

**Substance Abuse**
- A **maladaptive pattern of substance use** leading to **significant impairment or distress**, manifested by **one** (ie fairly low threshold) or more of the following occurring in the same 12 month period:
  - Recurrent substance use resulting in a **failure to fulfil major role obligations** at work, school or home
  - Recurrent substance use in which it is **physically hazardous** (eg driving)
  - Recurrent substance-related **legal problems** (eg arrests for disorderly conduct)
  - **Continued use despite** it causing or exacerbating persistent or recurrent social or interpersonal problems
- Symptoms have never meet the criteria for substance dependence for this class of substance

**Substance Dependence**
- A **maladaptive** pattern of substance use leading to **significant impairment or distress**, manifested by **three** or more of the following occurring in the same **12 month period**:
  1. **Tolerance**: either ↑ amounts to achieve intoxication or diminished effect with same amount
  2. **Withdrawal**: either characteristic withdrawal syndrome for that substance, or the same or a closely related substance is taken to avoid withdrawal symptoms
  3. Substance is taken in **larger amounts** or over a **longer period** than was intended
  4. There is a persistent desire or unsuccessful efforts to cut down or control use
  5. A great deal of time is spent obtaining, using or recovering from its effects
  6. Important social, occupational or recreational activities are given up or reduced as a result
  7. Use is continued despite knowing that has caused or exacerbated a physical or psychological problem

**Epidemiology**
- 2003-4 Substance Use Disorders in the NZ Mental Health Survey: **12.3% have had a substance use disorder in life so far**, 3.5% in the last year
- Higher incidence in **males, younger**, less education, lower income, social deprivation, MAP
- Co-morbidity or Dual Diagnosis:
  - 2003-4 Substance Use Disorders in the NZ Mental Health Survey found the lifetime co-morbidity of substance use disorders by specific diagnoses:
    | Disorder          | Percentage |
    |-------------------|------------|
    | Anxiety disorders | 40%        |
    | Alcohol dependence| 31%        |
    | Mood disorders    | 29%        |
    | Smoke tobacco     | 56%        |
  - In another study:
    - Those with a mental disorder have **twice** the risk of an alcohol disorder and **4 times** the risk of any other drug disorder
    - Those with a lifetime alcohol disorder have twice the risk of another mental disorder (37%) and 6 times the risk of another drug disorder (22%)
    - Those with a lifetime other drug disorder have a 4 times risk of another mental disorder (53%) and 7 times the risk of an alcohol disorder (47%)
    - Co-morbidity is higher in institutional settings (70- 80%) than in the community
    - Suicidal ideation is ↑
  - ➞ Dual diagnosis is an expectation not an exception

**Models of Aetiology of Addiction**
- **Disease model**: emphasises the biological and genetic basis of addiction. Loss of control is a central feature
- **Self-medication hypothesis**: use specific pharmacological effects to self medicate for psychological disturbance and painful effects
- **Biopsychosocial model**: multifactorial causality, interaction of **genetic** predisposition, **biological** factors, and **psychological** and **sociocultural** factors
- **Biological model**: **impact on mesolimbic reward system** – extends from the ventral tegmentum to the nucleus accumbens, with projections to areas such as the limbic system and the orbitofrontal cortex

**Factors Influencing Behaviour**
- **Early childhood** learning: **modelling** by parents and significant others
- **Current environment**: **reinforcement or punishment** for different practices (especially if immediate)
- **Views/knowledge/beliefs** about risk: usually over-rate our health and under-rate the risks
Our **resources** (usually an excuse)
- Physical environment (work/home)
- Social influences (friends/media)

**History Taking**
- Attitude of interviewer important: non-judgemental, empathic, detached, normalising behaviour, start estimates of use at a high level, person can then say ‘no, not that much’ – feels less judgemental
- Often illegal: won’t tell unless good rapport
- Signs of Substance Abuse:
  - Changed behaviour
  - Skipping work/school
  - Drug seeking behaviour
  - Money problems
  - Relationship problems
- Questions:
  - Reason for presentation
  - Which drugs
  - Ever intravenous
  - What are the useful effects – why do you continue to use
  - Quantity and frequency, pattern of use (regular or binge)
  - Cost per week
  - Duration of use, age at first use, reason for first use
  - Heaviest use
  - Have you or others ever been concerned about your use
  - Attempts at cutting down and duration of abstinence, what made you start again
  - Problems associated with use, including relationships, job, legal considerations, etc
  - Any withdrawal effects
  - Past treatment and outcome, what was and wasn’t helpful
  - Relationship to psychiatric symptoms. Do they drink when they’re anxious? Have panic attacks followed ↑ drug use, etc
- If alcohol, ever been in an accident, had a head injury or fracture
- Medical history, psychological history, social situation
- Family History: check psych, suicide and A&D history
- Corroborative interview
- Drug users have high mortality: health consequences, accidents, suicide, high-risk neighbourhoods, etc
- Physical examination: yellow fingers/teeth, injection marks, liver, cardiac murmurs, pregnancy/STD, mental status, signs of intoxication/withdrawal

**Key Questions**
- **What** are you using: drug type, strength, route (need to ask IV)
- **Patterns** of use (quantity and frequency)
- **Other** substances (eg alcohol, smoking)
- Usual social and physical **environment of use**
- What happens if you **don’t take**?
- WTF CULT
- What are the **GOOD AND THE BAD THINGS** about use?
- Do you find yourself **taking more** than in past? **Increased time** spent getting/using?
- Ever had any **INJURIES** whilst under the influence/trouble with the law?
- Impact on life: work/relationships?
- **CAGE** questions

**Investigations**
- Alcohol abuse: ethanol level, also LFT (↑GGT) & FBC (macrocytes), nutrition (eg Fe)
- **Blood tests for drug levels**: benzodiazepines & morphine levels
- Cannabis: creatinine/cannabis ratio over time
- If any **intravenous use** check for viral serology: Hep B, C, HIV
• Urine tests: useful for tracking abstinence, but not reliably effective as a treatment strategy. Can do a full drug screen (drugs + prescription medications) for $160. Verification of sample source is important—minimise the risk of substitution (e.g., giving you someone else’s urine sample).

<table>
<thead>
<tr>
<th>Drug</th>
<th>Time after which urine screen will be negative</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amphetamine</td>
<td>1–2 days</td>
</tr>
<tr>
<td>Cannabis</td>
<td>4–28 days</td>
</tr>
<tr>
<td>Cocaine</td>
<td>1–2 days</td>
</tr>
<tr>
<td>Diazepam</td>
<td>2–4 days (longer with prolonged use)</td>
</tr>
<tr>
<td>Heroin</td>
<td>1–2 days</td>
</tr>
<tr>
<td>LSD</td>
<td>1–3 days</td>
</tr>
<tr>
<td>MDMA (ecstasy)</td>
<td>2–4 days</td>
</tr>
<tr>
<td>Methadone</td>
<td>2–4 days</td>
</tr>
</tbody>
</table>

**Drugs of Abuse**

• If therapeutic index is wide, then it’s good for addiction: good effect but few side effects
• **IV drugs:** opiates, methamphetamines, speed, and benzodiazepines. Health risks include infection and non-infectious sequelae
• Heroin not available in NZ
• Marijuana
• Ecstasy—amphetamine (party scene)
• Fantasy—GHBA
• Solvents: younger, failing at school, worried parents, neurological impairment
• Tobacco (See Smoking, page 122)

**Drugs of Abuse**

**Category & Name**

<table>
<thead>
<tr>
<th>Tobacco</th>
<th>Nicotine</th>
<th>Found in cigarettes, cigars, bidis, and smokeless tobacco (snuff, spit tobacco, chew)</th>
<th>Not scheduled/smoked, snorted, chewed</th>
<th>Increased blood pressure, and heart rate/chronic lung disease; cardiovascular disease; stroke; cancers of the mouth, pharynx, larynx, esophagus, stomach, pancreas, cervix, kidney, bladder, and acute myeloid leukemia; adverse pregnancy outcomes; addiction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alcohol</td>
<td>Alcohol (ethyl alcohol)</td>
<td>Found in liquor, beer, and wine</td>
<td>Not scheduled/swallowed</td>
<td>In low doses, euphoria, mild stimulation, relaxation, lowered inhibitions; in higher doses, drowsiness, slurred speech, nausea, emotional volatility, loss of coordination, visual distortions, impaired memory, sexual dysfunction, loss of consciousness/increased risk of INJURIES, VIOLENCE, FETAL DAMAGE (in pregnant women); depression; neurologic deficits; hypertension; liver and heart disease; addiction; fatal overdose</td>
</tr>
<tr>
<td>Cannabis</td>
<td>Marijuana (cannabis)</td>
<td>Blunt, dope, ganja, grass, herb, joint, bud, Mary Jane, pot, reefer, green, trees, smoke, sinsemilla, skunk, weed</td>
<td>I/smoked, swallowed</td>
<td>Euphoria; relaxation; slowed reaction time; distorted sensory perception; impaired balance and coordination; increased heart rate and appetite; impaired learning, memory; anxiety; panic attacks; psychosis/cough, frequent respiratory infections; possible mental health decline; addiction</td>
</tr>
<tr>
<td>Hashish</td>
<td>Boom, gangster, hash, hash oil, hemp</td>
<td>I/smoked, swallowed</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Opioids</td>
<td>Heroin</td>
<td>Diacetylmorphine: smack, horse, brown sugar, dope, H, junk, skag, skunk, white horse, China white; cheese (with OTC cold medicine and antihistamine)</td>
<td>I/injected, smoked, snorted</td>
<td>Euphoria; drowsiness; impaired coordination; dizziness; confusion; nausea; sedation; feeling of heaviness in the body; slowed or arrested breathing/constipation; endocarditis; hepatitis; HIV; addiction; fatal overdose</td>
</tr>
<tr>
<td></td>
<td>Opium</td>
<td>Laudanum, paregoric: big O, black stuff, block, gum, hop</td>
<td>II, III, V/swallowed, smoked</td>
<td></td>
</tr>
<tr>
<td>Stimulants</td>
<td>Cocaine</td>
<td>Cocaine hydrochloride: blow, bump, C, candy, Charlie, coke, crack, flake, rock, snow, toot</td>
<td>II/smoked, snorted, smoked, injected</td>
<td>Increased heart rate, blood pressure, body temperature, metabolism; feelings of exhilaration; increased energy, mental alertness; tremors; reduced appetite; irritability; anxiety; panic; paranoia; violent behavior; psychosis/weight loss, insomnia; cardiac or cardiovascular complications; stroke; seizures;</td>
</tr>
</tbody>
</table>
### Methamphetamine
Drivers, uppers
*Desoxyn:*  'P' meth, ice, crank, chalk, crystal, fire, glass, go fast, speed

### Club Drugs
- **MDMA** (methyleneoxy-methamphetamine)
  - Ecstasy, Adam, clarity, Eve, lover’s speed, peace, uppers
  - I/swallowed, snorted, smoked, injected
  - MDMA—mild hallucinogenic effects; increased tactile sensitivity; empathic feelings; lowered inhibition; anxiety; chills; sweating; teeth clenching; muscle cramping/sleep disturbances; depression; impaired memory; hyperthermia; addiction

- **Flunitrazepam***
  - Rohypnol: forget-me pill, Mexican Valium, R2, roach, Roche, roofies, roofinol, rope, rorphies
  - IV/swallowed, snorted, smoked
  - Flunitrazepam—sedation, muscle relaxation; confusion; memory loss; dizziness; impaired coordination/addiction

### Dissociative Drugs
- **Ketamine**
  - Ketalar SV: cat Valium, K, Special K, vitamin K
  - III/injected, snorted, smoked
  - Feelings of being separate from one’s body and environment; impaired motor function/anxiety; tremors; numbness; memory loss; nausea

- **PCP and analogs**
  - Phencyclidine: angel dust, boat, hog, love boat, peace pill
  - Not scheduled/chewed, swallowed, smoked
  - Also, for ketamine—analgesia; impaired memory; delirium; respiratory depression and arrest; death

- **Salvia divinorum**
  - Salvia, Shepherdess’s Herb, Maria Pastora, magic mint, Sally-D
  - Not scheduled/swallowed
  - Also, for PCP and analogs—analgesia; psychosis; aggression; violence; slurred speech; loss of coordination; hallucinations

- **Dextromethorphan (DXM)**
  - Found in some cough and cold medications: Robotripping, Robo, Triple C
  - I/swallowed, absorbed through mouth tissues
  - Also, for DXM—euphoria; slurred speech; confusion; dizziness; distorted visual perceptions

### Hallucinogens
- **LSD**
  - Lysergic acid diethylamide: acid, blotter, cubes, microdot yellow sunshine, blue heaven
  - I/swallowed, snorted, smoked
  - Altered states of perception and feeling; hallucinations; nausea

- **Mescaline**
  - Buttons, cactus, mesc, peyote
  - Magic mushrooms, purple passion, shrooms, little smoke
  - I/swallowed, smoked
  - Also, LSD and mescaline—increased body temperature, heart rate, blood pressure; loss of appetite; sweating; sleeplessness; numbness, dizziness, weakness, tremors; impulsive behavior; rapid shifts in emotion

- **Psilocybin**
  - Magic mushrooms, purple passion, shrooms, little smoke
  - I/swallowed
  - Also, for LSD—Flashbacks, Hallucinogen Persisting Perception Disorder

### Other Compounds
- **Anabolic steroids**
  - Anadrol, Oxandrin, Durabolin, Depo-Testosterone, Equipoise: roids, juice, gym candy, pummers
  - Solvents (paint thinners, gasoline, glues); gases (butane, propane, aerosol propellants, nitrous oxide); nitrites (isomyl, isobutyl, cyclohexyl):/laughing gas, poppers, snappers, whippets
  - III/injected, swallowed, applied to skin
  - Steroids—no intoxication effects/hypertension; blood clotting and cholesterol changes; liver cysts; hostility and aggression; acne; in adolescents—premature stoppage of growth; in males—prostate cancer, reduced sperm production, shrunken testicles, breast enlargement; in females—menstrual irregularities, development of beard and other masculine characteristics

### Inhalants
- Not scheduled/inhaled through nose or mouth
- Inhalants (varies by chemical)—stimulation; loss of inhibition; headache; nausea or vomiting; slurred speech; loss of motor coordination; wheezing/cramps; muscle weakness; depression; memory impairment; damage to cardiovascular and nervous systems; unconsciousness; sudden death

### Prescription Medications
CNS Depressants
* Schedule I and II drugs have a high potential for abuse. They require greater storage security and have a quota on manufacturing, among other restrictions. Schedule I drugs are available for research only and have no approved medical use; Schedule II drugs are available only by prescription (unrefillable) and require a form for ordering. Schedule III and IV drugs are available by prescription, may have five refills in 6 months, and may be ordered orally. Some Schedule V drugs are available over the counter.

** Some of the health risks are directly related to the route of drug administration. For example, injection drug use can increase the risk of infection through needle contamination with staphylococci, HIV, hepatitis, and other organisms.

*** Associated with sexual assaults.

**Marijuana:**
- **Marijuana enhances the senses and brings on feelings of relaxation and well-being.** Marijuana is also used medicinally to relieve pain, reduce nausea and vomiting, and stimulate appetite. However, there are drawbacks to extended use, including learning and memory impairment, lung and respiratory problems caused by the smoke, and infertility. Marijuana abuse has also been linked to low achievement, delinquent behavior, and poor family relationships.
  - Types and street names:
    - Marijuana (pot, dope, weed)
    - Hashish

**Depressants and downers:**
- **Depressants, commonly known as downers, are substances that slow down the central nervous system.** Sleeping pills and prescription medications for anxiety such as Xanax and Valium fall into this drug category, as do Rohypnol and GHB, known as “date rape” drugs due to their frequent use in sexual assaults. Individuals suffering from anxiety and low self-esteem often abuse downers. But while downers induce relaxation, they also impair the user’s ability to think clearly and react quickly.
  - People abusing depressants may appear to be drunk—exhibiting signs such as losing their balance and slurring their words. Additionally, they may suffer from amnesia and delusions.
  - Downers are highly addictive, and withdrawal is severe, with symptoms including nausea, vomiting, and cramps. Downers are lethal in high doses, particularly when mixed with alcohol.
  - Types and street names:
    - Barbiturates (downers, sedatives)
    - Benzodiazepines (downers, tranqs)
    - Methaqualone (Qualudes)
    - Rohypnol (roofies)
    - GHB (liquid ecstasy)

**Stimulants and uppers:**
- **Stimulants, or uppers, are drugs that speed up the central nervous system.** Commonly abused uppers include cocaine, methamphetamine, crack, and prescription ADHD medications such as Ritalin and Adderall.
  - While stimulants initially boost energy and confidence, their use over time leads to symptoms of anxiety, aggression, sleep difficulties, hallucinations, and paranoid thinking. As uppers wear off, users experience a “crash,” characterized by depression, fatigue, and irritability.
  - Types and street names:
    - Amphetamines (uppers, speed)
    - Cocaine (coke, blow)
    - Crack cocaine
    - Methamphetamine (meth, crank)
    - Crystal meth
    - Ritalin and other ADHD drugs

**Hallucinogens and dissociative drugs:**
- **Hallucinogens and dissociative drugs, also known as psychedelics, are mind-altering drugs that affect the user’s sensory perceptions and thought processes.** Hallucinogens such as LSD and peyote can promote insight, contemplation, and euphoria—with some users reporting spiritual or out-of-body experiences. But on the flip side, these same drugs can result in “bad trips” characterized by panic and psychotic breaks with reality.
Ecstasy, a popular club drug with both hallucinogenic and stimulant properties, boosts empathy and feelings of interpersonal closeness. Risks include a dangerous increase in body temperature, liver damage, and heart problems. The dissociative drugs PCP and ketamine block perception of pain and induce a trance-like state. Adverse effects can be severe and include violent reactions, complete disorientation, and terrifying delusions and hallucinations.

- **Types and Street Names**
  - PCP (angel dust)
  - LSD (acid)
  - Mescaline (peyote)
  - Psilocybin (magic mushrooms)
  - MDMA (ecstasy)
  - Ketamine (Special K)

**Narcotics and opioids:**

- Narcotics, or opioids, are powerful pain relievers that mimic the effects of endorphins, the body’s natural “feel-good” chemical. Commonly abused narcotics include heroin, morphine, codeine, and prescription painkillers such as Vicodin and Oxycontin. These drugs elevate mood and induce a tranquil, relaxed state. Side effects include nausea, vomiting, and severe itching. Tolerance and physical dependency will develop if opioids are used for any extended period of time. If a narcotics abuser quits “cold turkey,” he or she will experience withdrawal symptoms.
- While not dangerous, withdrawal from heroin and other narcotics is extremely unpleasant, with symptoms including muscle and joint pain, fever, nausea, sweats, chills, stomach cramps, and diarrhea.
- Overdose is another risk of narcotic abuse, especially if the user is shooting the drug. Another danger of intravenous opioid or heroin use is infection from dirty needles. Intravenous drug users are at a higher risk of contracting viruses such as HIV and hepatitis, and often suffer from abscesses, collapsed veins, and bacterial infections.

- **Types and street/brand names:**
  - Heroin (smack, junk)
  - Opium
  - Morphine
  - Codeine
  - Fentanyl (Duragesic)
  - Oxycodone (Oxycontin, Percocet)

**Inhalants:**

- Inhalants are chemicals that cause intoxication when sniffed or inhaled. They include common, household solvents, aerosols, and gases such as paint thinner, dry-cleaning fluid, gasoline, glue, felt-tip marker fluid, deodorant and hair sprays, spray paint, air fresheners, butane lighters, and propane tanks.
- Other abused inhalants include medical anesthetics such as “laughing gas,” ether, and chloroform. While “huffing” gives users a brief high, this high often comes with side effects including nausea, vomiting, delusions, confusion, and loss of consciousness. Prolonged inhalant abuse can also cause damage to the brain and other organs of the body.
- But the biggest risk involved with inhalant use is death by overdose. Inhalant use can cause sudden heart failure, or “sudden sniffing death syndrome,” even in individuals who are young and healthy.

- **Types and street names:**
  - Solvents (paint thinners, gasoline, glues)
  - Aerosols (hair spray, spray paint)
  - Gases (butane, propane)
  - Nitrous oxide (laughing gas)
  - Nitrites (poppers)

**Anabolic steroids:**

- Unlike other drugs of abuse, anabolic steroids don't have any intoxicating effects. They are used, not to get “high,” but to improve athletic performance and build muscle. But while steroids may help would-be athletes bulk up or obtain an edge on the field, they come with serious side effects and health risks.
- Steroid abuse causes blood pressure to skyrocket, increases bad cholesterol (LDL) while decreasing good cholesterol (HDL), triggers violent and aggressive behavior, results in severe acne, and brings growth to a halt in adolescents.
- Women taking steroids can develop facial hair, a deep voice, and male-pattern baldness. Men, on the other hand, can develop breasts, infertility, shrinking of the testicles, and baldness.

- **Types and street names:** anabolic steroids (roids, juice)
Withdrawal Symptoms

- Cocaine:
  - Agitation, insomnia, anxiety, depression, anger, cravings, fatigue, nausea, vomiting, shakes, irritability, muscle pain.
- Methamphetamine:
  - Extreme fatigue, disturbed sleeping patterns, irritability, restlessness, intense hunger, moderate to severe depression, anxiety, angry outbursts, lack of motivation, mental confusion, psychotic reactions, depression, intense cravings for the drug.
- Opiates:
  - Dysphoria (more prominent than physical symptoms), watery eyes, runny nose, yawning, sweating, chills, stomach cramps, shakes, feeling jittery, irritability, panic, tremors, anxiety, restlessness, insomnia, dilated pupils, goose bumps, rapid heart beat, high blood pressure, nausea/vomiting, diarrhea, muscle aches and pains.
- Benzodiazepines:
  - Sleeplessness, irritability, anxiety, feeling shakily, headache, dizziness, loss of appetite, rapid heartbeat, sweating, agitation, and in extreme cases seizures.

Dependence Resulting from Various Drugs

<table>
<thead>
<tr>
<th>Drug Class</th>
<th>Physical</th>
<th>Psychological</th>
<th>Tolerance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alcohol</td>
<td>3</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>Sedatives</td>
<td>3</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>Benzodiazepines</td>
<td>1</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>Opioids</td>
<td>4</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>Stimulants</td>
<td>1</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Hallucinogens</td>
<td></td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Solvents</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Nicotine</td>
<td>1</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Cannabis</td>
<td></td>
<td>2</td>
<td>1</td>
</tr>
</tbody>
</table>

- Approximate addictivity (highest to lowest): nicotine → opiates → stimulants → alcohol

Cannabis/Marijuana

- Prevalence: abuse 0.9%, dependence 0.5% in past year; 20% of young people at least weekly or over 100 occasions
- Patterns of use:
  - Intoxication:
  - Withdrawal:
  - Physical complications:
  - Mental complications: ↑ risk of psychosis (OR 1.41, if frequent use, 2.09)
- Treatment:
  - Psychoactive ingredient is Δ9 tetrahydrocannabinol (Δ9 THC)
  - Receptor targets in the CNS = CB1, in PNS = CB2
  - Synthetic cannabinoid drugs used therapeutically for appetite stimulation (eg in cancer), anticonvulsant/antispastic, analgesic
- Effects:
  - Minimal for occasional use, greater for longer-term heavy use
  - Respiratory system: hot irritating smoke → all the effects of cigarette smoke (inflammation, ↑ mucus, thickened basement membrane, squamous cell metaplasia, destruction of cilia)
  - CNS: enhanced feelings of well being, disputed dose-dependent effects – reduction in energy, drive and motivation, psychosis, ↓ learning and attention, dependence with associated social and psychological dysfunction, acute adverse reactions (eg anxiety/panic attacks)

Opioids

- Opiates vs opioids
- Patterns of use: “chasing the dragon”; bleeding poppies, acetylation
- Intoxication:
  - Withdrawal: irritability, anxiety, agitation, myalgia, abdo pain, hot/cold, nausea + diarrhoea, yawning, lacrimation, piloerrection, rhinorrhoea, dilated pupils, insomnia
- Physical complications:
- Mental complications:
• Treatment: OST, detox, naltrexone

**Benzodiazepines**
• Prevalence:
• Types:
• Intoxication:
• Withdrawal: seizures, delirium, anxiety, agitation, sensitivity to light/sound, paresthesia, myalgia, myoclonic jerks, Insomnia, dizziness
• Physical complications:
• Mental complications:
• Treatment:

**Methamphetamines**
• Prevalence = 0.6% of global population, 97% of IVDU have used it
• Pattern of use:
• Intoxication:
• Withdrawal:
• Physical complications:
• Mental complications:
• Treatment:

**Others**
• Cocaine
• Hallucinogens (LSD, daytura)
• Party pills
• Gamma hydroxybutyrate
• Solvents
• Inhalants
• Steroids
• Gambling

**Regulation of Addictive Drugs**
• See Regulation of Drugs of Abuse, page 860

**Treatment of Substance Abuse**

**Treatment Rationale**
• Treatment must be for the underlying addictive disorder, not just detoxification and withdrawal
• Addiction is a chronic not acute illness. Requires long term follow-up and behaviour modification (as with diabetes/hypertension)
• Often unsympathetic response because addiction is perceived as self-afflicted: but there are numerous involuntary components in the addictive process. Loss of voluntary control turns a drug misuser into drug addicted. There is a compulsive, often overwhelming, involuntary component
• Involves genetic, biological, behavioural and environmental components
• Success rate for treatment depends on type of drug and variables inherent in the population being treated (e.g. better for professionals than for poorly educated). Nicotine has the poorest success rate. Success rates are comparable with other chronic diseases
• Treatment is cost-effective

**Brief Intervention**
• = a rapid assessment of AOD use, assessment of motivation, provision of education/support, referral if appropriate
• Is effective (can ↓ consumption by 30-40%); generally takes ~ 5min
• Ideal for all health care workers to use when there isn’t a lot of time for pts with binge or regular use, those with dependence at the less severe end of the scale, for any behaviour or lifestyle change
• The 5 ‘a’s:
  - **Ask**: all pts if using psychoactive drugs (illicit and licit)
  - **Assess**: pt’s willingness to change
  - **Advise**: of potential harms associated with their patterns of use
- **Assist:** pts in accordance with their readiness to change
- **Arrange:** for follow-up/referral

Structure of the BI:
- **Give information** – about drinking or other intake guidelines (eg ALAC), how easy it is to slip into using in excess, mention the pt’s intake level in regard to guidelines (if any)
- **Discuss cutting down, an appropriate goal,** changes to behaviour associated with AOD intake
- **Negotiate when to start** for the goal, how to make the changes, arrange a time for f/u

**Issues in Treatment**
- Compliance with treatment. Those who comply with treatment have best prognosis – as with other chronic diseases
- Who should be involved: multidisciplinary approach
- Managing the environment: peer pressure, money, job, supports, triggers to former behaviours, family relationships (can they be helped, education about illness)
- The most significant predictor of treatment success is an empathic, hopeful, continuous treatment relationship
- Must also treat any co-morbid diagnosis simultaneously

**Types of Treatment**
- Medical, psychological, and social (eg get a job, help with finance etc)
- **Medication:** Antabuse (stops alcohol dehydrogenase), naltrexone, opioid substitution
- **Detoxification** (inpatient/outpatient)
- A&D counselling: motivational interviewing, strategies for change, relapse prevention
- **Psychotherapy:** CBT, psycho-education
- **Self-help** groups (eg 12-step programme)
- Addressing specific issues: grief, anxiety, childhood sexual abuse, sexual assault, anger, relationship problems, parenting issues, financial, housing, employment issues, etc

**Readiness to Change/Motivational Interviewing**
- See Behavioural Change, page 19
- Stages of change: precontemplation → contemplation → planning → action → maintenance → ? relapse

**Safer Prescribing of Controlled Drugs**
- Frequent dispensing (closed control)
- Send prescription direct to pharmacy
- Write quantity and strength in words

**Services for Dependency**
- Detox: Kenepuru (inpatient)
- AA
- Narcotics anonymous
- Queen Mary – Hamner: uses 12 step process
- Odyssey House (Auckland)
- Alcohol and drug service

**Making the Change**
- Takes a long time
- Involves changing lifestyles, supports, habits
- GP can assist with motivation for change

**Methadone Treatment**
- Methadone: oral bioavailability = **80-90%** as cf 30% with other opioids
- Methadone is highly addictive, but is regular, long acting (a dose a day holds for 24 – 48 hours), free (→↓crime), legal, more effective taken orally than other opiates, no risks from injection
- Doesn’t give a high – just stops ‘hanging out’ (withdrawal)
- Has to be taken every day
- Can cause high mood, drowsiness, ↓pain, small pupils, constipation, histamine release (sweating, itching, etc), ↓saliva →↑tooth decay, ↓libido – it is a powerful drug
- It doesn’t affect senses, or damage body organs, shouldn’t affect pregnancy or breast-feeding
- Is dangerous in conjunction with tranquillisers and/or alcohol → overdose situation (eg vomit and choke while sedated)
- Is taken as part of a planned programme, including counselling, to build a life away from opiate abuse — can concentrate on sorting out debt, relationships, gives patients some measure of control

**Alcohol**
- Rapidly absorbed by simple diffusion: jejunum and duodenum > stomach
- BAL varies with: **body weight**, dose, rate of consumption, presence of food, rate of alcohol metabolism

**Safe Limits and Metabolism**
- Men and women have different blood alcohol levels given the same dose due to lower Vd in women

<table>
<thead>
<tr>
<th>Standard Units</th>
<th>Per Day</th>
<th>Per Week</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>6</td>
<td>21 (ie up to 210 g ethanol)</td>
</tr>
<tr>
<td>Female</td>
<td>4</td>
<td>14 (ie up to 140 g ethanol)</td>
</tr>
</tbody>
</table>

- Standard Unit = **10 g of alcohol**. Eg 1 can normal strength beer, 1 glass (120 ml) table wine, 1 glass sherry/port, 20 ml spirits (hotel nip)
- **Effects** (if no tolerance):
  - 50 mg: relaxation, emotional lability, ↓ concentration, reaction time, decision-making, vision
  - **80 mg**: legal driving limit
  - 100 mg: ataxia and poor coordination
  - **150 mg**: amnesic blackouts (can’t remember afterwards)
  - 200 mg: ataxia, vomiting, nystagmus, drowsiness
  - 350 mg: coma, respiratory depression, death
  - Intoxication can be life threatening
- **Driving**:
  - Legal blood limit = **80 mg/100ml (17.4 mmol/L)**
  - Legal breath limit = **400 µg/L breath**
  - Driving skills impaired from 40 – 50 mg/100 ml
- **Metabolism**:
  - CH3CH2OH → CH3- C – H → Acetate
  - **10 g per hour**, zero order kinetics
  - 10g = 15 – 20 mg/100 ml blood/hour (3 – 4 mmol/hr) = **one standard drink/hr**
  - Twice this rate of clearance with chronic alcohol consumption, less in liver disease
  - Alcohol changes NAD/NADH ratio → alters redox potential → widespread effects (eg ↑ lipids, ↓ sugars, etc)
- **Memory loss**:
  - BAL > 150mg
  - Alcohol induced amnesia, hours to days, carry out complex tasks with no recall
- **Alcohol binge medical effects**: AF, gout, hangovers, death etc etc

**Classifying Alcohol Use and Abuse**
- **AUDIT** tool
  - Use
  - Hazardous use (8+ on AUDIT)
  - Abuse
  - Dependence
Alcohol Dependence: need to drink every day

Important features:
- Tolerance: due to pharmacodynamic and pharmacokinetic (e.g., enzyme induction) processes
- Physical dependence: Withdrawal syndrome on abstinence
- Cross-tolerance, e.g., alcohol and BZDs
- Psychological dependence: Emotional need to compulsively take a drug (even if no physical withdrawal syndrome)
- Using more than intended
- Unsuccessful attempts to cut down
- Continued use despite contraindication (social/medical impairment)

### Questions

<table>
<thead>
<tr>
<th>Questions</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. How often do you have a drink containing alcohol?</td>
<td>Never</td>
<td>Monthly or less</td>
<td>2 to 4 times a month</td>
<td>2 to 3 times a week</td>
<td>4 or more times a week</td>
</tr>
<tr>
<td>2. How many drinks containing alcohol do you have on a typical day when you are drinking?</td>
<td>1 or 2</td>
<td>3 or 4</td>
<td>5 or 6</td>
<td>7 to 9</td>
<td>10 or more</td>
</tr>
<tr>
<td>3. How often do you have six or more drinks on one occasion?</td>
<td>Never</td>
<td>Less than monthly</td>
<td>Monthly</td>
<td>Weekly</td>
<td>Daily or almost daily</td>
</tr>
<tr>
<td>4. How often during the last year have you found that you were not able to stop drinking once you had started?</td>
<td>Never</td>
<td>Less than monthly</td>
<td>Monthly</td>
<td>Weekly</td>
<td>Daily or almost daily</td>
</tr>
<tr>
<td>5. How often during the last year have you failed to do what was normally expected from you because of drinking?</td>
<td>Never</td>
<td>Less than monthly</td>
<td>Monthly</td>
<td>Weekly</td>
<td>Daily or almost daily</td>
</tr>
<tr>
<td>6. How often during the last year have you needed a first drink in the morning to get yourself going after a heavy drinking session?</td>
<td>Never</td>
<td>Less than monthly</td>
<td>Monthly</td>
<td>Weekly</td>
<td>Daily or almost daily</td>
</tr>
<tr>
<td>7. How often during the last year have you had a feeling of guilt or remorse after drinking?</td>
<td>Never</td>
<td>Less than monthly</td>
<td>Monthly</td>
<td>Weekly</td>
<td>Daily or almost daily</td>
</tr>
<tr>
<td>8. How often during the last year have you been unable to remember what happened the night before because you had been drinking?</td>
<td>Never</td>
<td>Less than monthly</td>
<td>Monthly</td>
<td>Weekly</td>
<td>Daily or almost daily</td>
</tr>
<tr>
<td>9. Have you or someone else been injured as a result of your drinking?</td>
<td>No</td>
<td>Yes but not in the last year</td>
<td>Yes during the last year</td>
<td></td>
<td></td>
</tr>
<tr>
<td>10. Has a relative or friend or a doctor or another health worker been concerned about your drinking or suggested you cut down?</td>
<td>No</td>
<td>Yes but not in the last year</td>
<td>Yes during the last year</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Risk Level vs. Intervention

<table>
<thead>
<tr>
<th>Risk Level</th>
<th>Intervention</th>
<th>AUDIT Score*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zone I</td>
<td>Alcohol education</td>
<td>6–7</td>
</tr>
<tr>
<td>Zone II</td>
<td>Simple advice</td>
<td>8–15</td>
</tr>
<tr>
<td>Zone III</td>
<td>Simple advice plus brief counseling and continued monitoring</td>
<td>16–19</td>
</tr>
<tr>
<td>Zone IV</td>
<td>Referral to specialist for diagnostic evaluation and treatment</td>
<td>20–40</td>
</tr>
</tbody>
</table>

### Score Interpretation

- **Score of:**
  - Means
  - 0–7: Low risk of alcohol-related harm
  - 8–10: High risk of experiencing alcohol-related harm
  - 11–19: A person scoring in this range will already be experiencing significant alcohol-related harms
  - 20+: A person scoring in this range may be alcohol-dependent and is advised to see a health-care professional about their drinking.

Characterised by: ↑tolerance (CNS adaptation and pharmacokinetic), narrowing of drinking pattern (stereotyped drinking), amnesic blackouts, withdrawal symptoms, awareness of loss of control, failed attempts at abstinence, preoccupation with drinking, drinking to relieve withdrawal symptoms

Look for: compulsive binges with ↑ frequency, stereotyped drinking, intake over 60 g ethanol/day, chronic social and health problems, neurological problems

Use CAGE questions to assess dependency: Have you ever tried to Cut Down, Annoyed by others telling you to cut down, Guilt, Eye-opener (need a drink in the morning to get you going)

- Hazardous Drinking:
  - Heavy drinking with no “obvious” problem. 8+ on AUDIT
  - Characterised by prolonged (eg 5 years or more), regular (eg almost daily, or weekend binges), excessive consumption with a high risk of physical mental and social implications, but no dependency features – but maybe some ↑tolerance and occasional amnesic blackouts, may not be associated with acute intoxication
  - Look for: episodic heavy social drinking to intoxication, ↑ psychosocial problems, accidents, inflammation of stomach, liver, pancreas

- Problem Drinking: problems related to alcohol without dependency and with or without excessive regular consumption. May result from isolated acute intoxication or drinking with medical contraindication – injury, aggression, binge drinking, family, financial, occupational problems

- Remember: Drug abusers often abuse multiple drugs (eg alcohol, BZDs, and marijuana)

Alcohol Misuse Impact

- People on whom the drinking impacts:
  - The drinker: physical problems, psychological problems, marital problems
  - The spouse/partner/children
  - Society: homelessness, intersection with drug problems, crime and public safety issues, driving, public order (drunkenness, noise etc)

Assessment

- For liver and pancreatic effects see Alcoholic Liver Disease, page 281
- Differential of drowsiness/confusion in alcoholic:
  - Alcohol intoxication
  - Sedatives
  - Post-ictal (eg seizures with alcohol withdrawal)
  - Wernicke’s encephalopathy
  - Subdural haematoma: grow slowly, compounded by global atrophy due to alcohol
  - Hepatic encephalopathy
  - Alcoholic hypoglycaemia

- Assessment of co-existing disease is vital:
  - Other drug use (BZD, sedatives, opioids → also have withdrawal features)
  - Primary depressive disorder (in addition to alcohol-induced depression which resolves quickly)
  - Gastro disorders: oesophagitis, pancreatitis, liver disease, small bowel dysmotility
  - Respiratory: obstructive sleep apnoea, aspiration pneumonia, TB
  - Musculoskeletal: chronic proximal myopathy, osteoporosis
  - Carcinomas: larynx, oesophagus, lung
  - Neurological: peripheral neuropathy, dementia, cerebellar atrophy, Wernicke-Korsakoff syndromes, Head injury (subdural haematoma), haemorrhagic stroke
  - Cardiovascular: arrhythmias, congestive cardiomyopathy, hypertension
  - Blood and nutritional: macrocytosis, folate and iron deficiency, impaired leucocytes, hypocalcaemia, hypokalaemia, electrolyte disturbances

- Investigations:
  - Alcohol levels
  - LFTs (AST > ALT)
  - Electrolytes (low K or Na)
  - B12, B1
  - FBC (anaemia)
  - Glucose (→ hypoglycaemic)
  - Coagulopathy: INR
  - Other drugs, eg BZD
Drug Interactions

- ASA/NSAIDS: gastritis
- Opioids/benzos: CNS depression etc
- Insulin: potentiates hypoglycaemia
- Disulfiram (Antabuse)

Pathological Effects of Alcohol on the Brain

- Cerebral atrophy:
  - **Common.** Seen in over ¼ of long term alcoholics at post-mortem
  - Ventricular dilation, widening of the cerebral and cerebellar sulci
  - No specific cortical changes have been described. No classical changes of multi-infarct dementia or Alzheimer’s (see Dementia, page 731)

- Wernicke-Korsakoff Syndrome (Wernicke’s encephalopathy):
  - Due to ↓Vitamin B1 (Thiamine) – Marmite and Cereals are good sources
  - Thiamine is not stored in the body, signs of deficiency can appear within a month – especially in **beer** drinkers (high carbohydrate intake →↑ thiamine requirement)
  - Rare triad of:
    - 1. Ophthalmoplegia/VI nerve palsy (→ vertical/horizontal nystagmus)
    - 2. Ataxia (also see **broad-based gait**; vestibular dysfunction)
    - 3. Confusion
  - Pathology:
    - Acute: petechial haemorrhages in the grey matter surrounding the third and fourth ventricles and aqueduct
    - Chronic: shrinkage and haemosiderin staining (especially of mamillary bodies)
  - If prolonged leads to **Korsakoff’s amnesic psychosis** (unable to lay down new memories)

- Vitamin B12 (cobalamin) deficiency:
  - Leads to:
    - Peripheral neuropathy, demyelination and degeneration of the posterior and lateral columns of the spinal cord
    - Variety of confusional, amnestic and psychotic alterations

Treatment of Alcohol Abuse

- Drug treatment of alcohol abuse:
  - Effects of chronic alcohol:
    - ↑Dopamine activity
    - ↑Opioid activity (⇒ ?naloxone/naltrexone →↓ craving)
    - ↑Sensitivity to GABA
    - ↓Serotonin activity
  - ie, lots of potential neurotransmitter targets in reward pathways to ↓ cravings, etc
  - **Antabuse** (disulfiram):
    - Blocks second step of metabolism pathway →↑ acetaldehyde → flush, vomiting, ↓ BP
    - Takes 12 hours to block enzyme system. Has effect within ½ hour of a drink (one drink is enough)
    - Contraindications: heart disease (can’t cope with ↓ BP), makes depression/psychosis worse
    - Administration needs to be supervised: if taken at own discretion then little impact on abstinence
  - Naltrexone:
    - Blocks opioid receptors → ↓ craving
    - Leads to fewer drinking days, ↓ consumption
    - Improved outcomes 3/12 post drug
  - Acamprosate (Campral): ↓ craving, must be taken 3 times daily (a pain!), start 7 days post detox. Not in elderly, pregnant, liver or renal disease. No hypnotic, anxiolytic or antidepressant effects

- For non-drug treatment, see Treatment of Substance Abuse, page 748

Alcohol Withdrawal

- Most common drug withdrawal state. **Can be life threatening** (unlike opioid withdrawal). Most dangerous drug from which to withdraw (seizures, hallucinations, delirium)
- Detoxification is only the first step in treatment
- Aetiology of alcohol withdrawal syndrome poorly understood
- Features of withdrawal:
  - A spectrum
Psychological Medicine

- **Minor withdrawal (peaks at day 2):** craving, restlessness, anxiety, nausea, disordered sleep, headache, tachycardia, hypertension, tremor
- **Major withdrawal (peaks at day 5):** agitation, behavioural disorders, confusion, sweating, fever, paranoia, hyperventilation
- **Delirium Tremens** describes severe withdrawal only (severe agitation, confusion, visual hallucinations, fever/sweating, tachycardia, nausea/diarrhoea, dilated pupils)
- **Seizures:** if they occur (in ~ 15%), are most likely in first 48hrs, usually only one, usually grand mal, status rare
- **Hallucinations:** usually visual (auditory unlikely: visual > tactile > auditory), on day 2 – 4
  - CIWA: clinical institute withdrawal: alcohol
  - Score of withdrawal (not intoxication)
  - Benzos + alcohol interaction = respiratory depression

### Symptoms of Alcohol Withdrawal Syndrome

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Time of appearance after cessation of alcohol use</th>
</tr>
</thead>
<tbody>
<tr>
<td>Minor withdrawal symptoms: insomnia, tremulousness, mild anxiety, gastrointestinal upset, headache, diaphoresis, palpitations, anorexia</td>
<td>6 to 12 hours</td>
</tr>
<tr>
<td>Alcoholic hallucinosis: visual, auditory, or tactile hallucinations</td>
<td>12 to 24 hours</td>
</tr>
<tr>
<td>Withdrawal seizures: generalized tonic-clonic seizures</td>
<td>24 to 48 hours</td>
</tr>
<tr>
<td>Alcohol withdrawal delirium (delirium tremens): hallucinations (predominately visual), disorientation, tachycardia, hypertension, low-grade fever, agitation, diaphoresis</td>
<td>48 to 72 hours</td>
</tr>
</tbody>
</table>

### Management

- There is a management protocol based on CIWA score
- Get pre-detoxification blood alcohol level. Helps with assessment (how tolerant are they?). Avoid too much sedative if high.
- Previous withdrawal severity good indicator of likely current severity. Other indicators of severity: > 15 standard drinks a day, early morning drinking, hypokalaemia, intercurrent illness
- If likely to be severe, or co-existing medical, psychiatric illness or other addiction, withdrawal should be medically supervised (ie admit them). **Mattress on floor with constant nursing attention.** If dehydration or constant sweating then iv fluids. Non-stimulatory environment
- Otherwise at home or outpatients if good social support
- Routine blood tests: FBC, ESR, U+E, B12/folate, LFT, AST, GGT, PT, BS
- Give IV fluids and correct electrolyte disturbances as required
- **Parenteral thiamine** followed by short oral course (25 mg po twice daily) → ↓ chance of Wernicke’s encephalopathy
- Treat withdrawal with drugs which have cross-tolerance with alcohol (ie BZDs) once they’re no longer intoxicated
- Use BZDs or chlormethiazole:
  - Give sedatives with extreme caution if measurable blood alcohol levels
  - **Diazepam** 10 – 20 mg/4 hourly for moderate withdrawal, 20 mg/2 hourly iv for severe. Resist protracted sedatives, otherwise → addiction. If liver disease then reduce dose
  - Oral chlormethiazole 1 gm 6 hourly
- Additional treatments:
  - β-blockers for tremor, hypertension (except if COPD or CV disease)
  - Haloperidol 1 – 5 mg 6 hourly if hallucinations
  - **Sodium Valproate** (Epilim) 600 mg stat po, then 400 mg 8 hourly for 5 days, if history of seizures – care if liver disease. Likely to occur early in withdrawal, especially if history of seizures with previous withdrawal

### Other Disorders

#### Eating Disorders

#### Screening Questions

- **SCOFF questionnaire:**
  - Do you make yourself **Sick** because you feel uncomfortably full?
  - Do you worry you have lost **Control** over how much you eat?
  - Have you recently lost more than **One** stone (14 pounds, 6.35kg) in a 3/12 period?
  - Do you believe youself to be **Fat** when others say you are too thin?
Would you say that **food** dominates your life?
- If yes to 2 or more questions → 100% sensitive, 87.5% specific for eating disorder
- Ask re eating attitudes and behaviours:
  - Food intake
  - Weight loss methods: dieting, vomiting, exercise, laxatives, pills, caffeine, diuretics
  - Past weight, current weight, **preferred weight**
  - BMI
  - Exercise habits: intensity, hours worked per week
  - Mood and other psych screen (CAMP SAND)
  - Habits and behaviours: smoking, alcohol, drugs, sexual activity

**Anorexia Nervosa**
- Low weight not due to other illness
- **Persistent refusal to maintain weight** (cf depression – don’t want to eat). Obsession with food, weight and thinness
- Incidence rates have ↑ in last 25 years
- Affects **1% of adolescent females**, rates for men are **10% of those for women**; 90% female, usual onset from 11 – 19 years but as young as 6
- Mortality = ~10% (worst of any psychiatric disorder)
- FAB 15:
  - Fear of weight gain
  - Amenorrhoea
  - Body image disturbance (body seen as predominant measure of self-worth)
  - 15% below ideal body weight
- DSM-IV Criteria:
  - Refusal to maintain weight within a normal range for height and age (more than 15% below ideal body weight [IBW] or BMI below 17.5 – variation in definitions; normal is 18.5 – 25)
  - Fear of weight gain
  - Severe **body image disturbance** in which body image is the predominant measure of self-worth with denial of the seriousness of the illness
  - In postmenarchal females, amenorrhoea (> 3 cycles)
- Subtypes:
  - Restricting: restriction of intake to reduce weight
  - Binge eating/purging: vomiting, laxatives, diuretics or compulsive exercise
- Key psychological features are:
  - Relentless drive for thinness
  - Extraordinary fear of fatness
  - Distorted body image
- Medical DDx:
  - Cancer
  - Malabsorption syndromes
  - Endocrine disorders (eg hyperthyroid, diabetes, etc)
  - Connective tissue disorders
  - HIV/AIDS
- Comorbid conditions or primary psychiatric disorders that can present with unintended weight loss:
  - Affective disorder (eg MDD) with change in appetite or energy
  - Psychosis-driven eating changes
  - OCD
  - Somatisation disorder
  - Substance abuse – particularly stimulants
- Aetiology:
  - Media message: thin = beautiful
  - Already painfully aware of body image due to changes in puberty
  - Stressful life situations
  - Genetics
  - Family dynamics
  - Something they can have control over when they don’t have control in other areas of their lives
  - Failure to achieve weight control → ↓sense of failure → try harder
- Signs and symptoms:
Learn a good deal of these! Go from head to toe
- Bradycardia
- Dry skin
- Cold intolerance
- Blue hands and feet
- Sunken eyes due to ↓ ocular fat pads
- Constipation/bloating
- Dental caries, oral ulcers, Russell’s sign
- Brittle nails
- Delayed puberty
- Primary or secondary amenorrhoea
- Fainting/orthostatic hypotension
- Lanugo hair (fine, downy hair as in fetuses and malnutrition)
- Scalp hair loss
- Early satiety
- Weakness, fatigue
- Short stature
- Osteopenia
- Easy bruising (TCP)
- Breast atrophy
- Pitting oedema
- Atrophic vaginitis
- Cardiac murmurs/sinus bradycardia
- Hypothermia

- Features:
  - Deliberate self-starvation
  - Fear of gaining weight
  - Denial of hunger
  - Constant exercising
  - Self-perception of being fat
  - Absent or irregular periods
  - May purge (vomiting, laxatives)

- Complications: starvation, heart, osteomalacia, ↓ fertility

- Mental status changes related to malnutrition:
  - Mild/moderate depressed mood and social disinterest
  - Poor concentration and decision making
  - One-channel preoccupation with food
  - Poor insight
  - Irritability, especially around food and eating issues
  - Occasional pseudo-hallucinations (a hallucination that is recognized as a hallucination, as opposed to a "normal" hallucination which would be perceived as real. Eg the hearing of voices which are inside the head according to the patient; in contrast, a hallucination would be indistinguishable to the patient from a real external stimulus, e.g. people were talking about me) – “the anorexic voice”

- Treatment:
  - Weight + nutrition restoration
  - Treatment of any medical consequences (NB. Physical signs often come late)
  - Education and mental health therapy and treatment

**Bulimia**

- Binging and purging more dominant features
- Don’t usually lose so much weight
- Occurs in 1-5% of high school girls
- As high as 19% in college women
- DSM-IV criteria does not include a weight proviso
- DSM-IV criteria:
  - Episodes of binge eating with a sense of loss of control
  - Binge eating is followed by compensatory behaviour of the purging type (self-induced vomiting, laxative abuse, diuretic abuse) or non-purging type (excessive exercise, fasting, or strict diets)
Binges and the resulting compensatory behaviour must occur a minimum of **two times per week for three months**

- Dissatisfaction with body shape and weight

**Signs and symptoms:**
- Mouth sores, pharyngeal trauma, dental caries (erosion of dental enamel)
- **Russell's sign:** calluses on the knuckles or back of hand due to repeated self-induced vomiting arising from knuckles making contact with the incisors during gag reflex
- Heartburn, CP
- **Haematemesis** and sometimes oesophageal rupture
- Muscle cramps, weakness
- Bloody diarrhoea
- Bleeding or easy bruising
- Irregular periods
- Fainting/hypotension
- Swollen parotid glands

**Eating Disorder NOS**

- MOST COMMON
- Occurs in **3-5% of women** between the ages of 15 and 30 in Western countries, as minority cultural groups assimilate into Western societies, rates ↑

**DSM-IV criteria:**
- All criteria for anorexia nervosa except has regular menses
- All criteria for anorexia nervosa except weight still in normal range
- All criteria for bulimia nervosa except binges < twice a week or for < 3/12
- Patients with **normal body weight who regularly engage in inappropriate compensatory behaviour** after eating small amounts of food (eg self-induced vomiting after eating two cookies)
- A pt who repeatedly chews and spits out large amounts of food without swallowing

**Aetiology of Eating Disorders**

- Combination of psychological, biological, family, genetic, environmental and social factors
- Hx of dieting is a predictor of eating disorder
- Sports and artistic endeavours in which being thin are emphasised eg ballet, gymnastics are a/w ↑ rates
- Genetic: those with FDR with eating disorders were at 6-10 fold ↑ risk; MZ twins have higher rates
- Family characteristics: high parental expectations regarding achievement and appearance, poor conflict management, family discord
- Associated factors: **hx of dieting** in adolescence, childhood preoccupation with a thin body and social pressure about weight
- **Associated psychiatric conditions:** mood disorders, anxiety disorders, OCD, personality disorders, substance abuse

**Lab and Special Investigations**

- FBC: anaemia
- U & E + Cr
- Mg, PO4, Ca
- **Albumin**, serum protein
- B-HCG
- Urine: specific gravity
- TFTs
- Serum prolactin, FSH
- Bone density
- US of liver, gastroscopy, colonoscopy, CT brain

**Differential Diagnosis**

- New onset diabetes
- Adrenal insufficiency
- Primary depression with anorexia
- IBD
- Abdominal mass
- CNS lesion
HIV/AIDS

Hyperthyroidism

**Complications**

- **Fluid and electrolyte imbalance**: hypokalemia, hyponatremia, hypochloremic alkalosis, ↑ urea, ↓ ability to concentrate urine, ↓ GFR, ketonuria
- **CV**: bradycardia, orthostatic hypotension, arrhythmias, prolonged QT, TW abnormalities, HF, pericardial effusion
- **GI**: constipation, bloody diarrhoea, delayed gastric emptying, intestinal atony, oesophagitis, MW tears, oesophageal/stomach rupture, Barrett oesophagus, fatty liver, acute pancreatitis, gallstones
- Dermatologic: acrocyanosis, hypercarotenemia, brittle hair and nails, lanugo, hair loss, Russell’s sign, pitting oedema
- Endocrine: growth retardation and short stature, delayed puberty, amenorrhoea, low T3 syndrome, partial DI, hypercortisolism
- Skeletal: osteopenia
- Haematologic: BM suppression, mild anemia, leukopenia, TCP, ↓ ESR, impaired CMI
- Neurologic: seizures, myopathy, peripheral neuropathy, cortical atrophy
- Specific complications:
  - Osteopenia:
    - One of the most severe complications
    - Difficult to reverse
    - Treatment: weight gain, 1200-1500 mg/d of elemental Ca, multivitamin with 400IU vit D, maybe oes/prog replacement
  - Secondary amenorrhoea:
    - Happens in ~ 90% of pts with anorexia
    - Caused by low levels of FSH and LH
    - Withdrawal bleeding with progesterone challenge does **NOT** occur due to hypooestrogenic state
    - Menses resume within 6/12 of achieving 90% of IBW

**Anorexia Treatment**

- **Needs MDT approach**: clinician, dietician with experience in ED, mental health professional
- **CBT**:
  - Emphasises the relationship of thoughts and feelings to behaviour
  - **Limited** efficacy
- **Pharmacotherapy**:
  - Not that effective
  - Treat comorbid conditions of depression and OCD
  - Case reports support use of olanzapine
- **Hospitalisation**:
  - Severe malnutrition: < 75% IBW
  - Dehydration
  - Electrolyte disturbance
  - Cardiac arrhythmias
  - Arrested growth and development
  - Bradycardia, hypotension, hypothermia
  - Failure of outpt treatment
  - Self-harming, suicidal
- **Nutrition**:
  - Goal: regain to 90-92% of IBW → this is the mainstay of treatment
  - Inpatient treatment varies
  - Oral liquid nutrition
  - NG tube feeds
  - Gradual caloric ↑ with regular food
  - Parenteral nutrition **rarely** indicated
  - Beware the complications of refeeding too rapidly

**Anorexia Outcome**

- **50% good** outcome: return of menses and weight gain
- **25% intermediate outcome**: some weight regained
25% poor outcome: a/w later age of onset, longer duration of illness, lower minimal weight, overall mortality rate: 6.6%

Bulimia Treatment

- CBT is effective
- Pharmacotherapy: can be useful: Fluoxetine at high dose can result in ↓ in binge eating and a ↓ in vomiting; TCAs; Topiramate → can ↓ binge eating; Ondansetron

Impulse Control Disorders

Gambling

- Reference: General Practitioners Manual on Problem Gambling, Compulsive Gambling Society of NZ
- = The addiction you can’t see. The new mental disorder on the block

- Epidemiology:
  - 1 – 3 % of population are pathological gamblers. There are no longer stereotypical groups – young and women also now affected
  - Maori 3 times more likely, Pacific Islanders 6 times more likely (heavy socio-economic confounding)
  - 2/3 of presenting problem gamblers are under 30. Average age is decreasing
  - 90% of the population gamble (Dept Internal Affairs figures). $600 per family per year (cf $200 in the US)
  - Gambling has increased by 700% in the last decade. There has been significantly increased access to all forms of gambling (without social research)
  - Mode of gambling of people with pathological gambling disorder: 60% non-casino pokies

- Diagnosis:
  - Should screen early on in relationship with GP: later on won’t tell due to embarrassment
  - Features: Preoccupation with gambling, needs to gamble more to get the same excitement (ie tolerance), repeated and unsuccessful efforts to cut back or control, restless or irritable when trying to cut down (ie withdrawal), gambles as a way of dissociation, after losing returns to chase their losses, lies to conceal extent of gambling, has jeopardised or lost a job or relationships, etc
  - Other features:
    - Impacts for physical health: can’t afford to go to doctor, usually heavy smokers, often have co-morbid anxiety, depression, alcohol or drug disorder (NB – screen for depression in affected families), high suicidality
    - Will use their own money then may resort to crime (usually fraud, forgery & theft). Crimes unsophisticated, effected in haste and often first offence

- Theories re aetiology:
  - Reward deficiency syndrome
  - General theory of addiction: unresolved/maladaptive issues from the past
  - Behavioural/environmental conditioning
  - Social learning (eg permissive culture)

- Phases in the course of the illness:
  - For gambler: winning, losing, desperation, critical, rebuilding, growth
  - For spouse: denial, stress, exhaustion, critical, rebuilding, growing

- Problems with thinking in gamblers:
  - Irrational style of thinking
  - Illusions of control (“if I study the horses enough I’ll win)
  - Superstitious beliefs (“I feel lucky today”)
  - Biased evaluations
  - By the time gambling is pathological, they don’t care whether they win or lose, just want to do it

- Help to offer:
  - Treat depression
  - Financial/budget advice: easy way to engage, encourage contemplation
  - Information (eg about ‘controlled gambling’ as an option for ‘early’ problem gamblers)
  - Helpline: 0800 NOGAMBLE
  - Referral services: outpatients, Compulsive Gambling Society, Odyssey House

Factitious Disorder

Munchausen Syndrome

- Dramatic presentations of apparently severe illnesses
- Reported symptom patterns that fit diagnoses too perfectly and are too much like a textbook presentation
• A history of extensive surgical procedures and inpatient workups for a variety of diseases, particularly when the workup spans multiple hospitals and cities
• Notable vagueness or inconsistency in the details of the medical problems
• Evidence of pathological lying in areas other than the presenting symptoms

Factitious Disorder by Proxy
• = Munchausen By Proxy
• Criteria:
  ➢ Intentional production or feigning of physical or psychological signs or symptoms in another person under the individual’s care
  ➢ Motivation is to assume the sick role by proxy
  ➢ No external incentives for the behaviour (economic gain, avoiding legal responsibility)
• Warning signs: child aged 15 months to 6 years, baffling multisystem symptoms, taken to lots of health care providers, over attached parent, no symptoms when parent absent, strange poisonings, reported seizures

Personality Disorders
• Axis II diagnoses

Personality
• Personality = ingrained patterns of thoughts, feeling and behaviour characterising an individual’s unique lifestyle and mode of adaptation, and resulting from constitutional factors, development and social experience
• Personality development:
  ➢ 40-50% of phenotypical variation is due to genetics
  ➢ Some variation due to environment
  ➢ Innate temperament (eg resilience or affective lability or nervousness) + quality of early relationships (eg secure/insecure or nurturing/neglectful) + early life experiences (eg traumas such as illness, death, abuse, accidents or non-traumas such as treats, celebrations, holidays) = personality development

Diagnosis
• Personality disorders: TB RP ISAC (pattern of thinking and behaviour that is rigid and pervasive, manifest by impulsivity or social impairment, or affect or cognitions)
• Personality disorder:
  ➢ = An enduring pattern of inner experience and behaviour that deviates markedly from the expectations of the individual’s culture
  ➢ Is inflexible and pervasive across a broad range of situations
  ➢ Has its onset in adolescence or early adulthood, is stable over time and leads to distress
  ➢ And is manifested in two or more of the following:
    o Interpersonal functioning
    o Affectivity (emotionality)
    o Impulse control
    o Cognition (style of thinking)
• Key characteristics:
  ➢ Rrigidity: pervasive rigidity of cognitions and behaviours
  ➢ Avoidance: don’t want to look at or experience their thoughts or feelings → problem for therapy
    (compulsory treatment won’t change anything)
  ➢ Long-term interpersonal difficulties
• Differentiating from axis 1:
  ➢ There is substantial comorbidity with axis 1 – but must be distinguished from axis 1 (which is episodic, different from normal state. Personality disorders ARE the normal state)
  ➢ Need to exclude other possible factors: eg substance abuse, head injury, general medical condition, mood or psychotic disorder (ie must not occur exclusively in the course of an axis 1 disorder)
  ➢ Consider axis 2 if: ongoing non-compliance, client unaware of effect of their behaviour on others, client acknowledges need for change but motivation is questionable, always blame others for their behaviour
• Can’t diagnose before age 19 (much of the description of the disorders is also descriptive of adolescence)
• Requires longitudinal assessment and collateral information
• Can assess someone using either “Type” or “Trait” models using self-rating questionnaires or interviewing someone who has known the individual for years
  ➢ Traits: openness, conscientiousness, extraversion, agreeableness, neuroticism
• Must evaluate **within a cultural and religious context** (DSM 4 is white & American)
• Labelling someone with a personality disorder can be difficult, given limited information and possible reactions → often people labelled ‘traits of disorder X’
• Presentation is often not for the disorder (as it could be, for example, for depression), but for the degree of impairment due to excessive or little compliance with treatment
• Treatment is difficult and long-term: given deeply embedded nature and genetic predisposition to personality
• Explanation to client:
  ➢ **Behaviours were probably adaptive to survive difficult childhood experiences** (at some point behaviours were helpful – but they’ve got stuck). Take care to look for an explanation, not someone, to blame (people usually do the best they can)
  ➢ But it is now more functional to use different strategies in different situations
  ➢ Take care of criticising non-compliance: few are proud of ‘doing what they’re told’ – would you rather be a sheep or an eagle?

### Classification of Personality Disorders

- ~ 40-70% of psychiatric inpatients will have a PD
- 30-40% of psychiatric outpatients will have a PD
- 10-30% of GP patients will have a PD

### Classification Overview

- DSM uses categorical model, currently 10 PD types with 2 categories for further study
- Cluster A (**odd**): paranoid, schizoid, schizotypal
- Cluster B (**dramatic**): antisocial, borderline, narcissistic, histrionic
- Cluster C (**anxious**): avoidant, dependent, obsessive-compulsive
- For further study (**negativistic**): depressive, passive-aggressive
- Diagnosis is made by a “**symptom counting**” as for Axis I
- Standard assessments using **responses to questions or self-report are used**. Can be issues with reliability of answers to questions
- **Aetiology: genes, brain structure and NT, environment** (eg abuse, violence, alcoholism in parents etc)

<table>
<thead>
<tr>
<th>Disorder</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cluster A: Suspicious, seem odd or eccentric</td>
<td><strong>Generally distrustful, suspicious, loners.</strong> Non-compliant with treatment as doesn’t fit their worldview. See less of them in GP – don’t call attention to themself</td>
</tr>
<tr>
<td>Paranoid</td>
<td>0.5-2.5%. Distrust &amp; suspicious such that <strong>other’s motives are interpreted as malevolent</strong>. Feel that other people are being nasty to them, <strong>sensitive to rejection, hold grudges</strong></td>
</tr>
<tr>
<td>Schizoid</td>
<td>0.4-1.7%. <strong>Withdrawal</strong> from social relationships and <strong>restricted range of emotional responses</strong> (eg can’t express anger, seem directionless). <strong>Emotionally cold, prefer own company.</strong></td>
</tr>
<tr>
<td>Schizotypal</td>
<td>0.1-5.6%. Odd ideas, eccentric behaviour. <strong>Acute discomfort in close relationships</strong>, cognitive or perceptual distortions, eccentricities of behaviour. Often have ideas of reference (belief that casual events, people’s remarks, etc are referring to oneself when, in fact, they are not; but not with delusional conviction) eg preoccupied with paranormal phenomena or have special powers. Important differential to psychosis. May be suspicious/paranoid, may seek treatment for associated depression or anxiety.</td>
</tr>
<tr>
<td>Cluster B: Dramatic, emotional, impulsive</td>
<td>Call attention to themselves, vocal in asking for help, other people want them to change but may see their behaviour as functional (will bear the cost of dysfunction because they get what they want)</td>
</tr>
<tr>
<td>Antisocial</td>
<td>0.6-2.0%. Disregard for, and violation of, the rights of others (usually male). Don’t care about other’s feelings. Easily frustrated. Aggressive, commit crimes, impulsive</td>
</tr>
<tr>
<td>Borderline</td>
<td>0.7-2.0%. <strong>Instability</strong> in interpersonal relationships, self-image, and affects, and marked <strong>impulsivity</strong> (usually female). Hard to control emotions, <strong>feel bad about self. Self-harm, suicide attempts</strong></td>
</tr>
<tr>
<td>Histrionic</td>
<td>2-3%. <strong>Excessive emotionality and attention seeking</strong>. Self-centred, suggestible. Worry about appearance, crave new things and excitement. Can be seductive</td>
</tr>
<tr>
<td>Narcissistic</td>
<td>1%. <strong>Exaggerated sense of self worth</strong> – pattern of grandiosity, <strong>need for admiration</strong>, and lack of empathy. <strong>Exploit</strong> others</td>
</tr>
<tr>
<td>Cluster C: Anxious and fearful</td>
<td>May come to attention due to <strong>anxiety</strong></td>
</tr>
<tr>
<td>--------------------------------</td>
<td>----------------------------------------</td>
</tr>
<tr>
<td>Avoidant 0.5-5%. Social inhibition, feelings of inadequacy, hypersensitivity to negative evaluation. Very anxious and tense. Feel inferior. Have to be liked and accepted</td>
<td><strong>grounds for arrest</strong></td>
</tr>
<tr>
<td>Dependent 1.0-1.7%. <strong>Submissive &amp; clinging behaviour</strong>, related to an excessive need to be taken care of. Rely on others to make decisions. Feel hopeless and incompetent, hard to cope with daily chores</td>
<td></td>
</tr>
<tr>
<td>Obsessive-Compulsive 1.7-2.2%. Pattern of <strong>preoccupation with orderliness, perfectionism and control</strong>. <strong>Rigid</strong> in what you do, cautious, preoccupied with <strong>detail</strong>. High moral standards, judgemental and sensitive to criticism. Can have <strong>obsessional thoughts and images</strong>. <strong>Not to be confused with OCD</strong>. People experiencing OCPD do not generally feel the need to repeatedly perform ritualistic actions—and usually find pleasure in perfecting a task, whereas OCD patients are often more distressed after their actions.</td>
<td></td>
</tr>
<tr>
<td>Disorder not otherwise specified</td>
<td>Meet criteria for a personality disorder, but are a <strong>mixture of the above</strong> or don’t fit any of the above (eg passive-aggressive)</td>
</tr>
</tbody>
</table>

**DSM-IV Criteria for Antisocial Personality Disorder**

- Failure to conform to social norms with respect to lawful behaviours as indicated by repeatedly performing acts that are **grounds for arrest**
- **Deceitfulness**, as indicated by repeatedly lying, use of **aliases**, or **conning** others for personal profit or pleasure
- **Impulsivity** or failure to plan ahead
- **Irritability** and **aggressiveness**, as indicated by repeated physical fights or assaults
- Reckless disregard for safety of self or others
- Consistent irresponsibility, as indicated by repeated failure to sustain consistent **work behaviour** or honor **financial obligations**
- **Lack of remorse**, as indicated by being indifferent to or rationalising having hurt, mistreated or stolen from another

**Borderline Personality Disorder**

- Borderline between neurotic and psychotic
- Incidence: 3 – 5 % (cf 1% for Schizoid)
- Criteria include:
  - Frantic efforts to avoid real or imagined abandonment
  - **Unstable and intense relationships** alternating between extremes of idealization and devaluation
  - Impulsivity in areas that are potentially self-damaging: eg spending, sex, substance abuse, binge eating
  - Recurrent suicidal behaviour, parasuicides, threats or self-mutilations
  - Marked **reactivity of mood**, difficulty controlling anger
- Characterised by:
  - Schema: I can’t control myself → overdeveloped emotional responsiveness & underdeveloped self-identity, impulse control
  - Core belief about self: I’m defective, helpless, vulnerable, bad
  - Belief about others: other people will abandon me, can’t be trusted
  - Combination of these two leads to extremes of behaviour: **need to depend on others but fears will be abandoned**
  - **Hate being alone**: may attend A & E or ring friends late at night for company
- **Self-harm**:
  - Begins between 10 and 16: often following a major life change
  - ‘Toxic self-soothing’: **eases the inner pain** – powerful way to feel better. Can either help the dissociation (**turn off emotions**) or **help them feel real**
  - Communication strategy: there is chaos within family and have never asked for help → can’t ask for help now. But **self-harm is not always a cry for help**. For most, self-harm is a private matter
  - Strategy in the game of life: to manipulate people or drive them away
  - Always need to **screen for concurrent depressive episode**: this will need treatment
- **What helps in situations of self-harm**:
  - Non-judgemental acceptance
  - Teach other ways to self-sooth

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**Psychological Medicine** 762
Dealing with trigger event: what causes the negative feelings
Address underlying issues: but shouldn’t do trauma counselling without also improving coping skills

Aetiology:
- Genetic loading in temperament: ↓perseverance, ↑impulsivity, ↓affect regulation, ↑stimulation seeking
- Sexual abuse in 75% (but not all severely abused develop the disorder): feeling unsafe, victimisation, trauma, terror
- 75% are female (men more likely to react by becoming antisocial – same motivation but take it out on others rather than themselves – or substance use). Behaviour in collusion with dominant western values (eg emotionality, dependence)
- Other societal factors eg invalidating environments (eg neglect), marginalisation
- Most affected people have this cluster of factors, but someone can still get it even if the best of upbringings ⇒ ?stronger than normal predisposing temperaments

DSM-IV Criteria for Borderline Personality Disorder
- Frantic efforts to avoid real or imagined abandonment (not including suicidal or self-mutilating behaviour)
- A pattern of unstable and intense interpersonal relationships characterised by alternating between extremes of idealisation and devaluation
- Identity disturbance: markedly and persistently unstable self-image or sense of self
- Impulsivity in at least 2 areas that are potentially self-damaging (eg promiscuous sex, eating disorders, binge eating, substance abuse, reckless driving)
- Recurrent suicidal behaviour; gestures, threats or self-mutilating behaviour such as cutting, interfering with the healing of scars (excoration) or picking at oneself
- Affective instability due to a marked reactivity of mood (eg intense episodic dysphoria, irritability, anxiety usually lasting a few hours and only rarely more than a few days)
- Chronic feelings of emptiness, worthlessness
- Inappropriate anger or difficulty controlling anger (eg frequent displays of temper, constant anger, recurrent physical fights)
- Transient, stress related paranoid ideation, delusions, or severe dissociative symptoms

Psychodynamic Ideas in BPD
- Some useful psychodynamic ideas: transference, counter transference, splitting
- Interpersonal dynamics:
  - Clients with BPD (borderline personality disorder) struggle interpersonally
  - Struggles are related to painful, overwhelming feelings related to past relationship trauma
  - Subtle signs (real or perceived) of hostility, rejection, lack of acceptance or controlling authority will be magnified strongly
  - Staff will respond to clients with reactions of their own which can be used therapeutically or untherapeutically

Transference
- = "transference" of past feelings, conflicts, and attitudes into present relationships, situations, and circumstances (from one person to another)
- Unconscious transfer of experience from one interpersonal context to another
- Re-living past interpersonal relationships in current situations
- Unconsciously attributing desired qualities onto another

Countertransference
- = a normal occurrence, involves the therapist’s reactions, behaviours, thoughts, and feelings toward the pt
- Definitions include:
  - The staff person’s reactions to the transference of the client
  - All of the staff person’s reactions to the client
  - Automatic thoughts and feelings arising in response to the client that may be conscious or unconscious

Management of Transference and Countertransference
- Reflect on the countertransference
- Check that your responses are consistent and therapeutic, rather than reactive
- Don’t dismiss all client reactions as being of their own making
- Acknowledging our own inconsistencies and mistakes will assist the client to feel validated
Use the transference and countertransference to understand the client’s inner experience
Hang in, be real and consistently supportive

Splitting

- An unconscious separation or split within the psyche
- Seemingly contradictory aspects of the self are split apart, usually “good” and “bad” aspects
- The self or others are viewed as all good or all bad, with failure to integrate the positive and negative qualities of self and others into cohesive images
- Corresponding split in how they see other people. Important others can be idealised or devalued
- Natural developmental stage in childhood. Lack of integration of split for those with too many “bad” experiences in early years
- When “splitting” is used in the sense of something that is “done” to others, we often hear that a borderline patient is “splitting the staff” on an inpatient psychiatric ward or other healthcare facility. Yet, the process by which this happens is often not explained. Here is an example of how it happens: A patient is admitted to an inpatient psychiatric ward. In a private, one-to-one interchanges or assessments, the patient praises certain people, who in turn feel good about the patient. In other private, one-to-one interchanges or assessments, the patient condemns other people, who in turn, feel bad and thus, do not like the patient. Because the patient has treated the staff in these polarized ways in private unobserved interactions, different members of the staff come to have very opposite opinions of the character of the patient. Thus, the patient has “split” the staff. However, if all members of the staff could have witnessed ALL of the patient’s interactions, they would have seen how inconsistently the patient was behaving, depending on the particular member of the staff with whom the patient was interacting.

- Management of splitting:
  - Important to recognise and synthesise polarised positions. Both are valid but incomplete. Bring differences into the “healthy difference” domain
  - Maintain a non-judgemental stance. View the split as useful information about the client’s inner conflicts
  - Team cohesion is crucial. Helps clients to resolve their splits and staff to feel happy
  - Third party or consultant, if necessary, to resolve the split

Treatment

- Pat answer:
  - Establish a therapeutic alliance
  - MDT approach (biopsychosocial)
  - Discuss diagnosis
  - Exclude Risk factors
  - Etc

- Some specific models of treatment eg DBT (dialectical behavioural therapy) for BPD

- Psychotherapy is the general treatment for personality disorder:
  - Counselling: talking and listening
  - Dynamic psychotherapy: looks at how past experiences affect present behaviours
  - Cognitive therapy: a way to change unhelpful patterns of thinking
  - Cognitive analytical therapy: a way to recognise and change unhelpful patterns in relationships and behaviour
  - Dialectical behaviour therapy: use a combination of cognitive and behavioural therapies with some techniques from Buddhism
  - Treatment in a therapeutic community: like an inpatient unit, lots of group therapy

- Medication:
  - Antipsychotics can ↓ the suspiciousness of the cluster A PDs (paranoid, schizoid and schizotypal); can also help with BPD if people feel paranoid or have hallucinations
  - Antidepressants: can help with the mood and emotional difficulties that people with cluster B PDs (antisocial, borderline, histrionic, narcissistic) have. Some of the SSRIs can help people to be less impulsive and aggressive in BPD and antisocial PDs
  - Mood stabilisers: ie Li, carbamazepine, and sodium valproate can also ↓ impulsiveness and aggression

- Management of the person’s environment
- Treatment of co-morbid conditions
- Support and education for carers
- Self-help:
  - Unwind when stressed
  - Good sleep and diet

Psychological Medicine 764
Treatment of Mental Illness

The Basics

- Exercise
- Avoid too much alcohol, drugs
- Talk to people
- Key clinical points:
  - Keep and open mind re dx
  - An understanding of the person’s nature is much better than a category
  - Self-monitor
  - Police your colleagues
  - Chaotic people need stability around them

Care for the Mentally Ill

- Illness (especially initially) is very traumatic for individual and family (eg may not cope as normal or remember anything you say)
- Families will often blame themselves or feel guilty
- Knowledge/education is key: without it people are powerless
- ‘Recovery’: issue may not be getting rid of all the symptoms, but getting rid of or managing those symptoms which are disruptive or distressing

Stigma

- Feeling created by stigma is a significant reason for the loss of hope and relapse experienced by those with mental illness
- Stigma leads to discrimination and sense of shame
- Common misconceptions:
  - People with mental illness are dangerous and violent
  - People with mental illness never recover: vast majority do recover, some require ongoing treatment
  - It’s got nothing to do with me: but mental illness affects people of all ages and backgrounds

Drug Treatment

- When using medication:
  - Don’t make assumptions about what people want – ask them
  - What have they used before and what has worked. What’s worked for family members?
  - Need to consider side effects: will benefits outweigh costs/risks?. Side effects are often significant, and will be a major cause of problems with compliance. Be ready to change medications if side effects are intolerable
  - Need to consider the long term (ie when/how will they come off) as well as the short-term
  - Make sure alternative/adjunct treatments are considered
  - Optimal initial dose: the level at which there are maximum therapeutic benefits for minimum side effects
  - Maintenance dose: lowest possible dose that provides relief/remission. Will vary from person to person, and due to psychosocial factors (ie may need to increase it under when under stress)
  - Regular review is important, until the patient is stabilized on the medication
- Drug education:
  - Understanding the medication’s purpose is vital to informed consent and to adherence to treatment
  - Patient needs to know why the medication is needed, what the medication is expected to achieve, when and how to take it, and possible side effects or restrictions (eg diet), the likely duration of treatment, how long until an effect should be noticed, whether the medication is addictive, what are the alternatives
Some medication (e.g. fat soluble anti-psychotics) clears very slowly from the body, so a patient can stop taking them without immediate relapse. Patient’s need to understand that the drugs are effective only if taken regularly.

**Cognitive Behavioural Therapy (CBT)**

- See also Treatment of Depressive Disorders
- Principles of Treatment of Major Depressive Disorder, page 712
- Was developed as a structured, problem-orientated psychotherapy by Aaron Beck in the 1960s
- Focuses on cognitive and behavioural influences on human experience, as well as interpersonal processes and ‘unconscious’ motivation/underlying schema
- **CBT treatment:**
  - Includes a comprehensive assessment and shared formulation/conceptualisation
  - Usually includes both behavioural and cognitive interventions
  - There are specific treatments for separate disorders
  - Helps people recognise the thoughts, emotions, and behaviours behind problems and that maintain them. Works to break the cycles and alleviate distress
- **Basic principles of CBT:**
  - The situation itself does not determine how we feel (rather feelings are determined by thoughts about events)
  - Emotions and behaviours are influenced by how people perceive events
  - Information processing biases lead to, or maintain, depressed affect and behaviour
- **Efficacy of CBT well supported:**
  - At least as effective as antidepressants in depressed outpatients
  - Good evidence for major depressive disorders
  - Strong evidence for anxiety disorders
  - Can be helpful for other conditions including eating disorders, psychotic disorders, PDs
- Individuals for whom CBT works best are generally highly motivated and value a problem-solving approach: requires that the patient learns the skills of self-observation and of becoming a personal scientist, learns cognitive and behavioural coping skills, and learns to repeatedly practice the skills in anxiety-provoking contexts outside of the therapy setting
- **Characteristics:** active, short-term, structured, problem oriented, homework, collaborative, emphasis on self-help, relapse prevention
- Cognitive therapy helps the patient identify and correct distorted, maladaptive beliefs about their relationships, view of the future, competency and self-worth. Evaluation of automatic thoughts and the underlying core and intermediate beliefs
- Behavioural therapy is aimed at reinforcing positive behaviours and eliminating behaviours which prolong or worsen the condition

**Typical Mistakes in Thinking: Automatic Thoughts**

- All or nothing thinking: black and white, dichotomous, concrete “if I’m not a total success, I’m a failure”
- Catastrophising: predict future negatively “I’ll be so upset, I won’t be able to function at all”
- Etc

**CBT in Depression**

- **Common targets are:**
  - Addressing poor sleep hygiene
  - Engagement in physical exercise
  - Increasing behaviours that provide pleasure
  - Increasing behaviours that provide a sense of mastery
  - Improving social skills and social involvement
- Can be used individually or in combination (CBT)
- CBT includes education, relaxation exercises, coping skills training, stress management, or assertiveness training
- Duration normally 12-16 weeks
- Process in depression: early experience → formation of dysfunctional assumptions (core beliefs) → critical incident → assumptions activated → negative automatic thoughts → behavioural, motivational, affective, cognitive and somatic symptoms of depression
- **Cognitive triad** in depression: negative view of self, of the world, and of the future

*Psychological Medicine* 766
CBT Model

- Shows that there are a variety of physical, emotional and behavioural responses depending on underlying cognitions and thoughts
- Think of it like a **hot cross bun** (NB cognitions/thoughts = automatic thoughts)

**Context: friend late for movie**

**Three Levels of Beliefs**

- **Like an onion**
- **Early life experiences** (eg neglect) lead to → CBs → IA → ATs
- **1. Core beliefs** (CB’s): global, rigid, overgeneralised:
  - **Global, overgeneralised, absolute**, self-referent, rigid, influenced by socio-cultural background
  - When activated, data supporting is processed and data contradicting is distorted
  - Core beliefs affect view of self, world, future, other people
  - Affect what aspects of a situation we attend to, what we encode, what we remember
  - Once core beliefs are activated they **introduce biases in the processing of information** (systematic logical errors)
  - Biases in information processing maintain belief in NAT's, thus distorting interpretations consistent with dysfunctional beliefs and appraisals
- **2. Intermediate assumptions** (IB’s): attitudes, rules/expectations, assumptions
  - Rules, attitudes, assumptions that guide our daily actions & expectations
  - Often expressed as “If...then...” and “Should” statements
  - Often unarticulated ideas/rules that give risk to specific automatic thoughts
  - Are often rules that “make sense” in terms of the patient’s behaviour, affect and general presenting problem
- **3. Automatic thoughts** (AT’s): actual words or images, situation specific, superficial:
  - Reflect actions, are instant commentaries, are **habitual, automatic, involuntary, plausible**
  - Not at the forefront of the mind, may accompany more conscious mental activities
  - People can learn to identify automatic thoughts and the effect they have on mood and behaviour
  - Influence behaviour, emotions, physiological processes
  - Are usually accepted as true without evaluation
Interpersonal Therapy/Psychotherapy

- IPT applies a model which states that depression occurs when patients with a biological vulnerability to the illness experience adverse life events of sufficient severity.
- The therapy emphasizes current relationships and the connection between them and recent adverse life events and depression.
- The putative mechanism of action is that **mood improves as the patient resolves interpersonal problems that are associated with the onset or maintenance of depression**: grief (complicated bereavement), role disputes, role transitions, and interpersonal deficits.

Psychodynamic Psychotherapy

- Based upon the theory that childhood experiences, past unresolved conflicts, and previous relationships significantly influence an individual’s current situation in life. Thus, adult relationships are understood to be a byproduct of unconscious patterns that are ingrained from childhood.
- Involves identifying and making patients aware of these patterns in relationships, as well as unconscious meanings, conflicts, and desires that cause depression.

Problem Solving Therapy

- For ‘problems of living’ causing or contributing to current symptoms
- Regaining control → ↑ mood and less overwhelmed
- 3 Steps:
  - Realise symptoms are linked to problems in their life
  - Define and clarify problems
  - Solve problems in a structured way
- Stages:
  - Explanation of treatment and it’s rationale
    - Recognition of emotional symptoms
    - Recognition of problems: eg relationships, work, money, housing, legal, alcohol, etc
    - Acceptance of a link between symptoms and problems
  - Clarification and definition of problems:
    - List problems in a concrete form
    - Break down big problems into more manageable parts
  - Choose achievable goals given patients resources and obstacles
  - Patient generates as many solutions as possible
  - Choose the preferred solution
  - Implement the preferred solution – set deadlines, etc
  - Evaluation and encouragement. If unsuccessful consider: low motivation, inappropriate goals, unsuitable choice of solution, inappropriate implementation

Electroconvulsive Therapy

- History: insulin shock therapy → chemically induced seizures. Early ECT done in asylums when few meds available
- Relieves symptoms in 80% of all severe depression (**not just those resistant to medication**)
- **MOA:** NT levels all ↑ in CSF after seizure, results in downregulation of β-adrenergic receptors. *After seizure, blood flow and metabolism is ↓ especially in the frontal lobes* → research shows this is correlated with response
- **Indications:**
  - **Major depression** with or without psychotic features
  - **BAD** – manic or depressed phase. Bipolar mania: indications for first line treatment include *recent MI with acute mania or pregnancy with acute mania*
  - Acute or catatonic schizophrenia
  - Some studies have shown efficacy in treating OCD, delirium, NMS, chronic pain syndromes, and intractable seizure disorders
- Pre-ECT workup:
  - Physical exam
  - CXR
  - FBC, U & E
  - ECG
Psychological Medicine

- CT head
- No absolute contraindications but relatively contraindicated with recent MI, berry aneurysm, brain mass or ↑ICP
- Number of treatments: 2-3/week; 5-12 sessions although up to 20 is possible
- Adverse effects: death (very low rates), sore muscles, headache, short term confusion/delirium, memory impairment
- Response is proportional to length and quality of seizure. Usual course is about 6 cycles. If no response after 12 cycles then stop
- Also need to establish on an antidepressant that they haven’t failed on

Compulsory Treatment

- Features of the Mental Health (Compulsory Assessment and Treatment) Act 1992:
  - Specific legal definition of mental disorder (not a diagnostic definition)
  - Even if committed, must be treated in the least restrictive environment (→ community orders)
  - Rights of patients are listed: eg to information, to respect for culture, to second opinion, to legal advice, ability to communicate (phone, letters, visitors, etc)
  - Can’t treat without consent (which you must try and get) without a second opinion
  - Review procedures are specified, including the Mental Health Review Tribunal
- Definition of Mental Disorder (Section 2):
  - An abnormal state of mind characterised by continuous or intermittent delusions, disorders of mood, volition (energy, drive, will), cognition, or perception, etc
  - And to such a degree that it poses a serious danger to person or others, or seriously ↓ability to take care of themselves
  - Exclusions include (Section 4): if due only to intellectual disability or substance abuse, criminal behaviour, sexual preferences, political and religious views
- Process:
  - Application must be made by anyone over 18 (section 8)
  - Medical certificate must be provided by any doctor (who may be the applicant, section 8)
  - Reviewed by a psychiatrist designated under the Act within 24 hours (section 9)
  - 5 day compulsory assessment period (although can be released, become voluntary, appeal, section 11)
  - Following reassessment can be held for a further 14 days (section 13)
  - To extend beyond this require review by family court
  - Compulsory treatment orders:
    - Community treatment orders (section 29)
    - Inpatient orders (section 30)
  - Duly Authorised Officer = usually an experienced CPN in CATT team – carry out assessments, start process

Recovery

- READ OVER PAGES 116 - 124
- Defined as: the ability to live well in the presence OR absence of mental illness
- Recovery is woven through all elements of mental health in such a way that an expectation of recovery should accompany all clients
- The person with the illness can recover even when the illness is not cured; the process of recovery can proceed in the presence of continuing symptoms and disabilities
- Our language should reflect this: “when you get better” etc etc
- Recovery happens when people with mental illness take an active role in improving their lives, when communities include people with MI, and when MH services can enable people with mental illness and their communities and families to interact with each other
- Course of a Psychiatric disorder:
  - Phase 1: Moratorium: where pts experience stability in symptoms and function. In these situations, pts seem to be reconstituting their identity, accumulating supports and strengthening their skills. Can get stuck at this phase due to a lack of support or too much support (become comfortable)
  - Phase 2: Change points: these involve considerable shifts in functioning or symptoms over a brief period. Often symptoms become worse at a change point, but one has to decide if it is a prodromal symptom (ie about to become really unwell) or simply a normal reaction to a life event
  - Phase 3: Ceilings: the highest level of functioning reached in a given period of time. Often difficult to surpass the ceiling with experiencing major decompensation and symptom exacerbation
- Essential elements of recovery:
Hope (there is hope for recovery; you can lead a ‘normal’ life; like living with a physical condition, need to learn to manage it; positive language)

Support (biopsychosocial treatments, family/friends/work/support groups etc)

Education (to pt and supports: about the condition/treatment, it is common, it can be managed [like any physical condition], relapse prevention: triggers and action plans for triggers)

Self-advocacy (gives sense of control and empowerment: internal locus of control)

Personal meaning

Personal responsibility

Grief and Bereavement

- Reference: Material from Mary Potter Hospice, obtained in GP run, and Te Omanga Hospice Material
- See also Palliative Care, page 786

Theories of Grief

- Freud: work of mourning: detachment from person who has died. Healthy resolution when this is completed
- Kuebler-Ross: Stages of terminal illness: denial, anger, bargaining, depression, and acceptance. But it’s not sequential, and this only talks of emotions, not physical or behavioural dimensions
- Worden: Tasks of mourning:
  - Accept reality of loss (harder if no body etc)
  - Experience pain of grief
  - Adjust to an environment in which the deceased is missing (often very practical – change in roles etc)
  - Withdraw emotionally and invest in new relationships (later he revised this to emotionally relocate the deceased and move on) – put the deceased in another place
- Silverman:
  - There is a continuing bond between deceased and survivor
  - Stages:
    - Impact: this is not real
    - Recoil: I’m going crazy, why am I worse now (can be months later)
    - Accommodation: what do I carry with me? Being a living memorial – don’t have to cut off – can move on and still carry something with them
- Stroebe et al: Dual process moving between expression of grief and containment of grief (women prefer former, men latter)

Characteristics of Grief

- Reassure bereaved person that these are normal. If overwhelming, seek help
- Emotional: bewildering and intense range or emotions without warning - shock, numbness, relief, anxiety, anger, blame, guilt, loneliness, helplessness, hopelessness
- Physical: hollow stomach, tight chest, breathlessness, weakness, lack of energy, ↓ sexual desire, sleep disturbances, symptoms similar to person who died (this can be pathological)
- Cognitive responses: disbelief, confusion, ↓ concentration, going crazy, preoccupation
- Behaviours: searching, crying, sighing, absent minded, restless, ↓ socialising, visiting/avoiding places that are reminders

Coping with Loss

- Losses are a common cause of illness – they often go unrecognised
- Conflicting urges lead to a variety of expression of grief – but there is a pattern
- Understanding factors that predict problems in bereavement enables these to be anticipated and prevented
- Grief can be avoided or it may be exaggerated and prolonged
- Doctors can help to prepare people for the losses that are to come
- People may need permission and encouragement to grieve and to stop grieving

Factors Complicating Grief – Risk Factors for Pathological Grief

- Dependent family members (children, handicapped, elderly)
- Loss of primary care giver/constant companion
- Loss of financial provision
- Loss of home (feared or actual)
- Anxiety about decisions
- Unable to share feelings
• Family discord
• Uncontrolled pain/emotional distress before death
• Concurrent life crisis
• Prolonged reaction/suicidal thoughts
• Lack of community support

Children’s Grief
• It is not possible not to communicate to children (ie not telling them is not an option)
• Help should start at the time of diagnosis
• Talk about what won’t change as a result of the illness
• Maintain things that are important in a child’s life (e.g. routines)
• Talk about practical concerns
• Provide extra stability, order, routine and physical affection
• They need to know who will take care of them if key people leave or die
• Offer reassurance
• Children often assume responsibility for what has happened and feel very guilty
• Offer clear, simple, truthful information: repeat, repeat, repeat
• Don’t use euphemisms (e.g. asleep – explain death, body stops working)

Signals for attention from a grieving child
• Marked change in behaviour: illegal behaviour, persistent aggression (> 6 months), tantrums, withdrawal, drug abuse
• Inability to cope with problems and daily activities
• Many complaints of physical ailments
• Persistent depressions, panic attacks
• Change in school performance
• Fearfulness for self, or for loved ones

Helping Families
• Listen effectively
• Foster communication
• Engage siblings
• Check social supports
• Address symptoms
• Provide constant factual data
• Help build positive memories
• Don’t take offence

5th Year Written Exam Model Answer
• These questions normally give a small vignette and then ask the following questions

What is the Diagnosis?
• List the factors from the vignette which support your diagnosis
• List what other factors you would ask about on further history taking (eg what criteria for your diagnosis where not mentioned in the vignette)
• What risk factors for the diagnosis are there in the vignette or that you would ask about
• Is there a significant impairment in social and occupational functioning
• Is there a change from previous functioning

What are the Possible Differentials?
• Always consider including the following:
  ➢ Alcohol and Drug use disorders or withdrawal
  ➢ Other psychiatric disorders (eg anxiety for depression, etc)
  ➢ Conversion disorder
  ➢ Axis 2 disorders (personality disorders)
  ➢ Medical conditions:
    o Endocrine: thyroid, cortisol, calcium
    o Cerebral insult: dementia, stroke, tumour, SLE, AIDS
Medications: β-blockers, steroids, etc

What is Your Recommended Management?

- Establish a positive therapeutic relationship based on a shared understanding of the problems
- Establish an accurate diagnosis:
  - Take a full history (including past psych history) and mental state exam
  - Get a corroborative history if necessary
  - Consider a drug screen if indicated
  - Do a physical exam and investigations to exclude medical causes
  - Assess for comorbid psych illness (especially alcohol and drug use)
- Establish a formulation:
  - Why has this person presented in this way at this time
  - Assess predisposing, precipitating, perpetuating and protective factors across a biopsychosocial framework, eg genetic factors, coping and relationship skills, stress, risk factors
  - Consider cultural aspects. Assess their needs and treatment within their cultural context
  - Assess insight, willingness to change or accept help
  - Assess severity
- Immediate management:
  - Safety issues: Use of CAT team, Mental Health Act, etc
  - Do they need admission to stabilise and assess/observe?
  - Immediate drugs for psychosis: antipsychotic +/- lorazepam
- Longer term management:
  - Multidisciplinary approach
  - Lifestyle modification: stress management, ↓alcohol and drug, sleep hygiene, exercise
  - Maintain function and integration with communities of interest
  - Education for patient and their family
  - Drugs:
    - Side effects, contraindications, duration
    - Watch for and treat complications
  - Psychotherapy:
    - Modify exacerbating or precipitating behaviours
    - CBT, coping skills, structured problem solving, relaxation training, breathing retraining, deconditioning, desensitisation, graded exposure, cognitive restructuring
    - Psychodynamic psychotherapy: elucidate mental processes outside the person’s conscious awareness so as to alter core conflicts
    - Stop ↓self esteem and manage stigma from having a psychiatric illness
  - Secure employment, housing
  - Community support: support groups, psych nurse
  - Consider referral to specialist services
- On-going review:
  - Plan for follow-up to reassess illness and monitor treatments
  - Identify warning signs for a relapse
  - Plan and prepare for relapses
  - Set and prioritise goals
Genetics and Cancer

Background

- Chromosomes are the packaging for our genetic material, our genes
- Each gene has a specific location on a chromosome
- Genes carry instructions that tell our bodies how to grow, develop and function. Each gene gives specific instruction for the production of a particular protein which has a job in the body
- Just like the chromosomes, there are two copies of each gene, one on the maternal chromosome and one on the paternal
- Usually the information from both copies are actively being used
- When a gene actively gives the instructions to create a protein, we say that it is being expressed

DNA

- Our genetic code
- Has a backbone of deoxyribose sugars with purine + pyrimidine bases
- Is cross-linked by H bonds
- Triplet codons of bases (pur + pyr) make up the code and encode amino acids
- Transcription = in nucleus DNA code is read onto mRNA
- Translation = on ribosomes mRNA is read by tRNA carrying the AA → proteins formed
- Genes:
  - Paired (alleles) located on each pair of chromosomes
  - ~ 30000
  - Exons (coding) + introns (non-coding)
  - Frequently rearranged (mutations) + tightly controlled (eg promoters)

Miscellaneous

- Mosaicism = 2 cell lines (2 populations of cells each with different genotypes) eg a down’s cell line + a normal line (will produce a milder phenotype)
- Genetically unfit = incompatible with life
- Phenotypic risk = whether disease will manifest
- Reproductive risk = whether disease will be passed on
- FISH = probes which bind to a specific gene or area of chromosome
- Linkage disequilibrium = non-random association of alleles at two or more loci, not necessarily on the same chromosome; the occurrence of some combinations of alleles in a population more often or less often than expected from a random formation of haplotypes from alleles based on their frequencies

Epidemiology of Genetic Disorders

- Prevalence of genetic disease:
  - ~5% of pop will have a genetic disease by the age of 25
  - ~60% of pop will experience a genetic-related disorder in their lifetime
  - ~2500-3000 genetic d in NZ each year

DNA

- There is frequent mutation in rapidly dividing cells: but repair mechanisms ‘mop up’
- If there is a sustained mutation in:
  - Essential gene → lethal
  - Non-coding gene → no effect
  - Non-essential gene → human variability/disease

Chromosome Disorders

Numerical Chromosomal Abnormality

- Euploidy 2 copies of each chromosome
- Aneuploidy gain (trisomy) or loss (monosomy) of a whole chromosome
  - One missing or additional chromosome

Genetics and Cancer
Trisomy 13: next most common, trisomy

Turner’s Syndrome: 45, XO
- Puffy feet, poor toe nails, webbed neck, kidney and cardiac malformation (bicuspis aorta – systolic murmur), shield chest
- Later: short, infertile, normal mental ability (unless 2nd X ring chromosome → mental disability)
- The 10% that survive to term are the good end of the spectrum
- Differential: Noonan’s Syndrome – similar symptoms but karyotype is normal

Klinefelter Syndrome: 47, XXY
- 1/3 present in childhood with learning difficulty
- 1/3 present in adolescent: failure of puberty due to no testosterone (ie hypogonadism)
- 1/3 present in adulthood due to infertility

Polyplody: gain whole sets of chromosomes (triploidy) – not compatible with life

Mosaicism: euploidy + aneuploidy

Origins of numerical abnormality:
- Gametogenesis (↑maternal age):
  - Eggs reach meiosis I in foetus + suspended here until puberty
  - Increasing age can cause damaged meiotic spindle + abnormal meiotic pairing (nondisjunction)
- Fertilisation:
  - Polyploidy (usually triploidy – double paternal leads to large placenta + growth delay; double maternal leads to tiny placenta + significant growth delay + macrocephaly therefore female genes for fetus, paternal for placenta)
  - Molar pregnancy (haploid sperm + empty egg → haploid zygote → diploid zygote with double paternal genome; leads to a conceptus without an embryo)
  - Errors at early cleavage (post zygotic non-disjunction)

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  - Errors at early cleavage (post zygotic non-disjunction)

Summary of numerical abnormality:
- Meiosis (ie gametogenesis): gain or loss of a single chromosome
- Fertilisation: gain of whole chromosome sets
- Post-fertilisation (ie early cleavage): gain or loss during mitosis

Chromosome Rearrangement

- Balanced:
  - Translocation
    - Reciprocal (break + exchange; 10% phenotype risk; reproductive risk)
    - Robertsonian (whole arm exchange in acrocentric chromosomes [one arm shorter than other]; no phenotype risk; reproductive risk)
  - Inversion (2 breaks, rotation then rejoining; 5-10% phenotype risk; reproductive risk)
  - Insertion

- Unbalanced:
  - Deletions – loss of segment (interstitial or terminal)
  - Duplications – gain of segment
  - Rings – breakage then circularisation
  - Markers – extra unidentified chromosome
  - Isochromosomes – mirror image of one chromosome arm
  - Dicentrics – 2 centromeres
  - Fragile sites

Summary:
- Balanced rearrangements = 10% phenotype risk but reproductive risks
- Unbalanced rearrangements = will see a phenotype

Patterns of Inheritance

Autosomal Dominant
- Single gene abnormalities expressed in heterozygotes
- Does not skip generations
- M = F, 50% risk of passing it to kids
- 1 mutated allele causes disease
- Eg Huntington Disease, Marfan Syndrome, Achondroplasia (disturbance of epiphyseal chondroblastic bone formation)
- But:
- Variable expression, variable age of onset (see below)
- Non-penetrance happens (see below)
- Gonadal mosaicism (esp if old paternal age) → somatic genes normal, mutation in gonads

**Autosomal Recessive**
- Both alleles of gene mutated (homozygous)
- M = F; each parent carries at least 1 mutated allele; 1 in 4 (25%) chance
- Skips generations
- Must have mutations in both genes ⇒ both parents are carriers
- Shows up early (no normal genes)
- Eg cystic fibrosis, phenylketonuria

**X-linked Recessive**
- 1 mutated gene on x chromosome
- Only affects males
- 1 in 2 risk for son of carrier mother, daughter of carrier mother also has 1 in 2 risk of being a carrier
- Carrier females may manifest some signs of disease
- Females are carriers (random X inactivation should mean that 50% of cells are abnormal. But they’re usually in the minority. 50% normal cells generally is more than enough to function normally; may have mild phenotype)
- Turner’s females or non-random x inactivation of the good chromosome – leaving the mutant chromosome active
- Impact early (no normal gene)
- Eg haemophilia, Duchenne muscular dystrophy (wasting muscle disease – most dystrophies are X linked)

**X-linked Dominant**
- eg Fragile X

**Multifactorial**
- Genetic predisposition + environmental influence
- May be polygenic
- Seen in common disorders: DM, congenital heart d, neural tube defects
- Eg Cleft lip/palate

**Others**
- Mitochondrial, tumour predisposition

**Congenital Malformations and Syndromes**
- Malformations:
  - Common, major or minor
  - If 1 major, check other systems for others; if >3 minor, look for a major malformation
  - May be a familial predisposition; may be developmental error
- Syndromes:
  - Recognisable pattern of congenital malformations with a known (chromosomal, metabolic, DNA mutation) or unknown cause (developmental error, mutation)
- Teratogens:
  - Special group of malformation syndromes
  - Causes: meds (thalidomide), drugs (ETOH), infection (CMV), maternal disease (DM, PKU)

**Penetrance and Expressivity**
- Incomplete penetrance = in autosomal dominant diseases with incomplete penetrance, the person either expresses the disease phenotype or not
- Variable expressivity = each patient may express all of the symptoms, or only a few
- Incomplete penetrance should not be confused with variable expressivity. In diseases with variable expressivity the patient always expresses some of the symptoms of the disease and varies from very mildly affected to very severely affected
- Incomplete penetrance and variable expressivity are phenomena associated only with dominant inheritance, never with recessive
Novel Genetic Mechanisms

- Triplet repeats:
  - Genetic code occurs in triplets (3 bases makes an AA)
  - Prone to expansion + shrinkage b/w generations
  - Changes in repeat number are influenced by parent of origin (imprinting)
  - The presence of variable repeat numbers amongst family explains observed clinical variability to an extent
  - Number of repeats may help prediction of likely clinical outcome eg HD – need >41 repeats to be sure HD will manifest
  - Fragile X, Friedreich’s ataxia etc other examples

Non-Mendelian Genetics

Genetic Imprinting

- = Differential expression of genetic material depending on whether it has been inherited from mum or dad
- ⇒ Parent of origin of mutation matters for many genes
- Imprinted genes are genes whose expression is determined by the parent that contributed them
- Some genes only expressed when inherited from the father (or mother) → differential expression depending on the parent of origin
- Some chromosomes, sections of chromosomes or genes are stamped (methylation) with the parent of origin
- Chromosomes, sections of chromosomes or genes can be turned on and off depending on the parent from which the component was inherited
- Affected genes are usually highly conserved (ie the same genes appear in mice and humans – conserved through evolution)

Angelman’s/PWS:
  - Allele turned off by methylation, syndrome determined (ie AS or PWS) by whether paternal or maternal gene switched off
  - Both conditions are the result of a deletion in the same area on chromosome 15 (15q11-q13)
  - If the deleted area is inherited from an individual’s father the patient will have PWS (parental – PWS). The PWS gene is "switched off" on the maternally inherited chromosome 15, so this individual has no working copies of the PWS gene
  - On the other hand, if the deleted area is maternal in origin the patient will have AS. The AS gene is "switched off" on the paternally inherited chromosome 15, so this individual has no working copies of the AS gene

- Myotonic dystrophy:
  - Autosomal dominant
  - Progressive weakness from 3rd decade
  - Unstable triplet repeat on 19 (upper limit of normal is 50 repeats)
  - Most unstable when it’s from mum (ie parental imprinting)
  - As number of repeats increases goes from normal → premutation carrier → affected

Fragile X Syndrome:
  - Abnormal if triplet repeat > 200
  - Only expands when passed from mother to son, not to daughter

Huntington’s:
  - Unstable triplet repeat syndrome
  - If father passes it on then greater risk of ↑ number of repeats
  - See Dementia, page 731

Uniparental Disomy (UPD)

- = Presence of a cell line containing 2 chromosomes both inherited from only one parent
- Has been demonstrated in cystic fibrosis, haemophilia (ie got both mutated genes from the one parent)
- Prader-Willi Syndrome:
  - Floppy baby, low birth weight, retarded, ↑↑appetite →obesity, short statue
  - Caused by deletion on father’s Chr 15, or have both normal Chr 15 from mum (ie no 15 from dad)
  - Angelman Syndrome caused by maternal deletion of the same chromosome →low birth weight, unusual cry, stiff legged gait, tremor and seizures

Mitochondrial Disorder

- Mitochondria:
Genetics and Cancer

- Subcellular organelles, generate ATP, electron transport chain, CAC etc
- Has own double stranded circular DNA – codes for 13 subunits of the ETC (of a total of 60 or 70 total subunits – rest are from normal DNA)
- Maternally inherited; high mutation rate – leads to heteroplasmic populations (mixed pop of mitochondrial DNA)

- Clinical presentation: unexplained association of neuromuscular and or non-neuromuscular symptoms; progressive course; involving seemingly unrelated organs or tissues; wide range of age of onset
- Associated with ageing, PD, alzheimer’s
- Screening tests: plasma lactate, ketones, BG, FFA, urinary organic acids
- Diagnostic tests: muscle bx: histo, EM for mito morphology, enzyme analysis; DNA from above tissues plus blood for mutation analysis
- Rx: largely symptomatic, megavitamin cocktail (vit K, coenzyme Q, riboflavin, carnitine), dietary manipulation

Genetic Testing

- Types of test:
  - Screening tests: done on normal population to identify those at risk (not diagnostic)
  - Diagnostic tests to confirm the presence of disease
- Guthrie Card – for screening all neonates:
  - Should be done around 48hrs
  - Second test needed in about 1 in 100 babies (usually due to poor sample)

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<thead>
<tr>
<th>Disease</th>
<th>Treatment</th>
<th>Risk</th>
</tr>
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<tbody>
<tr>
<td>Biotinidase Deficiency</td>
<td>Take vitamin H (biotin)</td>
<td>1:50,000</td>
</tr>
<tr>
<td>Congenital Adrenal Hyperplasia</td>
<td>Steroids</td>
<td>1:20,000</td>
</tr>
<tr>
<td>Cystic Fibrosis</td>
<td>Pancreatic enzymes etc</td>
<td>1:3,000</td>
</tr>
<tr>
<td>Galactosaemia</td>
<td>Diet</td>
<td>1:120,000</td>
</tr>
<tr>
<td>Hypothyroidism</td>
<td>Thyroid replacement</td>
<td>1:4,500</td>
</tr>
<tr>
<td>Maple Syrup Urine Disease</td>
<td>Diet</td>
<td>1:250,000</td>
</tr>
<tr>
<td>Phenylketonuria (PKU)</td>
<td>Diet</td>
<td>1:15,000</td>
</tr>
</tbody>
</table>

- Galactosaemia:
  - Absence of the enzyme galactose-1-phosphate uridyl transferase.
  - It is an autosomal recessive condition.
  - This leads to galactose intolerance, and the main source of galactose is lactose found in milk.
  - Galactosaemia is associated with jaundice, hypoglycaemia and cataracts.
  - A positive Babinski response may be present up to the age of one year.
- Indications for neonatal genetic testing: Physical, growth or developmental disorders:
  - Still birth
  - Multiple congenital abnormalities
  - Small for age
  - Facial dysmorphia
  - Significant mental retardation
  - Post-natal growth retardation
  - Microcephaly

Other

- Agenesis: complete absence of an organ
- Aplasia: absence of an organ with the persistence of an undeveloped rudiment
- Anencephaly: congenital absence of cranial vault – with cerebral hemispheres completely missing

Genetic Counselling

- Aim: provide information for an individual/couple to make informed choices about their reproductive options, and to assist them in coming to terms with the options they face
- Requires:
  - Diagnostic precision
  - Estimation of risk: either Mendelian or multifactorial (eg cardiac abnormalities, neural tube defects, etc)
  - The likely burden of care for a child with the disorder: variability, life expectancy, quality of life, treatment
  - Alternatives: childless life style, adoption, intrauterine diagnosis, donor sperm, donor ova
Cancer

- See also Childhood Cancer, page 988
- See also Breast Cancer, page 669
- See also Colorectal Cancer, page 254
- Malignancy requires:
  - Presence of invasion
  - Ability to metastasise

Epidemiology

- In NZ:
  - Over 16,000 new cases diagnosed per annum, 7000 deaths
  - Commonest cancers (incidence):
    - Male: prostate, large bowel, lung (incidence ~ mortality)
    - Female: breast, large bowel, melanoma
  - Commonest cause of death:
    - Male: lung, large bowel, prostate
    - Female: breast, lung, large bowel
- Prognosis of cancer is determined by:
  - Tumour related factors: accurate diagnosis, stage, grade, risk factors (eg biochemical markers), cytogenetics
  - Patient related factors: age, sex, co-morbidities

Oncogenesis

- Cancer causing agents:
  - ‘Natural’ – eg fungus and plant toxins. Eg aflatoxin from fungus contaminating peanuts in Africa → liver cancer
  - Man-made: enormous diversity. Mainly the metabolites/intermediates in the body that are carcinogenic. Very often organ specific. Most precarcinogens detoxified to non-carcinogenic metabolites.
- Cancer = uncontrolled cell proliferation due to genetic change
- The more uncontrolled the proliferation, the more mutations – in final stages anuploidy, translocations, etc will be very common
- Oncogenes: cells related to normal cell proliferation and differentiation. If one allele is mutated then uncontrolled proliferation (autosomal dominant)
- Tumour suppressor genes: regulatory genes that inhibit cell proliferation. Need to lose both alleles to have an effect (autosomal recessive)
- Carcinogenesis:
  - Multifactorial – needs multiple DNA mutations
  - P53 Gene:
    - Regulates cell cycle
    - Inactivated in over ½ human tumours
    - Activated by hypoxia, DNA damage, viruses
    - If there is minor cell damage → small amount of P53 → arrest cell cycle and repair
    - If major damage → P53 → apoptosis
    - Activated P53 binds to DNA activating other genes
    - Normal P53 can be inactivated by mutating co-factors
  - Philadelphia Chromosome:
    - Arises from balanced translocation t(9, 22)(q34,q11)
    - Brings C-ABL gene beside BCR gene. C-ABL is an oncogene, and is now regulated by BCR → normal regulation has failed
    - Causative in CML, also seen in other tumours. See Chronic Leukaemia, page 480
  - Telomere
    - Non-coding cap to genome
    - During replication, an enzyme binds and prevents replication → telomere shortens with each replication
    - Telomerase can produce telomere – usually only in germ cells. But also active in cancer cells → unlimited potential to divide
    - Research aim: find drug to inhibit telomerase → give cancer cells a limited number of divisions
Tumour starts with single clone, quickly becomes heterogeneous. Only a few descendants will be able to metastasise.

Growing tumour needs blood supply – secretes angiogenic factors. Research aim: find ways of inhibiting this process. An advantage would be that this would kill all tumour cells, whereas chemotherapy is selective, leaving resistant cells to grow.

Anatomic Pathology and Neoplasia

- Describing a histologic section – always include:
  - Architecture (eg gland formation, infiltration – eg sheet like, cords)
  - Cytologic features of malignancy:
    - Coarse chromatin/hyperchromatic
    - Nuclear pleiomorphism
    - Abnormally mitotically active
    - ↑N:C ratio
    - Cellular aggregation
    - Prominent nucleoli
  - Tissue reaction (fibrosis, inflammation, etc)
- Macroscopic signs of invasion:
  - Variegated
  - Poorly circumscribed, not encapsulated, irregular border
  - Crab like
  - Areas of haemorrhage
- Microscopic signs of malignancy:
  - Nuclear pleiomorphism
  - Hyperchromatic nuclei
  - Invasion
  - Poorly differentiated (anaplastic)
  - Mitoses
- Tumor prognosis:
  - Stage (how much infiltration, metastasis)
  - Grade (what type, how well differentiated)
  - Resection margin
  - Brisk inflammatory response is good
- Hamartoma = overgrowth of tissue native to that site (NOT clonal proliferation/neoplasm)

- Headings for answering pathology exam essay questions:
  - Incidence
  - Aetiology
  - Pathogenesis
  - Macroscopic description
  - Microscopic description
  - Natural History
  - Outcome
  - Complications
  - Special types

Staging of Cancer

- = Determining the extent of cancer
- Why stage:
  - Affects prognosis
  - Affects treatment
  - Allows comparison of results between centres (eg audit)
- Staging Systems:
  - TNM system:
    - Nomenclature:
      - T: Size and invasion eg 1 = small, 4 = large
      - N: which nodes are involved
      - M: no metastases or metastases present
    - Variations applied to many cancers (eg NSC lung cancer, breast, etc)
Guides treatment: eg T1N0M0 → wide local excision; T3N1M0 → may start with chemo/RT

TNMs are grouped to give stage groups ranging from IA to IV

**FIGO System**
- Gynae malignancies, eg cervix:
  - Stage I: confined to cervix
  - Stage II: Not involving the pelvic wall or lower 1/3 of vagina
  - Stage III: extends to pelvic side wall
  - Treatment:
    - I & IIa: surgery or radiotherapy
    - IIb & III: radiotherapy

- Ann Arbor classification for lymphoma (see Lymphoma, page 490)
- Dukes Classification for bowel cancer, see Prognosis of Colorectal Cancer, page 257

**How to stage:**
- **History**: symptoms suggestive of local extension or distant metastases
- **Exam**: nodal involvement, metastatic involvement (bone tenderness, hepatomegaly)
- **Bloods**: FBC (blood loss, marrow involvement), LFT, ALP and albumin (liver involvement), tumour markers
- **Imaging**:
  - CXR, mammography
  - CT Scanning – to determine primary disease, nodal involvement, mets
  - MRI: especially CNS and spinal cord tumours
  - Nuclear medicine: bone scan
  - US: good for differentiating cystic from solid, especially in the abdomen
  - Contract studies (barium swallow, enema): largely surpassed by endoscopy

- **Special investigations**:
  - Bone marrow: lymphomas, small cell lung
  - FNA: either US or CT guided
  - Laproscopy: node sampling
  - Endoscopy
  - Surgery: role in staging tumours largely overtaken

**Tumour markers**:
- Generally only reliable for **monitoring treatment** in cancer demonstrated to produce a tumour marker. Generally poor for screening
- **βHCG**: germ cell tumours; used for diagnosis and monitoring treatment
- **AFP**: produced during liver regeneration: hepatocellular cancer, testicular embryonic cancers, yolk sac tumours
- **CEA**: produced by epithelial elements (colon, ovary, pancreas). Usually in advanced disease so no use for screening. Also in gastritis and UC
- **CA125**: ovarian cancer (good response marker). Also in endometriosis, hepatitis
- **PSA**: levels correlate well with disease extent. > 10 ⇒ 80% chance of cancer
- **CA 19-9**: pancreatic cancer monitoring

**Type, Grade, Stage**

- **Three foci**:
  - **Type**: what is the cell of origin?
    - Carcinoma – epithelial origin
    - Sarcoma – connective tissue (mesenchymal) origin
  - **Grade**: how well does the tumour resemble the tissue of origin?
    - Indicator of aggressiveness – likelihood of infiltration
    - Well differentiated
    - Moderately differentiated
    - Poorly differentiated
  - **Stage**: what is the extent of spread throughout the body?
    - TNM
    - Best **prognostic indicator**

**Cancer Treatment**

- **Treatment objectives**:
  - Cure
  - Prolong life expectancy
  - Palliate: relieve symptoms/↑QOL
• Treatment modalities:
  ➢ Chemotherapy
  ➢ Radiotherapy
  ➢ Surgery
  ➢ Symptomatic/Supportive
• For Treatment of:
  ➢ Colorectal cancer, Treatment of Colorectal Cancer, page 257
  ➢ Breast cancer, see Treatment of Breast Cancer, page 672

Radiotherapy
• Superficial X-ray: for skin cancers
• Cobalt: no longer used in the west. Max 1.2 MV
• Linear accelerators:
  ➢ 6 MV to 18 MV
  ➢ Skin sparing
  ➢ Produces electrons and photons. Biological effect of photons is to create free radicals
  ➢ Does lots of damage to the cell – but only damage which affects reproductive integrity is DNA damage
  ➢ Most DNA damage is repaired within 6 – 8 hours, but if lots of damage then non-repair
  ➢ More damage is done to cells in G2 (ie in mitosis) as DNA is super coiled
• Effective use requires:
  ➢ Good planning: how to maximise dose to the lesion while minimising dose to unaffected tissue
  ➢ Immobilising the patient
• Use of multiple fractions (ie lots of small doses) spares normal tissue as this has time to repair, but tumour tissue doesn’t repair so well
• Uses:
  ➢ Aim is curative in head and neck, skin, cervix
  ➢ Anal (with chemo), rectal (with surgery)
  ➢ Adjunct in lung, stomach cancer
• Toxicity:
  ➢ Acute: builds up during treatment and settles within ~ 6 weeks
    o Affects rapidly dividing cells and secretory function
    o Skin: erythema, desquamation
    o Mouth: mucositis and dryness
    o Gut: diarrhoea, colic, ileus
    o Bladder: cystitis
    o Marrow (only if widespread dosing): leukopaenia, thrombocytopenia
  ➢ Late: Months to years
    o Due to healing with fibrosis or ↑aging of tissues
    o Affects slowly or non-dividing cells and causes permanent damage
    o Skin: Telangiectasis, fibrosis
    o Mouth: Dryness (↓parotid function), caries, osteoradionecrosis
    o Gut: strictures, fistula
    o Bladder: contracture, haematuria
    o Nerves: myelitis, necrosis, neuropathy

Chemotherapy
• = cytotoxics: interfere with DNA/RNA protein synthesis → cell death/apoptosis. Not tumour specific
• Systemic treatment with single or multiple agents (allows less side effect profile)
• Predictable side effects depending on the schedule. Side effect management has improved greatly
• Can be oral, sc, im, iv, continuous iv
• Adjuvant treatment = after local therapy has removed cancer but where there is a statistical chance of relapse (eg due to micro metastases)
• Decisions re chemo are based on: What is the disease? What is the goal of treatment? What are the side effects? What is the response rate expectation?
• Key themes: quantity vs quality; risk vs benefit; response vs toxicity
• Uses:
  ➢ Curative: in lymphoma (esp Hodgkin’s), leukaemia (including ALL), sarcomas of childhood, Germ cell tumours (Testicular teratoma, Seminoma), etc
- **Adjuvant:** in breast, large bowel and ovarian cancer (deals to micrometastases; can be neo-adjuvant [before] or after other therapy eg surgery/RT)
- Paliiative:
  - Improving QOL
  - Prolongation of life: ovarian, lung (small cell lung cancer is sensitive to chemotherapy), bowel, breast
  - Relief of symptoms: shortness of breath, pain/discomfort, local disease
- Not in melanoma, renal cell carcinoma

- Grouped into families:
  - Anthracyclines eg doxorubicin
  - Platinums eg cisplatin
  - Anti-metabolites eg methotrexate
  - Fluoropyrimidines eg SFU
  - Topoisomerase inhibitors eg irinotecan
- Majority are **cell cycle specific** ie interferes at a specific stage in the cell cycle
- **Side effects:**
  - General:
    - Feeling terrible till 2 – 3 days later
    - Nausea and vomiting: 5HT3 antagonists (ondansetron) to help
    - Lethargy, anorexia
    - Rash
    - Hospital attendance
  - Affect on fast growing tissues:
    - Mucous membranes: mouth ulcers, diarrhoea
    - Hair loss: not inevitable (depends on regime) but always temporary
    - Bone marrow: myelosuppression, anaemia, neutropenia, thrombocytopenia (NB these can be managed with transfusion, gCSF, ABs etc)
  - Peripheral neuropathy
  - Irritant effects: haematuria, sore eyes
  - Neutropenia: typically 1 – 3 weeks following. See Fever in a Neutropenic Patient, page 482
  - ↓Fertility (especially in men) but no risk of future fetal abnormality (unless pregnant at the time). NOT a reliable contraceptive
  - Toxicity profile depends on the drug and is either acute, medium or long term:
    - Acute: n + v, diarrhoea, allergy, skin rash; BM suppression (anaemia, leukopenia, TCP)
    - Medium term: diarrhoea, mucositis, alopecia, skin rashes, LFT derangement
    - Long term: fertility issues, premature menopause, peripheral neuropathy, second cancers

- Targeted therapy:
  - Designer drugs eg imatinib to treat GIST tumours
  - Side effect profile is different
  - May result in cytostasis rather than cytoreduction
  - Expensive

**Other treatment options**
- Hormones
- Immunotherapy

**Symptom Management in Cancer**
- See also Constipation, page 263

**Principles of Symptom Management**
- Principles of symptom control:
  - Assessment: identify each problem/pain and make sure it’s managed
  - Explanation
  - Individualised treatment
    - Treat the cause if possible
    - Treat the symptom
    - Enhance coping skills
  - Monitoring progress
  - Attention to detail
  - Anticipate problems

*Genetics and Cancer*
Remember the family

**Pain Management in Cancer**

- See also Pain Management, page 866

  - Common problems:
    - Physical symptoms: pain, anorexia, nausea, insomnia, incontinence, weight loss, dyspnoea, effusions, weakness etc
    - 84% with advanced cancer have pain (most common symptom) but often have multiple other symptoms
    - Pain is subjective and contextual (eg in the setting of terminal illness; depends on social support etc)
    - Compounded by anger, losses, fear, financial insecurity, anxiety, isolation, bewildered by treatment
    - Always consider emotional, intellectual and spiritual components

  - Causes of pain:
    - Destructive/obstructive effects of the cancer
    - Debility: pressure sores, constipation
    - Due to treatment
    - Unrelated (eg toothache)

- WHO analgesic ladder:
  - Step 1: **mild** pain. Non-opioids: paracetamol, aspirin, NSAIDs
  - Step 2: **moderate** pain. Weak opioids: codeine, tramadol, +/- non-opioids eg combination drugs:
    - Paradex (Digesic): dextropropoxyphene plus paracetamol
    - Panadeine: codeine plus paracetamol
  - Step 3: **severe** pain:
    - Morphine:
      - Actions: analgesia, respiratory depression, drowsiness, vomiting, miosis, convulsions, euphoria or dysphoria, smooth muscle stimulation (→GI muscle spasm, biliary and renal tract spasm)
      - **Rapid acting oral**: morphine elixir (start at 2.5mg and work up; 4 hourly) or oxynorm (synthetic); breakthrough dose when using slow release is 1/6 of daily dose (as given 4hrly)
      - **Longer acting/slow release**: m-eslon (average out total 24hr dose based on morphine elixir + split into bd; 12hrs) or oxycotin (cont = continuous)
      - Parenterally: SC syringe driver infusion (if not tolerating oral due to vomiting/other illness), IM (onset in 10 – 15 minutes, lasts 4 hours), IV
      - Bioavailability: half parenteral dose cf oral (1:2)
      - Anticipate constipation + co-prescribe laxative (eg laxsol)
      - Metoclopramide is an useful anti-emetic in conjunction with morphine as it ↑ GI motility
      - Neuropathic pain is typically unresponsive to opioids (use gabapentin, amitriptyline)
      - Signs of morphine overdose: RR < 12, if RR < 8 then Naloxone
      - Methadone (difficult titrating the dose) – useful in withdrawal from opioids
      - Fentanyl: less constipation than morphine, but not subsidised, transdermal fentanyl patches lasting 72 hours are well suited to patients with stable pain and low to medium opiod requirements
      - +/- non-opioids + adjuvant
    - Adjuvants at any stage: TCAs, gabapentin, anticonvulsants, steroids, muscle relaxants, antiarrhythmics
  - **Anticipate pain and give regular analgesia, plus PRN medication for acute-on-chronic pain (‘breakthrough’ pain)**

- Enhance coping skills:
  - Listen and acknowledge the symptoms
  - Explanation, information
  - Shared decision making
  - Calm supportive environment
  - Complementary therapies: relaxation, art therapy, music, OT diversional therapy
  - Spiritual support, counselling
  - Treat anxiety, depression
  - Support the family
Management of Nausea

- Risk of acute emesis can be influenced by patient-related factors including: (i) poor control of nausea and vomiting with prior chemotherapy, (ii) female sex and (iii) chronic alcohol intake in addition to the nature of the chemotherapeutic agent and its dose
- Identify the right pathway and treat it specifically
- From a 2002 review of anti-emetics:

<table>
<thead>
<tr>
<th>Emesis</th>
<th>Risk</th>
<th>Prophylaxis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute</td>
<td>High</td>
<td>5-HT3 + corticosteroid</td>
</tr>
<tr>
<td></td>
<td>Intermediate</td>
<td>Corticosteroid</td>
</tr>
<tr>
<td></td>
<td>Low</td>
<td>None</td>
</tr>
<tr>
<td>Delayed</td>
<td>High</td>
<td>Corticosteroid + metoclopramide or 5-HT3</td>
</tr>
<tr>
<td></td>
<td>Intermediate/low</td>
<td>None</td>
</tr>
<tr>
<td>Anticipatory</td>
<td>All</td>
<td>Prevention of acute or delayed emesis</td>
</tr>
</tbody>
</table>

- “Drugs of choice”:
  - H1 antagonist: cyclizine
  - D2 antagonist: prochlorperazine (stemetil), haloperidol
  - 5-HT3 antagonist: ondansetron
  - Prokinetic: oral domperidone, iv metoclopramide (also has anti-D2 effect)
- Chemical cause (stimulation of chemoreceptor trigger zone by uraemia, opioid induced, hypercalcaemia, toxins): stimulates dopamine receptors. Haloperidol is a dopamine antagonist, as is chlorpromazine, metoclopramide and cisapride
- Mechanical cause (squashed stomach, delayed emptying, regurgitation): metoclopramide and domperidone → prokinetic action
- Emetogenic chemotherapy: stimulates release of serotonin in the gut: 5HT3 antagonists are used (ondansetron, granisetron, tropisetron)
- Vestibular and ↑ICP: use antihistamines eg cyclizine
- Non-drug therapy: prophylactic treatment of constipation, keep away from sight or small of food; small, frequent, attractive meals, relaxation therapy, acupressure

Management of Breathlessness

- Due to lung, circulation, neuromuscular, psychological: effusion, anaemia, mass or irritant effect, anxiety, fatigue
- Compounded by fear of fighting to breathe. Can also be PE (but don’t anticoagulate them – it’s better to die from a clot than a bleed)
- Treatments:
  - Treat underlying cause eg drain effusion, give blood transfusion if anaemic
  - Low dose morphine → ↓irritant respiratory reflexes
  - BZDs/anxiolytics for panic (eg lorazepam for intermittent breathlessness, diazepam for chronic)
  - Steroids for anti-inflammatory effect
  - Nebulised saline: shift sticky secretions, humidify dry airways
  - Oxygen if symptomatic hypoxia – but commits the patient to the equipment
  - Advice from physio, especially re controlling expiration
  - Fan on face, open window

Management of Cachexia

- = Marked weight loss and muscle wasting, especially in advanced GI and lung cancers
- Due to ↑metabolic rate and ↓food intake, plus abnormal metabolism and cytokine production
- May also see altered taste sensation, lose dentures causing difficulty eating, oedema due to hypo-albuminaemia, pressure sores over bony prominences, etc
- Body changes may generate feelings of fear, isolation or difficulty with relationships
- Management:
  - Dietary supplements and NG feeding are unlikely to achieve anything. Patients should eat and drink as they wish
  - Corticosteroids in a reducing protocol may help (as well as reducing tumour oedema)
  - Relining dentures
  - General support: education, new clothes, aides to maintain independence
Cancer Emergencies

- See also Fever in a Neutropenic Patient, page 482

Spinal Cord Compression:
- Irreversible damage occurs quickly. Even if poor prognosis from cancer mobility makes a key difference to quality of life and to ease of nursing at home, etc
- Symptoms: pain (often dermatomal at the level of the lesion), weakness, autonomic dysfunction, sensory loss
- 95% is extramedullary compression. Thoracic > lumbosacral > cervical
- Primary tumours: lung, breast, prostate, lymphoma (very radiation sensitive), myeloma, kidney
- Differential: infective or mechanical
- Contraindications to radiotherapy: previous RT (already irradiated to spinal tolerance), radio-resistant tumour (eg myeloma), no tissue diagnosis (ie don’t know what you’re treating)
- Contraindications to surgery: widespread systemic disease, multiple levels, vertebral body collapse, known radio-sensitive tumour
- CXR usually done but MRI is investigation of choice

Cauda Equina Syndrome

Superior Vena Cava Syndrome:
- Compression causing thoracic and neck vein distension, facial and arm (maybe unilateral) oedema
- Causes: CNS symptoms (Headache, visual disturbance, dizziness, blackout, altered conscious state), venous thrombosis
- Usually due to lung cancer, also lymphoma and metastases. Benign causes include goitre, fibrosis, sarcoidosis, syphilis, etc
- Investigations: examination, CXR, CT (rather than MRI), biopsy (maybe US guided)
- Treatment:
  - Anticoagulant + thrombolysis if established clot (eg neck veins not compressible)
  - Endovascular stent if recurrent
  - Chemotherapy: small cell lung cancer (80% response), Hodgkin’s Lymphoma or Non-Hodgkin’s lymphoma
  - Radiotherapy: any other malignant cause (80% response)

Hypercalcaemia:
- Occurs in 20 to 30 percent of patients with cancer
- Most commonly is associated with multiple myeloma and cancers of the lung, breast, and kidney
- Mechanisms that are thought to be important include bone-resorbing cytokines; parathyroid hormone-related peptide, secreted by the tumor → binds to parathyroid hormone receptors; tumor-mediated calcitriol production; and, occasionally, ectopic parathyroid hormone secretion
- Symptoms of this condition include nausea, vomiting, constipation, progressive decline in mental function, renal failure, and coma → stones, groans and moans, also thirst
- Tx: vigorous rehydration + frusemide + bisphosphonates

Pathological fracture: orthopaedic referral to stabilise

Haemorrhage: tumours bleed easily, erosion into an artery

SIADH:
- Bronchogenic carcinoma often is the ectopic source of antidiuretic hormone production, although certain chemotherapy agents can cause SIADH
- Patients may present with anorexia, nausea, myalgia, headaches, and severe neurologic symptoms (e.g., seizures, coma)

Hyperviscosity syndrome:
- Most common in patients with Waldenström’s macroglobulinemia, leukemia, or multiple myeloma
- Elevated levels of circulating serum immunoglobulins coat the cells, causing increased blood viscosity, sludging of blood, and hypoperfusion
- Signs and symptoms of hyperviscosity syndrome include spontaneous bleeding, neurologic defects (e.g., peripheral neuropathies), and vision changes (“sausage-like” hemorrhagic retinal veins are pathognomic)
- Treatment includes plasmapheresis followed by targeted chemotherapy

Tumour lysis syndrome:
- Acute cell lysis caused by chemotherapy and radiation therapy, usually presenting in the first 5d of chemo/RT
- The release of intracellular products (e.g., uric acid, phosphates, calcium, potassium) overwhelms the body’s homeostasis mechanisms
- Commonly present with azotemia, acidosis, hyperphosphatemia, hyperkalemia, hypocalcemia, and acute renal failure
- Treatment includes inpatient monitoring, vigorous fluid resuscitation, allopurinol or urate oxidase therapy to lower uric acid levels, urinary alkalization, and hemodialysis

**Obstruction:**
- Trachea $\rightarrow$ stridor. Mainly extrinsic compression. Options: RT, steroids (↓oedema), tracheostomy
- Bronchus: dyspnoea
- Oesophagus: dysphagia. Usually progressive, not an emergency. Lodged bolus can present acutely
- Bowel
- Ureter

**Palliative Care**
- See also:
  - Breaking Breaking Bad News, page 20
  - See Grief and Bereavement, page 770
  - The Dying Child, page 894
- Palliative care: care of patients with active, progressive, far advanced disease and a limited prognosis and for whom the focus of care is the quality of life
- Regards death as a normal process
- Integrates physical, emotional, social, cultural and spiritual aspects of care
- Offers support to help families and care givers
- Provide relief from pain and other distressing symptoms
- Neither hastens death nor prolongs life
Emergency Management

- References: A New Zealand Guide to Resuscitation Practice, Wellington School of Medicine, New Zealand Resuscitation Council.

**Trauma**
- Resuscitation and primary survey → secondary survey → tertiary survey
- DRS ABCDE
- Assess for **danger**
- Assess for **response** (if pt responds, tells you they have a patent airway, sufficient air in their lungs, + cerebral perfusion ie **ABC**)
- **Send** for help

**Airway**
- Consider CSp injury: jaw thrust best when injury suspected → do not flex the neck
- Open
- Clear
- Maintain

**Breathing**
- Give O2 using reservoir – respiratory function may be compromised
- Examine chest + CXR

**Circulation**
- Includes haemorrhage management → stop external bleeding
- Insert minimum 16g cannulae
- Replenish circulating volume (crystalloid first; the best colloid is blood)
- Cross-match according to urgency
- In penetrating trauma, best to give less fluid as can blow off clot from damaged vessels: aim for SBP of 90mmHg
- In traumatic brain injury, aim for SBP of 120mmHg as oedematous brain is harder to perfuse, therefore need more volume replacement
- Occult blood loss: think chest, abdo, pelvis, multiple or open #

**Disability**
- GCS or AVPU (alert, responds to voice, pain or unconscious)
- Glucose
- Pupillary responses
- Lateralising abnormalities (eg R vs L)
- Longitudinal abnormalities (eg arms vs legs)
- Cushing’s response: ↑BP ↓HR

**Exposure/Environment**
- Examine whole pt
- Keep uninspected parts covered: cold can impair circulation

**Secondary Survey**
- **Before** secondary survey, ensure pt resuscitated; do CSp, CXR, pelvis; ensure connected to O2, monitors, IDC etc
- Top-to-toe assessment
- Remember to look in ears for blood (haemotympanum)/CSF and behind ears: Battle’s sign (mastoid ecchymosis: basal skull #)
- NB Orangish urine could be myoglobinuria → rhabdomyolysis (crush injury, electrocution)
- Priapism = SC injury until proven otherwise

**Resuscitation**
- Objective: keep oxygenated blood flowing to the brain – otherwise cell death in 2 – 4 minutes
- CPR only achieves ~ 30% flow to the brain; ~ 20% to the heart
- Basic life support = no special equipment
- Advanced life support = basic support + equipment + drugs
- Early defibrillation is vital: ↑ly non-doctors are being trained to use it outside hospital setting

Cardiopulmonary Resuscitation (CPR)

Current Guidelines

Advanced Life Support for Adults

Start CPR
30 compressions : 2 breaths
Minimise Interruptions

Attach Defibrillator / Monitor

Assess Rhythm

Shockable

Shock

CPR for 2 minutes

CPR for 2 minutes

Non Shockable

CPR for 2 minutes

Return of Spontaneous Circulation?

Post Resuscitation Care

Advanced Life Support for Infants and Children

Start CPR
15 compressions : 2 breaths
Minimise Interruptions

Attach Defibrillator / Monitor

Assess Rhythm

Shockable

Shock (4 J/kg)

CPR for 2 minutes

CPR for 2 minutes

Non Shockable

Adrenaline 10 mcg/kg (immediately then every 2nd cycle)

CPR for 2 minutes

Return of Spontaneous Circulation?

Post Resuscitation Care

December 2018

CPR only achieves ~ 30% flow to the brain; ~ 20% to the heart

Basic life support = no special equipment

Advanced life support = basic support + equipment + drugs

Early defibrillation is vital: ↑ly non-doctors are being trained to use it outside hospital setting

Cardiopulmonary Resuscitation (CPR)

Current Guidelines

Advanced Life Support for Adults

Start CPR
30 compressions : 2 breaths
Minimise Interruptions

Attach Defibrillator / Monitor

Assess Rhythm

Shockable

Shock

CPR for 2 minutes

CPR for 2 minutes

Non Shockable

CPR for 2 minutes

Return of Spontaneous Circulation?

Post Resuscitation Care

Advanced Life Support for Infants and Children

Start CPR
15 compressions : 2 breaths
Minimise Interruptions

Attach Defibrillator / Monitor

Assess Rhythm

Shockable

Shock (4 J/kg)

CPR for 2 minutes

CPR for 2 minutes

Non Shockable

Adrenaline 10 mcg/kg (immediately then every 2nd cycle)

CPR for 2 minutes

Return of Spontaneous Circulation?

Post Resuscitation Care

December 2018
Summary

- Ensure safety
- Check responsiveness
- Send for help
- Open Airway
- Check breathing/circulation: no longer than 20 seconds
- Precordial thump (if arrest within last 90 secs)
- Go for help
- Start compressions, followed by rescue breaths (adults = 30:2; children 15:2)
- ASAP: attach monitor Defibrillator and assess rhythm
- VF or VT or AED ‘shock advised’:
  - Defibrillate: max energy every time (generally 360J; if unsure though, use 200J): 3 x shocks in a row for adults, 1 only for children
  - Adrenaline every 3 minutes
  - 2 minute CPR
- Not VF or VT or No Shock Advised
  - Adrenaline
  - 2 minutes CPR
- Reassess rhythm or circulation

Basic Life Support: BLS Summary

- D: Check for danger.
  - If there is no danger
  - Then move on to R

- R: Response: verbal and/or painful stimulus
  - Determine if responsive (conscious) or unresponsive (unconscious)
  - If conscious, place in recovery position
  - If no response, call for help then move on to S

- S: Send for help

- A: Airway
  - It is reasonable to assume the unconscious patient has an obstructed airway until proven otherwise so you must do something to open the airway, headtilt with chin lift or jaw thrust.
  - Once an airway has been established, move on to B

- B: Breathing
  - Hold airway open and Look (at chest), listen (with ear) and feel (with side of face) for no more than 10 seconds
  - If breathing is present, then continue to maintain the airway
  - If not breathing (respiratory arrest) then you must breathe for them. Give 2 slow breaths
  - If there are no signs of life move on to C

- C: Circulation
  - This person has had a cardiorespiratory arrest so you must continue to breathe for them and pump the blood ie. CPR 2 breaths to 30 compressions rate of 100 per min.
  - Once compressions have been commenced, do not interrupt CPR to check for signs of life.
  - If more than one rescuer, rotate compressors every 2 mins to reduce fatigue.
  - CPR is continue until - signs of life return - qualified help arrives - impossible to continue due to exhaustion - authorised person pronounces life extinct

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A – Approach, Assess, Airway
- Ensure own safety, summon help
- Assess for responsiveness (gently shake, shout, be careful of other injuries). An arrest may present as a short grand mal seizure
- Cervical spine injury should be suspected, and assumed in unconscious patient esp. trauma. However, airway management takes precedence
- Urgent airway support may be indicated by: respiratory distress, hypoventilation, absent response to pain or stimuli, major skull, face or neck trauma, chest injuries, high spinal cord injury
- Open airway: CNS depression will diminish muscle tone in upper airway →tongue and epiglottis will obstruct airway →further hypoxia (faster in kids due to higher metabolic rate)
- Tilt head back, chin lift, jaw thrust

Airway Management Techniques
- Oropharyngeal airway insertion:
  - To maintain airway or prevent biting
  - Use Guedal airway. Male size 4, female size 3
  - If they tolerate oropharyngeal airway without gagging or coughing ⇒ no protective reflexes and need to be endotracheally intubated as soon as practical to protect from aspiration
- Laryngeal mask insertion:
  - For failed endotracheal intubation where Positive Pressure Ventilation indicated
  - Doesn’t protect from aspiration
  - Male size 4, female size 3
- Endotracheal intubation:
  - For control of airway, ventilation, protection from aspiration and prevention of gastric distension (e.g. in bag mask ventilation)
  - Sizes: Adult male size 9, female size 8, child (age in years)/4 + 4
  - If conscious and struggling may require sedative (e.g. thiopentone) and relaxant (suxamethonium)
  - Always check chest movements and CO2 return to check you haven’t got it in the oesophagus
  - Watch for pressure necrosis of tracheal mucosa from too large a tube or ↑inflation
  - Never attach O2 directly to tube (⇒ over inflation) – always via a ventilation/bag mask system
- Bag mask ventilation (AMBU Bag)
  - Always check chest rising: watch for leaks around mask, check patent airway
  - Too much pressure ⇒ gastric distension and aspiration into unprotected trachea
- Cricothyrotomy:
  - Use to gain access to airway where other methods have failed
  - Clean skin with antiseptic solution
  - Find cricothyroid membrane, between thyroid cartilage and cricoid ring immediately below it
  - Make horizontal incision through membrane. Insert handle of scalpel into incision and rotate 90 degrees
  - Insert largest possible endotracheal tube and attach to ambu bag. Ventilate with O2
  - Alternatively, use size 14 cannula, at angle of 45 degrees pointing down towards lungs. Attach cannula to syringe and syringe to ambu-bag

B – Breathing
- Ear over mouth and nose and look for chest to rise and fall. Slow gasping respirations may persist after arrest but these are ineffectual
- Assess whether trachea central, breath sounds bilateral, and check for crepitus (⇒pneumothorax)
- Exclude life threatening chest injuries: tension or open pneumothorax, flail segment

C – Circulation
- Check carotid pulse.
- Look for signs of circulation: movement, colour, etc

Action Plan
- If breathing and circulation but unconscious ⇒recovery position, and maintain airway
- If not breathing but there is circulation ⇒ventilate with 10 expired air ventilations over a minute and reassess
- If chest moving but there is no flow of air then obstruction ⇒head tilt, chin lift, jaw thrust forward
- If breathing absent or deteriorating and no or unsure of circulation then presume arrest
- Commence CPR/defibrillation, but consider (if you can):
Use O2 if at all possible – they will be hypoxic. Cylinders are black with white shoulder. Connect to ventilation bag at 4 atm. or to mask if breathing spontaneously (minimum 4 – 5 L per minute). NEVER connect directly to endotracheal tube (would →barotrauma)

Gaining iv access e.g. antecubital vein. Give saline flush after each access and hold limb up (circulation will be sluggish). Nothing more distal on arm, and don’t use femoral (unless needed for fluid replacement in trauma). If can’t get access, use carotid (subclavian interferes with CPR), or down endotracheal tube (2 to 2.5 times iv dose) with 10 ml saline

Adult CPR

- If defibrillator available, consider immediate use
- If no defibrillator and arrest has occurred within 90 – 120 seconds then single precordial thump – may convert ventricular arrhythmias in small number of cases, should never break bones, never in presence of palpable pulse (as may cause VF if delivered on T wave – commotio cordis)
- Get help: it is most likely a VF (and other things have a poor prognosis) and you need to defibrillate
- Continue with cycles of:
  30 chest compressions:  
  o Raise legs →↑venous return  
  o Press over junction of middle and lower thirds of sternum  
  o Use only heel of hand with thumb side lower  
  o Lock elbows, push straight down, move from hips not shoulders. Get on bed if you’re too low  
  o Consider putting board under patient or place on floor – soft mattress will impair compression  
  o Depress 4-5cm or one third of chest thickness: it is depth not force that is important, equal compression and relaxation times, not too jerky. Start gentle to determine correct pressure. Rib fractures impede filling, cause pneumothorax, lacerations of liver and spleen, and fat emboli
  o Rate of 100 per minute for adults and children.  
  o Can achieve systolic pressure of 60 – 80 mmHg, but low diastolic pressure so brain perfusion is maintained but heart perfusion poor. Adrenaline improves diastolic pressure
  2 expired air ventilations (mouth to mouth or nose, normal not big breath otherwise inflate stomach →gastric reflux, allow time for expiration). Theoretical risk of infection →take precautions
  After 2 minutes, stop for 10 secs to assess circulation. Continue with assessments every 2 minutes until defibrillator arrives
  Administer adrenaline 1 mg iv with every 1/2 minute loop

Paediatric CPR

- Respiratory distress/failure much more common cause of cardiac arrest than cardiac problems. Hypoxia and global ischaemia therefore often precede arrest (in adults it follows arrest), which results in asystole – not VF. Also caused by hypovolaemia, poisoning, drowning, etc
- Ventilation therefore more important than defibrillation. Kids have a higher metabolic rate and O2 reserves consumed quicker
- Survival associated with duration of arrest (after 5 minutes it plummets), not more than one dose of adrenaline, and presence of VF
- Procedure:
  - Assess your and patient’s safety
  - Assess responsiveness. Don’t shake a baby. If unresponsive, shout for help
  - Open airway: head tilt (not too much extension) and chin lift. Jaw thrust instead if cervical trauma. Check for obstruction
  - Assess breathing. If chest moves but no breath, recheck airway
  - Ventilate: 5 attempted breaths 1 – 1.5 seconds. In babies and infants, give through nose or nose and mouth. Slow breaths at low pressure better than fast/high pressure (↓gastric distension). Ventilate just sufficiently to make chest rise and fall
  - For no more than 10 secs, check circulation. Infants: brachial, femoral, axillary arteries or apex beat. If over 8, carotid best
  - If no circulation or less than 60 bpm, external chest compression. Over junction of middle and lower 3/4 of sternum.
    o In neonates, use two fingers to depth of 1 – 1.5 cm. Rate of 100 bpm, ratio of compressions to ventilations is 5:1  
    o Kids over 5, heel of one hand, depth approx. 2 – 3 cm  
    o Larger kids, two handed compression, depth of 3 – 4 cm, rate of 80 – 100 bpm, and ratio of 15: 2
  - After one minute alert emergency services
Resume CPR: reassess circulation after 3 minutes. Give adrenaline. If iv access time consuming, then 18 gauge perpendicular into anterior surface of tibia, 1 – 3 cm below tibial tuberosity. Failing this, give 10 times iv dose down endotracheal tube. Repeat cycle and adrenaline

When defibrillator arrives, assess rhythm. Use paediatric paddles if < 10 kg. ONLY if rhythm is VF or VT deliver 3 shocks at 2, 2, then 4 joules per Kg. Perform CPR for one minute, reassess rhythm. Every 2nd loop give adrenaline

Ventilation: Harder in kids – use two people to do bag-mask. Beware of barotrauma
If hypovolaemia →20 ml/kg saline or Ringers

Defibrillation

Works by applying current across the heart: one ½ depolarises while the other ½ repolarises
A successful shock induces asystole → SAN hopefully kicks in
Ideally within 90 seconds, preferably within 8 minutes. DON’T delay defibrillation to allow period of CPR
Apply ECG monitor
Switch on defibrillator (do this in transit)
Check its NOT in synchronised (cardioversion) mode
One paddle (doesn’t matter which) to right of upper sternum below the clavicle
Other paddle just to the left of the normal apex beat
Use a conducting aid (either electrode gel or pads), wipe up any gel that may short circuit between the pads
First, use paddles to assess rhythm (check settings on defibrillator). Classify as:

Ventricular fibrillation or ventricular tachycardia (wide QRS complex):
Charge defibrillator to max energy (for kids 4J/kg)
’S stand clear’: make sure you’re not touching patient or bed
Recharge defibrillator
Observe ECG
If VT or VF persists, deliver a second shock
If still persisting, deliver a third shock
If VT/VF persists, 2 minutes of CPR (attach ECG leads during this, insert artificial airway, iv access etc)
Repeat sequence, but with one shock then 2 minutes CPR
Adrenaline, 1 mg, with every 2nd loop (i.e. every 3 minutes)
Amiodarone 300mg after 2 lots of failed shocks or after refibrillation
If following a shock an organised rhythm appears which could be associated with cardiac output, check circulation. If absent then 3 minutes of CPR
If following a shock, the rhythm changes from VF/VT to asystole, perform 1 minute CPR and assess with NO adrenaline. ‘Stunned myocardium’ may take 20 – 30 secs to start again
If following a shock, is there an electrical fault, low gain on ECG. If in doubt deliver 3 defibrillating shocks
If asystole with P waves (ventricular standstill) consider emergency transcutaneous electrical pacing
Atropine, 3 mg iv, provides complete vagal blockade, as profound bradycardia may result from intense vagal over activity
Treatment of precipitating condition

Cardioversion

Is timed via ECG to occur on the R wave – must avoid the T wave (otherwise can → VF)
Is used for:
Ventricular tachycardia where pulse is present,
Supraventricular dysrhythmias (SVT, atrial fibrillation, atrial flutter)
Won’t fire unless it can detect the QRS. So if trying to defibrillate and it’s not working – check defibrillator is not set to cardioversion

Cardiac Arrest Rhythms

See also Arrhythmias, page 56
Due either to:
Disordered electrical activity (arrhythmia) such as following an MI, or
Impaired mechanical performance:
  o Pulseless Electrical Activity (PEA) or

Emergency Management
Electro-Mechanical Dissociation (EMD) – primary (damaged myocardium, e.g. ischaemia) or secondary (e.g. hypovolaemia, pneumothorax, anaphylaxis → ↓afterload, pulmonary embolus). EMD has worst prognosis. *ECG may be normal but patient is still arresting*

**Ventricular Fibrillation (VF)**
- Most non-traumatic arrests are ventricular fibrillation. Only effective treatment is defibrillation
- No organised depolarisation → doesn’t contract as a unit. But still contracting ⇒ still using O2
- **Coarse VF**: irregular, large amplitude ECG waves → onset recent. *Responds well to defibrillation* (if given within 5 – 8 minutes). CPR not sufficient to maintain the coronary artery perfusion necessary to offset O2 consumption → rapid ischaemia. *Precordial thump* MAY revert VF
- **Fine VF**: progressively lower amplitude VF until indistinguishable from asystole. 5-10% decrease in likelihood of successful defibrillation per minute
- Treatment:
  - Defibrillation
  - *CPR and adrenaline* help maintain diastolic BP and thus ↑ cardiac perfusion
  - If failing, consider *sodium bicarbonate* and *lignocaine* (antiarrhythmic)
  - Discontinue after **30 minutes**

**Ventricular Tachycardia**
- **Fast** (100 – 220/minute) and **wide QRS** complexes (> 0.12 sec) with **no p waves**
- Causes: ischaemia, K or Mg disturbances, PE, etc.
- Can be confused with supraventricular tachycardia with bundle branch block
- Dangerous precursor of VF
- Treatment:
  - If stable (i.e. still sufficient cardiac output → pulse):
    - Oxygen
    - *Amiodarone* or *Lignocaine* (1 mg/kg) stat plus 0.5 mg/kg every 8 minutes up to 3 mg/kg
    - If this fails then DC **cardioversion**
    - If little cardiac output/no pulse: same as for VF
  - If pulse but unstable:
    - Sedation
    - Cardioversion: starting at 50J, then 100 then 200 then 300. If recognisable regular rhythm then synchronised
    - If recurrent, give lignocaine, then procainamide 20 mg/min up to 1000 mg then brettylum 5 – 10 mg/kg and magnesium

**Torsade de Pointes**
- ECG like VT – but QRS amplitude changes due to *rotating electrical axis*
- May be self-limiting for periods of 5 – 10 secs
- Can → VF
- **May be due to anti-arrhythmics** prolonging the QT interval (if so, stop them)
- Treat by **correcting electrolyte abnormalities** and by ↑ basic heart rate (i.e. over-pacing)
- **Magnesium sulphate** 1-2gms given over 1 – 2 minutes may reverse drug-induced torsade
- Defibrillate for sustained episodes or use over-drive pacing

**Asystole**
- Complete absence of ventricular electrical activity
- Usually end result of major disturbance/myocardial damage
- Usually a wandering straight line (if completely flat check ECG)
- Invariably fatal after 15 minutes
- **Atropine + CPR** may bring back rhythm

**Drugs in Cardiac Arrest**
- No drug has been shown to consistently improve patient survival after cardiac arrest. CPR, defibrillation and airway control are therefore most important
- **Adrenaline**: peripheral vasoconstriction raises afterload, aids cardiac perfusion in diastole during CPR. Short duration of action → give 1 mg every 3 minutes. For kids, 10 µg/kg, subsequent doses 100 µg/kg. Effect wears off as local mediator dilator effects predominate in distal arteries
• Sodium bicarbonate: but major acidosis is usually respiratory, in which case bicarbonate →↑CO2 so will make this worse. Consider after prolonged hypoxia. Also in severe ketoacidosis. Don’t give via endotracheal tube

• Amiodarone

• Lignocaine, 1 mg/kg: for ventricular ectopy and stable ventricular tachycardia. No clear evidence of value in VF. ↑Shock energy required for successful defibrillation. Makes VF less likely – but harder to get out of

• Calcium: if massive blood transfusion will be calcium depleted

**Care Following Arrest**

• Transfer to ICU or CCU

• May need short period of elective ventilation

• Monitor cardiac rhythms, urine output, cerebral oedema, acid-base balance

• Prognosis of neurological function often clear from 24 hours after arrest

**Secondary survey**

• Check BP, respiratory rate, temperature

• Check for palpable pulse, capillary return to compressed fingernail bed, and neck veins

• Work **systematically** from head, to chest, abdomen, pelvis

• Check limbs and vertebrae for fractures

• External haemorrhage: pressure bandages, splints for fractures, if Military Anti-Shock Trousers (MAST) used for pelvic/femoral fracture, should only be very temporary and let down slowly (to avoid hypotension)

• Non-obvious injuries to exclude (as they may be life threatening): aortic dissection, pulmonary contusion, spinal injury, penetrating wounds (esp to back), and intra-abdominal bleeding (e.g. if persisting shock)

• Complications can occur insidiously: hypothermia, acidosis, sepsis, coagulopathies, shock

• Need 2 iv access sites with 14 gauge: arms, femoral, jugular, saphenous, subclavian vein, or cutdown to medial basilic or long saphenous vein (1 cm anterior to medial melleolus). Intraosseous in infants

• Fluid replacement: warmed crystalloid (watch for cerebral oedema) or colloid, blood where indicated

• Monitor pulse, BP, skin colour, capillary refill and **urine output**

• Check for neurological disability
  ➢ Very common, esp in road trauma
  ➢ Check: AVPU: alert, responding to vocal stimuli, pain, or unresponsive
  ➢ Moving limbs doesn’t exclude spinal injury
  ➢ Check pupils

**Glasgow Coma Scale (GCS)**

• **Eye opening:** E4 spontaneous, E3 to speech, E2 to pain, E1 nil

• **Verbal response:** V5 orientated, V4 confused conversation, V3 inappropriate words, V2 incomprehensible sounds, V1 nil

• **Best motor response:** M6 obeys, localises M5, Withdraws M4, Abnormal flexion M3, Extension M2, M1 Nil

• **8 or less = severe** head injury

• There is also a trauma score, includes GCS, respiratory rate, respiratory expansion, systolic BP and capillary refill

**Diagnosis of Death**

• Must be made by a doctor

• Must have all of:
  ➢ No respiration
  ➢ No BP
  ➢ No HR
  ➢ No pupillary reflex
  ➢ No response to pain

**Resuscitation Ethics**

**CPR Efficacy**

• Wide variation in outcome depending on clinical circumstances. Discharge rate is 15%. Biased by large number of ‘futile’ resuscitations

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<tr>
<th>Outcome</th>
<th>Comment</th>
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<tr>
<td>Elective cardiac surgery</td>
<td>100% Heart deliberately stopped</td>
</tr>
<tr>
<td>Out of hospital arrest, immediate CPR, ambulance &lt; 2 min</td>
<td>80% Early defibrillation key predictor of</td>
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Emergency Management

Survival. Survival ↓ by 10% per minute
Arrest under anaesthesia 20% Would already have had severe physiological assault prior to arrest
Out of hospital arrest, no CPR, ambulance > 6 min < 6%
Malignancy, severe chronic disease, chronic renal failure, pneumonia, trauma < 5%

• Poor outcomes (e.g. brain damage, organ failure) are inversely correlated with chances of survival
• Age per se is not an independent predictor of survival after CPR – but is correlated with illness

**CPR and Consent**

- Family members are not able to give consent (either for treatment or withdrawal of treatment) under common law in NZ, although HDC Code has provision for taking into account “the views of other suitable persons who are interested in the welfare of the consumer…”
- Doctor must make a ‘substituted professional judgement’: immediate decision on available information (usually not much) of what is in the patient’s best interests
- Ethically wrong to undertake resuscitation in patients in whom it is possible to predict a very low rate of intact survival
- Futile treatment diverts resources from other people. It is the principle of justice not the principle of autonomy that creates a right to treatment
- Doctor’s should not make decisions based on their assessment of the patient’s quality of life. Only the patient can make this assessment. However, this information is not usually available in acute setting. Revise further resuscitation/treatment decisions when this becomes available (i.e. the decision to resuscitate or not is not static)
- There is no ethical difference (may be other differences) between withholding and withdrawing treatment. Can revise decision to resuscitate as the probability of poor outcome grows or other information (e.g. patient’s wishes) comes to light

**DNR Orders**

- = Do not resuscitate, DNAR = Do not attempt resuscitation
- Reasons for DNR orders:
  - Refusal by a competent and informed patient
  - Poor quality of life after CPR (patient’s, not doctor’s view)
  - Futility: a clinical decision – so should the patient be involved or not?
- Decision to resuscitate should consider the likelihood of a beneficial outcome
- Prior discussion is key
- DNR orders should be discussed where:
  - Requested by a competent patient
  - Considered on grounds of poor quality of life
- Circumstances where it is not necessary to discuss DNR orders:
  - Patient is incompetent
  - Competent patient but grounds of quantitative futility
  - Where discussion of CPR would be detrimental to patient’s well being
  - Where patient indicates they do not wish to discuss CPR
- Role of family/friends: get their input, but doctor makes the decision regarding CPR unless the patient has a welfare guardian or has an advance directive
- Other points:
  - A DNR doesn’t mean other treatment is withdrawn
  - DNRs must be clearly documented in notes, including discussion of decision making process
  - DNRs should be reviewed regularly and may be withdrawn if warranted by change in clinical circumstances

**Shock**

**Clinical Signs**

- CNS: agitation, anxiety, confusion, changed consciousness, convulsions, focal signs, pupillary dilatation
- Respiratory - ↑RR, ↑respiration effort, ↑cyanosis, SOB, cough
- CV5 - ↑HR, ↓BP, ↓pulse pressure, ↓capillary return, pailor, sweaty, cool extremities, arrhythmias. Systolic BP < 90 and HR > 100. Treatment should aim to keep BP above 80 mm Hg
• Renal - ↓ urine output (< 30 ml/hour or < 0.5 ml/kg/hr)
• Cutaneous: flush, angioedema (swelling of face/mouth)
• GI: abdominal cramps, diarrhoea, vomiting, urinary/faecal incontinence
• See Adult Respiratory Distress Syndrome (ARDS), page 116

**Septic Shock**
• Systemic Inflammatory Response Syndrome (SIRS) is the presence of 2 or more of:
  ➢ Temp >= 38 C or < 35
  ➢ HR + 90 bpm
  ➢ RR >= 20/min or PaCO2 <= 32 mmHg
  ➢ WBC > 12,000 cells/ml
• Septic shock evolves from SIRS when BP <= 90 mmHg despite adequate fluid but need inotropes to raise BP
• Hyperdynamic circulation: may present early on with warm peripheries because of mediator-induced vasodilation – confusing as they’re not cold and clammy
• Infection: 70% due to G –ive: endotoxin release → inflammatory mediators → SIRS → changed haemodynamics
• Management:
  ➢ O2 + ventilation
  ➢ Circulatory support
  ➢ Nutrition
  ➢ Treat infection
• Mortality = 30 – 40 %

**Cardiogenic Shock**
• Causes:
  ➢ MI or ischaemia: need to lose 40 – 50% of functional ventricular mass
  ➢ Trauma
  ➢ Cardiomyopathy/myocarditis
  ➢ Dysrhythmia
  ➢ Valvular/septal defects
  ➢ Post cardiac surgery: stunned myocardium
  ➢ Drugs
• ↓ Contractile mass → ↓ CO → shut down → hypoxia, ↓ LVEDP → pulmonary oedema (more acute than heart failure)
• Management:
  ➢ Maximising coronary perfusion: ↓ afterload, maintain CO (inotropes), vessel patency (drugs, stents, etc), intra-aortic balloon pump
  ➢ Treat other factors: dysrhythmias, hypertension
  ➢ Support organ failure

**Hypovolaemic shock**
• Causes:
  ➢ Blood loss (usually trauma)
  ➢ GI (vomiting, diarrhoea)
  ➢ Renal (diuretics)
  ➢ Surface (burns)
  ➢ Maldistribution (e.g. sepsis, anaphylaxis)
• Estimated losses from fractures:
  ➢ Femur: 1000 – 1500 mls
  ➢ Pelvis: 1500 – 2500 mls (usually venous)
  ➢ Tibia and fibula: 750 – 1200 mls
  ➢ Humerus: 500 – 750 mls
  ➢ Also chest, abdomen, retroperitoneum, scalp
• Management: ABC, O2, iv fluids, minimise losses
• Initial bolus for paediatric shock is 20 ml/kg (unless DKA)

**Severe Anaphylaxis**
• = Severe allergic reaction
• See also Allergy and Hypersensitivity Disorders, page 496
Problems:
- Acute CV collapse: hypotension, myocardial ischaemia, arrhythmias
- Lower airway: bronchospasm → respiratory difficulty. Respiratory problems account for 70% of fatalities.
- Asthmatics at higher risk
- Upper airway: laryngeal oedema (ie angioedema)
- Also skin problems (urticaria, erythema, itch), nausea, vomiting, diarrhoea, anxiety, etc

Pathogenesis:
- Type 1 allergic reactions mediated by IgE antibodies
- Previously sensitised → IgE antibodies against allergen → mast cell activation → massive mediator release (histamine, leukotrienes, prostaglandins, kinins)
- Histamine leads to:
  - Smooth muscle contraction → bronchospasm
  - Vasodilation & ↑ permeability (can lose 1½ L of blood volume straight away)
  - ↑ HR and arrhythmias
  - ↑ Noradrenaline
  - Itch & oedema

Anaphylactoid reaction: activation of mast cells and release of mediators without IgE involvement. Only relevant to investigating cause – not to treatment

Examples of allergens:
- Drugs: 50% of fatalities. Includes penicillin, muscle relaxants (can be sensitised by exposure to similar drugs), aspirin, contrast media, blood products, streptokinase, preservatives (e.g. in adrenaline)
- Foods: 25% of fatalities. Peanuts, milk, eggs, fish
- Insect bites: 25% of fatalities (may be allergic)
- Also latex, semen, blood products, physical stimuli (eg exercise, cold, heat)

Presentation
- Anaesthetics: If IV – then as fast as 1 minute, but normally 5 – 10 minutes. Food up to 30 minutes
- 1 in 2,500 surgical patients in Wellington. Death rate 4 – 6 %

Treatment
- Stop administration of antigen. Call 777
- Adrenaline:
  - If no current venous access then 0.5 ml 1:1000 IM. 0.01 mg/kg for kids
  - If venous access: 0.3 – 0.5 mls iv of 1:1,000, slowly, repeat until BP > 100. Start low (eg 10 µg) and titrate up
  - Can be nebulised for laryngeal oedema
  - If on TCAs then ↑ sensitivity to adrenaline
  - α agonist → vasoconstriction – but not too much otherwise cardiac vasoconstriction
  - β agonist → bronchodilator
  - ↑ Force of heart contraction (inotropy)
  - ↓ Mediator release
  - T½ is short: common error is to give too little too infrequently
- Also:
  - Metaraminol (α agonist) to stop arrhythmias
  - Steroids: prevent late symptoms
  - Promethazine 25 mg slow iv or im (H1 antagonist) + H2 antagonist (e.g. ranitidine), or
  - Antihistamines: Phenergan 25 mg iv slowly for itch
- If bronchospasm alone:
  - Salbutamol: 5 – 20 µg/min
  - Hydrocortisone 200 mg iv
  - Aminophylline 5 mg/kg over 30 minutes
- Elevate legs → ↑ venous return
- O2 10 l/min by mask: intubate if necessary
- Wide bore cannula → 1 – 2 l iv colloid rapidly
- If anaesthetic reaction, always investigate so next anaesthetic is safe. Should have skin tests, etc. Cross reactivity between muscle relaxants is not uncommon

Differential Diagnosis
- Measure serum tryptase (longer T½ than histamine) to confirm anaphylaxis
Emergency Management

- Anaesthetic overdose: tryptase raised in anaphylaxis, normal in overdose
- Respiratory: pulmonary oedema/embolism, asthma, foreign body
- Heart: pericardial tamponade, MI, arrhythmia, vasovagal faint
- Venous air embolism
- Septic shock
- Pneumothorax
- Transfusion reaction
- Hypoglycaemia, CVA, epilepsy

**Prevention**
- Avoid treatment with β-blockers – makes treatment of anaphylaxis difficult
- Carry and use adrenaline (eg Epi-pen)
- Medic alert bracelet
- Call an ambulance, don’t ‘wait and see’

### Special Resuscitation Situations and Common Emergencies

#### Airway Obstruction
- Always consider in rapid cessation of breathing and unconsciousness. Also consider fainting, stroke, MI, epilepsy and drug overdose
- In adults especially related to meat, dentures and alcohol. Will grip throat not chest

**Adult obstruction**
- Partial obstruction → distressed and coughing. If conscious and adequate air → encourage coughing and spitting – nothing else
- Ask if they are choking: if can’t talk, breath or cough then:
  - Remove obvious obstruction from mouth (only if unconscious – may bite). Grasp tongue and mandible between thumb and fingers and lift up. Hook with other hand
  - **Back blows**: lean well forward onto one hand, 5 sharp slaps between shoulder blades with heel of other hand. If lying down, roll face down onto your thigh
  - **Abdominal thrusts** (Heimlich manoeuvre): fists over midline above naval, always below xiphoid process and ribs. Upwards thrust. May vomit. If on ground, lie on back and sit astride their thighs. If pregnant or obese, use chest thrusts
- If obstruction is not relieved: check mouth, 5 back slaps, 5 abdominal thrusts, repeat

**Paediatric Obstruction**
- Suspect in any airway distress with coughing, gagging, or stridor with rapid onset. May also be caused by infections (e.g. croup or epiglottitis). If infective cause then medical emergency
- Only intervene if child’s attempts to clear the obstruction are clearly ineffective and there is inadequate respiration
- For infants (<1 year) and children:
  - **5 back blows** with the child’s head below the level of the chest if possible
  - Then 5 chest thrusts to sternum in supine position: sharp, vigorous and rate of 20 bpm
- Check mouth: grasp tongue and jaw and lift. Don’t put finger into mouth unless foreign body is clearly visible
- Reassess airway. If not breathing, attempt to ventilate
- Repeat back slaps, chest thrusts, attempted ventilation. In children, alternate abdominal and chest thrusts

#### Alcohol Withdrawal
- See Alcohol Withdrawal, page 753

#### Asthma
- Arrest due to: bronchospasm (→ asphyxia), tension pneumothorax (often bilateral), β agonists → arrhythmias
- Arrest prevention:
  - SOS (salbutamol + O₂ + steroids) + adjuncts
  - Maximal O₂
Nebulised salbutamol (beware overdose → tachycardia and VF/VT) or iv 5 μg/min up to 20 μg if necessary (but regular nebs are better than iv)
- IV hydrocortisone
- Adrenaline
- IV sodium bicarbonate (acidosis prevents action of sympathomimetics)
- IV magnesium (bronchodilates)
- Intubation and IPPV: sedate with ketamine or benzodiazepines, paralyse with suxamethonium
- During arrest:
  - Consider assisted exhalation (bilateral manual squeeze over lower chest at end of inspiration)
  - Plus normal routine
- See also Asthma, page 107

Burns
- Caused by: thermal, electricity, chemical, mechanical, radiation
- History:
  - Timing – start fluid maintenance calculations from time of injury not time of presentation
  - Circumstances – eg any risk of inhalational injury
  - Tetanus immunisation
- Classification:
  - Assessing depth:
    - 1° degree burns: erythema (like bad sunburn)
    - 2° degree: blistering
    - 3° degree: skin goes like leather
  - Now classified as:
    - Partial thickness burns (either 1° or 2° degree): superficial; heal in 2 – 3 weeks, deep need grafting
    - Full thickness burn
- Body area covered: Rule of nines to estimate surface area burnt: head 9%, arms 9% each, thorax 18%, abdomen 18%, legs 18% each
- Admit if:
  - Major burn (>15% of adult, > 10% of child)
  - Special areas (hands, face, over joints, etc)
  - Circumferential – Require escharotomy to release pressure
  - Other medical conditions, etc
- Respiratory complications:
  - Upper airway burns: watch for oedema and obstruction. Prophylactic intubation if severe
  - Lower respiratory tract burns: Suspect if closed space fire, smoke inhalation or upper RT burns.
    - Treatment: humidified O2, PEEP, pulmonary toilet and physiotherapy. Avoid steroids
  - Inhalational injury a big killer – eg chemicals from burning materials → ARDS 24 hours later
- Watch for:
  - Hypovolaemia. See Replacement fluids, page 875 for fluid resuscitation
  - Good nutrition critical: ↑↑ calorie and protein requirements. Use NG tube
- For minor burns:
  - Analgesia
  - Wash gently
  - Dress with paraffin gauze and padding
  - Tetanus jab
  - Review in 3 – 4 days

Coma
- Immediate actions:
  - Establish unresponsiveness
  - Act as though cervical spine injury
  - Check ABC
  - If arrested → CPR
  - Consider ventilation/intubation
  - 100% O2
- IV access. Take blood for glucose, U&E, drug levels
- Access depth of coma: GCS
- Expose and examine patient
- Look for localising neurological signs, ↑intracranial pressure
- Bladder catheterisation

- Further diagnostic options:
  - Chest, skull and cervical spine X ray
  - CT scan
  - Gastric lavage after protection of airway by intubation
  - See Tests in Comatose Patients

- Consider:
  - Drugs/toxic (See also Poisoning and Overdose, page 801):
    - Alcohol: thiamine 100 mg iv
    - Opioid overdose: naloxone 0.4 mg iv
    - Benzodiazepine overdose: flumazenil
    - Also CO, fumes, antidepressants
  - Metabolic: renal failure, endocrine (eg hypoglycaemia – Dextrose 25g iv), renal/hepatic encephalopathy, porphyria
  - Miscellaneous: hypoxia, post epileptic fit
  - Extracranial: hypoxia (due to arrest, asphyxia), hypo/hyperthermia, electrocution

**Convulsions/Status Epilepticus**
- See Status Epilepticus, page 204

**Diabetic Ketoacidosis**
- See Management of Diabetic Ketoacidosis, page 136

**Electrolyte Abnormalities**
- See Electrolytes, page 155. Includes Hyperkalaemia and Hypokalaemia

**Electrocution**
- Depending on shock, reasonable chance of survival from arrest
- Ensure your safety, start ventilation and compression ASAP
- Watch for airway if face, mouth or neck burns → swelling
- Rapid iv fluids if hypovolaemic shock or tissue destruction

**Head Injury**
- See Head Trauma, page 194

**Hypertensive Crisis**
- Signs: headache, vomiting, visual changes, convulsion, coma, angina, pulmonary oedema, CVA, eclampsia
- Treatment: sublingual captopril. Labetalol (α & β blocker), etc
- Caution: vasodilators may increase ICP. May need iv fluids with vasodilators. Don’t lower blood pressure too fast – cerebral autoregulation may have been reset to a higher blood pressure

**Near Drowning**
- Effective immediate resuscitation critical. Use standard CPR procedure
- Remove foreign bodies from airways, don’t attempt to drain fluid
- Suspect spinal injury if diving or in surf
- Early tracheal intubation may be indicated. 100% O2
- Recovery may occur even after long immersion times, especially in cold water
- In hospital, cerebral oedema may require hyperventilation and diuretics
- Remember, alcohol or epilepsy may be involved
- Avoid steroids, consider antibiotics

**Hypothermia**
- Signs: hypotension, bradycardia, J wave on ECG, SV arrhythmias, VF at 28 C, metabolic acidosis, loss of consciousness at 28 – 30 C, shivering replaced by rigidity at 33 C, pupils dilated
- Lengthens tolerance of arrest: don’t discontinue till they’ve been warmed
- **Arrest prevention:**
  - Prevent further heat loss
  - Transport avoiding rough movement, which can precipitate VF
  - If core temperature < 34°C, can rewarm with oesophageal rewarming tubes, peritoneal lavage (warmed saline or gas). Warm trunk not peripheries. Reduce movement (risk of VF). Rewarm slowly – 0.5 degrees/hour (unless fit and sudden hypothermia)

- **During arrest:**
  - Take 30 – 45 secs to confirm cessation of ventilation and pulselessness
  - Don’t assume death until resuscitation has failed in an adequately rewarmed patient
  - If < 30°C give maximum of 3 shocks until core temperature increases
  - Reduced responsiveness to defibrillation and drugs. Impaired drug metabolism → watch for toxicity
  - Monitor fluids during rewarming

**Hyperthermia**
- Heat exhaustion: hypovolaemic shock due to fluid loss through sweating. Cool, restore volume, position supine with legs raised
- **Heat stroke:** *failure of heat regulation through failure to sweat*. Hot, flushed and dry. If temperature > 40 degrees → neurological disturbances. Rapid cooling, cool iv fluids
- Reduces tolerance time for arrest
- Cooling can be external or internal
- Watch electrolytes and fluid replacement following arrest
- Watch for tendency to cerebral oedema and multi-organ failure

**Poisoning and Overdose**
- Accidental vs intentional vs iatrogenic
- Cause of significant proportion of arrests in 18 – 35 year olds
- Duration of arrest and dose of toxin determinants of survival
- Analgesics most frequently implicated although sedatives/antipsychotics kill more people
- Do general management
- Manifestations of poisoning:
  - Exaggerated therapeutic response (eg sedation with BZD)
  - Pharmacological effects (eg respiratory depression, convulsions)
  - Accidental: children, single poison
  - Intentional: adult, often multiple, taken in conjunction with alcohol

**Management**
- Identify the drug:
  - History: find out the drug if you can (has someone brought in the packet?): but only a few will change management (paracetamol, salicylates, lithium, paraquat, quinine, phenobarbitone, iron salts)
  - Exam: on occasions might give a clue eg dilated pupils with tricyclic OD
  - Blanket measurement of drug levels is not done
- Supportive treatment:
  - ABC: respiratory depression is the most common cause of death in the community, arrhythmias in-hospital
  - Maintain airway, check blood gases. Check for hypotension (OD a/w vasodilation; → raise legs except in heart failure, volume expanders). Monitor electrolytes
  - Maintain safety: close supervision, no access to drugs on ward, etc
- Intensive support treatment:
  - IV fluids, ?NG tube, ?ventilation, maintain vital functions, nursing care (eg suction, pressure sores, limb movement →↓thrombosis)
- Treat complications:
  - Hypothermia, hyperthermia (salicylates and stimulants – sponge down, use fan), seizures (iv diazepam), arrhythmias (leave bradycardia, tachycardia – correct acidosis, try amiodarone), hypoglycaemia (salicylates, oral hypoglycaemics)
- Removal of unabsorbed drug:
  - Gastric lavage + emetics are not used due to risk of aspiration
- Enhancement of drug elimination:
  - Activated charcoal:
    - Porous, large SA, mops up (adsorbent) from GIT
Use for paracetamol, salicylates, theophylline, digoxin, anticonvulsants, anti-depressants
- 1mg/kg stat, followed by 50g 4hrly, best within 1hr of OD

- **Dialysis:**
  - Haemodialysis or haemoperfusion
  - Has to be a LMW drug (ie small) with a small Vd and minimal protein binding
  - Use with alcohols, salicylate, lithium

- **Forced diuresis:** not really done
- Plus treatment specific to poison
- Mental health assessment
- **Investigations:**
  - Blood levels: sometimes useful (eg Li, aspirin, theophylline, carbamazepine). Waste of time for TCAs
  - Urine screen: rarely changes management, no quantitative information, really only for criminal cases (eg after MVA)

### Antidotes
- Opioids → naloxone
- Paracetamol → N-acetylcysteine
- Fe → desferrioxamine
- BB → glucagon
- Digoxin → Fab fragments
- Methanol → ethanol
- Cyanide → cobalt
- Metoclopramide → anticholinergics
- BZDs → flumazenil

### Specific Management
- **Corrosives:**
  - *Never* induce vomiting
  - Drink copious fluids
  - Soak eyes, skin, mucous membranes
  - Petroleum/kerosene: beware of inhalation (chemical pneumonitis), cup of milk; kerosene (paraffin) is a laxative

- **Eliminating poisons.** If sure it’s not petroleum products, caustics, corrosives or acids, then options may include:
  - **Activated charcoal:**
    - Better than emesis
    - Charcoal powder, mixed with H2O: needs to be within 60 minutes. Give SINGLE 50 g dose in an adult (1 g/kg)
    - Reduces GI absorption of paracetamol, aspirin, phenytoin, digoxin, TCAs, theophylline, carbamazepine
    - Don’t use for volatile hydrocarbons or corrosives or an unprotected airway
    - Good for un-ionised drugs. Does not bind with acids, alkalis, alcohols, lithium
    - Generally safe but constipation, aspiration may be problems (protect airway)
    - Multiple doses only for drugs undergoing enterohepatic circulation or diffusing into the gut ⇒ drugs with a small Vd, low clearance, low protein binding and long T½. Eg Theophylline, carbamazepine, quinine, phenobarbitone. NOT Paracetamol.

  - **PH adjusted diuresis:**
    - Alkaline diuresis: aspirin, phenobarbitone
    - Acid diuresis: amphetamine, methadone. Doubtful use and dangerous

  - **Dialysis:** Haemodialysis. *Only useful if low Vd,* small molecule and low protein binding (eg lithium, theophylline, salicylates, alcohol and barbiturates)
  - Whole bowel irrigation: ‘Go Lightly’ – Xray prep

- **Questionable effectiveness:**
  - *Emesis:* Not effective? Ipecac – never if airway reflexes not intact. Causes emesis in 90% within 15 – 30 minutes
  - *Gastric lavage:* large bore catheter through mouth. 1ml/kg of body temperature water, recover, repeat. Little evidence of benefit and ↑ risk of aspiration. Contraindicated if acid, alkali, or petroleum
Common Poisons

- Anticonvulsants: carbamazepine
- **Aspirin**: risk is *pH balance*
- Barbiturates → flumazenil (can cause seizures – so not if SSRIs/TCAs/antihistamines as well – which also cause seizures)
- Benzodiazepines: diazepam, temazepam → post-0D “cerebellar syndrome” (dizziness, confusion, ataxia, nystagmus, bullous lesions). Supportive treatment
- Bronchodilators: theophylline
- Carbon Monoxide → 100% oxygen, treat cerebral oedema. Presentation: pink, headache, vomiting, tachycardia, seizures, arrest
- Chelating agents for arsenic, copper, lead, iron, cyanide
- Cocaine → benzodiazepines
- Cyanide → 100% O2 + cobalt edetate
- Dibenzazepine antidepressants: Rapidly absorbed, high Vd, protein bound. Look for myocardial toxicity, hypotension, hyperreflexia, convulsions. Treatment supportive + naso-gastric tube and charcoal (up to 24 hours later). Monitor ECG, iv propranolol and NaHCO3
- MAOIs: see MAOIs (Monoamine Oxidase Inhibitors), page 716
- Methanol and ethylene glycol poisoning → correct acidosis, ethanol

**Paracetamol:**
- Walk in, conscious
- RUQ/epigastric pain, nausea & vomiting
- Liver damage is evident by day 2
- Predictors of LD: paracetamol level + time since ingestion
- At subtherapeutic doses → ↑ amount of highly reactive metabolite seen with glutathione depletion → liver damage
- Conjugation pathway easily saturated. Of the remainder, 15% is metabolised to a metabolite that combines with glutathione. If glutathione is depleted, metabolite causes hepatic damage
- Toxic dose 140 mg/kg (textbook), 200 mg/kg (Starship), lower if chronic alcoholism, enzyme inducing drugs or fasting
- Measure plasma concentration. **Treat if > 200 µg/ml, 100 if liver disease, anorexia, etc.** Threshold declines for each hour after ingestion
- Absorbed quickly so activated charcoal only effective within 45-60 minutes
- **N-acetylcysteine (NAC) best antidote** – saturates alternative pathway so all the paracetamol is metabolised through the main pathway. Normal dose is 10 - 15 mg/kg per 4 hours acutely, per 6 hours at home
- If NAC given within 8hrs → survival guaranteed
- Monitor AST/ALT, PT (INR)

- Opioids:
  - Marked sedation, pinpoint pupils, ↓↓ respiration (differential: stroke)
  - **Naloxone** (but short T½ → will lapse back)
- **Stimulants** (cocaine type drugs): ↑BP, tachycardia, arrhythmia, dilated pupils [sympathetic effects], seizures
- TCAs: see Tricyclic Antidepressants, page 715

**Pulmonary Oedema**

- **Sit** patient up and give O2
- Medication:
  - **IV furosemide**: 40 – 80 mg if not on any already
  - **IV morphine**: 5 – 10 mg – calming effect, ↓ respiratory rate, venodilator → ↓ preload
  - Sublingual nitroglycerine
  - If BP > 100 mmHg then captopril 6.25 mg
- Occasionally CPAP or IPPV
- Pulmonary oedema resulting from near drowning and ARDS does not respond to morphine & diuretics – may require ventilation

**Renal Failure**

- Leads to: ↑ potassium, acidosis, uraemia, volume overload, toxic accumulation of drugs
- During arrest: give calcium chloride (to antagonise hyperkalaemia) + sodium bicarbonate

Emergency Management 803
Spinal Shock
- Due to a shutdown of cord function (e.g. following trauma): may last several days
- IV fluids to maintain blood pressure: but don’t overdo it. BP of 80/50 may be normal in spinal injury
- High dose methylprednisolone may be beneficial within 8 hours of spinal injury
- NG tube, urinary catheter (monitor output)
- Monitor ventilation, temperature, avoid pressure areas

Trauma to Abdomen
- Injuries may be blunt or penetrating
- Do a diagnostic peritoneal lavage (DPL) to look for bleeding
- A surgeon must evaluate all penetrating injuries of the abdomen
- Intra-abdominal visceral damage must be strongly suspected following blunt trauma to the abdomen. Multiple injuries are common and signs and symptoms guide diagnosis. Note that distracting injuries (e.g. fractures) may mask abdominal symptoms

Indications for Surgery
- Unstable patient
- Injury penetrates peritoneum
- Significant pancreatic injury on CT
- Significant splenic injury in an older patient
- Arterial injury

Specific Injuries
- Ruptured spleen (intraperitoneal haemorrhage)
  - Signs and symptoms: may be pain free, may have signs of blood loss
  - Treatment: splenectomy if elderly otherwise try to preserve it
- Ruptured liver: treatment: laparotomy and suturing individual vessels/packing etc
- Ruptured gut: presence of gas under diaphragm on x-ray, or history of penetrating wound needs laparotomy and repair/resection of affected bowel

Trauma to Chest

Tension Pneumothorax
- Signs:
  - Apex beat lost
  - Blocks IVC → ↓ venous return → ↑ JVP
  - ↓ Vocal fremitus
  - Hypotension
  - Hyper-resonance
  - Displaced trachea (maybe)
  - US may help with diagnosis
- On X-ray must have both of no peripheral vascular markings and a visceral pleural line
- Types:
  - Primary/spontaneous: apical sub-pleural blebs are common and occasionally rupture. Especially tall, thin, young males. Can occur at rest. Recurrence 20%
  - Secondary: in any lung disease
- Treatment:
  - Insert 14g iv cannula into midclavicular line at level of nipple (any lower and may get diaphragm)
  - Hissing of air is diagnostic
  - Remove needle and leave cannula in place. Attach tubing and put other end under water
  - PP ventilation will help reinflate the lung
  - Insertion where there wasn’t a pneumothorax will cause one!

Open Pneumothorax
- Sucking wound ⇒ can’t create –ive intrathoracic pressure
- Occlusive dressing and positive pressure

Massive Haemothorax
- 1500 ml in thorax or > 200 ml per hour
Mainly penetrating wounds of pulmonary vessels (e.g. intercostals). If great vessels affected usually don’t survive

Significant amount of blood needs surgical removal → thoracotomy

**Flail Chest**

- Needs lots of force – so suspect pulmonary contusion as well
- Independent segment of chest wall → paradoxical movement. Requires two breaks
- Treat with IPPV for at least a week

**Cardiac Tamponade**

- Commonly results from penetrating injury
- Commonly confused with a pneumothorax – think pneumothorax first – more common
- Signs:
  - Impaired diastolic filling →↓ stroke volume. Initially tachycardia and vasoconstriction maintain cardiac output and BP. Eventually hypotension and shock
  - Cardinal signs: Beck’s triad – hypotension, ↑ venous pressure (↑JVP), small quiet heart
  - Pulsus paradoxus: > 10 mmHg ↓ in systolic BP with normal inspiration
- Treatment:
  - Emergency pericardiocentesis (either via xiphisternum or into apical area). Surgery essential
  - Colloid fluid infusion →↑ filling pressure and stroke volume

**Pulmonary Contusion**

- Leads to non-compliance: V/Q mismatch, shunting →↓ PO2
- Ventilate

**Myocardial Contusion**

- Suspect if fractured sternum (requires big force)
- There will be a current of injury on ECG and cardiac enzymes
- Can → arrhythmias and ↓ CO
- Treatment: 24 hours observation under ECG – can be arrhythmias

**Rib Fracture**

- Commonest injury: pain impairs ventilation
- Complications: atelectasis, pneumonia, contusion, pneumothorax, secondary pleural effusion 2 – 3 weeks later
- Treatment: pain relief

**Traumatic Rupture of Aorta**

- Results from rapid deceleration, usually at ligamentum arteriosum
- Immediately fatal in 90% of cases. 50% further mortality per 24 hours thereafter untreated
- Diagnosis suspected on CXR: widened mediastinum, 1st & 2nd rib fracture, obliteration of aortic knob, deviation of trachea. Definitive diagnosis by aortogram
- Treatment: repair
- Complications: paraplegia due to ↓ blood flow to spine
Infectious Diseases

- References: Predominantly drawn from Dr M Humble’s Microbiology notes
- For notifiable diseases, see Communicable Disease Control, page 1028
- For infectious diseases of the skin, see Skin Infections, page 505
- For infectious diseases in children, see Infectious Diseases, page 950
- For respiratory infections, see Acute Pharyngitis, page 86 and Adult Pneumonia, page 89
- For urinary tract infections, see Urinary Tract Pathology, page 329
- For gastro-intestinal infections, see Diarrhoea, page 260 and Viral Hepatitis, page 281

Blood Culture

- Can enable detection of bacteraemia within 12 hours
- Allows targeted therapy
- Contamination (skin commensals) at the time of venepuncture can make interpretation difficult → thorough disinfection of the skin is essential
- Common skin commensals:
  - Staphylococcus epidermidis (coagulase-negative staphylococcus)
  - Corynebacterium spp ("diphtheroids")
  - Staphylococcus aureus
- When to take:
  - It takes 30 – 60 minutes for temperature to rise after introduction of bugs into the blood, but endothelial cells of the vascular system (spleen, kuppfer cells, etc) phagocytose cells in minutes
  - So when the temperature spikes, bugs may well be gone. So do random cultures in the hope of getting a hit
- Definitions:
  - Bacteraemia: no host response. Happens all the time (eg after cleaning teeth)
  - Septicaemia: sustained bacteria in the blood stream – ongoing delivery of bugs into the blood stream from a replicating focus (don’t multiply in blood). Leads to host response and disseminated loci of infection
  - Pyemia (older term): Spread of organisms via infected thrombi

Indications for Blood Cultures

- Infection of any degree of severity – especially if firm clinical diagnosis not possible
- Absence of fever doesn’t rule out infection (and not all febrile pts have an infection), so is not a contra-indication (eg confusion, feeling off)
- In hospitalised pts (especially elderly + post-op), sudden deterioration in conscious state, fall in BP etc may indicate bacteremia in the presence of a normal temperature
- Specific indications:
  - Acute generalised infection: fever, rigors, sweating, shock
  - Febrile illness + congenital or acquired heart disease where infective endocarditis suspected
  - Diseases with a bacteraemic phase (pneumonia, meningitis, acute pyelonephritis, etc)
  - Shock (especially post-operative following abdominal surgery)
  - Intercurrent illness in patients with compromised immunity
  - Febrile patients with infected IV drip sites
  - Febrile neutropenia
  - Named conditions: CAP, IE, cholecystitis/cholangitis, meningitis, osteomyelitis, cellulitis, pyelonephritis, fever in pregnant women with flu-like illness
- Usually unnecessary to do more than 2 sets at the time bacteraemia is suspected, 20 minutes apart. If infective endocarditis, take 3 sets over 24 hours

Procedure for Blood Culture

- Ensure everything sterile – contamination makes interpretation very difficult
- 5 – 10 mls of blood in two bottles, bottle one is the general purpose medium and the other anaerobic medium
- For kids, use single 3 ml paediatric bottle
- Choose vein (usually ante-cubital fossa)
- Swab with betadine (chlorhexidine if iodine allergy) and wait 3 – 4 minutes to dry (do not touch again!)
- Draw blood (15-20ml) and inject into bottles
- Write relevant clinical information on the form
- If already on antibiotics, notify lab
- In general, 2 sets taken 15-20 minutes apart is sufficient; if suspected IE, 3 sets should be taken in first 24hrs

**Common Sources of Bacteremia**

- **G+ve:**
  - Staphylococcus aureus =
    - Osteomyelitis, septic arthritis, cellulitis
    - Infected IV cannulae (esp CVP), surgical wound infection, subclavian lines in haemodialysis pts
  - Staphylococcus: coag negative =
    - Neutropenic cancer pts with hickman catheters
    - Premature neonates with long lines
  - Streptococcus pneumoniae = CAP, meningitis
  - Enterococcus faecalis = UTI, cholangitis, intra-abdominal sepsis
  - Strept agalactiae = neonatal septicaemia/meningitis
  - Strept pyogenes = cellulitis, nec fasc
  - Viridans strep = IE
- **G-ve:**
  - E coli =
    - Pyelonephritis, acute urinary retention with cystitis
    - Cholangitis, acute appendicitis, peritonitis, intraabdominal sepsis
  - Pseudomonas aeruginosa =
    - Catheter related UTI
    - Respirator-associated infection in ICU pts
  - Bacteroides spp = peritonitis, intraabdominal sepsis
- **Bugs isolated in Wgtn Hospital:**
  - Three most common G+ve: Staph aureus, Staph coag –ve (from lines), Strep pneumoniae
  - Three most common G-ve: E. Coli, Klebsiella, Other Coliforms
  - Candida albicans + spp are the most common fungi
  - Second most common is staph epidermidis (staph aureus is most common): It's a common contaminant, but also the most common pathogen in catheter related infections, neonates and neutropenic patients.
  - ↑Resistance to Flucloxacillin →↑use of vancomycin (expensive, side effects, etc)

**Infections Associated With Bacteraemia**

- CAP (treat strep pneumoniae with penicillin, except in children where > 30% resistance so use cephalosporin)
- Meningitis with petechial rash (treat meningitidis with penicillin)
- Osteomyelitis (treat S Aureus with flucloxacillin or vancomycin if MRSA)
- Leukaemia with infected Hickman line (Coag –ive staph, eg epidermidis, treat with vancomycin)
- Pyelonephritis (treat E coli with Gentamicin)
- Cellulitis (treat Strep pyogenes with Penicillin)
- Perforated appendicitis (treat B Fragilis with Metronidazole)
- Infective endocarditis (treat viridians Strep, eg S sanguis, with penicillin + maybe gentamycin)
- Epiglottitis (treat HIB with cephalosporin)
- Premature baby with respiratory distress syndrome (treat Lancefield group B strep with penicillin)

**Healthcare-Associated Infections**

**Types of HAI**

- UTI
- Wound infection
- Respiratory tract infection
- Blood stream infection
- GIT infection
- ~10% of patients admitted will acquire an infection
Transmission of Infection

- F = fingers
- F = phlegm
- F = flies, fleas, flying insects
- F = fomites
- F = faeces
- F = sex

Microbial Causes of HAI

- **NB.** Handwashing is the *most effective way* to prevent HAI
- *Resistance to ABS is the biggest problem* we currently face → bacterial conjugation leads to transfer of AB-resistant genes
- Fast becoming only two effective ABS:
  - Vancomycin for gram positive bacteria
  - Imipenem for gram negative bacteria

**Group A Streptococci**

- Eg impetigo + necrotising fasciitis
- GAS a problem in the *early 20th century*, much less so now → due to *better hygiene* mostly, penicillin only had a small effect

“H” Bug – *Staphylococcus Aureus*

- Eg boils, abscesses, wound infections
- In the 1950s, “phage 81” initially the strain causing all the problems; *better infection control* → ↓++ rates of phage 81 infections
- In the 1970s, after phage 81 had all but disappeared, MRSA surfaced

**Gram Negative Rods**

- I.e. e.coli, enterobacter, klebsiella, pseudomonas, proteus
- A problem now, especially extended spectrum beta-lactamases (ESBL)
- **Imipenem** the only drug these bugs are susceptible to
- Need to **screen for ESBL** in patients being admitted to hospital

**Fungal Infections**

- Eg candida albicans + aspergillus

**Viral Infections**

- Eg rhinovirus, rotavirus, norovirus, HSV, HBV/HCV, HIV, CMV, influenza

**Infections of the CNS**

**Bacterial Meningitis**

**Signs and Symptoms**

- Rapid onset of:
  - **Meningism:** Headaches, photophobia, stiff neck
    - **Kernig’s sign:** Pain on *straightening knee with hip flexed*
    - **Brudzinski’s sign:** flex pt’s neck → causes hips and knees to flex
  - ↑ICP: HA, irritable, drowsy, vomiting, fits, ↓pulse, ↑↓BP, ↓LOC, pin-point pupils, papilloedema (late sign), tense fontanelle
  - Septicaemia: fever, arthritis, DIC, ↓BP, ↑pulse, tachycardia, rash (ultimately 80% will have a purpuric rash, 10 – 15% will have a maculo-papular or urticarial rash, 5 – 10% will have no rash). NB. Can have purpuric rash/meningococcal septicaemia without meningitis
  - In different age groups:
    - **Infants/toddlers:** fever, lethargy, poor feeding, vomiting, toxic (drowsy, pallor), rash. *Only 30 – 50% have signs of meningism ⇒ absence doesn’t exclude.* Bulging anterior fontanelle – but *if vomiting may be normal or reduced*
    - **Children > 3:** fever, headache, vomiting, photophobia, stiff neck, confusion (may be combative), non-blanching rash (initially blotchy macular rash that rapidly becomes petechial or purpuric)
- Adolescents: may present as acute mania or appearance of drug induced psychosis

Pathogenesis
- Organisms:
  - Meningitis neonate
    - *strep agalactiae, e.coli* (ascending uterine infection from normal vaginal flora of mother)
  - Meningitis children
    - Hib, n.men, s. pneumoniae
  - Meningitis adults
    - n.men, s.pneumoniae, s.aureus, cryptococcus neoformans
  - Meningitis depressed CMI
    - AIDS (cryptococcus), lymphoma (listeria, crypto)
  - Meningitis trauma
    - # (s.pneumoniae), CNS surgery (s.aureus), CSF shunts (s.epidermidis)

- Pathogenesis:
  - Pathology: inflammation of pia mater and arachnoid
  - Most common are N Meningitidis and S pneumoniae
  - Nasopharynx → blood → subarachnoid space (via choroid plexus): N meningitidis, HIB, S. pneumoniae
  - Middle ear → blood → subarachnoid space: S Pneumoniae, HIB
  - Congenital abnormalities (eg spina bifida): coliform bacilli, pseudomonas, Strep agalactiae
  - Trauma: Skull fracture + CSF leak, CNS surgery, shunts: Staph aureus
  - Depressed immunity: listeria monocytogenes, cryptococcus neoformans
  - Neonatal meningitis from vaginal flora (especially with prematurity, prolonged ROM, delayed 2nd stage):
    - Strep agalactiae, coliforms (E coli), listeria monocytogenes
  - If recurrent:
    - Consider immunosuppression (eg hypogammaglobulinaemia or complement deficiency)
    - Look for lumbosacral defects, especially if enteric bacteria or S aureus

Investigations
- Do blood culture before presumptive treatment if possible, but NOTHING should delay presumptive treatment. Tell lab about antibiotics
- Must do:
  - Urine: supra-pubic aspiration or catheter
  - If antibiotics have already been administered:
    - a. Needle aspirate purpuric lesions for gram stain and culture
    - b. Throat swab
  - Bloods:
    - Blood cultures
    - Blood glucose sample – may be hypoglycaemic [ABC DEFG = Don’t Ever Forget Glucose]
    - FBC, electrolytes, clotting time, ABGs
  - Lumbar puncture:
    - Contraindicated if:
      1. Signs of ↑ICP (all meningitis will have ↑ICP) causing cerebral herniation (eg very ↓LOC, very bad headache, focal signs including abnormal papillary reflexes, tonic seizures, decerebrate or decorticate posturing, irregular respirations, bradycardia, papilloedema). If in doubt then CT
      2. Severe cardiovascular compromise with DIC/coagulopathy (eg fulminant sepsis)
      3. Infection over the injection site
    - Tests of CSF: Gram stain, Tb, cytology, virology, glucose, protein, Indian ink (Cryptococcus), culture (if clear then ?virus), antigen testing (especially if partially treated)
    - May be normal, repeat if symptoms persist
    - Typical CSF (lots of variation):
      | CSF                  | Normal                  | Bacterial               | Viral (aseptic) | TB/Fungal          |
      |---------------------|-------------------------|-------------------------|----------------|-------------------|
      | WBC                 | 0-5 lymphocytes         | PMNs                    | Lymphocytes    | PMNs/Lymphocytes  |
      | RBC                 | None                    | -                       | -              | -                 |
      | CSF protein         | 0.1 – 0.6G/L            | ↑↑↑                     | ↑ or →         | ↑↑                |
      | CSF glucose         | 2.8 – 5.0 mmol/L        | ↓↓↓                     | ↓↓ or →       | ↓↓                |
      | Blood glucose       | 3.9 – 6.1 mmol/L        | -                       | -              | -                 |
  - NB: early viral meningitis may have predominantly polymorphs
  - RBCs: None. If there are then either traumatic (more in 1st of 3 tubes) or bleed (new if red, yellow if old – xanthochromia)
  - Appearance on Gram stain:
    1. *N Meningitidis:*  | G –ive diplococci
2. *H influenzae*: Pleiomorphic G–ive bacilli
3. *S pneumoniae & S agalactiae*: G+ive diplococci
4. *Listeria monocytogenes*: G+ive bacilli
5. *TB*: Acid fast bacilli very scant – take at least 5 mls of CSF
6. *Cryptococcus neoformans*: Indian ink stain shows capsules

- Imaging: To identify subdural collections, abscess, hydrocephalus, thrombosis and infarction. Only if LP contraindicated and suspected mass lesion or persistent or focal neuro signs

**Management**

- See When is a Child Really Sick?, page 891
- Management (based on protocol for a child):
  - Standard infection control precautions plus surgical mask when examining throat, intubating etc
  - ICU if:
    - Coma
    - Circulatory collapse
    - Persistent, recurrent seizures
    - SIADH with cerebral oedema or seizures
  - Shock or ↑ICP is what kills
  - Maintain perfusion:
    - Colloid bolus (20 – 40 ml/kg 4% albumin iv), then colloid + glucose
    - Inotrope eg dobutamine (10 μg/kg/min)
    - Watch for ↑ ADH secretion → hyponatraemia and cerebral oedema if too much fluid given
    - Check Na 6 – 12 hourly. If Na < 135 mmol/l then ↓iv rate. If Na > 145 then ↑rate
  - Respiratory support:
    - O2
    - Early elective intubation if persistent shock (but may exacerbate hypotension due to vasodilation and ↓sympathetic drive)
    - Immediate intubation if ↑ICP, hypoxia and/or respiratory failure, pulmonary oedema or hypertension (uncompensated shock)
  - Correct abnormalities: anaemia, hypoglycaemia, coagulopathy (FFP), acidosis (NaHCO3), hypokalaemia
  - Seizures: anticonvulsants
  - Watch for ↑ICP:
    - ↓Conscious state, focal neuro signs, abnormal pupils, hypertension and relative bradycardia.
    - Treatment: ICU, ↓PCO2, diuretics (Mannitol, frusemide), head up, deep sedation, inotropes. But priority is to correct the shock (CBF = MAP – ICP)
  - Weight and measure head daily in an infant
  - Isolate patient, ensure analgesia
  - Dexamethasone treatment controversial (most benefit in HIB). Not routinely used. Reduces fever and gives misleading impression of clinical improvement

**Antibiotic Regimes**

<table>
<thead>
<tr>
<th>Bugs and AB therapy</th>
<th>Gram positive</th>
<th>Antibiotic</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Streptococcus pneumoniae</em> &lt;br&gt;NB. PCR used to detect SP when ABs given prior to dx</td>
<td>Gram-positive diplococci</td>
<td>Initial treatment until AB sensitivities known is: ceftriaxone + vancomycin (Vancomycin + rifampicin if penicillin-R)</td>
</tr>
<tr>
<td><em>Streptococcus agalactiae</em></td>
<td>Gram-positive diplococci</td>
<td>Penicillin</td>
</tr>
<tr>
<td><em>Staph aureus</em></td>
<td>Gram-positive cocci clusters</td>
<td>Flucloxacillin</td>
</tr>
<tr>
<td><em>Listeria monocytogenes</em></td>
<td>Gram-positive bacilli</td>
<td>Amoxycillin</td>
</tr>
<tr>
<td><em>Neisseria meningitidis</em> &lt;br&gt;NB. PCR used to detect NM when ABs given prior to dx</td>
<td>Gram-negative diplococci</td>
<td>Ceftriaxone or penicillin</td>
</tr>
<tr>
<td><em>E. coli</em></td>
<td>Gram-negative bacilli</td>
<td>Ceftriaxone</td>
</tr>
<tr>
<td><em>Haemophilus influenzae type B</em></td>
<td>Gram-negative bacilli (pleiomorphic)</td>
<td>Ceftriaxone</td>
</tr>
</tbody>
</table>

- **Others**

<table>
<thead>
<tr>
<th>Antibiotic</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Cryptococcus neoformans</em></td>
</tr>
<tr>
<td><em>Mycobacterium tuberculosis</em></td>
</tr>
<tr>
<td><em>HSV</em></td>
</tr>
</tbody>
</table>
Empiric antibiotic treatment:

- **Neonate** – 3 mths: *Amoxicillin* 50 mg/kg (for listeria) + *Ceftriaxone* 50 mg/kg (E coli and Strep). 2 weeks for G +ve, 3 weeks for G –ve.

- **Older child:**
  a. *Cefotaxime* 50 mg/kg/6hr, max 2 g, iv for 7 – 10 days or
  b. *Ceftriaxone* 50 mg/kg/12hr, max 2 g, iv for 7 – 10 days or
  c. *Penicillin G* 50 mg/kg/4hr iv for 7 – 10 days

- If *strep pneumoniae* suspected: *Vancomycin* 15 mg/kg/6hr, max 500 mg, iv + *cefotaxime/ceftriaxone* – synergistic, necessary due to ↑resistance to 3rd generation cephalosporins

- If still failing consider adding Rifampicin

Specific treatment according to culture and susceptibility results:

- **N Meningitidis, S agalactiae:** Penicillin (Cefotaxime if allergic to penicillin) for 5-7 days. For meningococcaemia only can use penicillin or cefotaxime

- **S pneumoniae:**
  a. Penicillin susceptible: penicillin (but 20% are resistant) for 7 – 10 days
  b. Penicillin resistant, 3rd generation susceptible: Cefotaxime
  c. Penicillin and 3rd generation resistant: Cefotaxime + Vancomycin

- **H Influenza:** Cefotaxime, Ceftriaxone

- **L Monocytogenes:** amoxycillin

- **Staph Aureus:** Flucloxacillin

- **M Tuberculosis:** Rifampicin, Isoniazid, Pyrazinamide, Ethambutol

- **Coliforms:** 3rd generation Cephalosporin (ie Cefotaxime, Ceftazidime)

- **Pseudomonas:** Ceftazidime

- **Cryptococcus Neoformans:** fluconazole or amphotericin B

- **NB:** Erythromycin and gentamycin don’t have good CSF penetration

- If not responding, or non-susceptible strain of pneumococci or receiving dexamethasone than repeat LP after 24 – 48 hours

### Complications

- **Seizures:**
  a. **First suspicion should be hyponatraemia (also hypoglycaemia):**
  b. **SIADH (Na < 130 and urine Na > 20)** →exacerbates cerebral oedema
  c. **Prevent by restricting fluids to 50% of maintenance**
  d. **Treatment:** severe fluid restriction (10 ml/kg/day), in an emergency consider hypertonic saline, Mannitol or frusemide

- **Hypoventilation can further ↑ ICP** →hypoxia, hypercapnea, acidosis

- **Anticonvulsants can also exacerbate these metabolic changes**

- **Management options:** diazepam, clonazepam, phenobarbitone, dextrose to control hypoglycaemia, intubation and ventilation

- **Major disability in 15%:** Deafness, brain damage, peripheral necrosis, etc. All cases should have audiologist check within 6 – 8 weeks of discharge

- **Death in 5%, 10 –15% pneumococcal meningitis, 20% in fulminant meningococcaemia**

### Meningococcal Disease

- **Cause:** *Neisseria Meningitidis*

- **Epidemiology:**
  a. 10-year epidemic started in 1990 with about 50 reported cases. Since then 3696 cases and 163 deaths. Current case fatality rate is 3 – 5 %
  b. Leading infectious cause of death in children
  c. 500 reported cases in 2000. NZ rate is 13.3 per 100,000. UK rate is 4 per 100,000
  d. Regional variation: East Cape and Central North Island the highest
  e. Rates per 100,000 < 1 year olds:
    a. Pacific Island: 570
    b. Maori: 230
    c. European: 80

- Healthy people can be carriers

- Transfer via respiratory secretions
- Kids and teenagers more susceptible than adults
- Not a cause of otitis media
- Pathogenesis: endotoxins (lipopolysaccharides in the cell wall) activate complement and release of PAF causing endothelial injury → immune activation and ↑vascular permeability
- Notifiable to public health (as is HIB)
- Prophylaxis to stop nasal carriage of the bug – not to cure incubating illness. Nasal carriage higher in adults than children
  - Rifampicin: 4 doses, 600 mg bd for adults, 10 mg/kg bd for kids (very high dose). Broad spectrum antibiotic
  - Offer to index case (if only treated with penicillin), all intimate, household and day-care contacts during last 10 days
  - Contraindications: pregnancy (use single dose ceftriaxone), liver disease.
  - Side effects: nausea, vomiting, diarrhoea (GI effects), turns urine/tears/sweat orange/red (will stain contacts)
  - Interactions: asthma, blood clotting and oral contraceptives (continue pill, use barrier method until 7 days after antibiotics finished)

**TB Meningitis**
- Rare
- Most common < 5 years
- Slow onset: malaise and fever progressing to drowsiness, neck stiffness and seizures over 2 weeks
- Mantoux testing may be normal, and CXR normal in ½ of cases
- Investigations:
  - Gastric lavage, urine and CSF for Acid fast stain and culture
  - CT
- Treatment: isoniazid, rifampicin, pyrazinamide
- Notifiable disease

**Brain Abscess**
- Aetiology:
  - Chronic otitis media, sinusitis or dental sepsis
  - Trauma: foreign body, skull fracture, CNS surgery
  - Haematogenous spread (may be multiple abscess) from congenital heart disease (with R-L shunt), bronchiectasis, abdominal abscess, endocarditis, etc
- Bacteria:
  - Temporal lobe (from chronic otitis media):
    - Anaerobes: Bacteroides fragilis
    - Aerobes: Proteus mirabilis + HIB and E faecalis
  - Frontal lobe (from chronic sinusitis):
    - Anaerobes: Bacteroides melaninogenicus
    - Aerobes: Strep milleri
  - Traumatic: Staph aureus
  - Haematogenous spread: Staph aureus, Viridians Strep, Bacteroides fragilis, etc
- Treatment:
  - Surgery
  - Antibiotics:
    - Anaerobes: Metronidazole
    - Aerobes:
      - Strept: Amoxycillin
      - Coliforms: Cefotaxime
      - Staph aureus: Flucloxacillin

**Viral CNS Infections**

**Viral Encephalitis**
- HSV encephalitis:
  - Symptoms: short hx, acute onset of fever and HA, disturbed LOC w confusion (as cf. meningitis), ataxia, focal convulsions → coma (if clouding of consciousness consider encephalitis in addition to meningitis)
  - Dx: raised WCC – lymphocytes; PCR for HSV DNA; CT – oedema of temporal lobes
- **Rx:** *acyclovir* 10mg/kg IV 8hrly for 14d, low threshold for treatment

- **HIV:**
  - Most AIDS patients have a subacute encephalitis caused by direct brain infection
  - Symptoms: mood changes, depression, lethargy, confusion, dementia

- **Other viruses:** Mosquito born (Murray Valley Encephalitis, Japanese Encephalitis), Rabies virus

- **Management:**
  - Full blood screen: Cr, electrolytes, glucose, LFT, ABG, urine drug & metabolic screen, blood and urine cultures, ammonia, cortisol, coagulation screen, ECG
  - Serology and viral cultures
  - LP if not contraindicated — may be normal in up to 50% of cases
  - Consider empiric *acyclovir* + cefotaxime — at least until HSV is excluded
  - CT (MRI better still) for focal lesions

- **Consider differential:**
  - Head injury
  - Toxic or metabolic encephalopathy
  - Hypoxic insult

- **Supportive treatment:**
  - Fluid restriction
  - Control of seizures
  - Cardio-respiratory support
  - Maintenance of nutrition

**Viral Meningitis**

- 85-95% of meningitis cases
- Enteroviruses — ECHO viruses most common, also coxsackie A and B and mumps
- Lab dx: PCR on CSF, throat swab, faeces
- DDx of lymphocytic (aseptic) meningitis:
  - Partially treated bacterial meningitis
  - Viral meningitis (as above)
  - Viral encephalitis (HSV, VZV, CMV) — will see confusion + maybe seizure as cf. meningitis
  - TB meningitis
  - Neurosyph
  - Leptospirosis
  - Tumour, sarcoidosis
  - Dx: CSF culture; PCR for HSV, VZV, CMV, TB, toxoplasma; latex test for crypto; serology (Ab) for leptospira, treponema pallidum (syph), toxoplasma

- **Causes:**
  - Most due to non-polio enteroviruses:
    - Faecal →oral ⇒ little kids at risk
    - ECHO viruses, Polio, Coxsackie A & B
  - Mumps
- **Presentation:** fever, headache, malaise, photophobia, abdominal pain and vomiting. Neck stiffness in older children. Maybe a macular or even petechial rash
- **Differential diagnosis of lymphocytic (aseptic) meningitis**
  - Viral meningitis (eg ECHO, Mumps, Coxsackie)
  - Viral Encephalitis (eg Herpes Simplex, CMV, Varicella Zoster)
  - TB meningitis
  - Fungal meningitis (eg Cryptococcus neoformans)
  - Neurosyphilis
  - Acute Leptospirosis
  - Cerebral toxoplasmosis
  - Neoplasm
  - Cerebral sarcoid

- **Lab tests:**
  - CSF Culture: Enteroviruses, mumps, fungi, TB
  - Throat culture and Faeces for enteroviruses
  - CSF Antigen tests: PCR for Herpes Simplex, CMV, VZV, TB, Toxoplasmosis
  - Serology: antibodies to Treponema pallidum, Leptospira, Toxoplasma gondii
- **Admit if:**
Infectious Diseases

- Diagnosis in doubt
- Antibiotics are being considered
- IV Rehydration is needed
- Ensure good analgesia

Post-Infective Encephalitis
- Immune hypersensitivity reaction to host cells containing viral antigens
- Late onset – 7 – 10 days after acute illness
- Viruses involved: Morbilli (Measles), Mumps, Rubella, Varicella-Zoster

Other
- Spongiform encephalopathies:
  - Caused by Prions (Proteinaceous infectious particles)
  - Histology: vacuolation of brain tissue, deposition of amyloid plaques
  - Eg: Kuru (in PNG), Creutzfeldt-Jakob Disease (CJD), Variant CJD
  - Symptoms: Insidious onset of ataxia, dysarthria and dysphagia. Progressive dementia
  - See Dementia, page 731
- Slow virus infections:
  - SSPE (Subacute sclerosing pan-encephalitis): Measles like virus affecting children and adolescents
  - PML (Progressive Multifocal Leucoencephalopathy): Affects adults from 40 – 70, Polyoma virus implicated.
- Neonatal Encephalitis:
  - TORCH Complex: Toxoplasmosis, Rubella, CMV, Herpes Simplex
  - Usually accompanied by disseminated disease
- Reye’s Syndrome: post-infectious encephalopathy with associated acute liver failure. Most common antecedent infection is Influenza virus

Bacterial Disease

Streptococcus

Streptococcal Skin Infections

<table>
<thead>
<tr>
<th>Streptococcus pyogenes skin conditions</th>
<th>Rx</th>
</tr>
</thead>
<tbody>
<tr>
<td>Impetigo</td>
<td>Superficial pyoderma (pus of the skin) characterised by vesicular + crusted lesions</td>
</tr>
<tr>
<td>Cellulitis</td>
<td>Acute spreading subcutaneous tissue skin infection</td>
</tr>
<tr>
<td>Erysipelas</td>
<td>Distinctive superficial cellulitis (usually on the face) with lymphatic involvement</td>
</tr>
<tr>
<td>Necrotising fasciitis</td>
<td>Severe + spreading infection of SC tissues involving both superficial + deep fascia – toxic shock can ensue</td>
</tr>
</tbody>
</table>

Streptococcus Pyogenes (Group A, β-Haemolytic)
- NB: Lancefield Groups only apply to β Haemolytic Streps
- Causes:
  - Commonly: acute pharyngitis, cellulitis, impetigo (also caused by group C)
  - Uncommonly: necrotising fasciitis (haemolytic strep gangrene), strep toxic shock syndrome, scarlet fever, erysipelas (= contagious skin infection with strep pyogenes), acute oitis media
  - Rarely: pneumonia, infective endocarditis
- Has remained sensitive to penicillin
- Identical strep can lead to a variety of infections:
  - Sore throat
  - Impetigo/Cellulitis. See Impetigo (School Sores), page 505
  - Toxic Shock Syndrome
  - Myositis
  - Necrotising Fasciitis
- Infection via throat (mainly) or via skin (impetigo/wound infection):
  - Suppurative: tissue invasion
  - Non-suppurative (after 2 – 8 weeks):
Infectious Diseases

Scarlet Fever

- **Direct response to Streptococcal toxins** (cf viral rash which is autoimmune and therefore delayed)
- **Presentation:** fever, exudative pharyngitis, scarlatina rash (**fine punctate rash with perioral sparing**), desquamation
- Skin feels like **sandpaper** then **desquamates**. May get purpura in flexures
- Tongue affected – white then **strawberry red**

Streptococcus Toxic Shock Syndrome

- **Also caused by S aureus** – see dermatology section
- First described in children. Now associated with **Tampon use**
- Early (1 – 7 days): vague, viral like illness: fever, chills, myalgia, diarrhoea
- Later: abrupt onset of pain (not necessarily associated with findings), redness, **hypotension**, renal failure, ARDS, coagulopathy. May lead to necrotising fasciitis. Also **skin diffusely erythematous** like sunburn, conjunctivitis
- **Desquamation** a week later characteristic
- Age group: 2-50 year olds, no predisposing or underlying disease
- Bacteriology:
  - Blood culture +ve in 60%
  - Swab or aspirate in 95%
  - M protein types 1 & 3: impedes phagocytosis by leucocytes, expressed on cell wall
- **Lab tests:** Haematuria, ↑Cr, ↓albumin and ↓Ca, serum CK for deep tissue infections
- **Treatment:** **Ceftriaxone**

Necrotising Fasciitis

- **Diffuse swelling and mild erythema**, followed by bullae filled with clear fluid. Spreads along fascial planes
- Skin may look normal but **tender+++**
- Infection of subcutaneous tissue → progressive destruction of fascia and fat but may spare the skin itself.
- 25 cases per year in NZ
- Requires aggressive surgical debridement
- Causative bacteria:
  - Group A strep most common
  - Staph Aureus
  - C. Perfringens
  - C. Sceptica
- Predisposing factors:
  - Diabetes
  - Peripheral vascular disease
  - Chicken pox
  - Minor trauma/surgical procedures
- Use of NSAIDs masks inflammation and delays diagnosis
- Treat with IV penicillin G + clindamycin

Streptococcus Lancefield Group B

- β Haemolytic Strep

  - Eg Strep agalactiae: differential in neonatal meningitis. Normal vaginal commensal

Streptococcus Pneumoniae

- Is α haemolytic but not classified as a Viridians
- **Causes:**
  - Commonly: acute otitis media, acute sinusitis, febrile convulsion in infants, community acquired pneumonia, infectious exacerbations of chronic bronchitis, meningitis (nasty type)
  - Uncommonly: peritonitis (2nd ary to chronic hepatic/renal disease of to infected IUCD)
  - Rarely: infective endocarditis
- Antibiotic sensitivity:
- **Parenteral:**
  - Penicillin resistance in 1% blood isolates in adults and 11% in kids ➔ Strep pneumonia penicillin resistance is not an issue in adults but is in kids
  - Ceftriaxone
  - Vancomycin (for penicillin resistant strains and MRSA)
- **Oral:** amoxycillin, erythromycin, cefaclor, tetracycline (not kids or pregnant)

- **Vaccination:**
  - Pneumovax
  - Polysaccharide-based subunit vaccine containing 23 serotypes covering 90% of strains causing invasive pneumococcal disease
  - Contains T-cell independent antigens ➔ non-immunogenic if < 2 years (and poor response for some serogroups up to age 6). Predominant IgM response without induction of memory. 5 yearly boosters recommended
  - Recommended for:
    - > 65 years
    - > 2 with asplenia, immunocompromised (including nephrotic syndrome) and chronic illness
  - Conjugate vaccines generating IgG response being worked on....

**Viridians Streptococci (plus also Enterococcus faecalis)**

- Causes UTI, abdominal wound sepsis, infective endocarditis (uncommon)

**Staphylococcus**

*Staphylococcus Aureus*

- **Sources of bacteraemia:**
  - Skin sepsis
  - Wound infection (esp hospital acquired)
  - Pneumonia (esp hospital acquired)
  - Osteomyelitis
  - Septic arthritis
  - Lines: Subclavian, IV drips (esp CVP)
  - Infective endocarditis
- **See also Impetigo (School Sores), page 505**
- **Neonatal impetigo:**
  - May spread through neonatal units – the “H bug” (hospital bug), especially due to moist skin + close contact
  - May spread to deeper tissues + umbilicus
  - May become blood-borne, can spread to bones/joints in babies
  - May required IV Abs
  - Prevention: attention to cross-infection
- **Skin infections caused by S aureus:**
  - Hydradenitis – infection of sweat glands, common in infants, leading to small abscesses
  - Folliculitis – see dermatology section
  - Furuncle/carbuncle – see dermatology section
  - Lymphadenitis – see dermatology section
  - Scalded skin syndrome – see dermatology section
  - Toxic shock syndrome – see dermatology section

*Staphylococcus coagulase negative (eg epidermidis)*

- Sources of bacteraemia: IV lines – Hickman, CVP lines, premature neonates with IV lines

**Haemophilus Influenzae**

- Uncapsulated type (not type B which is capsulated)
- **Causes:**
  - Commonly: acute otitis media, acute sinusitis, acute infectious exacerbation of chronic bronchitis
  - Uncommonly: community acquired pneumonia (more CORD patients)
  - Rarely: meningitis
- **Antibiotic sensitivity:**
  - 5% of isolates produce penicillinase ➔ resistant to amoxycillin
Infectious Diseases

- Augmentin
- Cefaclor
- Tetracycline (not kids or pregnant)
- Cefuroxime (iv)
- Is not sensitive to erythromycin

Moraxella Catarrhalis
- Previously known as Branhamella Catarrhalis
- Commonly causes: acute otitis media, acute sinusitis, acute infectious exacerbation of chronic bronchitis (same as Haemophilus Influenzae)
- Antibiotic sensitivity: 70% produce penicillinase, so use augmentin, cefaclor, tetracycline or cefuroxime (iv)

Other G-ivies
- Escherichia coli, klebsiella aerogenes, proteus mirabilis, other Coliform bacilli
- Cause: UTI, Pyelonephritis, abdominal wound sepsis, peritonitis, biliary tract infection (gallstones) or obstruction

Anaerobes
- Bacteroides fragilis, Clostridium perfringens, anaerobic streptococci
- Cause: Abdominal wound sepsis, peritonitis, pelvic sepsis, septic abortion, puerperal sepsis

Mycobacteria
- See Tuberculosis, page 92
- Classification:
  - Tuberculosis complex: M. Tuberculosis and M. Bovis
  - Other mycobacteria: M. Avium-Intracellulare (MAC), M. Kansasii, M Marinum
  - Leprosy: M. Leprae
- Resulting Diseases:
  - Tuberculosis Complex
    - Immunocompetent: In descending frequency: lung, lymph nodes, kidney, genital tract, CNS
    - Immunodeficient: Lung in > 70%, but extra pulmonary involvement > 70% in blood (25 – 40%), lymph nodes, faeces, CNS due to ↓cell mediated immunity
  - MAC:
    - Immunocompetent: Kids – cervical lymphadenitis, adults: chronic destructive lung disease (uncommon)
    - Immunodeficient: Infection common. Initial colonisation of GI tract, then spread to blood, lymph nodes, liver, spleen, less lung involvement but invariably fatal
    - Most strains of MAC are resistant to standard anti-mycobacterial drugs

Pathogenesis
- Inhaled → macrophage ingestion → cytokines (constitutional symptoms) → resist lysis (through waxy outer coat) → multiplication in macrophage → lysis of macrophage → LN spread → immune response → granulomas → latent

Diagnosis
- Tests
  - Quantiferon gold test (tests for interferon-γ release)
  - ZN stain
  - Culture
  - Immunofluorescence

Drug Treatment
- Standard drugs: Rifampicin, Isoniazid, pyrazinamide, ethambutol. Normally first 3, except if from Pacific Islands where use all 4 due to ↑isoniazid resistance. Rifampicin is the best, if resistant to this then poor prognosis
- Most strains of M Bovis are resistant to pyrazinamide
- Many strains of M Tb from AIDS patients in the US (especially NY) are resistant to Rifampicin and Isoniazid
- Other anti-mycobacterial drugs: ciprofloxacin, clarithromycin, amikacin, rifabutin, clofazimine
Vaccination

- **BCG:**
  - Live vaccine
  - Indicated for high risk infants: household has individuals from endemic areas of with past or current Tb
  - Neonatal BCG is 60 – 90% protective for extra-pulmonary Tb and 65% for pulmonary Tb. Protection lasts 10 – 15 years
  - Adverse effects: local abscess in 1%. Treated conservatively. Some require excision

Herpes Viruses

- All Herpes viruses exhibit latency
- Usually genital area, or in/around the mouth – but occasionally elsewhere
- **Closely grouped vesicles**, followed by **crusting**, and heal in 7-10 days
- May be preceded by **tingling** at the site
- Recurrences in 50% - may follow trauma infection or UV

Herpes Simplex Virus (HSV)

- Manifestations: systemic (fever, sore throat), gingivostomatitis (ulcers with yellow slough – cold sores), meningitis (uncommon, self-limiting), encephalitis (fever, fits, headache, dysphagia, hemiparesis – do PCR on CSF sample – refer urgently)
- Incubation: 2 – 25 days. Chronic infection is due to the virus remaining in the sensory nerve ganglia. Infectious period indeterminate →contact isolation
- Symptoms:
  - Blisters which become shallow painful ulcers, often preceded by itching or tingling
  - First episode may be accompanied by flu like illness, tender inguinal nodes and dysuria
  - Recurrences can be brought on by stress, fatigue, depression, immunosuppression and concurrent illness. Recurrences usually less severe and become less frequent
- Diagnosis: clinical suspicion. Swab the base of an unroofed ulcer and refrigerate in viral medium. This will be painful. Culture negative doesn’t exclude HSV as timing and collection technique important. Serology possible, but not routinely used
- Pathogenesis. There are two antigenic types of Herpes Simplex Virus:
  - Type 1 is associated with lesions on the face and fingers, and sometimes genital lesions. Treat with zovirax (topical cream). Prevalence: 70% of population
  - Type 2 is associated almost entirely with genital infections, and affects the genitalia, vagina, and cervix and may predispose to cervical dysplasia. 10% of oral lesions caused by type 2. Prevalence: 10 – 15% of population (depends on population – more in high risk)

**Type 1 Herpes Simplex Virus**

- Infection of fingers or thumb leads to a whitlow (vesicles coalesce)
- Can infect eczematous skin →eczema herpeticum
- Children:
  - HSV1 the most common type in children.
  - Primary infection in childhood leads to gingivostomatitis – may lead to dehydration as child won’t drink. May need NG tube
  - Dribbling can →perioral spread
  - Auto-inoculation can →conjunctivitis, genital lesions, skin infection with eczema (eczema herpeticum) can be severe
  - If neonate or immunocompromised can be life-threatening
  - Treatment: Oral analgesics (eg lignocaine) and Paracetamol. Acyclovir

**Genital Herpes (type 2)**

- Description:
  - Painful, recurrent condition.
  - Male – anus or penis – small grouped vesicles and papules + pain, fever, dysuria. Dysuria may be severe enough to cause urinary retention
  - 20% may have it, but 20% are asymptomatic and 60% mild or unrecognised
- 40% caused by type 1, 60% by type 2
• Transmission: spread through skin-to-skin contact, usually when skin is broken or lesions present, but asymptomatic viral shedding a possible route of transmission. Neonatal transmission is rare (1 in 10,000 live births), but carries risk of ophthalmic infection ☞ caesarean section indicated if active blisters at delivery.

• Prevention of genital herpes: Condoms with new partner (although doesn’t eliminate risk). Avoid sex during an outbreak.

• Can have extra genital lesions on thighs and buttocks. Can → radiculoneuropathy → urinary retention/constipation.

• Treatment of Genital Herpes (type 1 or 2):
   Acute: Acyclovir 200 mg 5 times daily for 5 days. Topical creams not effective. Symptomatic treatment: salt bathing, local anaesthetic creams, oral analgesia, oral fluids. Counselling and follow-up important – written information for patients and partners, Herpes Helpline (0508 11 12 13)
   Suppressive Therapy: Where frequent outbreaks or psychological morbidity. Acyclovir 400 mg BD for up to a year. Can reduce viral shedding by up to 95%
   Can be devastating. Refer to counselling at Sexual Health Service.

• Complications:
   ↑Risk of AIDS transfer
   Erythema Multiforme
   Neonatal Herpes: 1% transmission but 50% mortality
   In pregnancy:
    o If first primary episode: miscarriage, prem labour
    o If recurrent, tiny risk for baby
    o If lesions at delivery then Caesarean

Varicella Zoster

• Primary infection: Chicken Pox.
   Macules → papules → vesicles → crusts
   Incubation 10 – 21 days (usually 14 – 16)
   Infectious for 1 – 2 days before rash appears until it crusts over
   Highly infectious, in hospital requires strict respiratory/contact isolation
   Complications:
    o Commonly becomes super-infected (eg with scratching) with Staph aureus (or S Pyogenes) which leads to scarring
    o If immunocompromised → overwhelming infection, pneumonitis, hepatitis, encephalitis (treat with Ig and acyclovir)
    o Post-natal infection can be overwhelming
    o Immune response can → encephalopathy with cerebellar ataxia
    o Can lead to severe exacerbation of eczema
   Then remains dormant in dorsal root ganglia
   Treatment: Supportive, antipruritic lotion if itchy, cut fingernails short
   Prevention: Live attenuated virus, or im Ig within 96 hours of exposure if at risk and susceptible (immunocompromised, pregnant, newborn, prem babies)

• Tests: culture – swab transported in viral medium

• Vaccination:
   Live attenuated vaccine recently licensed for both children and adults
   Not recommended for general use, but role in protecting non-immune adults (more severe illness)
   Contra-indicated if immuno-suppressed or pregnant

• Shingles:
   Reactivation of infection: affects 20% at some time. Elderly and immunocompromised are high risk
   Symptoms:
    o Dermatomal pain, then fever + malaise for several days
    o Then macule-papules + vesicles, especially in thoracic or ophthalmic division of trigeminal dermatomes.
    o If sacral, then urinary retention may occur. Thoracic (50%), cervical (20%), trigeminal (15%)
   Complications:
    o If shingles around eye (especially end of nose), then are likely to have a dendritic ulcer on cornea. Stain with Fluorescein and shine on blue light, corneal abrasions will shine green. Don’t give steroid → blindness. Urgent referral to an ophthalmologist. See Eye Infections, page 218
    o Post-herpetic neuralgia – especially in the elderly and trigeminal
    o Recurrence rare and suggests HIV (or Dermatomal Herpes Simplex)
Treatment if needed: **acyclovir** as early as possible, 800mg 5 times a day for 5 days. Pain relief – analgesic or low-dose amitriptyline. Maybe prednisolone to reduce post-herpetic neuralgia. Report visual loss immediately

**Epstein Barr Virus**

- DNA virus
- One of Herpes Group
- Spread by **respiratory secretions** (e.g. sneeze, kiss)
- Pre-schoolers an important reservoir: usually just a non-specific URT infection. In later life (e.g. adolescent) get it more acutely plus hepatitis. 1 – 5% present as hepatitis
- Associated with Burkitt’s lymphoma & nasopharyngeal carcinoma

**Clinical**

- Highly variable course. Often asymptomatic if < 5 years
- **Sore throat** (often exudative)
- Fever
- Lymphadenopathy
- **Tender liver** (liver involvement → ↓ appetite and ↑ feeling unwell), maybe big spleen
- **Rash** in 10%
- Doesn’t resolve (especially after antibiotics)
- Will be tired for weeks/months
- Incubation 30 – 50 days
- Association with symptoms:

<table>
<thead>
<tr>
<th></th>
<th>Sore Throat</th>
<th>Lymphadenopathy</th>
<th>Atypical Mononucleosis</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>EBV</strong></td>
<td>+++</td>
<td>+++</td>
<td>+++</td>
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<tr>
<td><strong>CMV</strong></td>
<td>-</td>
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<tr>
<td><strong>HIV</strong></td>
<td>++</td>
<td>++</td>
<td>+</td>
</tr>
<tr>
<td><strong>Toxoplasmosis</strong></td>
<td>+</td>
<td>+++</td>
<td>+</td>
</tr>
<tr>
<td><strong>Viral Hepatitis</strong></td>
<td>-</td>
<td>+</td>
<td>+</td>
</tr>
</tbody>
</table>

**Investigations**

- Throat swab
- FBC: may be ↑ atypical mononuclear lymphocytes
- EBV serology (Monospot test)

**Treatment**

- Symptomatic
- **Don’t** give penicillin if risk of EBV: leads to rash that can be interpreted as penicillin allergy. (E.g. amoxycillin, rash in 80 – 90%)
- **Infectious for months.** No isolation required
- Steroids if upper airway obstruction in kids

**Antibodies to EBV**

- **IgM Anti-VCA** (Virus capsid antigen) and **IgG Anti-VCA:**
  - Usually appear in blood 7 days after symptoms develop in acute primary EBV infection
  - IgM: usually persists for 2 – 4 months
  - IgG: usually persists for life
- **Anti EBNA** (Epstein-Barr nuclear antigen): appears 2 months after primary infection and persists for life
- Profiles:

<table>
<thead>
<tr>
<th></th>
<th>IgM VCA</th>
<th>IgG VCA</th>
<th>EBNA</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>No infection</strong></td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td><strong>Acute Primary</strong></td>
<td>+</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td><strong>Past Infection</strong></td>
<td>-</td>
<td>+</td>
<td>+</td>
</tr>
</tbody>
</table>

  (ie EBNA +ive rules out acute infection)

- Paul-Bunell now largely obsolete (test for antibodies in dx of infectious mononucleosis). Negative in 10 – 15% of cases

**Associated Diseases**

- **Burkitt’s** lymphoma
- Nasopharyngeal carcinoma

*Infectious Diseases* 820
- Hodgkin’s disease (EBV in 40 – 60% of cases)
- Chronic EBV may occur but is very uncommon (recurrent sore throat, cervical lymphadenopathy)

**Chronic Fatigue Syndrome**
- Unknown cause: but key differential to EBV

**Diagnosis**
- Severe chronic fatigue over 6 months or longer, with other known medical conditions excluded, and
- 4 of the following during 6 consecutive months:
  - ↓Short term memory or concentration
  - Sore throat
  - Tender lymph nodes
  - Muscle pain
  - Multi joint pain: without swelling or redness
  - Headaches of new type/pattern
  - Unrefreshing sleep
  - Post-exertional malaise lasting > 24 hours

**Differential Diagnosis**
- Depression
- Psycho-social stressors

**Cytomegalovirus (CMV)**
- Transmission:
  - Blood: transfusions, intra-uterine, perinatal, needle sharing
  - Cervical secretions and semen
  - Saliva (eg close contact with kids)
  - Urine (eg infants to adults)
  - Organ donation (transplantation)
- Immunocompetent:
  - Kids:
    - Common in preschoolers, usually asymptomatic. May give URTI
    - Prolonged excretion in saliva and urine common
  - Adults:
    - Usually asymptomatic, if not then usually self-limiting
    - May be fever (up to 2 weeks, ie a differential of PUO)
    - Sore throat, cervical lymphadenopathy uncommon
    - Atypical mononucleosis on blood film
    - Differential: EBV, HIV, toxoplasmosis
- Pregnancy:
  - Congenital infection (ie crosses placenta) in 20 – 40%
    - > 90% show no signs at birth, but watch for long term neurological sequelae (eg sensori-neural deafness, retardation)
    - Severe cases: respiratory distress, jaundice, microcephaly, etc
    - Part of TORCH complex: Toxoplasmosis, Rubella, CMV, HSV
  - Perinatal infection (eg during vaginal delivery):
    - Full term: usually mild
    - Pre-term: may be severe
- Immunodeficient:
  - AIDS: one of the most common infections → CMV retinitis (common), CMV encephalitis (rare), CMV colitis (rare)
  - Transplant: greatest risk if they’re CMV negative and CMV positive organ → interstitial pneumonia and hepatitis (in liver transplant)
  - Transfusion: blood is not routinely screened for CMV antibody. Should give CMV –ive blood to prem babies (<1500 g) and seronegative transplant recipients with seronegative transplants
- Lab diagnosis:
  - Serology:
Infectious Diseases

<table>
<thead>
<tr>
<th></th>
<th>IgG</th>
<th>IgM</th>
</tr>
</thead>
<tbody>
<tr>
<td>No infection</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Past infection</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>Acute primary or reactivated infection</td>
<td>+</td>
<td>+</td>
</tr>
</tbody>
</table>

- **Cell culture** – slow (>7 days). Culture lung biopsy or peripheral blood leucocytes
- **PCR** for CMV DNA on peripheral leucocytes, amniotic fluid, CSF (very specific, less sensitive, very expensive)

**Treatment:**
- **Ganciclovir**: bone marrow toxicity
- Foscarnet (nephrotoxic)
- Ganciclovir prophylaxis used for −ive patients with +ive organs

### Parasitology

#### Toxoplasmosis

- A protozoon/parasite
- **Main source**: *cysts in meat*. Also *kitten faeces* (eg cyst in garden – pregnant gardeners should wear gloves)
- **Presentation:**
  - Immunocompetent:
    - *Lymphadenopathy* (eg unilateral)
    - Maybe: fever, myalgia, acute pharyngitis, hepatosplenomegaly, atypical mononucleosis
    - Usually self-limiting – may take months to settle
    - If persistent/recurrent lymphadenopathy →?Need for treatment
  - Immunodeficient:
    - Acquired or reactivated
    - AIDS most common: *CNS involvement* (*solitary space occupying lesion*, encephalitis), also myocarditis, hepatitis
    - Less common in transplants and encephalitis
  - Ocular toxoplasmosis: most cases in adolescents and adults → reactivation infection → blurred vision, photophobia, multiple retinal lesions
- **Congenital Toxoplasmosis**:
  - 29% fetal infection if mother has primary CMV infection
  - Highest risk in 3rd trimester (1st trimester may miscarry)
  - Complications: spontaneous abortion, premature, still birth
  - Surviving neonates: *bilateral chorido-retinitis*. In severe cases, TORCH type symptoms

- **Lab diagnosis:**
  - **PCR** test for toxoplasmosis: amniotic fluid, CSF (AIDS patients)
  - Lymph node biopsy → characteristic histology
  - **Serology:**
    - IgM antibody after 5 – 14 days, peaks at 2 – 4 weeks, traces for up to a year
    - IgG: high levels for up to 6 months, declines slowly over years
    - Avidity test: can differentiate between acute phase ‘immature’ IgG and ‘mature’ IgG

- **Treatment:**
  - **Pyrimethamine** (Gold standard, but gives bone marrow suppression + give folate) + sulphadiazine (not available in NZ)
  - Pyrimethamine + clindamycin (gives C. difficile diarrhoea)
  - Spiramycin (only one safe in pregnancy)

#### Malaria

- Transmitted by mosquito and very rarely transfusion
- See also Malaria, page 1030

**Clinical**

- **Irregular fever** – peaks on *release of parasite from infected RBCs*. May only be mild if person has immunity (ie previous exposure). Various strains have various periodicities
- Chills
- Headache
- Malaise
- Vomiting (20%)
Infectious Diseases

- Diarrhoea (<5%)
  - ie similar to Typhoid

**History**
- Travelled to a malaria country?
- What conditions did you stay in, rural/urban, etc?
- Was chemoprophylaxis taken, how was compliance?
- Diagnosed overseas?
- When did you return to NZ (Plasmodium Falciparum usually in 1 month, P Vivax up to a year)?
- Length of illness?

**Diagnosis**
- Blood film for plasmodium protozoa: a thick film is necessary as well as the standard thin film if parasites are scant (eg if have some immunity)
- Pointless if patient is afebrile
- If initially negative, repeat 12 hourly for 48 hours
- Critical that you find out which plasmodium species is present, eg:
  - Plasmodium Falciparum: common in Africa, can cause cerebral malaria (fatal)
  - Plasmodium Vivax: more common in Asia/Oceania
- Features of poor prognosis:
  - CNS signs: disturbed consciousness, repeated convulsions
  - Respiratory distress
  - Haemorrhage, shock
  - Biochemical markers: ↑Cr, ↓HCO3, ↑bilirubin, ↓glucose
  - High parasitic load

**Prevention**
- Assessment of risk:
  - Malaria geography: transmission rates vary by country (eg high in Sub-Sahara, PNG, Solomon Islands)
  - Likely extent of contact with mosquitoes (eg standard of accommodation)
- Anti-mosquito measures: long sleeves & trousers, insect repellent/sprays, nets
- Chemoprophylaxis:
  - Start 1 week beforehand and continue till 4 weeks after leaving
  - Mefloquine (effective against chloroquine resistant P Falciparum).
    - 250 mg weekly
    - At higher doses (eg for treatment) convulsions and sinus bradycardia
    - Contraindications: drugs altering cardiac conduction, psychiatric disease, epilepsy, pregnant, kids < 5kg, or where fine CNS co-ordination required (eg airline pilots)
  - Doxycycline, 100 mg daily
    - After food otherwise gastritis
    - In rural areas of SE Asia, where mefloquine-resistant strains of P falciparum are reported
  - Chloroquine + proguanil: Only one safe for first trimester. Low efficacy against drug resistant falciparum
  - Chloroquine weekly – countries without chloroquine-resistant P falciparum (Central America north of Panama)

**Treatment**
- P Vivax, P Ovale, P Malariae **outside** of Indonesia, Timor, PNG, Solomon’s, Vanuatu:
  - Acute treatment: 3 days of Chloroquine
- For radical cure in P Vivax or P Ovale:
  - Primaquine for 2 weeks (screen for G6PD deficiency first)
  - Eradicates exo-erythrocytic liver cycle. If you don’t, they will relapse
  - Relapse common (20%) – maybe several months later. If so, repeat 3 days of Chloroquine followed by 2 weeks of higher dose of Primaquine
- P Vivax, P Ovale, P Malariae **inside** of Indonesia, Timor, PNG, Solomon’s, Vanuatu:
  - Malarone (Atovaquone + Proguanil) four tablets daily for 3d
- P Falciparum:
  - Malarone 4 tabs/d for 3d
Infectious Diseases

- If pregnant, use quinine 600mg 8hrly + clindamycin 300mg 8hrly for 7d
- Cerebral malaria: Artesunate 2.4mg/kg IV, on admission + repeated after 12hrs + 24hrs, then oral therapy

- Drug resistance:
  - Chloroquine-resistant strains of plasmodium falciparum are widespread
  - Chloroquine-resistant strains of P Vivax reported in Indonesia and PNG

Other

Amoebiasis (Entamoeba histolytica)

- Diagnosis:
  - Intestinal amoebiasis: stool sample * 3, 48 hours apart, in PVA fixative
  - Cysts: frequently present asymptomatically (carrier state)
  - Extra-intestinal amoebiasis (eg amoebic abscess of the liver) maybe months later. Serum antibody test

- Treatment:
  - Intestinal amoebiasis: metronidazole then diloxanide furoate
  - Extra-intestinal: metronidazole (surgical drainage may be necessary)
  - Asymptomatic: Diloxanide furoate

Giardiasis

- Diagnosis:
  - Stool examination for Giardia Lamblia cysts, 3 samples 48 hours apart
  - Duodenal aspirate and direct examination for trophozoites

- Treatment:
  - Metronidazole 400 mg 8 hourly for 7 days
  - Test for cure with repeat stool sample. Relapse not uncommon

Filariasis

- Commonest is Wuchereria bancroft imported from Samoa
- Elephantiasis
- Diagnosis: Blood sample
- Treatment:
  - Ivermectin
  - Most cases are asymptomatic or low grade pyrexia and don’t require treatment
  - If severe, surgical relief of major lymphatic obstruction may be necessary

Intestinal Worms

- Hookworm:
  - Ancylostoma duodenale, necator americanus
  - Diagnosis: stool sample * 3
- Roundworm:
  - Ascaris Lumbricoides
  - Diagnosis: worms passed in faeces, or stool samples * 3 and examine for Ova
- Pinworm:
  - Enterobius vermicularis
  - Diagnosis: sellotape swabs of anus
- Whipworm:
  - Trichuris trichura
  - Diagnosis: stools * 3
- Treatment: medendazole 100mg BD for 3 days for Hookworm, Roundworm, Pinworm (treat whole family) and whipworm (only if severe)
- Strongyloides Stercoralis:
  - Diagnosis: Stools * 3
  - Treatment: Thiabendazole
- Taenia saginata, beef tapeworm
  - Diagnosis: Stools * 3, examine for worm segments
  - Treatment: niclosamide
Hydatid Disease
- **Aetiology:** *Echinococcus granulosa* (a flatworm). **Infected from ova excreted in dog faeces.** *Dogs infected from eating raw sheep offal* (ie liver) containing hydatid cysts
- **Clinical:** Often acquired in childhood, **present in older age with solitary cysts** (liver, lung, brain)
- **Treatment:** surgical drainage + alendazole as adjunct
- **Diagnosis:** Serology: haemaglutination test + complement fixation test

Cryptosporidium
- Common *protozoan* parasite
- Profuse watery diarrhoea for 48 hours. Very common cause of diarrhoea.
- Severe and persisting cases in AIDS
- **Diagnosis:** Stool microscopy with ZN stain for acid fast cysts
- **Treatment:** Paromomycin (an oral, non-absorbable aminoglycoside) has some efficacy

Pneumocystis Carinii
- Protozoan parasite probably part of normal respiratory flora
- Causes interstitial pneumonitis in immuno-compromised patients (transplant, leukaemia, AIDS)
- **Diagnosis:** Bronchial lavage or open lung biopsy
- **Treatment:** Cotrimoxazole (alternatively pentamidine). Relapse in 25%
- See also Other Pneumonias, page 94

Travel Medicine

<table>
<thead>
<tr>
<th>Tropical medicine</th>
<th>Information</th>
<th>Prophylaxis</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Malaria Epidemiology =</td>
<td>300-500mil infected/y</td>
<td>Anti-mosquito measures: Long sleeved clothing 20-30% DEET repellent Mosquito netting Screened/AC rooms Coils etc Chemoprophylaxis: Mefloquine: → Contraindicated in pregnant women in 1st trimester, children &lt;5kg, those w arrhythmias, epilepsy, schizaphrenia, those who require fine coordination to work → SE: vivid dreams, nausea, dizziness Doxycycline: → CI: pregnancy, children → SE: oesophago-gastritis, skin Photosensitivity Malarone: → CI: pregnancy → SE: HA, n + v Chloroquine + Proguanil: → Only safe regimen for women in 1st trimester → Not as effective against P. falciparum than the others</td>
<td></td>
</tr>
<tr>
<td>Symptom:</td>
<td>Irregular fever – peaks on release of parasite from infected RBCs. May only be mild if person has immunity (ie previous exposure). <em>P. vivax/ovale</em> = every 48hrs; <em>P. malariae</em> = every 72hrs; <em>P. falciparum</em> = continuous with spikes</td>
<td>→ Need to assess high-risk countries (=sub-saharan Africa, PNG, Solomons, Amazon) Anti-mosquito measures: Long sleeved clothing 20-30% DEET repellent Mosquito netting Screened/AC rooms Coils etc Chemoprophylaxis: Mefloquine: → Contraindicated in pregnant women in 1st trimester, children &lt;5kg, those w arrhythmias, epilepsy, schizaphrenia, those who require fine coordination to work → SE: vivid dreams, nausea, dizziness Doxycycline: → CI: pregnancy, children → SE: oesophago-gastritis, skin Photosensitivity Malarone: → CI: pregnancy → SE: HA, n + v Chloroquine + Proguanil: → Only safe regimen for women in 1st trimester → Not as effective against P. falciparum than the others</td>
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<td>Travel History:</td>
<td>→ Travelled to a malaria country? → Was chemoprophylaxis taken, how was compliance? → Diagnosed overseas? → When did you return to NZ? (Plasmodium Falciparum usually in 1 month, P Vivax up to a year) → Length of illness? → Diagnosis: Blood film for plasmodium protozoa: a thick film is necessary as well as the standard thin film if parasites are scant (eg if</td>
<td></td>
<td></td>
</tr>
<tr>
<td>→ Infection caused by P. vivax acquired OUTSIDE Indonesia, Timor, PNG, Vanuatu, Solomon Islands</td>
<td>→ Infection caused by P. malariae or P. ovale</td>
<td>→ Radical cure for P. vivax/P. ovale</td>
<td>→ Infection caused by P. vivax acquired INSIDE the above countries</td>
</tr>
<tr>
<td>Day 1: Chloroquine 600mg (base), followed by 300mg (base) after 6hrs</td>
<td>1. Day 1: Chloroquine 600mg (base), followed by 300mg (base) after 6hrs</td>
<td>1. Aim is to kill hypnozoites persisting in the liver which will cause relapse</td>
<td>1. Malarone (Atovaquone + Proguanil) four tablets daily for 3d</td>
</tr>
<tr>
<td>Day 2: 300mg (base) of chloroquine</td>
<td>2. Day 2: 300mg (base) of chloroquine</td>
<td>Use primaquine 15mg 12hrly for 14/7</td>
<td></td>
</tr>
<tr>
<td>Day 3: 300mg (base) of chloroquine</td>
<td>3. Day 3: 300mg (base) of chloroquine</td>
<td>NB. screen for G6PD before starting primaquine as can cause haemolysis</td>
<td></td>
</tr>
<tr>
<td>NB. one 200mg tablet contains 150mg base</td>
<td></td>
<td>It is pointless attempting a radical cure if pt returning to a malarious country</td>
<td></td>
</tr>
<tr>
<td>→ Infection caused by P. vivax</td>
<td></td>
<td>P. vivax relapse</td>
<td></td>
</tr>
<tr>
<td>→ Infection caused by P. malariae or P. ovale</td>
<td></td>
<td>May relapse, usually months following Rx</td>
<td></td>
</tr>
<tr>
<td>→ Radical cure for P. vivax/P. ovale</td>
<td></td>
<td>If &gt; 30d = possible primaquine resistance</td>
<td></td>
</tr>
<tr>
<td>→ Uncomplicated (not cerebral m) infection caused by P. falciparum</td>
<td></td>
<td>If &lt; 30d = possible chloroquine resistance</td>
<td></td>
</tr>
<tr>
<td>→ Infection caused by P. vivax</td>
<td></td>
<td>Malarone 4 tabs/d for 3d</td>
<td></td>
</tr>
</tbody>
</table>

Infectious Diseases 825
Infectious Diseases

Pointless if patient is afebrile
At least 2 blood samples, 12hrs apart
Critical that you find out which plasmodium species is present, eg:
- Plasmodium Falciparum: common in Africa, can cause cerebral malaria (fatal)
- Plasmodium Vivax: more common in Asia/Oceania

Cerebral malaria:
Caused by P.falciparum
Features suggesting = impaired LOC, convulsions, resp distress, haemorrhage, shock, jaundice, oliguria
Haematology = >100,000 parasites/cu.mm (>2% RBCs parasitized)
Biochem = Cr >265, HCO3 <15, BG <2, total bili >43, aminotransferases >3x normal

Women in 1st trimester should be advised about risk of travel to sub-saharan Africa where P.falc is most common
Ask all women of childbearing age if they could be pregnant!

Treatment of cerebral malaria
1. Artesunate 2.4mg/kg IV, on admission + repeated after 12hrs + 24hrs, then oral therapy

Dengue Fever
Now global pandemic
Dengue virus belongs to the flavivirus group; 4 serotypes
Transmitted via mosquito bite (Aedes spp. females)

Global distribution:
- Northern Queensland, Cook Islands, Samoa, Tonga, Fiji
- South-East Asia, India, Africa, South + Central America + Caribbean

Clinical features:
- Incubation period = 2-8d
- Sudden onset of high fever + HA – usually lasting 5-6d + accompanied by:
  1. Chills
  2. Retro-orbital pain, photophobia
  3. Myalgia + backpain
  4. Generalised maculopapular rash
- Dengue haemorrhagic fever + Dengue shock syndrome:
  1. Occur following a 2nd infection, usually a different serotype
  2. Due to the effects of antibody-mediated enhancement of the immune response
  3. See ↑ vasc permeability with severe haemorrhage (petechial rash, epistaxis, GI bleeding, TCP, DIC, positive tourniquet test)
  4. DSS results from sudden extravasation of plasma into extravascular sites (eg pleural/peritoneal cavities), leading to shock + death
  5. High mortality rates

Diagnosis:
1. Test paired serum samples 3 wks apart for IgM + IgG Ab to dengue virus (NB. cross-reacting Ab may be present in those w previous yellow fever vacination)
2. Test blood for dengue RNA by PCR

Risk factors for travellers:
1. Travel to rural and urban areas which lack effective mosquito control
2. Preferred feeding times for Aedes species are early morning and late afternoon

Prevention:
1. Similar anti-mosquito precautions as for malaria
2. No chemoprophylaxis
3. Vaccine: not yet developed

Amoebiasis
50 mil cases/yr; 40-100,000 deaths
Caused by protozoan = entamoeba histolytica – this has two forms: amoeboid trophozoite and cysts
Infection acquired via ingestion of cysts in food or water contaminated by human faeces

Pathophysiology:
1. Cysts are resistant to gastric acid + pass into colon where they form amoeboid trophozoites (“macrophage on steroids”)
2. Trophozoites adhere to colonic epithelial cells and kill them – they then invade the submucosal tissue and this results in flask-shaped ulcers on the mucosal surface
3. Trophozoites may penetrate into the portal circulation and form abscesses in the liver

Clinical features:
1. Amoebic colitis = bloody diarrhoea, cramping abdo pain
2. Fulminating amoebic colitis = profuse bloody diarrhoea, high fever, perforation in >75%

2. If pregnant, use quinine 600mg 8hrly + clindamycin 300mg 8hrly for 7d
NB. malarone should not be used for Rx of P.falciparum in pts who took this for prophylaxis
3. Amoebic liver abscess = most common extra-intestinal manifestation; may occur months-ys after travel; bowel function often normal; stool microscopy negative for cysts, trophozoites
   - Signs = fever, RUQ pain, liver tenderness, non-productive cough with dullness at R lung base

Diagnosis:
1. Amoebic colitis = presence of *E. histolytica* trophozoites on microscopy of faeces or mucosal bx
2. Amoebic liver abscess = US or CT (usually multiple abscesses); serum antibody to *E. hist* (haemagglutinin test – high sens & spec)

Treatment:
1. AC + liver abscess = metronidazole 750mg 8hrly for 10d
2. NB. warn pt about ETOH intake

### Schistosomiasis

#### Not really examinable, except TREATMENT

- 200mil people infected, 120mil symptomatic
- *Parasitic* trematode worms that live in the abdominal veins of their hosts; freshwater snails are the intermediate hosts
- 3 species (*s. Haematobium, mansoni, japonicum*) and they vary depending on location

**Life-cycle:**
- Infected snails → release cercariae into fresh water → cercariae penetrate human skin (legs) + develop into larval forms → enter capillaries/lymphatics → lungs → portal venous system → copulation + maturation → migration to SVC, IVC, vesical plexus

**Clinical features:**
1. Maculopapular eruption at site of penetration within hours of exposure
2. NB. swimmer’s itch is a dermatitis caused by cercarial penetration by schistosomes that are non-pathogenic for humans therefore systemic infection does not occur (has been reported in NZ)

#### Acute schistosomiasis (Katayama fever):
1. Incubation period: 14-80d
2. Onset of symptoms coincides with initial deposition of eggs in host tissues
3. Symptoms = fever, HA, myalgia, RUQ abdo pain, bloody diarrhoea
4. Signs = tender hepatomegaly, peripheral blood eosinophilia

#### Chronic schistosomiasis:
1. Results from the host’s immune response to schistosoma eggs + the granulomatous reaction they stimulate

#### GI disease (mansoni, japonicum):
1. Ulceration, micro-abscesses in gut wall = diarrhoea, colicky abdo pain in LIF
2. Migration of eggs to liver resulting in liver inflammation + fibrosis, portal HTN, oesophageal varices, splenomegaly

#### Genitourinary disease (haematobium):
1. Results from egg deposition in the vesical vein complex
2. Symptoms = haematuria (10-12/52 post infection), dysuria, haematospermia
3. Late = bladder calcification, ureteric obstruction, SCC

#### Risk-factors for travellers:
- Travellers to sub-saharan Africa most at risk, especially swimming in freshwater lakes (water nearest edge is worst)

**Diagnosis:**
1. *S.haematobium* = microscopy for eggs on early-morning urine, snips of bladder wall
2. *S.mansoni, japonicum* = concentrated faecal samples, rectal wall biopsies
3. Blood test for *s. Antibody* = less sensitivity than microscopy for eggs

**Treatment:**
1. Praziquantel 40mg/kg x 1 (*s. Haematobium*)
2. Praziquantel 20mg/kg 8hrly x 3 (*s.mansoni, japonicum*)

- **Categorisation of risk:**
  - **Trauma** is the most common cause of mortality and morbidity in travellers to developing countries
  - **Routine illness + exotic illness is possible**

- **Travel History:**
  - **General health** assessment (underlying conditions, meds, allergies, **pregnancy**)
  - **Where** are you going?
  - **How** are you getting there?
  - **How long** there?
  - **What** will you be doing?
  - **Where** are you staying?
  - **Have** you been there before?

- **Examples:**
  - 3 week package to Hong Kong, Singapore, Bangkok: Hep A and Tetanus up to date. Typhoid is overkill
  - 4 month Overland through from Thailand to Turkey (Vivax Malaria): Malaria, Hep A, Tetanus
  - 3 month TI in Tanzania: Hep A, Typhoid, Yellow fever (not Asia)
  - 3 year diplomatic posting in PNG: Malaria prophylaxis if going rural but not continuously

- **Advice to the traveller:**
  - Traveller’s diarrhoea:
    - Affects 30-60% of travellers to developing countries
Definition = passage of 3 or more unformed stools in 24 hours, may be accompanied by fever, cramps, blood for 3-4d

Aetiology: enterotoxigenic e.coli, also campylobacter, salmonella, shigella

Self-treatment = loperamide or norfloxacin if severe (>6 stools/d)

Prevention = avoid tap water + ice; buffets, salads, unpasteurised dairy/fruit juice; raw seafood; thin-skinned fruit; drink boiled water; eat hot food

Mosquito-borne infections:
- Include = malaria, dengue, yellow fever, JE
- Other insect-transmitted infection:
  1. Sandflies = leishmaniasis (India)
  2. Tsetse flies = trypanosomiasis (sleeping sickness; sub-saharan Africa)
  3. Ticks = rickettsial infection, lyme disease

Prevention:
  1. Lose fitting, long sleeved clothing
  2. 20-30% DEET repellent
  3. Use bed netting
  4. Take appropriate malaria chemoprophylaxis

Environmental risks:
- Swimming in freshwater lakes/rivers – leptospirosis, schistosomiasis
- Drowning is common in travellers
- Sun/heat/cold exposure
- Flying: DVT risk (esp pregnant, OCP, elderly, smokers)
- Trauma!

Insurance
First-aid kit
Pregnancy = 2nd trimester is safest; most airlines won’t allow travel in last 4/52 of preg
Scuba diving = dangerous marine life (box jellyfish, sea snakes etc); coral abrasions/cuts = infection

Vaccination

Mandatory
- Yellow Fever:
  1. Attenuated live strain (⇒ not if immunocompromised or pregnant or egg allergy)
  2. Mandated for travel to equatorial (sub-Saharan) Africa and South America
  3. Should be given >10d before departure
  4. 0.5ml sc
  5. Protection for 10 years
  6. Requires special certificate, stamp (before being allowed to travel to these countries) ⇒ only done in designated centres

Routine
- Polio:
  1. Travellers to India, Southeast Asia, some African countries
  2. IPV: Inactivated polio vaccine: 0.5 mls sc
  3. Booster every 10 years
- Tetanus/Diphtheria/Pertussis (Boostrix):
  1. If not given in the last 10 years
  2. Booster every 10 years. 0.5 mls im into deltoid muscle

For Healthcare Workers Intending to Work in Developing Countries
- Measles: give MMR-2 if sero-neg for measles Ab
- Rubella: give ervevax if sero-neg for rubella Ab
- VZV: give varilrix if sero-neg for VZV Ab
- Hep B: give booster dose if anti-HBs is <10
- Pneumococcal: give pneumovax to travellers >65 with chronic resp d

Recommended
- Hepatitis A:
  1. Most common vaccine-preventable illness 3/1000 risk
  2. Formalin inactivated HAV.
IM injection (1ml im) gives protection for one year.
Booster dose 6 – 12 months later gives long-term protection.

Typhoid:
Typhoid fever (enteric fever) has a worldwide distribution (India highest risk)
Transmitted by human carriers of s.typhi – excreted in faeces
Injectable: suspension of capsular Vi polysaccharide (0.5ml im)
3 yr immunity

Meningococcal Vaccine:
For types A, C, Y + W135 in sub-saharan Africa + mecca (compulsory for pilgrims to mecca)
0.5ml sc
3 yr immunity

Japanese Encephalitis Vaccine:
Infection with JE virus (flavivirus) endemic in India + southeast asia
Transmitted by mosquitos (pigs = reservoir)
Rare for travellers to get it – but high mortality.
Vaccine = suspension of inactivated JE virus – 3 im doses of 1ml at 0, 7, 28 days – booster at 1yr then every 3 yrs

Rabies:
Only for people intending to work (eg vets) longer term in rural/agricultural areas (esp in india + Africa)
Suspension of inactivated rabies virus – 3 im injections of 1ml at 0, 7, 28 days
Booster dose every 3 yrs
Post-exposure prophylaxis at 0 + 3d for immunised people

Illness in a Returning Traveller

Travel History
Dates of departure and return
Timing/sequence of clinical symptoms
Countries visited etc
Exposure to bites/animals/ill people
Type of food/liquids consumes
Immunisations
Malaria chemoprophylaxis + compliance
Etc

Incubation Periods
Short (<10d):
Influenza
Dengue
Travellers diarrhoea
Seafood poisoning
Medium (11-21d):
Malaria (esp p.falciparum)
Typhoid
Leptospirosis
Amoebiasis
Long (>21d):
Malaria (esp p.vivax)
Hep A, Hep E
Tb
Schistosomiasis
Amoebic liver d

Symptoms
Fever DDx:
Malaria
Dengue
Typhoid: usually constipated, used to die of peritonitis, bradycardia, high spiking fever, takes days for temperature to go down
• Respiratory symptoms:
  ➢ Viral URTI
  ➢ SARS
    o Travel within 10d to an affected country +
    o Resp symptoms eg non-productive cough, tachypnoea, rhinorrhea
    o Temp >38
    o Pulmonary infiltrates on CXR
  ➢ Aetiology = coronavirus (civet cat likely source)
• Diarrhoea >14d:
  ➢ Amoebiasis
  ➢ Giardiasis
• Rash or skin lesions:
  ➢ Dengue fever
  ➢ Rickettsial infections
  ➢ Cutaneous larva migrans (migrating serpiginous tracks on feet – hookworm)

**Lab Investigations**

• FBC + differential
• LFTs + electrolytes
• Blood film for malaria
• Urine: microscopy + culture
• Faeces: microscopy for ova/parasites + culture for enteric pathogens

**Serology:**
  ➢ Paired sera (3/52 apart) for dengue
  ➢ Leptospira spp
  ➢ Entamoeba histolytica

**Other Conditions to Consider**

• Ross River
• Syphilis
• Filariaasis (eg Samoa)
• Other imported infections from Pacific:
  ➢ Leprosy (mycobacterium lepraes)
  ➢ Yaws (Treponema pertenue)
  ➢ Eosinophilic Meningitis

**Antibiotic Treatment**

• NB. Penicillins and cephalosporins and carbapenems contain a beta-lactam ring that can be hydrolysed by beta lactamases (penicillinase is one of these)
• Patients with IgE-mediated allergy to penicillins may be reactive to the beta-lactam ring structure that is common to all penicillins, or to the R-group side chains that distinguish different penicillins from one another
• A beta-lactam structure is also found in cephalosporins and carbapenems
• The aminopenicillins amoxicillin and ampicillin each have R-group side chains that are identical to the side chains of certain cephalosporins

<table>
<thead>
<tr>
<th>Antibiotics</th>
<th>Antibiotic</th>
<th>Route</th>
<th>Antibiotic spectrum</th>
<th>Indications</th>
<th>NB</th>
</tr>
</thead>
<tbody>
<tr>
<td>Penicillin G</td>
<td>IV</td>
<td>1. Strep pyogenes</td>
<td>1. Community-acquired pneumonia (S pneumoniae)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>2. Strep pneumoniae</td>
<td>2. Cellulitis (S pyogenes)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>4. Strep viridans</td>
<td>4. Infective endocarditis (S pyogenes)</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>5. Treponema pallidum (syph)</td>
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<tr>
<td></td>
<td></td>
<td>6. Leptospira</td>
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<tr>
<td></td>
<td></td>
<td>7. N meningitidis</td>
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<td></td>
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<td></td>
<td></td>
<td>8. Anaerobes (Clostridium perfringens, Actinomyces)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Penicillin V</td>
<td>PO</td>
<td>S pyogenes</td>
<td>Acute pharyngitis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amoxicillin</td>
<td>PO/IV</td>
<td>As for penicillin +</td>
<td>1. Infections caused by e</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Infectious Diseases** 830
1. Enterococcus faecalis
2. Listeria monocytogenes

- faecalis (eg UTI, cholangitis, bacteremia, abdo sepsis)
- Infections caused by l mono (men, bacteremia)

**Resistant**

- Do not use for:
  1. Infectious exacerbation COPD
  2. Empiric Rx UTI

**Amoxycillin + Clavulonic acid (Augmentin)**

<table>
<thead>
<tr>
<th>Dose</th>
<th>1.</th>
<th>2.</th>
</tr>
</thead>
<tbody>
<tr>
<td>IV/PO</td>
<td>Haemophilus influenzae</td>
<td>1. Infectious exac COPD</td>
</tr>
<tr>
<td></td>
<td>Branhemella catarrhalis</td>
<td>2. CAP in those with COPD</td>
</tr>
<tr>
<td></td>
<td></td>
<td>3. Community-acquired UTI</td>
</tr>
<tr>
<td></td>
<td></td>
<td>4. Acute OM</td>
</tr>
<tr>
<td></td>
<td></td>
<td>5. Acute sinusitis</td>
</tr>
</tbody>
</table>

- Clav acid inhibits B-lactamases (penicillinase, cephalosporinase) + protects amoxy from hydrolysis

**Fluclaxacillin**

<table>
<thead>
<tr>
<th>Dose</th>
<th>1.</th>
</tr>
</thead>
<tbody>
<tr>
<td>IV/PO</td>
<td>S aureus (not MRSA)</td>
</tr>
</tbody>
</table>

- Infections caused by s aureus (cellulitis, skin, wound, bone, IE)

- Use penicillin rather than fluclax if infecting strain of s aureus is sensitive

**Piperacillin + Tazobactam (Tazocin)**

<table>
<thead>
<tr>
<th>Dose</th>
<th>1.</th>
</tr>
</thead>
<tbody>
<tr>
<td>IV</td>
<td>Pseudomonas aeruginosa</td>
</tr>
</tbody>
</table>

- Empiric therapy for suspected infection in neutropenic cancer pts

- Tazobactam is also an inhibitor of B-lactamases

**NB.** Penicillin allergy: always take thorough hx (common rx = itchy skin rash – urticaria – cephalosporins can generally be used safely; serious rx = anaphylaxis – do not use cephalosporins)

**Cephalosporins**

**Cefazolin**

<table>
<thead>
<tr>
<th>Dose</th>
<th>1.</th>
<th>2.</th>
<th>3.</th>
</tr>
</thead>
<tbody>
<tr>
<td>IV</td>
<td>S aureus (not MRSA)</td>
<td>S pyogenes</td>
<td>E coli, p mirabilis, klebsiella</td>
</tr>
</tbody>
</table>

- Cellulitis (monotherapy)
- Surgical prophylaxis

- A combined fluclox + pen alternative
- Cef is not hydrolysed by staph penicillinase
- Useful AB for home therapy

**Cefuroxime**

<table>
<thead>
<tr>
<th>Dose</th>
<th>1.</th>
<th>2.</th>
<th>3.</th>
<th>4.</th>
</tr>
</thead>
<tbody>
<tr>
<td>IV</td>
<td>S aureus (not MRSA)</td>
<td>S pyogenes</td>
<td>H influenzae</td>
<td>E coli, p mirabilis, klebsiella</td>
</tr>
</tbody>
</table>

- CAP in those w COPD
- CA systemic infections caused by e.coli

**Ceftriaxone**

<table>
<thead>
<tr>
<th>Dose</th>
<th>1.</th>
<th>2.</th>
<th>3.</th>
<th>4.</th>
</tr>
</thead>
<tbody>
<tr>
<td>IV</td>
<td>S pneumoniae</td>
<td>N men</td>
<td>N gonorrhoeae</td>
<td>H flu</td>
</tr>
</tbody>
</table>

- Men (n men, s pne)
- CAP
- Gonorrhoea (single IM dose)

- Given OD ; good for home therapy

**Ceftazidime**

<table>
<thead>
<tr>
<th>Dose</th>
<th>1.</th>
</tr>
</thead>
<tbody>
<tr>
<td>IV</td>
<td>Pseudomonas aeruginosa</td>
</tr>
</tbody>
</table>

- Systemic Rx of resp infections in CF, bronchiectasis – often w gentamicin

**Carbapenems**

**Imipenem, Meropenem, Ertopenem**

<table>
<thead>
<tr>
<th>Dose</th>
<th>1.</th>
</tr>
</thead>
<tbody>
<tr>
<td>IV</td>
<td>Broad spectrum</td>
</tr>
</tbody>
</table>

- Empiric therapy of infection in neutropenic ca pts
- Infections caused by multiple-resistant strains of coliform bacilli eg ESBL +ve e.coli (causing urosepsis in elderly)

- NB. Broadest spectrum AB available
- Ertopenem does not have activity against pseudomonas but the others do

**Macrolides**

**Erythromycin**

<table>
<thead>
<tr>
<th>Dose</th>
<th>1.</th>
<th>2.</th>
<th>3.</th>
<th>4.</th>
<th>5.</th>
<th>6.</th>
<th>7.</th>
<th>8.</th>
</tr>
</thead>
<tbody>
<tr>
<td>IV/PO</td>
<td>S aureus</td>
<td>S pneumoniae</td>
<td>S pyogenes</td>
<td>Mycoplasma pneumoniae</td>
<td>Chlamydia pneumoniae</td>
<td>C trachomatis</td>
<td>Legionella</td>
<td>Campylobacter jejuni</td>
</tr>
</tbody>
</table>

- CAP (especially atypical: mycoplasma, chlamydia, legionella)
- Campylobacter enterocolitis in children

- NB. Can be used in those w pen allergy
- Has poor activity against h flu ; don’t use in OM, COPD, sinusitis

**Clarithromycin**

<table>
<thead>
<tr>
<th>Dose</th>
<th>1.</th>
</tr>
</thead>
<tbody>
<tr>
<td>IV/PO</td>
<td>Combination Rx for infection caused by mycobacterium avium-intracellulare (MAC)</td>
</tr>
</tbody>
</table>

- These macrolides have better absorption + less gastric intolerance than erythromycin

**Azithromycin**

<table>
<thead>
<tr>
<th>Dose</th>
<th>1.</th>
</tr>
</thead>
<tbody>
<tr>
<td>PO</td>
<td>Single-dose Rx of STI caused by c trachomatis</td>
</tr>
</tbody>
</table>

**Roxithromycin**

<table>
<thead>
<tr>
<th>Dose</th>
<th>1.</th>
</tr>
</thead>
<tbody>
<tr>
<td>PO</td>
<td>Combination Rx w IV cefuroxime for CAP</td>
</tr>
</tbody>
</table>
| **Clindamycin** | IV/PO | 1. S aureus  
2. S pyogenes | 1. *Cellulitis* (monotherapy)  
2. *Nec fasc* (s pyo) | ➢ Not a macrolide, but a lincosamide AB  
➢ *A/w* AB-associated diarrhoea caused by C diff |
| **Fluoroquinolones** |  
| **Ciprofloxacin** | PO | 1. S aureus  
2. P aeruginosa  
3. E coli + other coliform bacilli  
4. S typhi  
5. Salmonella  
6. Shigella  
7. Yersinia enterocolitica  
2. Typhoid fever  
3. *Infectious diarrhoea* (campylo, yersinia, shigella) | ➢ *NB. All* fluoroquinolones *contraindicated* in pregnancy + children  
➢ Norfloxacin only achieves low serum levels ↓; should only be used for UTI Rx  
➢ Moxi + Gati are *small print* |
| **Norfloxacin** | PO | Similar to ciprofloxacin | 1. UTI caused by p aer  
2. UTI caused by coliform bacilli resistant to other ABs |
| **Moxifloxacin** | PO | PO | 1. Home Rx of CAP – typical + atypical but not used often to ↓ likelihood of resistance |
| **Others** |  
| **Vancomycin** | IV/PO | 1. S aureus (incl MRSA)  
2. S epidermidis (coag neg)  
3. S pneumonia  
4. E faecalis  
5. C diff | 1. MRSA infections  
2. Systemic IV catheter infections caused by s epidermidis (>50% of these are MRSA)  
3. Rx of *peritonitis* in CAPD pts (intraperitoneal infusion)  
4. AB associated diarrhoea (C diff)  
5. Rx of staph/enterococcal infection in pts w hx of anaphylaxis/reaction to pen | ➢ Ototoxic – need to measure levels prior to subsequent doses |
| **Rifampicin** | IV/PO | 1. M tuberculosis  
2. S aureus  
2. Severe s aureus inf w fluclox or other  
3. *Chemoprophylaxis for contacts of n men* |
| **Gentamicin** | IV | 1. All coliform bacilli (e coli, klebsiella, proteus)  
2. P aeruginosa | 1. *Acute pyelonephritis*  
2. Suspected gram –ve septicaemia  
3. Combination Rx for infections in neutropenic pts  
4. Synergistic Rx w pen for IE | ➢ Ototoxic – need to measure levels prior to subsequent doses |
| **Cotrimoxazole** | PO | 1. Pneumocystis carinii  
2. Nocardia species  
3. MRSA | 1. Chemoprophylaxis + Rx of pneumocystis carinii pneumonia (immunocompromised)  
2. MRSA | ➢ Trimethoprim + sulphamethoxazole |
| **Trimethoprim** | PO | 1. E coli  
2. P mirabilis  
3. Klebsiella pneumonia | 1. CA UTI | |
| **Doxycycline** | PO | 1. S pneu  
2. H flu  
3. B catarrhalis  
4. Chlamydia trachomatis  
5. Plasmodium falciparum (+ other p spp) | 1. STIs caused by c trachomatis  
2. Infectious exacerbations of COPD  
3. Chemoprophylaxis for malaria  
4. Acne | ➢ *Contraindicated* in pregnancy + children (as are all tetracyclines) |
### Infectious Diseases

| Metronidazole | IV/PO | 1. All anaerobic bact (except actinomyces spp) eg:  
| | | B fragilis  
| | | C perfringens  
| | | C diff  
| | | Fusobacterium spp  
| | | Peptostreptococcus spp  
| | 2. Gardnerella vaginalis  
| | 3. Trichomonas vaginalis  
| | 4. Giardia lamblia  
| | 5. Entamoeba histolytica | 1. Anaerobic infections  
| | | 2. AB-associated diarrhoea (C diff)  
| | | 3. Bacterial vaginosis (gardnerella)  
| | | 4. Vaginal discharge (trichomonas)  
| | | 5. Diarrhoea caused by protozoa (giardia, entamoeba) |  

#### Anti-fungals

| Nystatin | Topical | 1. Candida albicans | 1. Oral or vaginal thrush |  
| Miconazole | Topical | 1. C albicans  
| | | 2. Dermatophytes (trichophyton spp, microsporum spp) | 1. Thrush  
| | | 2. Tinea (ringworm) except tinea of scalp or nails |  
| Fluconazole | IV/PO | 1. C albicans, candida spp (except krusei, glabrata)  
| | | 2. Cryptococcus neoformas | 1. Systemic infections caused by candida spp  
| | | 2. Chronic vulvo-vaginal candidosis  
| | | 3. Prophylaxis of candida infection in BM transplant pts |  
| Terbinafine | PO | 1. Dermatophytes | 1. Tinea of scalp or nails (onychomycosis) |  
| Itraconazole | PO |  
| | 1. Active against most pathogenic fungi: eg yeasts (candida spp., cryptococcus)  
| | 2. Aspergillus spp  
| | 3. Mucor + other zygomycetes (eg rhizopus) | 1. Invasive fungal infections, esp in neutropenic BM transplant pts |  
| Voriconazol | IV/PO | 1. Similar to above – broad spectrum anti-fungal | 1. Invasive aspergillosis |  
| | | SE = transient visual disturbance, elevation of LFTs  
| | | Has function against fungi resistant to amphotericin B |  
| Caspofungin | IV | Small print |  

#### Anti-virals

| Acyclovir | IV/PO | 1. HSV  
| | | 2. VZV | 1. Genital herpes (1°): 200mg 5/day for 10d  
| | | 2. Genital herpes (recurrence): 400mg tds for 5d  
| | | 3. Genital herpes (suppression): 400mg bd  
| | | 4. HSV encephalitis 10mg/kg IV tds for 14d  
| | | 5. Shingles (VZV) 800mg 5/d for 7d  
| | | 6. Shingles in immunocompromised: 10mg/kg IV tds for 14d  
| | | NB. Rx should be started within 3d of onset of rash |  
| Ganciclovir | IV | CMV | 1. Prophylaxis for CMV-neg recipients of a CMV-pos organ transplant  
| | | 2. Pneumonia (BM transplant recipients)  
| | | 3. Hepatitis (liver transplant pts)  
| | | 4. Retinitis, colitis (AIDS pts) |  
| Ribavirin | PO | 1. HCV | 1. Chronic hepatitis C |  
| | | Given w interferon alpha |  
| Oseltamivir | PO | 1. Influenza A + B | Influenza (esp in immunocompr) |  
| | | | Inhibits neuraminidase of flu viruses  
| | | | Should be given within 2d of onset of Sx |  

#### Anti-retroviral drugs – small print

- Targeted at preventing viral replication + infection of CD4 cells
- Combination therapy is always used to prevent resistance
- Indications = all pts with a hx of an AIDS-defining illness or severe symptoms of HIV infection, regardless of CD4 count

| NRTIs (nucleoside reverse transcriptase inhibitors) |  
| | E.g. combivir (zidovudine + lamivudine)  
| | Mechanism = molecular mimics of nucleosides – incorporated into viral DNA by reverse transcriptase |  
| NNRTIs (non-nucleoside RTIs) |  
| | E.g. efavirenz |
Infectious Diseases

Mechanism = binds to RT and prevents catalytic activity

E.g. ritonovir

Mechanism = binds to protease + prevents post-translational processing of protein precursor

E.g. enfuvirtide

Mechanism = binds to gp41 preventing fusion of virus with cell membrane

E.g. raltegravir

Mechanism = prevent integration of viral DNA into host chromosome

E.g. maraviroc

Mechanism = bind to co-receptors (e.g. CCR5, CXCR4) preventing virus binding

Pls (protease inhibitors)

Fusion inhibitors

Integrate inhibitors

Entry inhibitors

Summary

G +ive

Cocci

Strep pneumonia

Oral: Amoxycillin. IV: Penicillin G
Allergy: Erythromycin. Resistant (eg kids): Ceftriaxone
Resistant and Meningitis: Cefotaxime + Vancomycin (act synergistically)
Resistant and Endocarditis: Vancomycin

Strep faecalis

Trimethoprim

Strep agalactiae

Penicillin. [β haemolytic. Normal vaginal flora]

Strep pyogenes

Penicillin. Erythromycin if allergic. Also sensitive to flucloxacillin

Strep sanguis

Penicillin [β haemolytic]

Staph aureus

Flucloxacillin. Allergy: Ceftriaxone. MRSA (resistant to penicillins and cephalosporins): Vancomycin

Staph epidermidis

Flucloxacillin. Resistant: Vancomycin

Bacilli

Listeria monocytogenes

Amoxycillin. Elderly/immunocompromised: ciprofloxacin (quinolone – not in kids)

Clostridium difficile

Metronidazole

Enterococcus faecalis

Amoxycillin

G –ive

Bacilli

E Coli

Trimethoprim. Cotrimoxazole (trimethoprim + sulphmethoxazole), Norfloxacin (Quinolone). 48% resistant to amoxycillin. Augmentin resistance growing.
Meningitis: Cefotaxime (good CSF penetration). Consider gentamycin or cotrimoxazole

Campylobacter Jejuni

Erythromycin

H Influenzae

Cefaclor, Augmentin, Tetracycline

5% resistant to penicillin, not sensitive to erythromycin

Legionella

Erythromycin. Add rifampicin if severe

Pseudomonas Aeruginosa

Ciprofloxacin. Maybe Tobramycin or piperacillin

Meningitis: Ceftazidine

Gardnerella Vaginalis

Metronidazole. Metronidazole is otherwise inactive against aerobes

Bordetella Pertussis

Erythromycin

Branhamella Catarrhalis

Augmentin, cefaclor, tetracycline, cefuroxime

70% penicillinase

Anaerobes

Bacteroides Fragilis

Metronidazole. Not penicillin or cephalosporins

Helicobacter Pylori

Clarithromycin + metronidazole + omeprazole (7 days)

Cocci

Neisseria Meningitidis

Penicillin. Cefotaxime if allergic.

Prophylaxis: Rifampicin, ceftriaxone if pregnant

Neisseria Gonorrhoea

Stat: Amoxycillin + Probenecid

Ciprofloxacin or tetracycline if penicillin allergy or resistant.

Azithromycin if concurrent chlamydia or pregnant

Not G-ive

Chlamydia Pneumoniae

Erythromycin

Chlamydia Trachomatis

STD: Doxycycline, azithromycin, pregnancy: Erythromycin

PID: Erythromycin + ornidazole

NB: Obligate intracellular parasite. Cellular wall similar to G-ive but not actually a G-ive bacteria
### Others

- **Mycoplasma**
  
  Erythromycin. 2nd line: Tetracyclines (eg doxycycline) except pregnant/kids

- **TB**
  
  Rifampicin + isoniazid + pyrazinamide (also ethambutol if isoniazid resistant). Prophylaxis: rifampicin

- **MAC**
  
  Clarithromycin = Syphilis. Penicillin G. Resistant: Tetracyclines (eg doxycycline)

- **Treponema pallidum**
  
  = Syphilis. Penicillin G. Resistant: Tetracyclines (eg doxycycline)

### Yeasts

- **Aspergillus**
  
  Amphotericin B. Itraconazole prophylaxis

- **Cryptococcus neoformans**
  
  Fluconazole (good CSF penetration), Amphotericin B

### Virus

- **HSV**
  
  Acyclovir

- **CMV**
  
  Ganciclovir

- **Toxoplasmosis**
  
  Pyrimethamine + clindamycin. Pregnant: Spiramycin

### Protozoa

- **Cryptosporidium**
  
  Nothing effective. Maybe Paromomycin (oral, non-absorbed aminoglycoside)

- **Giardiasis**
  
  Tinidazole stat or metronidazole 7 days

- **Trichomonas**
  
  Doxycycline, Metronidazole

- **Pneumocystis Carinii Pneumonia**
  
  Cotrimoxazole

- **Malaria Prophylaxis**
  
  Mefloquine weekly: good for chloroquine resistant falciparum.

  Not epilepsy, pregnant, babies

  Doxycycline daily: Esp Mefloquine resistant falciparum. Not kids or pregnant

  Chloroquine + Proguanil: if pregnant

  Chloroquine weekly: if no chloroquine resistant falciparum

- **Plasmodium Falciparum**
  
  Quinine sulphate + doxycycline

- **Plasmodium Vivax**
  
  Chloroquine 3 days then primaquine 2 weeks

- **Amoebiasis**
  
  Metronidazole + diloxanide furoate

### Worms

- **Filaria**
  
  Ivermectin

- **Intestinal worms**
  
  Hookworm, roundworm, pinworm: Medendazole

  Strongyloides Stercoralis: Thiabendazole

  Tapeworms: Niclosamide

### Antibacterials

#### Penicillins

<table>
<thead>
<tr>
<th>Penicillin G (iv/im)</th>
<th>Streptococci</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>(Oral form: Pen V)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Not Enterococcus faecalis, resistance in kids to strep pneumoniae</td>
</tr>
<tr>
<td></td>
<td>Staphylococci</td>
<td>But 80% produce penicillinase</td>
</tr>
<tr>
<td></td>
<td>N Gonorrhoeae</td>
<td>Some produce penicillinase</td>
</tr>
<tr>
<td></td>
<td>N Meningitidis</td>
<td></td>
</tr>
<tr>
<td></td>
<td>T Pallidum</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Leptospira</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Syphilis</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Anaerobes</td>
<td>Peptostreptococci, Clostridia, Fusobacteria, Bacteroides (not B fragilis), Actinomycyes</td>
</tr>
</tbody>
</table>

- **Amoxycillin**
  
  As above plus:

  Enterococcus faecalis

  Listeria monocytogenes

  Haemophilus influenzae 6% produce penicillinase

  Some E coli 48% resistant

  Most Proteus mirabilis 20% produce penicillinase
### Augmentin

<table>
<thead>
<tr>
<th>Haemophilus influenzae</th>
<th>Branhamella Catarrhalis</th>
<th>Clavulanic acid inhibits penicillinase. Principle use is infectious exacerbations of chronic bronchitis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>↑ E coli resistance</td>
</tr>
</tbody>
</table>

### Fluclaxicilllin

| Staph Aureus | Penicillase producers. MRSA resistant to Fluclaxicilllin and cephalosporins |

### Piperacillin Tazocin

<table>
<thead>
<tr>
<th>Pseudomonas aeruginosa</th>
<th>Systemic infection only</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neutropenic cancer patients</td>
<td>= Piperacillin + Tazobactam (a beta-lactamase inhibitor)</td>
</tr>
</tbody>
</table>

### Cephalosporins

<table>
<thead>
<tr>
<th>Gen</th>
<th>Examples</th>
<th>Use for</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td><strong>Cefazolin</strong>&lt;br&gt;Cephalothin (IV)&lt;br&gt;Cephradine (IV &amp; oral)&lt;br&gt;Cephalexin (oral)</td>
<td>Better for G+, poor for G-&lt;br&gt;Gram +ives: Streptococci (not E faecalis), Staphilococci, Anaerobes (Not B Fragilis)&lt;br&gt;Gram –ives: Some coliforms: E coli (20% resistant), Klebsiella&lt;br&gt;Inactive against: H Influenzae, Pseudomonas, Enterococcus faecalis</td>
</tr>
<tr>
<td>2</td>
<td><strong>Cefuroxime</strong>(IV+oral)&lt;br&gt;Cefamandole (IV+IM)&lt;br&gt;Cefaclor (Oral)</td>
<td>G +ive: as for 1st generation&lt;br&gt;G -ive: Better against coliforms&lt;br&gt;Active against H influenzae&lt;br&gt;Inactive against: Pseudomonas, E Faecalis, B Fragilis</td>
</tr>
<tr>
<td>3</td>
<td><strong>Ceftaxime</strong>&lt;br&gt;Cefotaxime&lt;br&gt;Ceftazidine&lt;br&gt;Cefpodoxime (oral)</td>
<td>Good activity against most coliforms&lt;br&gt;Activity against G+ &lt; 2nd generation&lt;br&gt;No activity against Bacteroides or Enterococcus&lt;br&gt;Ceftazidine good against pseudomonas aeruginosa&lt;br&gt;Ceftaxime has long T½, can be given once daily&lt;br&gt;Good CSF penetration ⇒ first choice for meningitis caused by coliforms or HIB</td>
</tr>
<tr>
<td>4</td>
<td><strong>Cefipime</strong>&lt;br&gt;Cefpirome</td>
<td>Highly stable against β-lactamases&lt;br&gt;Good against most aerobic G –ives (coliforms and <em>pseudomonas</em>)&lt;br&gt;Good against G +ive, incl staph aureus (similar to 1st generation) but not Enterococcus</td>
</tr>
<tr>
<td></td>
<td>Cefotetan</td>
<td>Broad spectrum cephamycin&lt;br&gt;Good against Bacteroides and Coliforms (not pseudomonas)&lt;br&gt;Indications: antibiotic prophylaxis for colonic and gynaecological surgery</td>
</tr>
<tr>
<td></td>
<td>Aztreonam</td>
<td>Active against G –ive bacteria only: including coliforms and to a lesser extent Pseudomonas&lt;br&gt;Indication: less toxic than aminoglycosides for G-ive infection</td>
</tr>
<tr>
<td></td>
<td>Imipenem&lt;br&gt;Meropenem</td>
<td>A cabapenem (not cephalosporins)&lt;br&gt;Inhibit nearly all G+ and G-&lt;br&gt;Restricted as its so good&lt;br&gt;Indication: Empiric therapy in neutropenic cancer patients</td>
</tr>
</tbody>
</table>

### Macrolides

- Effective against:
  - Staph aureus (up to 10% resistance in community strains)
  - Streptococci (not E faecalis)
  - Anaerobes (only moderately effective against B fragilis)
  - Mycoplasma pneumoniae
  - Chlamydia pneumoniae
  - Chlamydia trachomatis (but tetracycline is the drug of choice)
  - Campylobacter jejuni
- Ineffective against:
  - H influenzae
**Infectious Diseases**

- No CSF penetration
- Indications:
  - Treatment of susceptible bacteria if penicillin allergy
  - Atypical pneumonia (eg Mycoplasma, Chlamydia or Legionella)
  - Campylobacter
  - Chlamydia infection in pregnant women

**Erythromycin**
- New analogues:
  - Roxithromycin (Rulide)
  - Clarithromycin (Klaricid): Treatment of MAC, especially in AIDS patients
  - Azithromycin (Zithromax): Single dose treatment for STD’s caused by Chlamydia trachomatis or N. gonorrhoeae (especially in pregnancy)

**Vancomycin**
- G+ive wonder drug – active against G+ive only
- Indications:
  - Systemic infections caused by MRSA or MRSE (Epidermidis), or infected Hickman lines in cancer patients
  - Infective Endocarditis due to Strep or Staph with penicillin allergy
  - Clostridium difficile colitis (by mouth). First line is metronidazole
- Otto and nephrotoxic
- Teicopanin: similar drug, active against some Vancomycin Resistant Enterococci (VRE)

**Rifampicin**
- Always used in combination (except meningitis prophylaxis)
- Active against M. Tb, Staph aureus, Legionella
- Indications:
  - TB (in combination)
  - Severe Staph aureus infections (eg infective endocarditis) in combination
  - Severe legionella pneumonia (in combination with erythromycin)
  - Prophylaxis against N meningitides or HIB

**Aminoglycosides**
- Active against all coliform bacilli (eg E Coli), pseudomonas, staphylococci
- Inactive against: streptococci, anaerobes
- Indications: G- sepsis, perforated appendix
- Drugs:
  - Gentamicin
  - Tobramycin: more active against pseudomonas
  - Amikacin: reserved for Gentamycin resistant bugs
  - Spectinomycin: N gonorrhoeae (penicillinase producers)
- Otto and nephrotoxic

**Cotrimoxazole**
- = Trimethoprim + Sulphamethoxazole
- Broad spectrum: Staph, Strep, many coliforms (not Pseudomonas), HIB, Pneumocystis, Brucella
- Indications: Acute infectious exacerbations of chronic bronchitis, PCP in AIDS
- Trimethoprim on its own is the standard treatment against community acquired UTI (E Coli, Klebsiella, Proteus, Strep faecalis)

**Quinolones**
- Broad spectrum oral antibiotic
- Active against: most coliforms, pseudomonas aeruginosa (main use), Staphs (including MRSE and MRSA), N gonorrhoeae, HIB, Branhamella catarrhalis (good), Salmonella, Shigella, Yersinia, Campylobacter
- Poor activity against Anaerobes, streptococci
- Can damage growth cartilage ⇒ not licensed for children
- Indications:
  - Norfloxacin: resistant UTIs
  - Ciprofloxacin: Mainly pseudomonas
Tetracyclines

- **Eg doxycycline** (once a day on full stomach), very common in treatment of STIs
- Active against Staphs, Streps, Coliforms, HIB
- Other indications:
  - Syphilis and Gonorrhoea if penicillin allergy
  - Mycoplasma pneumoniae
- Contraindications: young children, pregnancy, renal failure (except doxycycline)

Metronidazole

- = Flagyl
- Active against all anaerobes (eg B fragilis)
- Inactive against aerobes (excl Gardnerella vaginalis, causing bacterial vaginosis, where it is drug of choice)
- Active against Protozoa: Trichomonas vaginalis, Giardia lamblia

Other

- Fucidin: active against Staph Aureus, must be used in conjunction with, eg Flucloxacillin. Use in bone/joint infections
- Chloramphenicol: for infections caused by Burkholderia cepacia

Antifungals

- **Nystatin** (topical): vaginal or oral candida
- **Miconazole** (topical): Candida and dermatophytes (except scalp or nails)
- **Terbinafine** (oral) Dermatophyte infections of scalp or nails (has superseded Griseofulvin)
- **Itraconazole** (oral): Dermatophyte infections of scalp or nails, prophylaxis in Candida and Aspergillus in immunocompromised
- **Fluconazole** (Oral/IV): active against yeasts (candida, cryptococcus). Good CSF penetration (eg Cryptococcal meningitis)
- **Amphotericin B** (IV): Very good but side effects, including nephrotoxicity
- See also Antifungals, page 536

Antivirals

- **Acyclovir**: active against HSV and VZV (less active)
- **Ganciclovir**: CMV in immunocompromised patients. Bone marrow suppression → neutropenia

Vaccination

- Reference: Public Health Module Notes

Vaccination Principles

- Jenner first vaccinated using cowpox against smallpox in 1796
- Characteristics of immunity:
  - Specificity: response to specific antigen
  - Priming
  - Memory: brisk secondary response
- Results of vaccine:
  - Most stimulate serum antibodies (IgG, IgM)
  - Some stimulate IgA (eg polio, rubella)
  - A few promote cell mediated reaction (eg BCG)
- Immunity:
  - Active: by disease or vaccination
  - Passive: by antibody transfer (in-utero, breast milk, Ig)
- Types of vaccine:
  - **Live attenuated vaccine** (eg OPV, MMR, VZ, BCG): full and long lasting immunity after a single dose (except OPV which requires 3 doses)
  - Inactivated vaccines (non-infectious):
    - First dose gives a predominantly IgM response. Further doses raise IgG level (depending on potency of the vaccine, maturity of the immune system and time interval)
    - Inactivated **whole cell** bacteria or viral vaccines: IPV, Hep A, whole cell pertussis (being replaced).
    - **Modified toxins (toxoids)** eg Diphtheria, Tetanus → antibody response to toxin not infective agent
Sub-unit vaccines: eg Hep B, Hib, Pneumococcus, Influenza – the main focus of modern vaccines – conjugated vaccines with fewer side effects and easy to grow from genetically engineered yeasts etc.

Recombinant: eg HBV, HPV

Conjugated: children under 2 yrs poor response to polysaccharide vaccines – enhanced if conjugated to protein (eg Hib, pneumococcal)

Also passive immunity available from injectable IgG. Immediate protection lasting from weeks to months

• Population protection/herd immunity:
  • Immunisation is delivered to individuals and provides individual protection and benefit
  • Also provides population protection (herd immunity):
    o Some level of immunisation protects unimmunised people who would otherwise have caught it ➞ don’t need to immunise those for whom its contraindicated (eg too young or sick)
    o ↑Virulence ➞ ↑coverage necessary to get herd immunity
    o ‘Free riders’ – because they perceive costs (needles, hassle, side effects) to be greater than perceived benefits ➞ weakens herd immunity

• Efficacy and effectiveness:
  • Efficacy: Does intervention provide a specific outcome (eg an IgG response) under ideal lab circumstances
  • Effectiveness: Does it work under normal clinical circumstances
  • Apparent paradox: as coverage ↑, so does the proportion of cases that have been vaccinated (but lower absolute numbers of disease), due to vaccination failure. Can create the illusion that the vaccine is ineffective

• Vaccine failure:
  • Primary vaccine failure: inadequate physiological response to the vaccine (eg freezing or overheating of the vaccine, or poor host response)
  • Secondary vaccine failure: waning immunity

• Degrees of protection:
  • Generally provides 80 – 95% protection (BCG 50%, Influenza 70%)
  • May protect against severe disease rather than infection (eg Diphtheria)

• Immunisation coverage:
  • = proportion of a population who have completed a specific course of immunisation
  • Coverage goal = 95% of children fully immunised by 2yrs (2010: 87%; Maori = 82%, PI = 89%)
  • Historically poor coverage in Maori + PI children
  • With measles: ↑coverage ➞ ↑time between epidemics as need a pool of 130 – 150,000 measles susceptible children to sustain an epidemic. Each epidemic ➞ 50,000 kids contract measles and therefore immune in future. 10,000 unprotected kids added to the pool each year.
  • Policy measures: revise schedule to reduce the number of visits, immunisation certificates on enrolment at school/early childhood centre.
  • Evidence-based strategies to ↑coverage:
    o ↑community demand (pt-oriented)
    o ↑access to imms service (system-oriented)
    o Provider-based interventions

• National Immunisation Register (NIR):
  • Commenced 2005, important for tracking the uptake + recall of children overdue for imms + for monitoring the effectiveness of imms programme

• Safety:
  • Gold standard for clinical trials includes 3 phases:
    o Phase 1 – small numbers of people take same vaccine to assess safety
    o Phase 2 – larger numbers to cf placebo to assess safety and immune response
    o Phase 3 – large RCTs to test safety and efficacy

• Surveillance:
  • Disease surveillance: NIR, notifications, discharge and mortality database, outbreak investigations, disease modelling
  • Coverage surveillance: NIR
  • Adverse event surveillance
    o CARM = centre for adverse reactions monitoring
    o Must report all unexpected, serious, clinically significant events following vaccination
    o AEFI = adverse events following immunisation – serious reactions are rare; can be coincidental event or caused by the vaccine process (vaccine itself, error in process, anxiety related to injection process)
    o Cold-chain monitoring
**Vaccination Practice**

- Practical vaccination standards:
  - Ensure correct storage and transport: maintain the ‘cold chain’ at 2 – 8°C. Eg have dedicated fridge and check its minimum and maximum temperature daily
  - Check vaccines due for each patient: either age groups (neonates, children, adolescents, adults, elderly) or specific exposure situations (occupational, travel, post-exposure)
  - Discuss and obtain informed consent: Written consent only required for children if care giver not present
  - Check contra-indications
  - Administer vaccine
  - Manage adverse reactions:
    - Observe for 20 minutes afterwards
    - Local or systemic reactions (fever, rash, joint pains): symptoms of immune activation. Offer Paracetamol. Especially whole cell pertussis. MMR may be followed about 7 – 10 days later by a 2 – 3 day fever and rash (but the vaccine is not infectious)
    - Anaphylaxis: Distinguish from fainting (which is common). Treatment: ABC, Adrenaline 1:1000 IM injection, 0.01 ml/kg, O2
    - Report to centre for Adverse Reaction Monitoring if serious (includes persistent screaming > 3 hours and > 5 cm swelling at injection site), but also convulsions, meningitis within 30 days
  - Manage records: practice notes, HBL claim record and immunisation certificate for parents

- Anti-immunisation views:
  - Risks outweigh benefits: some diseases now rare and specific vaccines have serious side effects
  - Alternative health views: disease part of growing up (so was death!) and natural infection develops immune system
  - Plus a variety of beliefs/values that will be hard to shift
  - Main reasons for non-immunisation is ‘passive rejecters’ – don’t get around to it

- **Risks of the MMR vaccine** (courtesy www.immune.org.nz):
  - Local injection site reactions are uncommon
  - The most common reaction (but still uncommon) is mild rash and fever (< 5 %)
  - Aseptic meningitis from the mumps component (1 per 100,000)
  - Encephalitis (1 per million) (much less risk than contracting this from the virus itself)
  - Anaphylaxis (<1 per million)

- FAQs re vaccines:
  - Does MMR vaccine cause mumps?
    - There has been one poorly documented case report of transmission of mumps vaccine strain from a vaccine that is no longer in production.
  - Can the MMR vaccine cause autism?
    - NO. There is no evidence that the MMR vaccine causes autism, Crohns disease or ADHD, or any other neurological or behavioural disorders.
  - Does the MMR vaccine contain thiomersal (or mercury)?
    - No.

- Contraindications:
  - Acute illness or fever > 38°C: defer vaccine. Otherwise will blame the illness on the vaccine!
  - Living with an immune suppressed person: use IPV rather than OPV
  - Reaction to previous dose: encephalopathy with 7 days of DTP vaccines or immediate severe allergic reaction. If true anaphylaxis seek specialist advice
  - Immunosuppression: don’t give live vaccine. Likely to have reduced response to inactivated vaccines
  - Pregnancy: theoretical risk from live virus vaccines
  - If in doubt, refer to a paediatrician

- False contraindications:
  - Mild illness, URTI, fever < 38.5°C
  - Asthma, hay fever, eczema
  - Prematurity and low birth weight in an otherwise healthy child – these especially need vaccination
  - Previous clinical history of illness: no harm done from vaccinating and many clinically diagnosed cases of an illness are in fact something else
  - On antibiotics, inhaled or low dose steroids
  - Stable neurological conditions (cerebral palsy, Down)

- Common side-effects:
  - Local inflammation
  - Mild fever
Infectious Diseases

- Restlessness/crying
- Rash (1-2/100 with MMR)

- Uncommon side-effects:
  - Brachial neuritis (tetanus; 1-2/200,000)
  - Encephalitis (MMR; 1/1,000,000)
  - Self-limiting thrombocytopenia (MMR; 1/30,000)
  - Guillain-Barre syndrome (Influenza; 1/1,000,000)

Immunisation Schedule

- Current Immunisation Schedule as at March 2011:
  - Covers Hep B, Diphtheria (child dose = D, adult dose = d – smaller), Tetanus, acellular Pertussis, Polio (now all intravenous = IPV, not oral), Hib, Measles, Mumps, Rubella

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>6 weeks</th>
<th>3 months</th>
<th>5 months</th>
<th>15 months</th>
<th>4 years</th>
<th>11 years</th>
<th>12 years –</th>
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<td>✓</td>
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</tbody>
</table>

- For unimmunised adults:
  - o Give jabs over same timeframe
  - o Don’t need HIB, don’t give paediatric dose of diphtheria (too big) and more inclined to use IPV

- Additional vaccination in specific age groups:
  - Neonates:
    - o Babies of HBsAg +ive mothers: Hepatitis B immune globulin (HBIG) and vaccine at birth, vaccine at 6 weeks, 3 months and 5 months. Also offer vaccination to household and sexual contacts.
    - o BCG if possible Tb exposure
  - Women of child bearing age who are susceptible to Rubella should be offered MMR
  - Adults: Td (after injury and at 45 and 65 – used to be 10 yearly) + annual influenza
  - Elderly: annual influenza + pneumococcal (5 yearly)

- Specific exposure situations:
  - Splenectomy: Pneumococcal vaccine
  - Occupational: Health care workers (eg Hep B) or HAV to food workers
  - Travel: See Travel Medicine, page 825

- Future Developments:
  - Inclusion of Varicella Zoster and pneumococcal for children
  - Research into Group B meningococcal (currently 10 year epidemic, 250 cases per year), Rotavirus and RSV, non-infectious diseases including cancer

Vaccine Preventable Diseases

- Vaccine preventable disease in NZ:
  - VPD continues to occur at higher rates in NZ than other developed countries
  - Mostly due to pertussis and to a lesser extent, measles

- Hepatitis B:
  - See Hepatitis B, page 283
  - Yeast derived subunit vaccine
  - Babies of HBV mothers receive vaccination and HB Ig at birth

- Diphtheria:
  - Corynebacterium diphtheriae → respiratory and cutaneous infection (grey membrane on throat).
  - Exotoxin can cause cardiac toxicity and ascending paralysis.
  - Spread by nasal droplets
  - 1 imported case in last 20 years. Till 1945 killed 100 babies a year.
  - Vaccine: inactivated diphtheria toxoid, boosters every 10 years. > 80% efficacy

- Tetanus:
  - Clostridium tetani from soil and animal faeces → muscular rigidity due to neuron specific toxin, 10% mortality
  - 3 notifications per year (old ladies in the garden). Common in environment ⇒ no herd immunity
- Vaccine: Inactivated toxoid, boosters every 10 years, 100% efficacy
- Pertussis:
  - See Pertussis, page 942
  - Acellular vaccine
- Polio:
  - Enterovirus spread by faeces and saliva
  - Presentation:
    - Usually asymptomatic or mild (fever, headache, nausea, vomiting)
    - Only 1% of infected get severe clinical disease: muscle pain, neck and back stiffness → flaccid paralysis
  - Last wild virus infection in 1962. Occasional imported and vaccine associated cases
  - Vaccine:
    - Live oral polio (OPV) > 90% protection after 3 doses. < 1% of recipients develop diarrhoea, headache or muscle pains. 1 in 2.5 million recipients or close contacts develop paralysis (more common in immunosuppressed) = Vaccine Associated Polio Paralysis (VAPP)
    - Inactivated polio vaccine (IPV) for immunocompromised (will be used more widely when it can be combined with other jabs)
- Haemophilus influenzae type B (Hib):
  - See Epiglottitis, page 941
  - >90% reduction in Hib since vaccine introduced
  - Subunit vaccine – polysaccharide conjugated to protein carrier
- Measles:
  - See Measles, page 951
  - Live attenuated vaccine
- Mumps:
  - See Mumps, page 951
  - Live attenuated vaccine
- Rubella:
  - Togavirus spread by nasal droplets
  - Presentation:
    - Incubation 2 – 3 weeks
    - Fever, headache, mild conjunctivitis, erythematous maculo-papular rash, lymphadenopathy (especially posterior triangle), arthritis, arthralgia
    - 50% develop the rash and lymphadenopathy
    - 50% of adolescents and adults have arthralgia or even frank arthritis
    - 1 in 5,000 have encephalitis
  - Complications:
    - Congenital rubella syndrome: 90% of embryos of mothers infected in 1st trimester will abort or have major abnormalities (severely retarded, seizures, deafness, cardiac defects). Frequent problems after birth
    - Rate of congenital rubella is 5 times the US rate
  - ~ 60 notifications per annum (1600 in 1995)
  - Vaccine:
    - Live attenuated vaccine
    - 98% protective
    - To protect the unborn child only – relies on herd immunity. Need to vaccinate guys as well otherwise they will maintain a population reservoir which women with vaccine failure will catch
    - 5% of adolescents and adults have arthralgia and 1% have non-infectious rash
    - Contra-indicated in pregnancy and immunosuppressed
- Influenza:
  - Virus types A (H3N2 and H1N1) and B
  - Causes: fever, rigors, headache, myalgia, protraction. Estimated 400 deaths per annum.
  - Vaccine: inactivated subunit vaccine for new strains (resulting from ‘antigenic drift’). 60 –90% effective.
  - Pandemics result from ‘antigenic shift’
- HPV:
  - Gardasil = recombinant quadrivalent HPV vaccine (Types 6, 11, 16, 18)
  - Highly effective against HPV 16 + 18 (~70% of cervical ca) + 6 + 11 (90% of genital warts)
- Tb: BCG:
  - See Mycobacteria, page 817
- **Neonatal BCG offered to babies likely to be exposed to TB** (high incidence countries, previous or current contacts with TB)

- **Pneumococcal Disease:**
  - See Streptococcus Pneumoniae, page 815
  - *S pneumoniae* causes invasive infections including **bacteraemia + meningitis + URTI**
  - Conjugate vaccine 7-valent (against 7 serotypes)

- **Varicella Zoster:** See Infectious Diseases, page 819
Generally, specific drugs are covered in the relevant systems chapter

Specific topics elsewhere:
- Antibiotics in infectious diseases, see Antibiotic Treatment, page 830
- Anticoagulant Treatment, page 103
- Antidepressant and Mood Stabilising Medication, page 713

Pharmacokinetics
- “What the body does to the drug”
- Deals with time course of the drug in the body:
  - Absorption: rate and amount absorbed
  - Distribution: amount in the body/volume of distribution
  - Metabolism
  - Elimination = Clearance: rate of metabolic and renal elimination
- Drug concentration usually plotted as plasma concentration versus time

Variability of Drug Response
- Disease, patient and doctor specific factors leading to the prescribing decision
- Absorption: formulation, GI motility, polypharmacy (eg Grapefruit juice)
- Distribution (ie Vd)
- Plasma protein binding (generally not important unless highly bound and low Vd)
- Metabolism: age, genetic factors, enzyme induction and inhibition, first pass metabolism, dose-dependent metabolism, active or toxic drug metabolites, biliary excretion, renal elimination
- Tissue Sensitivity

Volume of Distribution (Vd)
- = volume into which the drug appears to be uniformly distributed with a concentration equal to that of plasma
- Relates the amount of drug in the total body relative to that in the plasma. Explains where drug goes – not what it does. In one compartment model:
  - Vd = dose/plasma concentration L/kg, or
  - Amount in body = Vd * conc
  - Vd = Cl/Ke
- Examples:
  - Gentamycin has an apparent Vd of extracellular H2O
  - Digoxin has a Vd much larger than physical volume of body
  - Warfarin has a much smaller Vd than expected
- Use Vd to calculate loading dose: LD = Vd * target conc
- Vd is altered in cardiac, liver and renal disease and in obesity
- For obese patients, use total body weight for lipid soluble drugs and ideal weight for water-soluble

Vd Key Points
- Vd is the constant relating the amount of drug in the body to the plasma concentration
- Its major physiological determinant is the ratio of the strength of binding to plasma proteins and tissue binding
- It is used to calculate loading dose
- The rate of distribution from or to the site of action can be the determinant of the onset or offset of drug effects

Clearance (Cl)
- = Elimination
- Clearance of drug corresponds to the volume of plasma that appears to be cleared of its drug in unit time e.g. ml/s/min, l/hr
- Represents the size of the plug hole, rate of elimination (= rate of clearance) is the flow through the plug hole
- Depends on rate at which drug is transported to the organ of elimination and the efficiency of the eliminating organ in removing the drug
- Clearance = rate of elimination/drug concentration (as long as not saturable elimination, eg phenytoin, alcohol)
- Clearance can be:
Concentration dependent/ Capacity limited: saturable metabolic pathway (eg phenytoin)
Flow-dependent: organ elimination rate = concentration * flow * extraction ratio (fraction cleared on each pass through the organ). Eg will be eliminated on 1st pass \( \Rightarrow \) elimination dependent on blood flow. If Heart failure \( \Rightarrow \) vasodilation to maintain blood flow \( \Rightarrow \) liver flow \( \Rightarrow \) elimination (eg lignocaine, propranolol). Total body clearance can’t exceed cardiac output (5 l/min)
- Clearance and Volume of Distribution are independent of each other, but \( T\frac{1}{2} \) is dependent on both
- Maintenance Dose = clearance * desired concentration
- Compartments:
  - One or multi compartment models
  - \( Ka = \) absorption into compartment
  - \( Ke = \) elimination from compartment

Linear kinetics
- **First order kinetics**: rate of transport or elimination proportional to drug concentration in the compartment
- **Zero order kinetics**: elimination has maximum value \( \rightarrow \) rate is non-linear and it’s a capacity limited process. Eg alcohol is metabolised at 10 ml/hr. Beyond this the enzyme metabolism is swamped. So if dose rate is greater than clearance rate, then a small increase in dose rate leads to a dramatic increase in plasma concentration (ie accumulation)

Michaelis-Menten kinetics
- For a drug that undergoes zero-order elimination, when the concentration is low enough, elimination no longer occurs at its maximum rate (V max) but at a rate dependent on but not proportional to the plasma concentration. As the concentration reaches \( \frac{1}{2} \) the maximum rate (km), first order elimination occurs
- So, elimination will increase with \( \uparrow \) dose, but not proportional to the dose
- Zero-order kinetics will be approached \( \Rightarrow \) risk of accumulation
- Issue for any drug having zero-order kinetics within its therapeutic range
  - E.g. salicylic acid (especially in overdose), phenytoin, alcohol

Half Life (\( T\frac{1}{2} \))
- Time for drug concentration to decline by half \( \Rightarrow \) influences dosing interval
- Is dependent on clearance and volume of distribution:
  \[ Vd = T\frac{1}{2} \times \text{clearance} / 0.693 \]
- Rate at which drug leaves the body is dependent on Cl & Vd. In one compartment model:
- \( Ke = Cl/Vd \)
- = Measure of how the whole body handles the drug – how quickly it gets out
- But it doesn’t work in practice...
  - For slowly excreted drugs, 5 * \( T\frac{1}{2} \) and it will be eliminated for practical purposes
  - But for anaesthetic drugs that you want to switch on and off quickly the therapeutic window is often in the redistribution phase – not the elimination phase. Need a more complex model where the drug redistributes to (then from) slow and fast compartments, as well as being excreted from blood \( \Rightarrow \) context sensitive half-life. If drug is over infused, it builds up in other compartments and then takes a long time to wash out. So give a reducing amount over the duration of infusion as other compartments get saturated and stop ‘sucking it out’ of blood

Steady State Concentration
- Amount of drug absorbed = amount eliminated
- Takes 5 half lives to reach 97% of steady state, if each new dose given at half life spacings
- The shorter the \( T\frac{1}{2} \), the sooner theCss will be reached (steady state concentration)
- The shorter the \( T\frac{1}{2} \), the greater the plasma concentration will fluctuate between doses
- If \( T\frac{1}{2} \) is prolonged, dose should be reduced or dosage interval increased
- \( Css = (F \times D) / (Cl \times T) \) where \( F = \) bioavailability, \( D = \) dose, \( Cl = \) clearance and \( T = \) dosage interval

\[
As Cl = (Vd \times 0.693) / T\frac{1}{2}, \ then
\]

\[
Css = (F \times D \times T\frac{1}{2}) / (0.693 \times Vd \times T)
\]

Bioavailability (\( F \))
- = Fraction of drug that reaches the systemic circulation
- \( F = \) AUC (Area under curve) after an oral dose/AUC after IV dose
Absorption

3 routes:
- Passive diffusion:
  - Most important
  - Net transfer depends on concentration gradient and lipid:water partition co-efficient
  - Lipid soluble drugs absorbed more quickly
  - Non-ionised drugs absorbed quicker (more lipid soluble)
  - Absorbed along whole GI tract: basis for slow release preparations
- Active transport: highly specific – usually for transporting naturally occurring substances (e.g. amino acids)
- Filtration through pores: absorbed via paracellular route in small intestine. E.g. frusemide, atenolol, digoxin

Factors affecting oral absorption:
- Formulation: affects solubility and bioavailability. Presence of other drugs (e.g. Fe, Ca)
- Gastric emptying: ↓emptying →↓absorption rate
- Food: may slow gastric emptying, alter ionisation, decrease first pass metabolism. Affects different drugs differently

Alternative sites of absorption:
- Plasma concentration rises quickest for iv > im > sc (absorption similar to im but ↓blood supply)
- Intramuscular injection: affected by lipid solubility and blood flow
- Rectal absorption: avoids GI irritation, good in vomiting, doesn’t avoid 1st pass metabolism
- Pulmonary absorption: small particle size
- Absorption from mouth: nitrates/buprenorphine
- Absorption from nose: desmopressin & other peptides
- Percutaneous: zero order absorption – for nicotine, nitrates, scopolamine

Distribution

Drug can be bound or unbound in both plasma and tissues
- Drugs bind to albumin (acidic drugs), α1 acid glycoprotein (basic drugs), tissue proteins
- Lipid solubility:
  - Penetrate lipid membranes easily (e.g. placenta, blood/brain barrier)
  - Rapidly distributed, dissolves in fat →plasma levels fall quickly, and large volume of distribution
  - Is non-polar or unionised
- Water soluble:
  - Excreted by kidneys (some also metabolised by liver)
  - Redistributes in water, smaller volume of distribution
- Ionisation of acid or base:
  - Depends on pH and pKa (the pH at which 50% of drug is ionised)
  - As pH ↑ (becomes more alkaline) an acid becomes more ionised, and a base less ionised
  - Only unionised drug will diffuse across lipid membrane

Metabolism

Water soluble: excreted unchanged through the kidney
- Lipid soluble: Can’t be excreted by kidneys (reabsorbed straight away) so conjugated or metabolised →water soluble →excretion
- Metabolism:
  - May result in activation of a pro-drug, active metabolites or inactive metabolites
  - Phase 1: oxidation, reduction, hydrolysis
  - Phase 2: conjugation, eg methylation, acetylation, glutamine, etc
  - Occurs in mainly in the liver, also in the lung, kidney, blood, small intestine, gut bacteria
- 1st pass metabolism: high > 70%, e.g. lignocaine, GTN (no use taking them orally)
- Examples of drug metabolic reactions:

<table>
<thead>
<tr>
<th>Reaction</th>
<th>Substrates</th>
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<tbody>
<tr>
<td>Cytochrome P450 (oxidation)</td>
<td>Many drugs, carcinogens</td>
</tr>
<tr>
<td>Oxidation of alcohols/aldehydes</td>
<td>Ethanol</td>
</tr>
<tr>
<td>Oxidation of purines</td>
<td>Azathioprine</td>
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<tr>
<td>Oxidation by MAO</td>
<td>Tyramine, catecholamines</td>
</tr>
<tr>
<td>Hydrolysis</td>
<td>Suxamethonium</td>
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</tbody>
</table>
Acetylation  
Glucuronidation  
Dapsone  
Phenols, morphine

- Factors affecting metabolism: genetics, ethnicity, age, gender, pregnancy, liver disease, time of day, environment, diet, malnutrition, alcohol, other drugs

**Excretion of Drugs**

- **Excretion:**
  - Major routes renal, hepatobiliary, pulmonary
  - Minor routes: saliva, breast milk, tears
- **Renal:**
  - Few are excreted unchanged. Lipid soluble undergo tubular reabsorption
  - Only unbound particles excreted ⇒ if highly bound then slower excretion
  - Some are secreted by active tubular secretion e.g. penicillin, digoxin
  - Urine pH: alkaline urine →↑ weak acid excretion (eg salicylates) and visa versa
- **Biliary:**
  - Polar drugs likely to be excreted in bile, e.g. rifampicin, ampicillin
  - Some drugs undergo entero-hepatic circulation, e.g. oestrogens

**Drugs and the Kidney**

**Principles**

- 1. Identify pre-existing renal impairment (ie GFR <50 → halve dose)
- 2. Identify dehydration
- 3. Identify toxic drug combinations (eg diltiazem + statin)
- 4. Monitor renal function
- 5. Beware of elderly

**Examples of Renal Drug Toxicity**

- 1. Haemodynamic affect:
  - Acute RF: NSAIDs, ACEi, diuretics
  - Fluid retention: NSAIDs, vasodilators, steroids
- 2. Systemic allergic (hypersensitivity) reaction
  - DRESS/Drug hypersensitivity syndrome (Drug reaction with eosinophilia + systemic symptoms): severe, idiosyncratic multi-system reaction defined by the clinical triad of fever, rash and internal organ involvement (e.g. hepatitis, myocarditis, nephritis or pneumonitis), which may occur 1 - 8 weeks after medicine exposure
  - Acute interstitial nephritis: anti-convulsants, β-lactam Abs + allopurinol
- 3. Tubular injury + interstitial nephritis: lithium, aminoglycosides, omeprazole

**Renal Drug Clearance**

- Renal blood flow ↓ as we age
- Renal drug clearance = fraction of drug excreted unchanged (ie not metabolised)
- Any drug with > 70% excretion unchanged may accumulate in renal impairment
- Active drug metabolites also accumulate in renal impairment (eg morphine 3 + 6 glucuronides; nordiazepam)

**Drugs Requiring Dose Adjustment in Renal Impairment**

- Morphine, tramadol, LMWH, allopurinol, digoxin, metformin, gentamicin, lithium, fluconazole, sotalol/atenolol, methotrexate, bezafibrate, simvastatin, ciprofloxacin, ACEi (NB Cr ↑ when first starting as GFR ↓), diazepam

**Bad Drug Combos**

- NSAIDs:
  - → ↓ PG + therefore ↓ GFR
  - There is no safe dose or safe NSAID in the elderly (even COX-II)
  - NSAID risk factors:
    - Renal impairment
    - ACEi (leads to efferent arteriole dilatation), Frusemide (NSAIDs + ACEi + diuretics = “triple whammy” = BAD)
    - Elderly, dehydration, post-op, systemic infection, contrast media
Lithium:
- Can induce nephrogenic DI, also see chronic Li-induced interstitial nephritis
- Need to monitor serum Li (12hrs post dose; standard serum Li = 0.8 – 1.3mmol/L)
- ↓ clearance with NSAIDs, diuretics, ACEi → severe toxicity + RF

Aminoglycoside toxicity eg gentamicin:
- Acute non-oliguric RF 1-5 days after a dose → accumulates in proximal tubule; less likely with a single 24hr dose
- Can lead to RF if pre-existing renal impairment or in conjunction with other nephrotoxins eg Li, NSAIDs

Serum Creatinine & Renal Function
- GFR must ↓ by 50% before Cr ↑ above normal range
- Cr is therefore a poor predictor of renal function but a useful indicator of changing renal fx
- NB. Cr depends on age, gender, muscle mass, diet
- NB. Trimethoprim, cimetidine, fibrates ↑ Cr by ↓ tubular secretion (ie interfere with the Cr test)
- Cockcroft-Gault formula:140 – age x LBW (x 0.85 if female) / Cr x 50
- eGFR is not proven in drug dose prediction in those with impaired renal fx

Renal Drug Toxicity Golden Rules
- 1. Check drug fraction excreted unchanged: if >75%, then: calculate GFR (using CG) + halve dose or do not prescribe
- 2. If >80 years old, assume 50-60% ↓ in GFR ie they are at risk (consider halving dose)
- 3. Identify other risk factors eg hypotension, dehydration
- 4. If in doubt → halve dose
- 5. Monitor changes in renal function

Inter-individual Differences
- There are large inter-individual differences in the capacity to metabolise drugs, due to:

Genetic factors
- Characteristics can be autosomal dominant, autosomal recessive, sex-linked, etc
- Either polygenic or monogenic (present either as polymorphisms – more than 1% - or as rare phenotypes <1 %)
- Cytochrome P450: a group of enzymes located on the endoplasmic reticulum. Divided into families and sub-families
- 3 polymorphisms have been well defined:
  - Acetylation: enzyme: n-acetyl-transferase 2. Leads to slow and fast acetylators. 90% of Japanese are fast acetylators (autosomal dominant) compared with 55 – 60% of Europeans who are slow acetylators. Affects eg isoniazid and caffeine
  - Oxidation: poor metabolisers are deficient in enzyme CYP2D6, affects 4 hydroxylation pathway. Covers lots of drugs – TCAs, antipsychotics (e.g. haloperidol), β blockers (e.g. metoprolol). ↑Risk of accumulation. Rest of population are extensive metabolisers
  - Oxidation (CYP2C19): affects diazepam, omeprazole, others

Disease
- Absorption in disease:
  - Can affect gastric emptying rate: affects rate not extent
  - ↓Absorption rate in migraine, acute MI, labour, malabsorption syndromes (variable effect)
  - Low cardiac output → ↓IM absorption
- Distribution:
  - For drugs with low Vd and high binding (only), changes in protein binding: e.g. ↓albumin in hepatic disease, nephrotic syndrome, ↑α1AGP in RA, Crohn’s. Amount of free drug is the same. But normally total plasma concentration measured (and this will be reduced) → danger of overdose
  - Cardiac disease → altered distribution (eg due to reduced gut flow → poor absorption, ↓renal and hepatic perfusion → ↓clearance)
  - Obesity → increased Vd for lipophilic drugs
- Metabolism:
  - Most biotransformation occurs in liver. For some drugs, extraction depends on blood flow (where extraction ratio tends to 1)
- Liver disease →↓capacity of metabolising enzymes (eg ↑warfarin, phenytoin) and possibly shunting of blood around liver (affects drugs with high first pass metabolism)
- Thyroid diseases →↑or ↓metabolism
- Diabetes mellitus →fatty liver →change in metabolism
- Low clearance with high (>90%) degree of protein binding – generally ↓clearance
- Low clearance, low binding (e.g. paracetamol) – variable but can be ↓clearance

**Excretion:**
- For many drugs, reduction in clearance →↑half-life
- Adjust dose using creatinine clearance formula: Cockcroft Gault Formula (a prediction which saves doing a 24 hr urine):

\[
\text{Cr.Cl ml/sec} = \frac{(140 - \text{age}) \times \text{wt(kg)}}{50,000 \times \text{serum Cr (mmol/L)}}
\]

- Normal is 1.5 mls/sec. For mls/min, replace 50,000 by 815
- For females, multiply by 0.85
- Important for eg digoxin and aminoglycosides which are excreted unchanged. If elderly →↓excretion →↑plasma concentration
- Dose rate for a drug excreted 100% by the kidney (e.g. antibiotics) is:

\[
\text{DR} = \frac{(\text{Cr.Cl} / 1.5) \times \text{normal DR}}{\text{normal DR}}
\]

- This dose requires adjustment when not all the drug is excreted unchanged.

\[
\text{DR} = (1 - \text{fu}) + \text{fu} \times \text{Cr.Cl} / 1.5 \times \text{DR}
\]

**Liver disease: arbitrary rule:**
- ↓Dose by 50% for high clearance drugs (high 1st pass metabolism)
- ↓Dose by 25% for low clearance drugs (enzyme capacity only)

**Dosing in CV disease:**
- ↓Vd (vasoconstriction)
- ↓Renal flow →↓excretion
- ↓Mesenteric blood flow →↓absorption of frusemide

**Age**
- Epidemiology:
  - Elderly > 75 years
  - More likely to have multiple drugs (median per person over 65 is 3), 90% have one drug
  - 2 * incidence of adverse reactions (20 – 25%). ↑ in proportion to number of drugs
  - 30% of elderly admissions due to drug problems
- Absorption: little difference compared with young, except if other drugs interfere (eg ↓transit time)
- Distribution:
  - ↓Lean body weight. ↑Vd of fat soluble drugs (eg diazepam), possible problems with accumulation
  - May be ↑adipose compared with lean body tissue. Eg smaller loading dose of drugs with low Vd (eg digoxin and cimetidine)
  - Protein binding: Albumin declines with age →significant change only in tightly bound drugs (ie small Vd, eg phenytoin) or zero order elimination (eg warfarin)
- Metabolism: Hepatic clearance:
  - Liver has significant residual capacity so not much decline with age, especially given ↓lean body weight
  - But significant (50%) reduction in liver blood flow, so significant reduction in metabolism of 1st pass metabolism (eg propranolol) or capacity limited metabolism (phenytoin or theophylline). Problem if narrow TI
  - ↓Hepatic blood flow and hepatic mass
  - ↓First pass clearance: eg major tranquillisers, TCAs, antiarrhythmics
- Excretion:
  - Decline in renal function. ↓GRF by 50% (although wider spread of function →↑inter-individual variability). Problems with digoxin, lithium and gentamycin
- ↓Renal clearance (see creatinine clearance above). However, ↑variability in serum creatinine (eg proportional to lean body mass) →less reliable estimate of renal function
- Delayed action of renal acting drugs (eg diuretics)
- Tolerate renal side effects less well (eg NSAIDs)
- Need to adjust dose of: digoxin, cimetidine, ACE inhibitors, NSAID, Diazepam, aminoglycosides. Dose adjustment factor = \( \frac{1}{F (Fk - 1) + 1} \)
  - \( F \) = fraction of drug normally excreted unchanged
  - \( Kf \) = relative renal function of a patient = actual or derived Cr clearance \[ \text{use Cockcroft & Gault formula} \]
  - normal Cr clearance
- Principles of geriatric prescribing:
  - Full drug history
  - Reasonable therapeutic objective (ie forget management of long term risk factors if they’re 95)
  - Individual dose titration – beware ‘usual’ doses
  - Lowest possible dose
  - Simplest possible regime
  - Regular review of drug therapy

**Children**
- Clearance: functional maturity reached from 6 months to 1 year
- Vd: have more body water and less fat ⇒↑dose for H2O soluble and ↓for lipid soluble
- Guidelines:
  - If < 6 months: consult a paediatrician
  - 6 months to 1 year: use a nomogram for surface area. Estimates Dose = \([\text{wt (kg)} ^ 2/1.7 \text{ m} ^ 2] * \text{adult dose}\)

**Other Factors**
- Sex: Women clear BZDs faster, NSAIDs slower
- Pregnancy: more rapid clearance of oxidised drugs due to ↑liver flow. See Pharmacology of Pregnancy and Breast Feeding, page 852
- Obesity: Use ideal body weight if actual > 30% above ideal for drugs with low Vd
- Environment
- Diet: eg smoking, grapefruit juice, malnutrition, alcohol

**Controlled Release Formulations**
- Aim is to prolong short acting drugs, to reduce daily dose frequency
- Also a drug company ploy: introduce slow release formulation to extent patent
- Good points:
  - Increased compliance
  - ↓Side effects (but probably also decreased therapeutic effects)
- But:
  - Often more variability in plasma fluctuation. Eg Slower absorption + variations in 1st pass metabolism ⇒wider variation in clinical effect
  - Effect of variation in gastric emptying reduced
  - Adhesive patches cause skin reaction in 30%
  - Fixed dose: harder to titrate
  - ↑Cost

**Pharmacodynamics**
- “What the drug does to the body”
- =Study of drug/receptor interactions. Dimensions of time, concentration and effect (ie response intensity)
- Types of ‘receptors’ for drugs: enzymes, ion channels, receptors, carrier molecules. Most common targets are transmembrane receptors linked to G proteins
- Receptor interactions:
  - Agonists:
    - Bind and produce a full effect
- Partial agonists: bind and produce sub-maximal effect (ie lower dose-response curve)
- Inverse agonists: bind and have opposite effect to that of agonists
- Non-competitive agonists cannot be displaced
- Competitive agonists reversibly interact, can be reversed by an antagonist.

- Antagonists: bind and produce no effect.
  - Competitive: maximal response is still possible with an ↑ in dose of endogenous agonist (ie dose response curve shifts right). Eg ↑ adrenaline can over-ride β-blockers
  - Non-competitive: don’t allow a maximal response regardless (ie lower-dose response curve).
    Progressively lowers maximal response of agonist

- Agonist antagonist: has an agonist effect at one subtype of receptor and an antagonist effect at another
- Specificity = effect produced by interaction with a single receptor
- $K_a = \text{concentration required to occupy 50\% of receptor sites at equilibrium}$

- Up-regulation/down-regulation: a very common response to an antagonist/agonist. Watch for rebound when it stops

- Dose response curves:
  - Relationship between plasma concentration and drug’s effect
  - Efficacy: maximal ceiling of effect, regardless of dose. Effectiveness of drug once bound to a receptor
  - Potency: quantity required for maximal effect
  - Affinity: if a drug has lower affinity, it can still produce a maximal effect but will require a larger dose (ie pushes dose response curve to the right). Higher affinity $\Rightarrow$ higher potency.
  - Individuals vary considerably in the efficacy, slope (difference between small and maximal effect) and potency of drugs. Eg with ↑ age have ↓ receptors. So dependent on age, disease, environment, etc

- Concentration vs. response:
  - $EC_{50} = \text{drug concentration at 50\% of maximal effect (describes affinity of the drug for the receptor)}$
  - Therapeutic index is the ratio of the Adverse Effect $EC_{50}$ to the Therapeutic Effect $EC_{50}$
  - Rise in response intensity is normally less than proportional to drug concentration. It reaches a point where further increases in concentration have no further effect (but may prolong effect – but to double time may need 10 fold ↑ in concentration). Need to balance against ↑ adverse effects
  - Usually presented as Response vs log drug concentration – this linearises the central part of the curve
  - Combining with another drug with a synergistic effect changes the dose response – often allows ↓dose (eg ACE + diuretic)

- Dosing:
  - ‘Usual dose’: set at maximum profit for minimum toxicity. Always half New Ethicals starting dose!
  - Objective in chronic disease management: use the lowest possible daily dose of the appropriate drug. Building up slowly, but this is usually impractical in general practice (requires lots of visits until therapeutic effect satisfactory, so back titration used)
  - Loading dose dependent on volume of distribution
  - Infusion rate dependent on clearance
  - Constant infusion $\rightarrow$ gradually rising Cp. Bolus $\rightarrow$ instantly high Cp, then declining. Both $\rightarrow$ stable Cp

- Factors in Failure to respond:
  - Poor compliance: difficult dosage regimes, poor technique (eg inhalers), difficult to swallow, etc.
    Frequency critical. ↑ frequency $\rightarrow$ more forgotten. But if T½ < 24 hours, will get better overall control (avoiding peaks and troughs in Cp) with > once a day
  - Incorrect drug formulation
  - Altered drug handling due to disease state (eg impaired absorption of oral frusemide due to mucosal oedema)
  - Drug tolerance or bacterial resistance
  - Disease state too severe (eg thiazide diuretic in heart failure)
  - Toxicity may prevent attainment of the therapeutic dose

Changes with Age

- Blunted homeostatic reserve:
  - ↑Risk of postural hypotension with antihypertensives, neuroleptics, TCAs
  - Drugs have greater effect on postural control (eg sedatives)
  - Changes in neurotransmitters $\rightarrow$ ↑ risk of drug induced confusion

- Receptor changes. Eg ↓response to β agonists and antagonists
Pharmacology of Pregnancy and Breast Feeding

Pregnancy

- Risks are often unknown – although usually small
- Rule of thumb: DON’T use drugs in pregnancy
- Most drug induced abnormalities are subtle → don’t make link with drug

Effects of harmful drugs:
- Gametes → sterility
- Blastocyst (first 2/40) → death
- Embryo (3-8/40) → death or major abnormality (heart, limbs, brain, eye form during embryogenesis
- Fetus → functional abnormality

Teratogens: exogenous agents that have the ability to produce congenital malformations or functional defects during embryonic or fetal development

- Criteria for proof of teratogenicity: proven exposure to agent at critical times, epi studies, should make biological sense etc etc
- Difficult to ID also due to frequency of effects: eg thalidomide (20%), retinoids (38%), valproate (1-2%)
- Factors affecting dysmorphogenesis:
  - Critical dose
  - Timing of dose during development
  - Fetal susceptibility
  - Fetal environment (eg already at risk due to diabetes, smoking etc)
  - Placental drug transfer: all drugs get across but in widely varying amounts. Lipid drugs with polar metabolites are bad news (drug crosses in, but metabolites can’t get out, eg diazepam)

Testing safety:
- Validity of drug models
- RCTs assess efficacy not safety
- Can only pick them up with post-market monitoring and careful evaluation in clinical practice, case reports are the most common, also case-control etc

- Effects of pregnancy on drug handling:
  - 30 – 50% delay in gastric emptying
  - Minimal effect on absorption
  - Albumin reduced by 25% by 15 weeks
  - Altered Vd – plasma concentration
  - Excretion - ↑ clearance
  - Plasma volume increases by 50%
  - Total body water ↑ by 8 litres
  - 50% ↑ in renal blood flow

- Drug transfer by passive diffusion, facilitated diffusion or active transfer
- Anticonvulsants:
  - Seizures endanger mother and fetus → ↑ risk of stillbirth, microcephaly, seizures and mental retardation
  - ALL anticonvulsants ↑ malformations; carbamazepine (probably most safe) and valproate → NTDs
  - Drug levels should be monitored

- Antihypertensives:
  - Methyldopa is drug of choice
  - B-blockers generally safe
  - Hydralazine is safe but causes tachycardia
  - CCBs can delay labour
  - ACEi: should NOT be used in 2nd and 3rd trimester dur to risk of RF, oligohydramnios, growth retardation and skeletal abnormalities

- Analgesics:
  - No teratogenic effects
  - Opioids: resp depression, withdrawal in addicted mothers
  - Non-opioids: paracetamol is safe
  - NSAIDs: constriction of ductus arteriosus, oligohydramnios, necrotising enterocolitis

- Anticoagulants:
  - Heparin is safest drug as it doesn’t cross placenta
  - Warfarin is teratogenic and should be avoided

- Categorisation of risks of medicines prescribed in pregnancy
- A = safe drugs, used by many women
- B = drugs taken by a limited number of women without an ↑ in frequency of malformation
- C = take care, suspected of causing harmful effects, not malformations eg rifampicin, methadone
- D = cause or suspected to cause malformations or irreversible damage eg cytotoxics, vit A, nicotine
- X = do not use → high risk of permanent damage, should be avoided eg isotretinoin, misoprostol

- Fetal renal excretion:
  - Fetal kidney’s are functionally immature (Ccr = 2 – 4 mls at term – very small)
  - Renal blood flow only 5% of cardiac output (25% in adult)
  - Renal elimination not an important route of drug metabolism (baby swallows it again anyway)

- Hepatic metabolism:
  - Shunt 30 – 70% of umbilical blood flow (ductus venosus)
  - Oxygenation of the Left lobe (umbilical vein) > than right lobe (portal vein)
  - Slower metabolic rate than adult but extensive CYP450 metabolism

**Breast Feeding**

- Transfer affected by:
  - PKa: Base transfers more as pH of milk is lower than blood
  - Lipid solubility
  - Molecular weight (eg high molecular weight heparin doesn’t cross)

- Avoid:
  - Excess alcohol
  - Anticoagulants except heparin
  - Amiodarone
  - Antimalarials
  - Ginseng
  - Anti-thyroid drugs
  - Antibiotics: ciprofloxacin, chloramphenicol, tetracyclines (affect teeth and growth plates), sulphonamides and quinolones
  - β-blockers: atenolol, sotalol → bradycardia. Other antihypertensives OK
  - Diazepam
  - Lithium
  - Combined OCPs
  - Anti-metabolic agents
  - Ergot derivatives (eg anti-migraine medication)
  - ?Diuretics
  - ?SSRIs → insufficient information
  - Phenytoin
  - NSAIDs – effect breast milk production

**Adverse Drug Reactions (ADR)**

- Any noxious, unintended drug reaction that occurs at normal doses used for prophylaxis, diagnosis or therapy
- **Adverse drug event:** Includes adverse drug reactions AND the inappropriate use of medicines. An injury resulting from medical intervention related to a drug
- Responsibility of prescriber is to observe, record and report adverse drug effects and interactions
- Factors involved: age, # of drugs, renal function, hepatic function
- Includes:
  - Side effects
  - Intolerance (side effects occurring at levels normally well tolerated)
  - Anaphylaxis
  - Interactions with other drugs (e.g. pharmacokinetic reaction due to enzyme induction)
- Classification: includes mistakes (knowledge based errors) and lapses (skill based error)
- Grading them:
  - Serious: results in death, hospitalisation or persistent disability
  - Severity: intensity of reaction not seriousness of reaction (ie a severe skin reaction may not be serious)
- Incidence:
  - True incidence unknown
  - Estimated 3 – 5 % of all hospitalisations due to an ADR
  - Estimated 3 in 1000 hospital deaths due to a drug reaction
Common in elderly

Monitoring:
- Medicine Assessment Advisory Committee reviews new drugs prior to licensing
- Can be licensed for monitored use through the Intensified Medicines Monitoring Programme (IMMP). Requires reporting of all new clinical events in a patient
- Voluntary reporting to the Centre for Adverse Reactions Monitoring in Dunedin (reporting rate estimated <15%)
- Danger/WARNING Notification System with NHI number. Records potentially life-threatening reactions

Difficulties in recognising ADRs:
- May mimic a common symptom (eg headache)
- May be so bizarre that a common drug escapes suspicion
- May be a long delay (eg hepatoxic reactions)
- The ADR may be confused with the disease (eg antibiotic fever in meningitis)

Recognising an ADR: suspicion, how often does this occur without the drug (ie reference rate of the disorder), temporal sequence, what happens when drug is discontinued and/or rechallenged

Frequency of effect:
- Clinical trials are poor indicators of ADRs. Not sufficient numbers to find rare effects, so post market surveillance important
- Eg:

<table>
<thead>
<tr>
<th></th>
<th>GI bleed</th>
<th>Agranulocytosis</th>
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<tbody>
<tr>
<td>Reference Rate</td>
<td>1:100</td>
<td>1:100,000</td>
</tr>
<tr>
<td>Rate with NSAID</td>
<td>5:100</td>
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<tr>
<td>Rate Ratio</td>
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<td>5</td>
</tr>
<tr>
<td>Attributable Fraction</td>
<td>80%</td>
<td>80%</td>
</tr>
</tbody>
</table>

Determinants of ADRs
- The drug itself: rate, route, formulation, dose, PK
- The patient:
  - Age: young (immature conjugating enzymes) and elderly (↓clearance)
  - Gender: more common in women. ?Effect of sex hormones, ?less gastric acid, compounding effect of ↑health seeking behaviour  
  - Disease: diseases of heart, kidneys, liver all affect drug kinetics and dynamics. Eg, AIDS →↑risk of ADR with co-trimoxazole
  - Previous history: Previous reaction →↑risk
  - Genetic and ethnic factors, eg altered rates of metabolism
- Extrinsic factors:
  - Alcohol consumption, tobacco, pollutants
  - Multiple drug therapy: 1 – 5 drugs → 3.3% risk, 6+ drugs → 19.8% risks

Management of ADRs
- 1. Stop the drug and treat the reaction
- 2. Don’t re-challenge
- 3. Advise precautions
- 4. Maybe medic alert bracelet
- 5. Notify CARM
- 6. If dose-dependent, can ↓dose

Classification of ADRs
- Type A: dose dependent and predictable:
  - Exaggerated primary therapeutic effects. Risk is increased with ↑dose or ↓clearance. Rarely serious. Eg anticoagulants →bleeding, hypotension with antihypertensives
  - Primary drug effects that are not therapeutic. Eg β blockers →bronchospasm
- Type B: not dose dependent and unpredictable. Eg anaphylaxis to penicillins, carcinogenicity, dental discoloration from tetracyclines
- Type C: dose & time dependent
- Type D: delayed
- Type E: withdrawal
- Type F: failure of therapy
- Now includes DoTS:
Dose: dependent on the pharmacokinetics or pharmacodynamics of the drug
Time: dependent or independent
Susceptibility: eg polymorphisms, sex, age, disease

Drug Allergy
- An ADR mediated by immune mechanisms
- Recognition of an allergic drug reaction:
  - Always a delay in allergic reaction following initial exposure
  - Once established, a reaction can be precipitated by minute amounts of the drug
  - There is recurrence on re-exposure
  - The reaction doesn’t resemble the pharmacological activity of the drug
  - Symptoms suggest an allergic response
- Four main mechanisms for inducing an immunotoxic reaction:
  - Drug may be an immunogenic protein
  - Drug or metabolite may form a hapten by combining with endogenous proteins
  - Drug/metabolite may cause a reaction between a modified self-antigen and an antibody
  - Drug/metabolite may cause the synthesis of auto-antibodies, but its continued presence is not required for binding between the antibody and the antigen
- Four types of reaction (Coombs-Gel types): (See Allergy and Hypersensitivity Disorders, page 496)
  - Type I (immediate) hypersensitivity:
    - Drug or drug conjugate binds a specific IgE on the surface of basophils and mast cells → degranulation → mediator release → bronchospasm, urticaria, anaphylaxis, rash
  - Type II (cytotoxic) hypersensitivity:
    - IgG or IgM + drug-protein conjugate → complement release → complement activation → haemolysis or neutropenia or thrombocytopenia (depends on which cell surface reaction takes place)
    - Eg quinine
  - Type III (immune complex) hypersensitivity:
    - (Actually rare) protein complexes + Igs → insoluble matrices → complement activation → localised vascular damage with Serum Sickness/Antibiotic Fever (fever, joint pain, lymphadenopathy, neutropenia, glomerulonephritis)
    - Eg Presents 1 – 3 weeks after penicillin/cephalosporin/sulphonamide treatment.
  - Type IV: (delayed) hypersensitivity (cell mediated):
    - Drug-protein complex + target cell → recognised by T-lymphocyte → direct cytotoxicity/macrohage activation → fixed drug eruption, allergy to topical agents
    - Eg contact dermatitis due to chlorpromazine
- Symptoms:
  - Localised: urticaria (weals, always itch), bronchospasm, angioedema
  - Generalised: hypotension, bronchospasm, urticaria, laryngeal oedema
- Examples:
  - Haemolytic anaemia: eg levodopa, captopril (ACE inhibitor), penicillins
  - SLE: eg phenytoin, gold, procainamide (antiarrhythmic)
  - Glomerulonephritis: eg gold, drugs with sulphydril group
  - Aplastic anaemia: eg phenytoin
- Factors influencing occurrence of allergic reactions
  - Duration and the number of courses or treatment
  - Any route (although anaphylaxis more common with iv)
  - IV anaphylaxis occurs with the same frequency in the general population and atopic individuals.
  - Anaphylaxis by other routes more common in atopic individuals
  - More common in adults than children (?less exposure to drug antigens)
  - Previous history of any allergic reactions and co-existing disease states

Drug Interactions
- = Effect of one drug is increased or decreased by another
- Lots of interactions: the key is their significance
- Often caused by Polypharmacy:
  - = “Irrational concurrent use of several different drugs”
  - 6 or more drugs used in combination = 80% chance of interaction
  - Common in:
    - Multiple medical problems
o Long term care
  o “Standing orders”, sedatives, laxatives, antidiarrhoeals, cough medicine

- Guide to potential drug interactions:
  - How commonly are interacting drugs used together?
  - Does one of the drugs have a low TI? Eg probenecid reduces penicillin clearance, but who cares.
  - Erythromycin reduces theophylline clearance – critical
  - Has a potential interaction been validated in in-vivo studies?
  - Are there case reports of adverse effects?
  - Is there a reasonable mechanism for the interaction?

- Risk factors for drug interactions:
  - 1. Low volume of distribution (Vd) →↑ plasma concentration (esp if protein bound; eg warfarin)
  - 2. Predictable toxicity/narrow TI (toxicity with small changes)
  - 3. Saturable hepatic/renal elimination in therapeutic dose range
  - High protein binding (→↑↑ plasma concentration if protein binding disrupted)
  - Acidic drugs: readily displace basic drugs
  - Active renal tubular excretion (other drugs can compete for excretion pathways →↓clearance)
  - IV administration (risk of mixing drugs that shouldn’t be mixed)
  - Drug clearance is the key issue

- Pharmacokinetic mechanisms:
  - Drug Inactivation: Eg Cholestyramine (ion binding resin) binds oral anticoagulants
  - Altered absorption: Metoclopramide (↑gastric emptying) + digoxin (takes long time to breakdown in stomach) →↓absorption. Metoclopramide + paracetamol →faster absorption
  - Protein binding: Adverse reactions do not occur purely because of displacement from protein binding sites: Eg phenytoin + hypoalbuminaemia →↓binding →↑clearance →↓total concentration →↑free fraction but free concentration remains the same
  - Drug excretion: Probenecid + Penicillin – competition for limited capacity of active tubular excretion.
    Diuretics →↓Lithium clearance
  - Drug metabolism: Metabolic reactions are unpredictable and highly variable.
    o Multiple Cytochrome P450 enzyme phenotypes, each with its own selectivity for inhibitors
    (immediate effect) or inducers (takes weeks, requires transcription, etc). Eg sulphinpyrazone: inhibits tolbutamide, warfarin, and phenytoin. Induces theophylline and verapamil
    o CYP450: Mixed function oxidase system. Genetic polymorphism results in:
      - Extensive metabolisers (EM). Inhibition reactions will convert these to PMs
      - Poor metabolisers (PM). Inhibition reactions won’t affect these
      - Ultra-rapid metabolisers (eg CYP2D6). Marked differences in genetic polymorphism (eg CYP2D6 – 7 % Caucasian, 1% Asian)
    o Inhibition of CYP450 →↑risk of type A reaction to another drug metabolised by the same enzyme
    o CYP3A4 is the most abundant P450 enzyme (metabolises over half of all drugs):
      - Induced by carbamazepine, rifampicin, dexamethasone
      - Inhibited by grapefruit juice, azole antifungals, erythromycin
    o Enzyme inducers: chronic ethanol, anticonvulsants, rifampicin, isoniazid (Tb antibiotic)
    o Enzyme inhibitors: acute ethanol, ANTIBIOTICS: macrolides (eg erythromycin), metronidazole, sulphonamides, quinolones (eg ciprofloxacin), azole antifungals, cimitidine, MAOIs, SSRIs, amidarone, verapamil, omeprazole, grapefruit juice (inhibits CYP3A4)
    o Eg non-sedating anti-histamines (eg terfenadine / Teldane). Concentration dependent inhibition of K influx →prolongs action potential →↑QT interval →torsade du pois →sudden death (very rare). However, ↑Cp due to CYP450 inhibitors (eg erythromycin, cimitidine) →↑risk of sudden death

- Pharmacodynamic mechanisms:
  - = Additive or opposing effects at the same or different receptors
  - Majority of drug effects
  - Examples:
    o Combinations of agonists or antagonists at the same receptors: eg Anxiolytics (lorazepam) + hypnotic (triazolam) →↑BDZ adverse effects
    o Combinations of agonists and antagonists: eg phenothiazine + L-Dope = antagonism of anti-parkinsonian effect
    o Combinations of agonists or antagonists at different receptors: eg ethanol + benzodiazepines →↑sedation

- Pharmaceutic mechanisms: the interaction occurs prior to systemic availability
**Major Enzyme Inducers**
- Phenytoin
- Phenobarbital
- Carbamazepine
- Rifampicin
- Corticosteroids
- Others eg alcohol abuse, smoking etc
- CYP450 enzymes are inducible except CYP2D6, leads to $\uparrow$ first pass metabolism $\rightarrow$ $\uparrow$ clearance $\rightarrow$ $\downarrow$ T1/2 $\rightarrow$ $\downarrow$ steady state concentration ($\rightarrow$ around 2/52 for drug’s full affect)

**Major Enzyme Inhibitors**
- Macrolides + amiodarone
- Azole anti-fungals
- Fluoxetine
- Leads to $\downarrow$ FPM $\rightarrow$ $\downarrow$ clearance $\rightarrow$ $\uparrow$ T1/2 $\rightarrow$ higher steady state concentration $\rightarrow$ $\uparrow$ dose dependent effects

**Major Drug Interactions**
- $\alpha$-blockers + nitrates $\rightarrow$ syncope
- Ethanol + BZDs $\rightarrow$ sedation and driving impairment
- NSAID + diuretic + ACEi $\rightarrow$ renal failure
- Diltiazem + statin $\rightarrow$ rhabdomyolysis
- Morphine + BZD $\rightarrow$ respiratory failure
- SSRI + tramadol/morphine $\rightarrow$ serotonergic syndrome
- Antipsychotics + L-Dopa $\rightarrow$ loss of dopa effect
- Aminoglycosides + loop diuretics/cephalosporins $\rightarrow$ renal failure
- Lithium + ACEi $\rightarrow$ Lithium toxicity
- NSAIDs + ACEi $\rightarrow$ loss of ACEi effect
- Allopurinol + azathioprine $\rightarrow$ aplastic anaemia
- Tamoxifen + fluoxetine $\rightarrow$ loss of endoxifen effect
- Codeine + fluoxetine $\rightarrow$ loss of analgesia

**Drug/Disease Interactions**
- Contraindications
  - 1. Renal impairment + any drug with renal fraction unexcreted > 75% ($\rightarrow$ toxicity)
  - 2. Hypertension + ethanol/NSAIDs/licorice $\rightarrow$ accelerated HTN
  - 3. Elderly + $\alpha$-blockers $\rightarrow$ syncope
  - 4. Asthma + $\beta$-blockers $\rightarrow$ respiratory failure
- Common examples:
  - Ethanol/drug interactions:
    - CNS depressants: alcoholics need more to sedate but stay under longer
    - Anticonvulsants: unpredictable
    - Metronidazole gives a disulfiram reaction (Antabuse)
    - Warfarin: acute ethanol inhibits metabolism, chronic ethanol induces metabolism
    - Antihypertensives have decreased effect
  - Oral contraceptives:
    - 23% of OC failures associated with antibiotics
    - Mid cycle breakthrough bleeding may indicate important antibiotic effect ($\downarrow$ oestrogen level)
    - Should have alternative contraception for the antibiotic course and 7 days afterwards with no pill free period. No action required for stat antibiotic doses or POPs
    - Other interactions: antacids, H2 antagonists, NSAIDs, cough and cold remedies (pseudoephedrine)

**Therapeutic Drug Monitoring (TDM)**
- Used to titrate the ‘usual dose’ to an individual
- Monitoring Cp (plasma concentration) assumes no receptor tolerance, accurate determination of the biological effect and accurate determination of the plasma level
- Indications for TDM:
  - Availability of an accurate, precise, specific and inexpensive test
- Long term drug therapy where clinical definition of efficacy is difficult (ie won’t know if it’s working by observing the patient)
- Dose related adverse effects for which there are few clinical warning signs/symptoms
- Substantial inter- and intra-individual variability in pharmacokinetics
- Multiple drug interactions
- Drugs with a narrow therapeutic index: phenytoin, digoxin, theophylline, lithium, gentamicin
- Suspected non-compliance
- Unexpected lack of response or signs of toxicity
- But TDM should not replace clinical judgement

- Therapeutic index: top and bottom are blurred margins/probabilities
- Blood sampling for TDM:
  - Often done badly
  - When absorption and distribution phases are complete
  - Steady state plasma conc. (5 half lives after started)
  - Sample just prior to next dose when dosing 2 * T½. Sample 3 – 5 hours post dose for slow release formulations

- Examples:
  - Phenytoin: Has dose dependent kinetics. Dose changes should not exceed 20% of total daily dose. Metabolised by CYP450 with many interactions. CNS toxicity correlates well with blood concentrations (nystagmus, ataxia, atypical convulsions). Therapeutic concentrations controversival (based on studies in severe epileptics). Reduce in hypoalbuminaemia (Same dose → ↓ binding available → ↑ free conc.). Frequent error: sample in trough of plasma concentration – then appears to be below TI
  - Lithium: narrow TI for maintenance – 0.4 – 0.8 mmol/L. Minor symptoms (eg tremor, nausea) don’t predict serious toxicity. Renal clearance ↓ by diuretics, theophylline, caffeine, dehydration, low sodium diet. TDM mandatory when side effect, relapse, serious illness, dose adjustment. 3 monthly monitoring for Li levels, electrolytes, thyroid fn
  - Theophylline (bronchodilator): Dose related toxicity: seizures, arrhythmias. Elimination reduced with erythromycin, ciprofloxacin, cimetidine, smoking cessation, hypothyroidism (all ↓ P450)
  - Digoxin: variable bioavailability (eg with cholesterol binding agents, antacids) and large variability of clearance (↓ with NSAIDs, spironolactone, verapamil, amiodarone). ↑ Effect in hypokalaemia, hypothyroidism, elderly. ↓ Effect in hyperthyroidism and pregnancy. Sample 8 – 12 hours post dose (long distribution phase).
  - Aminoglycosides: Dose predictions performed by pharmacy

Poisoning and Drug Overdose
- See Poisoning and Overdose, page 801

Drug Withdrawal Syndromes
- Alcohol: tremor, sweats, tachycardia, ↑ BP, seizures, visual hallucinations, delirium
- Opioids: anxiety, lacrimation, fever, runny nose, muscle aches, nausea, vomiting, diarrhoea, dilated pupils, tachycardia. Give naloxone for overdose (give test dose first, in case its not opiates). Pentazocine and Buprenorphine also used
- BZD Withdrawal:
  - Anxiety, insomnia, depersonalisation, perceptual disorders, tremor, maybe seizures and confusion
  - Usually short acting (long acting less likely to give withdrawal affects)
  - Eg Triazolam: rebound wakefulness (can last 4 – 7 days). Also behavioural disinhibition, amnesia, confusion, etc
  - If severe then weight loss, autonomic dysfunction, ↓ BP, ↑ ↓ temp, tachycardia, psychosis, seizures. Have to restart drug and withdraw slowly
- Propranolol withdrawal:
  - All β blockers can do it: but more common with short acting (eg propranolol and metoprolol). Less common with long acting (atenolol) or slow release
  - On withdrawal, sympathetic activity overshoots due to receptor up-regulation while on drug
  - Palpitations, sweating, apprehension, arrhythmias, etc. Peak is 3 – 5 days following withdrawal, especially with physical activity
- Clonidine withdrawal:
  - Antihypertensive. Pre-synaptic α2 agonists → inhibits nor-adrenaline release
  - Withdrawal in 10% → sudden rise in BP 24 – 72 hours later, plus other symptomatic effects
  - Similar effect in methyldopa (antihypertensive used in pregnancy)
• Diuretics: eg frusemide, thiazides. ↑Na retention over 4 – 5 days. Returns to normal
• TCAs, phenothiazines, butyrophenones: headache, nausea, vomiting, confusion in elderly. Sleep disturbance

**Sleep**

• Changes in elderly sleep patterns:
  - ↑Stage 1 and 2 sleep (light sleep) – effects early morning
  - ↓↓Deep sleep and REM sleep
  - ↑↑ Wakefulness
• For elderly, less sleep is a normal physiological process – they’re sleeping the amount they need. Problem is often anxiety about and during wakefulness

**Treatment of Insomnia**

• See sleep section in respiratory
• Drug management:
  - 30% over 65 take sleeping pills
  - Not for persistent insomnia (common in personality disorders, depression, sleep apnoea, pain, gastro-oesophageal reflux – treat primary cause).
  - Hypnotics should only be prescribed for symptomatic temporary insomnia (no more than 2 – 3 weeks) and should only be part of an overall management strategy
  - If used, for defined period, perhaps intermittently, and should sustain sleep
  - Not:
    - o Short acting (eg midazolam) get them off to sleep – but don’t sustain sleep. Don’t have any impact on early morning wakefulness. So will wake, and take another – then hangover in the morning, ↑falls, etc
    - o Long acting (triazolam/Halcyon) - which leads to daytime anxiety
  - Use intermediate-acting hypnotics (eg zopiclone and temazepam)
  - Risk of addiction
  - Shift workers should avoid them

**Compliance Issues**

• Compliance = extent to which person’s behaviour coincides with medical advice
• Few people take their medication as prescribed
• Non-compliance is multi-factorial:
  - Rapport with doctor
  - Not knowing how to take medication
  - Not understanding the importance of the drugs
  - Taking many drugs
  - Anticipation or experience of side-effects
  - Forgetfulness
  - Impaired physical function or other disability
  - Community and family support
• Strategies for improving compliance:
  - Education about disease and treatments (spoken instructions are quickly forgotten)
  - Simplifying drug regimes (fewer drugs and fewer doses)
  - Involving carers
  - Education about common side effects which may subside
  - Use of drug diaries, calendars, medication charts
  - Use of ordinary bottle tops (not childproof) for elderly people
  - Large print labels
  - Dosage forms (eg small pill size, pleasant taste)
  - Compliance aids such as pill trays and blister packs
  - Return or destruction of old drugs

**Prescribing**

• Definition of a medicine:
  - Medicines Act 1981 and Medicines Regulations 1984
“Administered to one or more human beings for a therapeutic purpose”:
- Treating or preventing disease
- Altering the shape, size, structure or weight of the human body
- Cleaning, soaking or lubricating contact lenses

- Registered medicines:
  - Registered medicines are gazetted and approved by the Ministry of Health
  - Unregistered medicines can be used under section 29 – requires special consent process
  - Unregistered indication

- Classification of medicines:
  - Prescription medicines
  - Pharmacist only medicines (formerly restricted medicines)
  - Pharmacy medicines (formerly pharmacy only medicines)
  - General sales medicines
  - Controlled drug

- Legal requirements for all prescription types:
  - Legibly and indelibly printed
  - Signed personally by the prescriber and dated
  - Contain the address of the prescriber
  - Contain the surname, initials and address of the patient
  - If under 13, the child’s date of birth
  - Indicate the name and where appropriate the strength of the medicine
  - Indicate the total quantity to be dispensed on each occasion
  - Indicate the dose and frequency for medicines intended for internal use

There are special script pads and requirements for controlled drugs (see the Preferred Medicines List)

**Regulation of Medicines and Drugs**

- Medicines Act 1981: prescription medicines can only be supplied or possessed on the prescription of a doctor and dispensed in a pharmacy. Maximum amount = 3 months supply (6 months for oral contraceptive)

**Regulation of Drugs of Abuse**

- See also Drugs of Abuse, page 743
- Misuse of Substances Act 1975 defines and regulates controlled drugs - prohibits non-therapeutic use. Mainly Opiates, Ritalin, dexamphetamine and BZDs
- Prescriptions for opiates and stimulant-controlled drugs must be on a special triplicate form in the Doctors own writing. BZDs don’t require triplicate form
- Prescribed for maximum of one month, dispensed in 10 day lots
- It is illegal to supply a controlled drug for the treatment of maintenance of dependency (except for Gazetted drug clinics)
- Need good notes to avoid legal recourse (e.g. no automatic repeats)
- Many injected drugs have been prescribed ‘legally’ by doctors and diverted to illicit use (eg sold to dealers)
- Monitoring of prescription narcotics and abuse prone medicines is carried out by Medicines Control Advisors, reporting to the Medical Officer of Health
- They can issue a Restriction Notice – which prevents the supply of controlled or specified drugs to a named person – it is then an offence for this person to try and obtain this drugs, and a doctor to prescribe it for them

**Classes of drugs**

- Responsibilities of the prescriber:
  - To avoid creating dependence
  - To see that the patient doesn’t increase the dose, inducing dependence
  - To avoid unwittingly supplying the black market
- Misuse of Substances Act:
  - Grades drugs according to harmfulness when misused. Specifies recording, reporting and form filling requirements. Enforced by Customs, Police (where criminal acts) and by Medical Officer of Health in the Ministry of Health
  - Class A: Possession, prescribing, sale are prohibited – street drugs. Use is an offence (e.g. heroin). Large penalties
  - Class B: Can only be used for pain. Can only be prescribed for dependency by a gazetted person. Includes morphine, methadone
Class C: Controlled drugs which are less hazardous (eg codeine, BDZs, etc)

Clinical Trials
- Preclinical trials: testing toxicity and potential therapeutic benefit
- Phase 1: Human pharmacology
- Phase 2: On patients – focus is safety: dose level and frequency, unwanted effects, treatment duration
- Phase 3: On more patients – designed to test efficacy not safety
- Medicines licensed for use
- Phase 4: Adverse reaction monitoring – rare effects only show up with widespread general use ⇒ big responsibility on prescribers to report ADR

MedSafe
- = NZ Medicines and Medical Devices Safety Authority. Part of the Ministry of Health.
- www.medsafe.govt.nz - has data sheets for all drugs
- Medicine = any substance ... supplied wholly or principally to treat a human for a therapeutic purpose ... treating or preventing a disease
- Medsafe regulates:
  - From production to distribution
  - Access to medicines (eg prescription, restricted, pharmacy only, general sales
- Need to regulate to protect public health and to avoid counterfeit or inferior quality medicines
Anaesthetics

- References: Anaesthesia, Resuscitation and Emergency Management, Wellington School of Medicine, 2000
- See also Paediatric Anaesthetics, page 997

Anaesthesia

Types
- Local (infiltration)
- General (IV or inhaled)
- Regional (nerve block or neuraxial block → eg SC: epidural)

General Anaesthesia
- Anaesthesia = absence of all sensation
- The reversible induction of:
  - Hypnosis
  - Autonomic reflex suppression
  - Muscle relaxation
- One drug doing all (e.g. inhalational anaesthetic such as isoflurane) would require sufficiently high doses to cause major side effects (e.g. respiratory depression, prolonged recovery)
- Balanced anaesthesia: one drug for each component → minimal homeostatic depression and quick recovery
- Stages:
  - 1 – Confusion
  - 2 – Exaggerated reflexes, severe confusion
  - 3 – Light, surgical and deep anaesthesia
  - 4 – Medullary paralysis
- With ↑ depth there is:
  - Loss of reflexes causing cough and swallowing → aspiration
  - ↓Muscle tone → airway obstruction
  - Progressive depression of ventilation
  - At deep level, medullary paralysis with apnoea and cardiovascular collapse
- Major problem is awareness if anaesthetic too light: anaesthetist won’t know due to paralysis. Principal signs are stress responses: tachycardia, hypertension, mydriasis (large pupils), sweating, pallor. Additional hypnotic will remove consciousness of pain, additional opioid will suppress CNS reception of pain

Monitoring
- ECG: heart rate, rhythm and ischaemia
- Blood pressure: depressed by excessive depth, extensive local (e.g. spinal blocks), or blood loss, elevated by awareness, inadequate pain blockade or hypercarbia
- End tidal CO2: if ↑ then inadequate ventilation, if ↓ then excessive ventilation
- Pulse oximetry: O2 saturation
- Temperature: anaesthetic agents → vasodilation → loss of temperature, also cold iv fluids
- Muscle relaxation: neuromuscular block monitor
- Awareness: BIS (bispectral index) → EEG monitoring

Rapid Sequence Induction
- Intubation of someone not properly prepared for surgery (eg not fasted so risk of gastric aspiration/regurgitation)
- Drugs to paralyse (e.g. Suxamethonium – fast acting) and sedate (e.g. propofol)
- Cricoid pressure until intubated to stop aspiration (closes off oesophagus) – but not if actively vomiting (otherwise gastric or oesophageal rupture)

Phases of Anaesthesia
- Induction
- Maintenance
- Recovery (drugs are both metabolised + exhaled): gas/IV stopped and ventilation rate ↓ to ↑ CO2 + thus ↑ the drive to breathe
**Triad of Anaesthesia**

- **1. Hypnosis**: lack of awareness
- **2. Paralysis**: suppression of reflexes
- **3. Analgesia**

  + anti-emetics + maintenance of physiology/homeostasis (eg BP: anaesthetics are potent vasodilators therefore need vasoconstrictors eg phenylephrine to ↑ TPR + afterload)

**Hypnosis**

- Also suppress autonomic reflexes
- All act on the CNS, probably through GABA potentiation
- Can use:
  - Hypnotics eg propofol, etomidate, thiopentone
  - Benzodiazapines eg midazolam
  - Ketamine
  - Vapours eg sevoflurane, isoflurane (these are mostly used to maintain after propofol induction)
    - **Minimum Alveolar Concentration** (MAC) = the concentration that prevents movement in response to skin incision in 50% of subjects
    - Factors influencing MAC = age, other drugs, temperature (not gender or weight)

**Paralysis**

- Muscle relaxants
- Drugs act on either:
  - NMJ (depolarising) eg suxamethonium (fast acting → good for RSI)
  - NMJ (non-depolarising) eg atracurium, vecuronium, rocuronium
  - CV eg atropine or β-blockers

**Maintenance of Physiology**

- BP, RR, removal of CO2 etc
- O2: can deliver based on either pressure or volume; can give PEEP (as ventilation can cause barotrauma + atelectasis)
- CO = HR x SV; MAP = CO x TPR → can regulate all of these things
- α1-agonists = phenylephrine
- α + β agonists = ephedrine + adrenaline
- See Vasoactive Drugs, page 73

**Airway Management**

- Pre-op evaluation:
  - **History**: prior hx of difficult intubation, dental problems, neck masses, neck trauma, arthritis, last eat + drink (need 6hrs), general health, smoker, drugs/allergies
  - **Exam**: tongue vs pharynx size (Mallampati score: 1-4; 1 is good), atlanto-occipital joint extension (tilt head back), anterior mandibular space (thyromental distance: normal is 6cm), dental exam
  - **Consent**
- **Types**:
  - Bag + mask (for short cases)
  - LMA (sits over epiglottis, prevents airway closure)
  - ETT (for long cases)
  - ETT following RSI (for emergencies)
  - Fibre optic intubation (awake or asleep for difficult airways)
  - Awake tracheostomy
- **Pre-intubation**:
  - Prepare equipment
  - Hyper-oxygenate (to clear N + ↑O2 in lungs to give more time during intubation)
  - Position head (pillow under head)
- **Securing an airway**:
  - **Open + clear**: head tilt, chin lift, jaw thrust
  - **Maintain**: OP or NP airway
  - **Confirm**: lung sounds, condensation in tube, CO2, O2 sats
  - **Secure** the tube
Anaesthetic Agents

Dose Calculations of Anaesthetic Drugs

- Concentrations. Four most common methods of specifying concentration are:
  - Mg/ml: weight of drug per volume of diluent
  - % - number of grams of drug per 100ml. E.g. 50% = 50 grams per 100 ml or 500 mg/ml. 1% = 10 mg/ml. Multiplying by 10 gives mg/ml. Often used for lignocaine (Xylocaine)
  - 1:1000 is the same as 0.1% (1 mg/ml). Used for adrenaline and isoprenaline
  - mmol/l: used for electrolytes

- Infusions:
  - Use for drugs with very short T½ where fluctuations in dose of drug are dangerous
  - Common for adrenaline, dopamine, dobutamine & lignocaine
  - E.g. post arrest infusion of lignocaine at 2 mg/min with 2% xylocaine. This is 20 mg/ml, so want 0.1 ml per minute. Using a burette system can deliver 6 drops a minute (60 drops = 1 ml) or dilute 10 fold and run at 60 drops per minute (easier)

Inhalational Anaesthetics

- Gases = compounds in the gaseous state at a temperature above their critical temperature.
- Vapours = compounds in gaseous phase but can be returned to liquid by ↑ in pressure. Ambient temperature must be below the critical temperature for the compound
- The partial pressure in the brain necessary to achieve anaesthesia will depend on its potency (Potency is a measure of how much of a drug is required in order to produce a particular effect)
- Poorly soluble gases will have higher partial pressure at a given concentration and will have a fast onset.
- Lipid soluble drugs are more potent
- So more soluble drugs have slower uptake in blood and require lower partial pressure to achieve their effect
- Factors affecting uptake:
  - Inspired partial pressure
  - Alveolar ventilation
  - Circulation
  - Properties of the anaesthetic agent (e.g. blood solubility)

  - Nitrous Oxide (N2O):
    - Pleasant, non-irritating, non-flammable (but supports combustion)
    - Stored in blue cylinders
    - Poorly soluble in tissues → rapid uptake and elimination
    - Good analgesic but low potency (therefore need bigger dose for effect)
    - Always given with at least 30% O2 to avoid hypoxia
    - Expands in enclosed air spaces: so avoided for middle ear operations and where air embolism may occur
    - Give 100% O2 at end of N2O anaesthesia to avoid diffusion hypoxia – N2O rapidly leaves pulmonary capillaries → ↓ alveolar O2 concentration

  - Halothane:
    - High potency (Minimum Alveolar Concentration, MAC = 0.7% - level that produces immobility in 50% of people, NO2 is 105% ⇒ not so good)
    - No irritation and moderately rapid induction and recovery
    - Poor relaxant and analgesic properties
    - Requires accurate vaporisers
    - High concentrations produce profound respiratory and cardiac depression
    - Rare complication is hepatic necrosis

  - Isoflurane:
    - Similar to halothane, but more irritant so difficult to use for induction
    - More potent vasodilator ⇒ hypotension and tachycardia
    - Also sevoflurane: not so irritant, quicker onset, but more expensive. Use in kids if can’t cannulate

Intravenous Anaesthetics

- Can be given as bolus for induction or infusion for maintenance
- All have similar characteristics:
  - All are lipid soluble
  - Unionised fraction crosses the blood brain barrier
  - Loss of consciousness usually occurs in one arm to brain circulation time (approx. 30 secs)
  - Rapidly redistributed to tissues with high blood flow so rapid fall in peak plasma concentration
• **Thiopentone:**
  - *Barbiturate* derivative containing sulphur (→ yellow)
  - Highly alkaline in solution → thrombophlebitis
  - Blood level results from distribution (seconds), redistribution (e.g. from muscle to fat – minutes/hours) and metabolism (15%/hour by liver)
  - CNS depression - ↓cerebral O2 consumption, potent anticonvulsant
  - Respiratory depression: especially initially – may be apnoeic for short period
  - Circulatory effects - ↓cardiac output, ↓vasomotor depression → peripheral vasodilation → ↓BP
  - Poor analgesia and prolonged hangover
  - Dose: 4 mg/kg – less for elderly, more for robust male
  - Complications: acute intermittent porphyria and IgE mediated hypersensitivity

• **Propofol:**
  - White, oil in water emulsions, 20 ml ampoules, 1% solution = 10 mg/ml
  - Structurally different to barbiturates
  - Highly lipid soluble: so rapid onset – and short duration due to rapid distribution, metabolism (T ½ = 35 – 50 minutes) and delayed return from poorly perfused tissues (e.g. fat)
  - Smooth induction, rapid recovery
  - Poor analgesic
  - Apnoea for about 30 seconds common
  - More ↓BP but less nausea/vomiting than thiopentone
  - Induction dose: 2 mg/kg in young and 1.5 mg in elderly

• **Midazolam:**
  - H2O soluble benzodiazepine
  - Muscle relaxant, amnesic, anxiolytic, anticonvulsant
  - Rapid onset and rapid elimination (T½ = 2 hours) cf. other benzodiazepines
  - Unlike other iv anaesthetics can be reversed, with flumazenil
  - Used for minor procedures, ICU sedation
  - Slower, more variable induction cf. thiopentone. Small dose may → deep anaesthesia
  - Dose for sedation: 1 – 5 mg titrated
  - Dose for induction: 10 – 15 mg (highly variable)

• **Ketamine:**
  - Related to angel dust
  - *Dissociative* anaesthesia (characterised by catalepsy [prolonged maintenance of a fixed posture], amnesia and analgesia; pt seems disassociated from their environment)
  - BP and respiration well supported, bronchodilator
  - Dose for induction: IV 1 – 2 mg/kg, IM 5 – 12 mg/kg
  - Smaller doses → potent analgesia
  - A sympathetic stimulant, can have bad dreams

Neuromuscular Blockade

• Muscle relaxants are used to:
  - Facilitate intubation and artificial ventilation
  - To facilitate abdominal access during abdominal surgery
  - To allow lighter levels of anaesthetic to be used → rapid recovery and less cardiovascular depression

• Block neuromuscular transmission from motor nerve to voluntary muscle (ACh transmission across synaptic cleft, broken down by cholinesterase)

• **Train of Four:**
  - Method used to objectively monitor degree of chemical paralysis
  - Involves Peripheral Nerve Stimulation (PNS) e.g. if 4 twitches seen in response to stimulus, only up to 75% of receptors are blocked and there is potential for movement
  - Allows for correct dosage
    - Too little = movement
    - Too much = adverse effects
    - Lower doses
    - Faster recovery
  - The number of responses to the TOF stimuli indicates the degree of neuromuscular blockade
  - Only used for non-depolarising blockade

• **Non-depolarising blocking agents:**
- Competitive antagonists of the nicotinic cholinergic motor end plate receptors. E.g. rocuronium, pancuronium, atracurium, vecuronium
- Degree of block determined by train of four stimuli. Each successive twitch is a lower amplitude — trails off. No interference with twitch response until 75 – 80% receptors blocked. 90 – 95% block required for surgery
- Reversed by anticholinesterase drugs: neostigmine (onset in 2 minutes, lasts 20 minutes), pyridostigmine, edrophonium. Inhibit acetylcholinesterase →↑ACh, but also effects muscarinic sites in parasympathetic nervous system. Side effects include salivation, bronchospasm, ↑gut motility and bradycardia. These effects blocked by atropine – which blocks the parasympathetic system
- Analgesia ended with anticholinesterase (commonly neostigmine 2.5 mg) and atropine 1.2 mg

**Depolarising Neuromuscular Blocking Agents:**
- Faster onset and shorter duration (4 – 6 mins) than non-depolarising. Used for short procedures (quick intubation), supplemented with non-depolarising for long procedures or given by constant infusion
- Suxamethonium: reacts with ACh receptors to produce depolarisation (→fasciculation), but because it is not so rapidly eliminated as ACh, depolarisation persists → inexcitability of membrane around endplate. Repolarisation happens when suxamethonium is hydrolysed by pseudocholinesterase (unless atypical genetic variant → prolonged effect). If overdose or poor elimination → drug-receptor complex forms, unavailable for ACh → dual or phase II block. No antagonist to suxamethonium except fresh frozen plasma (contains pseudocholinesterase)
- Train of four different to competitive antagonists: each twitch the same height (although reduced over normal)
- Has other muscarinic side effects due to similarity to ACh: ↑BP, ↑intra-ocular pressure, ↑bronchial secretions, ↓heart rate, post operative muscle pain
- Suxamethonium is contraindicated in major burns, neurological injuries, hyperkalaemia, myasthenia and myotonic diseases, ↓pseudocholinesterase and history of malignant hyperthermia

**Reversal Drugs**
- Neostigmine: reverses non-depolarising anaesthesia (AChE inhibitor) → can ↓HR also though so give atropine also
- Flumazenil: reverses BZD
- Naloxone: reverses opiates
- Protamine sulphate: reverses heparin

**Pain Management**
- See also Symptom Management in Cancer, page 782

**Pain Physiology**
- Pain is vital to survival, but also an important source of human suffering
- Subjective response to:
  - Damage to body tissues → stimulation of somatic and visceral nociceptors (nociceptive pain)
  - Altered function of brain or nerve pathways → neuropathic pain
  - No detectable damage ⇒ psychological, social or environmental factors – idiopathic pain (diagnosis must include a psychological assessment)
- Three types of pain:
  - Acute pain: injury, surgery, acute illness
  - Cancer pain
  - Chronic non-cancer pain
- Nociceptive pain:
  - Nociceptors are free nerve endings stimulated by chemicals (e.g. H+), pressure or hot/cold
  - Sensitivity to noxious stimuli ↑ by prostaglandins (long chain fatty acids derived from arachidonic acid), e.g. PGE2 and PGF2
  - Conducted by
    - Fast, myelinated A fibres → sharp pain
    - Slow, poorly myelinated C fibres → dull persistent pain
  - Terminate in thalamus. Fast fibres then to sensory area of cortex → pain localisation. Slow fibres synapse with reticular formation → general arousal and → limbic system (autonomic responses and emotion)
- Facilitation:
  - Processes that ↑ pain sensation

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- Primary hyperalgesia: sensation heightened in discrete area due to histamine and serotonin sensitising adjacent nociceptors
- Windup: hyperalgesia beyond areas actually damaged – due to recruitment of other receptors, mediated by NMDA
- Cortical factors: facilitate pain in anxiety, stress, absence of other sensory input (e.g. at night)
- Long term changes in pain pathways →pain disorders persisting after tissue damage has resolved

- Inhibition:
  - Descending fibres activate encephalinergic neurones within dorsal horn
  - Release endorphins which inhibit passage of pain impulses, derived from endorphins (in turn derived from β-lipoprotein). Can be antagonised by naloxone
  - Gate theory: large fibres send inhibitory collaterals to presynaptic C fibres

- Referred Pain: visceral pain felt in somatic structures.

- Adverse effects of pain:
  - Psychological effects - adaptive behaviour may become dysfunctional →stress, dependency, isolation, sleep deprivation, psychiatric illness
  - Neurohumoral reflexes - ↑ sympathetic activity, CVS system stimulated, metabolism becomes catabolic (which can inhibit healing), changes in immune system
  - Cardiorespiratory effects: e.g. decreased ventilation, ↓secretion clearance →hypoxia (especially given ↑cardiac O2 requirements), infection
  - Musculoskeletal spasm
  - Gastro and urinary function - ↑secretions, ↑sphincter tone, ↓motility →stasis, urinary retention

Pain Pharmacology

- Choice of drug depends on pt and disease state: HA, post-op, renal stones, malignancy

- Opioid analgesics:
  - Main drugs used in severe pain
  - Act on Mu, kappa and delta receptors in substantia gelatinosa and solitary nuclei in spinal cord, thalamus, periaqueductual grey matter and amygdaloid
  - Different opioids have different affinities for different receptor subtypes →different effects. E.g. Morphine agonises all receptors giving strong analgesia, respiratory depression (both mediated through M receptor) and dependence. Pentazocine is a weak M-receptor antagonist and strong k-receptor agonist and produces weaker analgesia, low dependence and little respiratory depression
  - Moderate pain: codeine, tramadol
  - Severe pain short T1/2: morphine, oxycodone, pethidine, fentanyl
  - Severe pain long T1/2: methadone, long acting morphine, long acting oxycodone
  - Oxycodone is most potent
  - Uses of opioids:
    - Best for acute pain and dull continuous pain
    - To supplement regional and general anaesthesia
    - As primary anaesthetic agents
    - Premedication to allay anxiety and sedate
    - Specific indications e.g. pulmonary oedema
  - Alfentanil, fentanyl and remifentanil are opioids used intra-operatively because they are rapid and short acting
  - Side effects: respiratory depression (if dose greater than that necessary for analgesia), addiction (not a problem in severe or post-operative pain), sedation, nausea and vomiting, constipation, cough suppression, histamine release, tolerance and dependence, pethidine associated with serotonin syndrome if given with MAOIs
  - Well absorbed, liver metabolism to M6G and M3G and excreted by kidney
  - Clinical effects: CNS (analgesia, drowsy, confused, nausea, miosis, resp depression); CVS (peripheral vasodilation, ↓preload, releases histamine, can cause bradycardia/hypotension); GIT (contracts spincter of oddi, delays gastric motility)
  - Codeine: weak opioid, is a pro-drug. Used for mild to moderate pain. Constipation occurs frequently
  - Tramadol: weak opioid. Also inhibits reuptake of SHT and NA. Moderate to severe pain. ADR: GI symptoms, drowsy, postural hypotension and seizures
  - Methadone: acts at Mu receptors. Used in treatment of pain and opioid dependence. Resp depression can be seen
  - Oxycodone: semisynthetic opioid. Differs from morphine as metabolised by CYP450. Faster acting than morphine and more potent given orally. Oxycontin = slow release, Oxynorm = short acting
- Post-Operative pain relief:
  - Pre-empt pain: give ibuprofen etc. Aim to ↓ use of opiates
  - Can use epidural, morphine boluses or PCA
  - PCA: morphine/fentanyl. Lockout interval and 4 hour dose limit is decided. Morphinne preferred due to short duration of action of fentanyl. Fentanyl will accumulate if given for 5 days. PCA stopped when pt can take PO
  - Reasons for poor pain relief: lack of understanding/recognition, poor knowledge of drugs and doses, fear of overdose or addiction, logistic difficulties (e.g. access to controlled drugs), willingness to complain about pain, lack of time, problems with side effects, variation in plasma levels necessary to produce analgesia, wide variations in pharmacokinetics
  - Factors affecting response:
    - Lean body mass
    - Age: neonates sensitive, elderly have slower distribution and metabolism
    - Liver disease → slower metabolism, renal disease → slower elimination
    - Problems in shock: smaller blood volume, but poorer diffusion. Give little and often and titrate to effect
    - ↓ PaCO2 → ↑ plasma concentration
    - Drug interactions (e.g. phenytoin → ↓ pethidine clearance)
    - Personality type
  - Alternatives to IM opiates:
    - Continuous iv infusion: morphine 10 – 20 mg loading dose over 45 – 60 minutes followed by 2 – 3 mg/hour
    - PCA
    - Extradural or regional block
    - NSAIDs as adjuncts
    - TENS: transcutaneous electrical nerve stimulation, acupuncture and hypnosis

- Paracetamol:
  - Central COX
  - Mild to moderate pain, can use in conjunction with opioids/NSAIDs
  - PO/IV/PR
  - 4-6hrly
  - Efficacious and very safe

- NSAIDs:
  - COX1 (COX1 in blood vessels, stomach, kidney, ?brain; COX2 induced in inflammation)
  - Most NSAIDs inhibit COX 1 and 2, in theory, COX2 should be safer than a non-selective inhibitor
  - ASA irreversibly inhibits COX, other NSAIDs are reversible, competitive inhibitors
  - Pharmacokinetics: well absorbed, protein bound, liver metabolism, levels in synovium are 60% of those in plasma (therefore ASA used in RhF)
  - Uses: inflammatory states, RA, acute pain syndromes (gout, pleurisy), chronic pain (OA, cancer pain [bone]), post-op pain, fever, PDA closure, sports injury, migraine
  - No evidence that one drug is better than another, there is pt variability in response
  - SE: dyspepsia, PUD in 1.5%, ↑ in risk by approx 5x → mgmt options = COX2 inhibitors, H2 antagonists, PPIs, misoprostol; nephrotoxicity (seen in elderly, hypovolemia, diuretics, ACEis, chronic gout; beware ACEI + diuretic + NSAIDs + ↑ Cr); CVS (fluid retention), inhibit uterine activity, blood dyscracias (very rare eg aplastic anaemia), skin problems
  - NSAID interactions: Li, diuretics, ACEi, BB, sulphonylureas

- Chronic Non-cancer Pain relief:
  - Opioids: orally (morphine tablets, methadone, codeine), epidural, subcutaneous
  - NSAIDs
  - Chemical or surgical ablation of nerves: e.g. chemical coeliac plexus block for pancreas pain
  - Psychological/emotional support

- Neuropathic pain (e.g. nerve compression, post herpetic neuralgia, etc):
  - Burning, stabbing, shooting pain
  - Treatment:
    - Amitriptyline: 10- 50 mg nocte, increases descending inhibitory pathways, effect in 48 hours
    - Anticonvulsants (Carbamazepine, Gabapentin)
    - Sympathetic blockade
    - Steroids to reduce inflammation of nerves or adjacent tumour
    - Plus TENS, psychotherapy, rehabilitation, opioids
• Bone Pain:
  - NSAIDs
  - If bony metastases: bisphosphonates

Post Operative Nausea & Vomiting
• Risk factors:
  - Patient factors: F > M, age: children > adults, obesity, hx of PONV
  - Procedural factors: gynae, abdominal + ENT surgery
  - Anaesthetic factors: pre-med anti-emetics, opioids, inhalational agents, NOS, duration
  - Post-op factors: pain, pain relief, early ambulation

• Drugs + site of action:
  - 5HT3 antagonists: ondansetron; slows colonic transit time
  - Anti-histamines: cyclizine; see dry mouth, blurred vision, tachycardia
  - Anti-dopaminergics: metoclopramide, chlorpromazine
  - Anti-cholinergics: hyoscine
  - Others: dexamethasone, BZDs, acupuncture

Local Anaesthetics
• Reversible inhibition of conduction in peripheral nerve fibres and nerve endings
• If local and general GA used, then local can take the place of an opioid in balanced anaesthetic
• Methods of local anaesthetic:
  - Surface or topical anaesthesia
  - Infiltration anaesthesia
  - Conduction anaesthesia or regional nerve block
  - Intravenous regional anaesthesia (into limb with a tourniquet)
  - Central neural blockade (e.g. spinal or epidural)

Local Anaesthetic Agents
• Reversible inhibition of conduction in nerve fibres and endings
• Classification:
  - Esters of benzoic acid: cocaine, tetracaine
  - Esters of para-aminobenzoic acid: chloroprocaine, procaine
  - Amides: e.g. lignocaine and bupivacaine (Marcain)
• Bind to internal opening of Na channel, preventing threshold and progression of action potential
• Pharmacokinetics depends on:
  - Mass movement of drug around and away from nerve
  - Diffusion into axon: best if unionised (i.e. weak base)
  - Absorption is determined by route of administration, site of administration (e.g. vascularity), and presence of vasoconstrictors (some anaesthetics themselves have vaso-constricting/dilating properties)
  - Metabolism: esters hydrolysed by plasma cholinesterase, amides by liver
• Adverse effects:
  - CNS: first cause excitation due to suppression of inhibitory neurons
  - CVS: negative inotropy, depression of conduction, reduction in automaticity (∴ sinus bradycardia)
  - Vasoconstriction – decrease rate of absorption, ↓ bleeding. Never use adrenaline in digital extremities → ischaemia
  - Allergy: extremely rare
  - Fainting
• Treatment of overdose of local anaesthetic:
  - O2
  - Diazepam/thiopentone for convulsions
  - Other resuscitation: airway, ventilation, elevate legs, IV fluids, atropine for bradycardia
• Clinical uses:
  - Topical anaesthesia: slow. Good for cannulating kids but takes an hour
  - Infiltration: e.g. around suturing. Don't inject through wound edge of unsterile wound
  - Nerve block: large area of analgesia, fewer injections, smaller doses
  - ExtraDural: between dura mater and periosteum of vertebral canal. Also blocks autonomic efferent nerves ⇒ vasodilation ⇒ hypotension. If it goes into subarachnoid space ⇒ total spinal: respiratory paralysis, hypotension – treat with IPPV O2, IV fluids and vasopressors
Spinal/subarachnoid anaesthesia: direct into CSF. More potent, more pronounced motor block

Intravenous regional anaesthesia: tourniquet inflated to 100mmHg above systolic blood pressure

Obstetric Anaesthesia

Physiology of Pregnancy

- Respiratory:
  - Raised diaphragm \(\rightarrow\) ↓functional residual volume
  - ↑O2 demand: due to ↑maternal metabolism and foetal demands
  - ↑Respiration \(\rightarrow\) respiratory alkalosis (PCO2 approx. 32) with metabolic compensation
  - \(\Rightarrow\) Becomes apnoeic more quickly

- Cardiovascular:
  - ↑Blood volume, ↑Hb by not so much \(\Rightarrow\) physiological anaemia
  - Blood pressure: if normal pregnancy then small ↓in systolic, ↓↓in diastolic due to vasodilation
  - Minimum Alveolar Concentration (MAC) lowers in pregnancy
  - Volume of CSF reduces \(\rightarrow\) ↓dose of spinal by \(\frac{2}{3}\)

- GI: lower oesophageal sphincter less effective \(\rightarrow\) ↑regurgitation

General Anaesthetic in Pregnancy

- More difficult getting endotracheal tube in: throat is smaller, usually done at night in emergency, etc
- Mendelssohn’s syndrome: acid aspiration in surgery when pregnancy \(\rightarrow\) bigger A-a gradient compared with non-pregnant. Give H2 blockers to ↓stomach acid
- ↑Awareness: inhaled and induction agents cross placenta – so often more cautious dosing. But muscle relaxants don’t cross placenta. Usual dosing. But can’t tell if they’re aware
- So trend from GA to epidural in pregnancy
- If doing GA: use rapid sequence induction. Use anaesthetic agent, muscle relaxant and cricoid pressure to occlude oesophagus until tube in

Pathology in Pregnancy

- Pre-eclampsia: ↑BP, proteinuria, oedema
- Eclampsia: ↓circulating blood volume, swollen tissues, fits, death
- Placenta praevia: placenta over os \(\rightarrow\) big bleed
- Abruptio: placenta separates from uterus \(\rightarrow\) big bleed
- Amniotic fluid embolism \(\rightarrow\) equivalent of PE and DIC
- Aorta-caval occlusion/compression. \(\rightarrow\) faint when they lie down. Uterus compresses IVC \(\rightarrow\) ↓venous return \(\rightarrow\) ↑HR and vasoconstriction \(\rightarrow\) ↓perfusion pressure to uterus. Lie on left side, push uterus to left if doing CPR

Analgesic Drugs in Labour

- Mechanism of pain:
  - Ischaemic pain during contractions is due to ↓O2
  - Contraction against resistance \(\rightarrow\) colicky pain (like gallbladder)
  - Mechanical: pelvis and perineum

- Epidural:
  - Very effective
  - Good in eclampsia and where high suspicion of intervention
  - Complications:
    - ↑Rate of subsequent intervention
    - Hypotension
    - Paralysis, infection, haematoma, wrong drug
    - If into subarachnoid \(\rightarrow\) total spinal overdose
    - If into vein \(\rightarrow\) cardiotoxic drugs, CNS damage
    - If CNS drains out, positional headache
  - Can’t have epidural if:
    - Patient refusal
    - Hypovolaemic due to haemorrhage
    - On anticoagulants, in case puncture epidural vein \(\rightarrow\) haematoma
    - Septic: could transfer bug from blood to CSF
  - Inhalational – N2O/Nitrous Oxide: variable satisfaction, analgesia and dissociative, 50% vomit, 2 min to peak effect, no further effect once breathed out

Anaesthetics 870
Opiates (e.g. Pethidine): variable satisfaction, dissociative, safe (midwives can use it), can → respiratory depression in neonate
Psychoprophylaxis: very effective. If frightened and don’t know what’s going to happen, hurts more

Preoperative Assessment

Aim is to investigate and optimise treatment for pre-existing medical conditions before surgery – especially respiratory and CVS: Anaesthetic drugs have profound effects on the cardiovascular and respiratory systems — the main focus of questioning is therefore about cardiac or respiratory problems
Undertake a brief preassessment with a focus on CV, resp, previous anaesthetic experiences, smoking, check pregnancy if female, PMHx, drugs, allergies, FHx (anyone in the family with problems with anaesthetic eg malignant hyperthermia) etc
PMHx screen: MI or IHD, asthma, HTN, RhF, epilepsy, liver/kidney disease, dental problems, neck problems, GI reflux, past anaesthetic and associated problems
Ask when last ate
Cigarette smokers are difficult to anaesthetise because their upper airways are sensitive to the dry gases and their risk of hypoxia is greater

Cardiovascular Conditions Requiring Assessment

Ask CV screening questions eg CP, SOB, orthopnoea etc
Hypertension: 1/3 develop intraoperative hypotension, and ¼ develop post-operative hypertension. Predisposes to MI, stroke and renal failure. Resting diastolic pressure over 100 mmHg should delay elective surgery until better controlled. Continue previous antihypertensive therapy up to and following surgery to prevent rebound hypertension (esp beta blockers)
Coronary vascular disease: IHD → 10-fold increase of risk of perioperative myocardial infarction. Delay elective GA until 3 (preferably 6) months after MI
Cardiac failure: contra-indication to all but most necessary surgical procedures
Arrhythmias: resulting complications more related to underlying pathology rather than rhythm. If cardiac efficiency already reduced, GA can lead to ↓↓ cardiac output (e.g. atrial fibrillation with rapid ventricular response)
Valvular and congenital heart disease. E.g. aortic stenosis may require anticoagulant therapy (although this increases haemorrhage risk so stop during operation) and prophylactic antibiotics

Respiratory Conditions Requiring Assessment

Ask respiratory screening questions eg cough, recurrent infections, SOB etc
Ventilation, gas exchange, cough and mucociliary clearance impaired by GA and into post operative period
Major risks: sputum retention, lung collapse, infection, ventilatory failure
Preoperative management aims to:
  Eradicate infection
  Reduce excess sputum production
  Treat reversible obstructive disease
  Treat co-existing right heart failure
  Optimise ventilatory muscle function
Elective surgery should be cancelled if acute infections up to 5 weeks beforehand. (e.g. viral infections → ↓ mucociliary clearance)
PEFR (Peak expiratory flow rate), FEV1 and VC (Vital capacity) are useful preoperative measures

Other Conditions Requiring Assessment

Endocrine:
  Diabetics are at risk from:
    Poor perioperative control: e.g. during pre-operative fasting, stress response, etc. Poor control → poor wound healing, ↑ infection, etc
    Co-existing cerebral, coronary or renal vascular disease or autonomic neuropathy
  Hyperthyroid patients at risk of CVS collapse
Liver Disease: hepatic function commonly deteriorates post operatively. Infection risk to staff from hepatitis
Alcoholism: complications include withdrawal, nutritional abnormalities, existing cardiac and liver disease
Anaemia: increases risk of hypotension and hypoxia
Drugs: Corticosteroids suppress cortisol, so patients will require supplementation with hydrocortisone at induction and by infusion following
Physical Assessment

- Should be guided by history
- Airway assessment:
  - How easy or difficult it will be to intubate a patient depends on these important points
    - Do they have a short neck and small mouth?
    - Are they obese, and to what extent can they open their mouth?
    - Is there any soft tissue swelling at the back of the mouth or any limitations in neck flexion or extension (RA or ankylosing spondylitis)?
  - The Mallampati scoring system uses a simple visual scale to grade each patient based on the visual vertical distance between the tongue and soft palate or uvula at the back of the pharynx. Grade I shows a large vertical distance between the uvula and the base of the tongue.
- A general systems examination must be done to pick up any abnormalities—for example, heart murmur, abnormal breath sounds, abdominal masses, skeletal malformations such as kyphoscoliosis, previous scars, and any local skin infection
- Vital signs: with the exception of emergency surgery, patients should be haemodynamically stable and their vital signs normal before starting anaesthesia

Investigations

- Ordering unnecessary tests is neither helpful nor cost effective. Commonly used investigations are discussed below.
- Urine dipstick or analysis—Invaluable in detecting undiagnosed diabetes or urinary tract infection.
- Haematology:
  - Haemoglobin should be checked when the history or examination indicates anaemia or when the proposed operation is expected to cause substantial blood loss
  - Clotting and platelet function is relevant for the many patients who take aspirin
  - The decision about whether to cross match serum (to be used in transfusion) or to order group and save (kept ready in reserve) should be judged on the current haematology status of the patient as well as the estimated blood loss
- Biochemistry:
  - Deranged electrolytes are common in procedures, and it is usual to measure the urea, creatinine, and electrolytes before any major operation. Renal function is important because it may influence the choice of drugs given
- Lung function:
  - CXRs are not routinely ordered and are usually limited to patients with substantial cardiac or respiratory disease, depending on local policy
  - Radiographs of the cervical spine, to determine any instability, are useful in patients with rheumatoid arthritis because almost 90% of patients have some degree of involvement. Also, patients with ankylosing spondylitis can have a semifused spinal column, and the anaesthetist should bear this in mind when extending the patient’s neck during intubation
  - Spirometry tests are a good measure of pulmonary physiology and are useful in patients with obstructive or restrictive patterns of disease—for example, asthma may be reversible with bronchodilators.
- Heart function:
  - An electrocardiogram can identify underlying ischaemia or previous infarction and also abnormalities in heart rhythm. It should be taken in anyone with cardiovascular risk factors—for example, hypertension, smoking, high cholesterol, significant family history, diabetes, and obesity
  - Exercise stress testing and echocardiography are reserved for patients in whom a further cardiac assessment is needed before deciding whether or not to proceed

ASA Status

- The scale of the American Society of Anesthesiologists assesses the patient’s physical fitness for anaesthesia and is widely accepted
- ASA status = American Society of Anaesthetics: 1 = normal, 5 = expected to die, appended E = emergency
Pre-operative Optimisation

- **Cardiovascular system:**
  - People who have had an acute coronary syndrome within the past three months are at great risk of a perioperative myocardial infarction, with a mortality of more than 30%. The risk is sufficiently reduced to proceed at six months.
  - Uncontrolled hypertension (180/100 mm Hg) and uncontrolled cardiac failure are both contraindications to surgery. Diastolic blood pressure greater than 110 mm Hg is associated with a high risk of infarction, and surgery should be postponed until the hypertension is controlled.
  - Short acting antihypertensives should be replaced with longer acting ones (for example, atenolol) and these should not be stopped during the surgery.
  - Prophylactic antibiotics are required if there is a risk of infective endocarditis.
  - Arrhythmias, such as atrial fibrillation, need to be well controlled before proceeding.
  - Volume depletion is common in preoperative patients (starved, nasogastric tube aspiration, and bowel preparation) and this requires quick identification and treatment.

- **Lung function** and surgery:
  - Remember that postoperative pain and altered diaphragmatic function contribute to a reduction in functional residual capacity (FRC) of at least 40%.
  - FRC = ERV + RV (ERV—the expiratory reserve volume—is the additional volume of air that can be forcibly exhaled after a normal expiration. RV—the residual volume—is the air remaining in the lungs even after a maximal expiration; it cannot be expired no matter what the effort.)
  - This means that after the operation there is a reduced lung reserve, and, therefore, for the safe induction of a patient an adequate lung function needs to be obtained preoperatively.
  - People with asthma tend to have problems with the expiratory phase of breathing because of obstruction of the airways (from hypersensitivity and inflammation) and this can be optimised with a β2 agonist, such as salbutamol.
  - Also, long term smokers are at a much greater risk of postoperative atelectasis (collapse of lung tissue) as well as pneumonia. Encouraging these patients to stop smoking for as little as 24 hours before anaesthesia can optimise oxygenation of their tissues because the carbon monoxide in cigarette smoke, which reduces oxygen transport by up to a quarter, has a short half life.
  - URTI: the presence of an upper respiratory tract infection, particularly in children, often complicates the decision about whether or not to proceed. Excess secretions and mucous plugging can compromise the airway in the perioperative period. Usually only patients with key risk factors relating to their breathing (prematurity or airway obstruction) will have their procedure postponed.

- **Other considerations:**
  - Fluid shifts are almost inevitable, and volume depletion is important to recognise and treat.
  - Patients with diabetes should be first on the operating list and should have regular glucose monitoring; they usually need a change to their route of insulin administration (subcutaneous to intravenous infusion)
  - Patients with uncontrolled hyperthyroidism are at risk of developing a “thyroid storm,” and their resting pulse on the morning of surgery should be fewer than 80 beats/min.
  - Regurgitation and aspiration can be dangerous (remember the lower oesophageal sphincter is less competent in the unconscious patient). Be vigilant of patients not properly fasted or anyone at higher risk—for example, patients with hiatus hernia, bowel obstruction, oesophageal pouch, upper gastrointestinal bleeding, obesity, and pregnancy. These patients require antacid and antiemetic drugs.
Guidelines

- GP and RMO should:
  - Determine what medical conditions are present
  - Quantify any impairment and improve as much as possible
  - Make sure appropriate investigations are back in sufficient time before surgery
  - Advise patient of risks and benefits and obtain consent

- Conditions of note:
  - Cardiac: MI in previous 6 months, evidence of left or congestive heart failure, unstable or ↑ angina, diastolic blood pressure > 110 mmHg, digitalis toxicity, uncontrolled AF
  - Respiratory: respiratory infections, exacerbation of CORD/Asthma
  - Hepatitis
  - Recent stroke
  - Thyroid or adrenal dysfunction
  - Poor control of diabetes
  - Major nutritional disorders

- Are the following present:
  - Family history of anaesthetic problems
  - Previous anaesthetic problems
  - Malignant hyperthermia:
    - Hypermetabolic response to gases or suxamethonium due to Ca leakage from cytoplasmic reticulum), suxamethonium apnoea, porphyria (thiopentone precipitates a crisis)
    - Is a genetic abnormality of muscle, causes a substantial increase in metabolism and body heat
    - This response is often triggered by inhaled anaesthetics and can be dangerous
    - Suxamethonium apnoea occurs in patients who have abnormally low plasma cholinesterase, the enzyme that breaks down the drug. As a result, the action of suxamethonium (a paralysing agent) is prolonged, with dangerous consequences
  - Abnormal hepatic or renal function
  - Muscle disease
  - Previous jaundice following anaesthesia
  - Allergy to anaesthetic or related drugs
  - Disorders of blood or coagulation
  - On MAOIs or cholinesterase inhibitors

- Also investigate Hb, U+E, CXR, ECG and Respiratory function if indicated
Surgical and Fluid Management

Normal Values

Blood volumes

- Infant: 80-85 ml/kg
- Young child: 80 ml/kg
- Adult: 70 ml/kg

Child’s body weight

- Under 9 years: kg = 2*age + 9
- 9 and over: kg = 3*age

Electrolyte concentrations

<table>
<thead>
<tr>
<th>Electrolyte</th>
<th>Extracellular</th>
<th>Intracellular</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sodium</td>
<td>140</td>
<td>12</td>
</tr>
<tr>
<td>Potassium</td>
<td>4</td>
<td>155</td>
</tr>
<tr>
<td>Magnesium</td>
<td>1</td>
<td>28</td>
</tr>
<tr>
<td>Chloride</td>
<td>100</td>
<td>10</td>
</tr>
<tr>
<td>Bicarbonate</td>
<td>28</td>
<td>10</td>
</tr>
<tr>
<td>Phosphate</td>
<td>1</td>
<td>105</td>
</tr>
</tbody>
</table>

Fluid Compartments and Control

- Fluid Compartments in 70 Kg person:
  - Extracellular: 14 L
    - Intravascular: 3.5 L
    - Interstitial: 10.5 L
  - Intracellular: 28 L
- Female: 55% water, male 60% water
- Control through ECF osmolarity:
  - Thirst
  - ADH: controls H2O excretion
  - Renal Na excretion: renin-angiotensin-aldosterone system

Replacement fluids

Signs of extracellular fluid depletion

- Symptoms: oliguria (min 0.5 ml/kg/hr), thirst, tachycardia, dry tongue, weakness, confusion
- Signs: weight change, ↓tissue turgor, postural hypotension, cool peripheries, dry axilla and mucous membranes, ↓JVP
- Common in surgical patients due to: vomiting, ileus, stomal losses, etc. Not always naso-gastric losses. Frusemide is a flogging offence! It’s due to intravascular hypovolaemia
- Investigations:
  - Bloods: ↑Hb, ↑Urea/Creatinine, Na/K
  - Urine Na
  - Maybe ABG for acid/base balance
- Replace deficit quickly over 30 minutes – 1 ½ hours, not by ↑hourly rate
- Give boluses of 200-250 mls N/saline, Hartmanns or plasma expander
- Take care in older patients/CHD: don’t tolerate large Na loads (→pulmonary oedema)
- If on IPPV, this pushes up intra-thoracic pressure to 10 – 15 cm H2O (0 – 5 cm H2O is normal), so when using central venous pressure need to adjust for this before determining whether hypovolaemic

Depletion in children

- Can be rapid and profound. Described as:
  - Mild: loss of 4 – 5% body mass. History of diarrhoea/vomiting but few signs
  - Moderate: loss of 6 – 9% body mass. Sunken eyes & fontanelle. Urine output < 0.5 mls/kg/hour
  - Severe: 10% loss of body mass. Very ill. Hypotension and rapid weak pulse
Surgical and Fluid Management

See Management of Mild-Moderate Dehydration, page 991, for fluid management in children

Types of Replacement Fluids

- Crystalloids: isotonic, short intravascular T½. For replacement of extra-cellular loss. To replace blood give 3 times blood loss
  - 0.9% saline: 154 mmol/L NaCl (isotonic)
  - Hartmanns and Lactated Ringers: electrolyte mixture similar to plasma
  - Excessive replacement of plasma losses acutely with saline may →hyperchloraemic acidosis
- Dextrose containing solutions: not for replacing blood loss (hypertonic). For treatment of water loss or when sodium restrictions are present:
  - Barts: 4% dextrose/0.18% saline – 30 mmol/L NaCl + 168 Kcal/L
  - 5% dextrose: 200 Kcal/L (calories and water only)
- Synthetic Colloids: isotonic, long intravascular T½, for blood volume replacement. More readily available than blood and no infection risk, don’t require cross matching. Give 1:1 ratio with blood lost. If > 1 L required, consider albumin and/or blood. Kidneys take time to excrete, so watch for fluid overload, especially in renal impairment and kids
  - Haemaccel: polygeline (degraded gelatine) plus electrolytes (145 mmol/L NaCl + 5.1 mmol/L K + 6.25 mmol/L Ca). T½ = 4 hours, hypersensitivity rare
  - Dextran 40, 70: dextran with molecular weight 40K (T½ = 2 – 4 hours) or 70K (T½ = 6 hours), hypersensitivity reactions, impairs coagulation and cross match
  - Hetastarch (Hespan), Pentaspan: starch solution, MR = 70K, T½ = 17 hours, hypersensitivity rare
- Blood products: reserved for > 20% blood loss or continuing bleeding or Hb acutely < 70 g/L

Child Requirements

- Maintenance fluid: 4% dextrose + 0.18% saline + 20 mmol KCl/L at:

<table>
<thead>
<tr>
<th>Per hour</th>
<th>Per day</th>
</tr>
</thead>
<tbody>
<tr>
<td>First 10 kg</td>
<td>4 mls/kg</td>
</tr>
<tr>
<td>Second 10 kgs</td>
<td>2 mls/kg</td>
</tr>
<tr>
<td>All subsequent kgs</td>
<td>1 ml/kg</td>
</tr>
</tbody>
</table>

- Losses (e.g. nasogastric tube, fever, diarrhoea) replaced with an equal volume of 0.45% NaCl + 20 mmol KCl/L. Give as boluses of 20 ml/kg over 15 – 30 mins. Losses decrease with renal failure
- See Management of Mild-Moderate Dehydration, page 991

Adult requirements

- Adult daily requirements:
  - 2.5 - 3 litres of fluid
  - 100 mmol Na (60 mmol/day in elderly)
  - 60 mmol of K+ (max of 10 mmol per hour)
- Can be given as:
  - 2.5 – 3 litres of dextrose/saline (=0.18% saline + 4% dextrose) per day with 20 mmol/L KCl in each bag, or
  - 2 litres of 5% dextrose and 500 mls of saline
  - Run in at 50 – 100 mls per hour (NB, smaller daily requirements for a small person)
  - If concerned about heart failure/pulmonary oedema than monitor saturation
- Intraoperative fluid replacement:
  - Oral intake withheld before surgery
  - In major surgery, half the estimated 24 hour maintenance requirement should be given initially (600 – 1000 ml saline), followed by maintenance requirements plus losses
  - K is usually excluded for first few post-operative days: due to ↑ liberation from cells
  - Excess use of low Na fluids post-operatively may cause hyponatraemia given ↑ ADH

Abdominal losses

- GIT has huge internal economy of fluid secretion & absorption
- Losses through surgical intervention (stoma, leaking viscous, etc) replaced with iv solution of similar composition
mLs per day

Saliva 1500
Gastric 1500
Pancreatic 700
Biliary 500
Jejunostomy 2-3000
Ileostomy 500
Colostomy 300
Diarrhoea 0.5 – 15,000 (Normal ileum delivers 1200 – 1500 per day)

- See also Abdominal Physiology, page 228
- Diarrhoea and Vomiting
  - Leads to dehydration, hyponatraemia, hypokalaemia, hypochloraemia
  - Replace ½ calculated losses in first 24 hours with saline plus potassium. Maximum rate of potassium replacement is 20 mmol/hr

Burns
- Burns → rapid loss → secondary organ damage (e.g. renal)
- Give 2-4 mLs/kg * %burned area of Hartmanns: half over first 8 hours, rest over next 16, in addition to maintenance requirements. Consider blood transfusion
- See Burns, page 799

Monitoring adequacy of Fluid Replacement
- Monitor pulse, BP, respiratory rate and urine output (i.e. put in catheter):

<table>
<thead>
<tr>
<th>Per hour</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infants in Nappies 2 mLs/kg</td>
</tr>
<tr>
<td>Kids &amp; adults 1 mLs/kg</td>
</tr>
<tr>
<td>Elderly 0.5 - 1 mL/kg</td>
</tr>
</tbody>
</table>

- Na to K ratio in urine should be > 1. If < 1 then body frantically reabsorbing Na not in balance

Postoperative Hyponatraemia
- See Hyponatraemia, page 155

Blood Products

Blood loss

<table>
<thead>
<tr>
<th>Blood Loss</th>
<th>Clinical signs</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>10% loss (500 mL) ↑HR, BP normal</td>
<td>Crystalloids, 10 – 20 mL/kg</td>
<td></td>
</tr>
<tr>
<td>20% loss (750 – 1500 mL) ↑HR, moderate hypotension</td>
<td>Colloid +/- red cells, 20 mL/kg</td>
<td></td>
</tr>
<tr>
<td>20 – 50% loss (1 – 2.5 L) Severe hypotension, shock</td>
<td>Colloid and red cells 30 mL/kg</td>
<td></td>
</tr>
<tr>
<td>&gt; 50% loss ?Irreversible shock</td>
<td>Red cells + coag factors (FFP) and platelets</td>
<td></td>
</tr>
</tbody>
</table>

- Giving blood isn’t based on how much they’ve lost, but on Hb measurement and pre-existing cardiac/respiratory disease. A normal person could survive an Hb of 50 if volume was adequate (below this CO falls dramatically). But a sick, old person can’t use ↑CO to compensate, so CO starts to drop below 100

Blood Component Therapy
- Modern transfusion therapy is blood component therapy
- Blood components are used to:
  - Correct intravascular volume (usually non-human products e.g. crystalloids)
  - Correct O2 transport deficiency
  - Correct bleeding disorders
- Blood components available:
  - Red cells: one unit is the red cells from one unit of donated blood (450 mL). Hb increases by 10 g/L per unit transfused. Red cell transfusions – transfuse at 1 unit per 2 – 4 hours (if cardiovascularly healthy then 2 hours, if older then 4 hours as you don’t want to go too fast otherwise volume overload)
- Platelet concentrates: Prophylactic platelet transfusions – 10 g/L pretty good maintenance level in leukaemia.
- Fresh frozen plasma: 250 ml will provide approx 8% of an adult’s circulating clotting factors
- Cryoprecipitate: source of fibrinogen for DIC
- VIII & IX concentrates
- To separate these: centrifuge – take off plasma first, then platelets, then RBCs

**Decision sequence:**
- What factor is deficient?
- Is the deficiency physiologically significant (hard to decide. Not the same as below the normal range, as normal range includes functional reserve)
- What is the appropriate blood product
- What is the correct dose to transfuse
- Has the transfusion worked?

**When blood is required:**
- Type O immediately, type specific in 10 – 20 minutes and full X match in an hour
- If massive transfusion (> 50% loss) use reconstituted red cells and colloid and consult haematologist re fresh frozen plasma (FFP), platelets and coagulation factors
- Tests for coagulation during large transfusions should include:
  - Full blood count: baseline Hb and platelet counts before transfusion, and repeated throughout
  - APPT: intrinsic pathway
  - PT/INR: extrinsic pathway
  - Thrombin time: fibrinogen availability
  - Fibrin degradation products: for DIC

**Risks:**
- Most common reaction to transfusion: febrile ½ an hour later:
  - Due to leukocytes contaminating red cells. If necessary, insert leucocyte filter on line (@$50)
  - Leucocyte poor red cells
  - Febrile reaction more common if multiple blood transfusions or multiple children (more antigenically primed)
- ABO incompatibility (eg due to incorrect labelling):
  - Hypotensive, rash, tachycardia
  - Symptoms of major intravascular haemolysis: nausea, vomiting, low back pain (renal reaction to free haemoglobin), feeling very unwell
- If allergic to plasma proteins → washed red cells
- For immunocompromised: use irradiated red cells to stop leucocytes grafting into host & then attacking host
- Infection risks (depend on prevalence in population):
  - Bacteria:
    - Yersinia Enterocolitica: is cryophilic (likes cold) and blood is a great culture medium. Comes from transient bacteraemia in infected donor.
    - Other bacteria: Brucella abortus, salmonella, M. Leprae
  - Viruses: HBV, HCV, HIV, HTLV-1, CMV, EBV
  - Parasites: Malaria, Toxoplasma gondii, Trypanosome cruzi
  - Specific risks:
    - HIV infection via transfusion: 1 in 1 – 2 million
    - CJD: no documented case worldwide (although has been done in animals)
    - HBV: 1 in 200,000
    - HBC: 1 in 80,000
- Complications of massive blood transfusion:
  - Over transfusion → Fluid overload and pulmonary oedema
  - Coagulation defects: dilutional thrombocytopenia, ↓ factors V, VII & X, DIC
  - Hypothermia (blood products are stored at 4 C)
  - Hyperkalaemia: K moves out of red cells in storage
  - Acidemia: stored blood becomes acidic with age
  - Hypocalcaemia & citrate toxicity → cardiac depression and alkalosis
  - Hypomagnesaemia
  - Transfusion haemosiderosis (ie iron overload) if on chronic transfusions (eg thalassaemia)

**Management of major reaction (either anaphylaxis/haemolysis or sepsis):**
- If worried during the transfusion, stop it
- Call blood bank for advice
- Send back blood + samples from the patient
- Check for errors

- Strategies to stop transmission of infection:
- Donor screening – very effective
- Blood screening:
  - But tests not 100% accurate & window periods
  - Move from serologic tests to PCR for viral antigens

**IV Cannulation**

- Superficial veins of the arm: metacarpal, dorsal venous arch, cephalic (radial – thumb side), basilic (ulnar), median antecubital, antecubital
- Parts of a cannula: bevel, stylet, catheter, hub of catheter, flash back chamber, air vent
- Cannulation procedure: blood return, level off, advance catheter, release tourniquet, pressure upstream remove stylet
- ↓Haematoma by ↓angle of insertion, ↓force
- Keeping it going: if infusion stopped, blood can track back through cannula and clot. Intermittent flushing with saline helps
- If hemiplegia, or mastectomy, insert in good arm
- Infiltration/tissuing is leakage into surrounding tissues. Will be pale, cold, boggy, painful. If red and warm then infection
- Phlebitis = inflammation of the vein. Caused by
  - Infection
  - Chemical irritation (eg antibiotics, especially erythromycin)
  - Mechanical
- Consequences of infection: inflammation of skin, cellulites or bacteraemia
- Minimising infection: hand washing, sterile equipment, site care and regular inspection
- Always record in notes: date and time of insertion, what gauge, what vein
- Replace every 72 hours, unless inserted in emergency in which case replace in 6 – 8 hours
- Consent: check armband, explain reasons for iv therapy, duration, what’s being infused, possible complications. Obtain verbal consent
- Choice of gauge: age, flow required, what’s being infused.

<table>
<thead>
<tr>
<th>Gauge</th>
<th>Colour</th>
<th>Uses</th>
</tr>
</thead>
<tbody>
<tr>
<td>24</td>
<td>Yellow</td>
<td>Neonates, extremely small veins</td>
</tr>
<tr>
<td>22</td>
<td>Blue</td>
<td>Infants, elderly, fragile veins, small lengths</td>
</tr>
<tr>
<td>20</td>
<td>Pink</td>
<td>Most commonly used</td>
</tr>
<tr>
<td>18</td>
<td>Green</td>
<td>For viscous fluids (eg blood)</td>
</tr>
<tr>
<td>16</td>
<td>Grey</td>
<td>For large quantities of IV fluid. Painful at insertion.</td>
</tr>
<tr>
<td>14</td>
<td>Orange</td>
<td>As for 16</td>
</tr>
</tbody>
</table>

**Nutrition in Surgical Patients**

*Consequences of malnutrition*

- ↑Perioperative mortality (e.g. in 30 days post surgery)
- ↓Healing
- ↑Respiratory infection
- ↓Immune function
- ↑Wound infection

*Nutritional assessment*

- Observe: thin?, how strong is finger grip
- History: intake over preceding days compared to normal
- Anthropomorphic measurement (BMI, girth to hip ratio, skinfold thickness, compare actual to standardised 24 hour urine creatinine excretion.)
- Lab measurements (albumin, transferrin – only for gross malnutrition)
- Physiological assessment (PEFR, FEV1, hand grip)
Energy Metabolism

- Adult needs 25 – 30 kcal/kg/day
- Typical diet gives: CHO – 40 – 60% (4 kcal/g)
  Fat: 20 – 45% (9 kcal/g)
  Protein: 10 – 20% (4 kcal/g)
- Excess CHO stored as fat, otherwise broken down to glucose
- Short & medium chain FFA are directly absorbed into the portal vein: so if gut is malabsorbing, give them this – rapid and easy to absorb
- During starvation, FFA saturate Kreb’s cycle → ketones and acids

Protein Metabolism

- No body storage. Used, converted to energy or excreted
- Maintained by protein intake of 0.8 – 1.0 g/kg/day
- Nitrogen balance = nitrogen in equal nitrogen out
- Protein is 16% N2

Energy metabolism in Starvation

- Immediate use: liver and muscle glycogen
- Early starvation: Gluconeogenesis from AA, glycerol and lactate. Leads to catabolism. Only supports CNS and RBCs
- After few days: ↓ metabolism, ↑ FFA used by heart, kidneys and muscles
- Prolonged starvation: brain uses ketones. Protein catabolism ↑ as fat stores used up

Nutritional Requirements

- Basal Energy Requirement (BEE) for otherwise well and sedentary (↑ when challenged by illness):
  - Men = 66 + (13.7 * kg) + (5 * height in cm) – (6.8 * years)
  - Women = 655 + (9.6 * kg) + (1.8 * height in cm) – (4.7 * age)

Nutritional Support

- Protein/Calorie Requirements
- Well nourished patients without sepsis or injury: H2O and electrolytes OK for 5 days
- Non-depleted post-operative patients: 1.2 - 1.5 * BEE + 0.8 – 1.0 g protein/kg/day to prevent catabolism
- Malnourished patients without sepsis or injury: Cautious repletion – avoid refeeding syndrome due to depletion of co-factors → marked ↓ in PO4 and Mg – monitor
- Nutritionally depleted patients: 1.5 – 1.8 g protein/kg/day + 1.5 * BEE
- Patients with sepsis or injury: Well nourished can manage without feeding for a few days. Malnourished need feeding

Enteral Nutrition

- Adult energy requirements: 40 Kcal/kg/day (approx. 2,500 Kcal per day)
- Requirement ↑ in sepsis, burns, trauma by 50 – 100%
- Protein requirement: 1.5g/kg/day (approx. 105 g protein or 14g N2 per day)
- Enteral much safer and less expensive compared with parenteral
- Delivered by: NG tube, nasoduodenal tube (↓ risk of aspiration), PEG, jejunostomy
- Problems: aspiration, tube blockage, diarrhoea due to intolerance/inadequate digestion
- Feed by pump, starting slowly, at 30 – 45 degrees. Stop at night if they can tolerate increased flow during day
- Tradeoffs:
  - When sick, ↓ motility and ↓ emptying. Need to be minimal volume but still flow through tube
  - Don’t include lactose as ↓ lactase when sick. Lactose would → diarrhoea
  - ↑ Osmolar load → ↑ diarrhoea. So need ↑ Mr
- 3 types:
  - Intact nutrient formulas: Blenderised feedings (don’t flow well), lactose-free feedings (via tube), and nutrient-dense feedings (flavoured for oral use)
  - Pre-digested Nutrients (elemental diets): taste fowl, use NG tube
  - Feeding modules: concentrated sources of one nutrient (e.g. protein, CHO or fat)

Parenteral Feeding

- For nutritional support when GI tract can’t be used
Via central line: Total Parenteral Feeding (TPN) has very high osmolality. X-ray after insertion to check no pneumothorax and line is outside pericardium (above anterior third rib) to avoid cardiac tamponade following catheter erosion.

Complete nutrition: electrolytes, glucose, amino acids, fat emulsion, vitamins, etc. Fat a good way of giving calories without ↑glucose (which could →diabetes).

Other major risk: sepsis. Test for coagulase +ive staphylococci. Colony count should be 5 times higher in central line sample than in peripheral blood.

Metabolic problems common, e.g. hyper or hypo glycaemia, acidosis, etc. Alter constitution of TPN.

Post-Operative Care

- Eg following a laparotomy
- Know and watch for complications
- Analgesia:
  - Epidural: watch for low blood pressure
  - PCA/PRN narcotic (but watch for constipation from morphine/codeine)
- Wound care:
  - Check not too much blood from drain
  - Rough times to leave a drain in for:
    - Laparoscopic cholecystectomy/vascular surgery: 1 day
    - Rectal surgery: 3 – 4 days
    - Mastectomy: 4 – 7 days (can go home with it in)
    - T-tube for biliary surgery: if latex then 10 – 14 days, if silicon then 3 – 4 weeks
- Anti-coagulant (eg Clexane)
- Fluid balance: if elderly alternate normal saline and dextrose bags (+KCl)
- NG tube:
  - If no aspirate after 24 hours then take it out
  - If aspirate is green, leave it in
- Prophylactic antibiotics: for uncomplicated laparotomy usually one dose intraoperatively
- Consider rehabilitation, support at home, work re-entry
- Plan follow-up

Post-Operative Complications

Infection

- Usually takes 3 – 5 days
- Wound infection:
  - Redness, induration
  - Either:
    - Abscess: red, hard mass →needs drainage
    - Cellulitis: red, hot, painful →antibiotics
- Abdominal infection:
  - Often 5 – 7 days before apparent: pain, ileus, sweats, rigours
  - Investigations (to look for abscess): Maybe US. CT better
  - Treatment:
    - Small abscess: if deep and < 3 cm try antibiotics
    - Large abscess: if > 4 cm then drain either surgically or under radiological guidance. Depends on depth, if its loculated or presence of overlying bowel
- Peripheral line
- Central line: may look innocent – but consider if no other locus found. Can leave a central line in for 4 – 6 weeks if you look after it
- Chest infection:
  - Usually results from atelectasis following poor ventilation (especially immediately following extubation, especially if pain)
  - Look for ↓saturation and fever (especially if it occurs the night following surgery) – this is initially due to inflammation – so it presents quicker than the above infections
  - Management:
    - Effective analgesia
**Chest physio:** deep breaths and cough each hour

- Overall management:
  - Check wound, chest, iv sites, abdomen, UTI. Check for signs of meningism, endocarditis, DVT
  - Do FBC, culture. Consider MSU, CXR, abdo US

---

**Decreased Blood Pressure**

- Lie flat and give O2
- Check pulse and other vitals
- Consider:
  - Hypovolaemia: check fluid chart, replace losses
  - Haemorrhage: review wounds
  - Cardiogenic: any heart history?
  - Sepsis
  - Anaphylaxis

---

**Nausea/Vomiting**

- Causes: Mechanical obstruction, paralytic ileus, emetic drugs (opiates, digoxin, anaesthetics), systemic or GI illness
- Consider AXR, NGT, antiemetic (metoclopramide or cyclizine)

---

**Deep Vein Thrombosis**

- If it’s a long operation, a clot may start to form then and propagate →inflammation →mild fever
- If immobile or in pain, then may form post-operatively
- High probability of a DVT if:
  - Calf circumference > 3 cm than the other
  - Malignancy
  - Immobile
  - Local tenderness
  - Family history
- Test using Doppler US (for flow)
- See also Deep Vein Thrombosis (DVT), page 103

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**Confused Patient**

- Ie Delirium. See also Delirium, page 736
- Causes (especially if already borderline):
  - Infection
  - Hypoxia
  - Metabolic: glucose, K
  - CVA or MI
- Drugs:
  - Too little: eg withdrawal of sleeping pills, insufficient analgesia
  - Too much: eg morphine →↓respiration, pinpoint pupils. Treat with naloxone (but short T½ so may need to repeat)
  - Delirium tremens (alcohol withdrawal)
  - Urinary retention
  - No cause found
- Management: Quiet, gently lit area, familiar faces. Consider midazolam or haloperidol

---

**Decreased Urine Output**

- = < 30 ml/hour
- Causes:
  - Hypovolaemia: ↑HR, ↓BP, peripherally shut down
  - Urinary retention: ?palpable bladder
  - Catheter blockage (especially if sudden drop off)
  - Renal failure due to hypotension, nephrotoxic drugs, transfusion
- Management: If not overloaded then treat with fluids: normal saline unless significant blood loss. Don’t use dextrose – won’t stay in the blood for long
Dehiscence

- Wound breakdown (e.g., of a gut anastomosis). Usually after 5–7 days due to ischaemic tension, infection, etc.
- Symptoms: severe pain, ↓ bowel sounds
- Investigation: CT with gastrographin contrast
**Paediatrics**

Paediatric topics elsewhere:
- Skin conditions, including infections, eczema and other lesions, see Skin, page 504
- Consent and Children, see Consent, page 1059
- Other cross references are included in the relevant section

**Epidemiology and Health Systems**

**Epidemiology**

*Child Public Health*

- Why is child public health important?
  - The early years are important for lifelong health (eg CV disease etc)
  - The health status of NZ children compares poorly internationally
  - ↑/persistent *ethnic + SE inequalities in health* exist
    - Need for more prevention + early intervention (evidence of effective interventions + positive economic returns)
    - Need for multi-level interventions
- Child development key points:
  - Influenced by the *ecological model* i.e. development shaped by many factors at different levels
  - Rapid brain development occurs during the early years
  - Relationships are key – loving, secure, responsible

**Measures of Child Health**

- Measures of death/disease:
  - Mortality
  - Disease specific mortality/morbidity (eg SUDI)
  - Hospital discharges
  - Disparities: ethnic, gender, age, location, etc
- Measure of health interventions:
  - Immunisation coverage
  - Well child checks
- Measures of health or its determinants or impacts:
  - Breast feeding at 3 months, 6 months
  - Participation: early childhood education, school, sport, etc
  - BMI: marker of appropriate nutrition
  - Self-report (eg questionnaires)

**NZ Statistics**

- Numbers of children:
  - 26% of NZers are aged <18, 22% <15, absolute number is ↑, proportion of total population is ↓
  - 35% of Maori population are aged <15; 38% of PI peoples <15
  - Until 2050, expected fall in the number of children, and fast fall in their proportion of the total population (from 23 –16%) → future conflict over resources: essential needs of children should be given high priority in the allocation of resources
- Social context:
  - Major social + economic changes from ’80s-’90s disproportionately affected children, Maori and PI families:
  - Increased income and health inequalities
  - Rapid ↑ in number of children living in homes experiencing poverty +/-unemployment
  - ↑ in one parent families
  - Child poverty rates had been gradually ↓ until 2008
  - Despite a period of economic prosperity, child poverty levels remained elevated
  - Important to consider needs of children during current economic downturn
- Mortality:
  - Infant mortality = deaths in the first year of life (includes neonatal mortality: <4/52 and post-neonatal: 4-52/52)
All child mortality rates in NZ are declining but this is slow in comparison with other countries.

Major causes of death (old data – from Tripp days):

- < 1 year: SUDI (29%), Congenital abnormalities (28%), Perinatal conditions (27% - prematurity, neonatal infection, hypoxia, etc)
- 1 – 4 years: Injury and poisoning (46%), Congenital abnormalities (18%), Cancer (11%). Maori injury and poisoning rate 3.5 x Non-Maori

SIDS/SUDI:

- SIDS now known as SUDI (sudden unexpected death in infancy)
- SUDI rate has fallen – linked with SIDS health education messages (national cot death campaign).
- Ethnic inequalities ↑

Majority of SUDI deaths have one or more preventable risk factors

Key messages for parents/caregivers:
- 1. Smoke-free during pregnancy
- 2. Sleeping position – "back to sleep"
- 3. Safe sleeping environment (cot near parent’s bed, no co-sleeping)
- 4. Sleep in same room for 1st 6/12
- 5. Breastfeed

Child injury deaths:

- Leading cause of death in developed countries (~ 40% of deaths for 1-14 yr olds)
- Marked inequalities in injury mortality
- Much scope for prevention

Morbidity:

- Top 5 causes of hospitalisation in children aged 4/52 – 14 years = injury/poisoning, gastro, asthma, bronch, viral infection
- Ethnicity patterns same as for mortality: Maori rates much higher

Child abuse and neglect:

- NZ has a 4-6-fold higher rate of child maltreatment deaths compared to countries with the lowest rates
- Risk is highest for infants
- Maori children – 2-fold higher rate of maltreatment-related deaths, hospitalisation, and CYF notifications cf non-Maori

Exposure to tobacco smoke:

- Estimated to result in 500 hospital admission for chest infections in <2yr olds; 15,000 episodes of child asthma; 27,000 GP consults; 1500 glue ear operations; 50 cases meningococcal disease
- In utero exposure linked to IUGR + SUDI
- Parental smoking ↑ risk of smoking during adolescence

Conclusions:

- Despite improvements, New Zealand hasn’t made the gains that other countries have
- Ethnic and socio-economic disparities are growing
- Improvements in curative medicine are unlikely to have an impact on this inequality

Health Systems

Determinants of child health:

- Biology: genetic potential, development in utero
- Socio-economic:
  - Housing
  - Income
  - Education (especially maternal – key issue in 3rd world)
- Environment:
  - Social
  - Physical
- Health Behaviours
- Health Services

Impact of determinants:

- Perinatal complications and family adversity have an independent impact on cognitive ability
- Social adversity is a bigger factor in mild mental retardation than biological factors
- Variations in family social background is a:
  - Weak determinant of specific problems
  - Pervasive determinant on generalised vulnerability to a wide range of problems
• Large differences in absolute income have little or no effect on mortality. Small increases in income equality have a large effect

• Improving health equality through health services:
  • Population based measures:
  • Resource allocation
  • Intersectorial collaboration
  • Community development
  • Data collection on deprivation
  • Salaried GP services for deprived areas
  • Individual health services:
  • Site and mode of provision of services
  • ↑Communication with consumers
  • Targeting of preventative services

International Agreements

• Alma Ata Declaration on Primary Health Care:
  • Declaration to protect and promote the health of all people
  • ‘Health for all by the year 2000’ through quality primary care
  • Defined primary care and gave principles for health services

• Ottawa Charter on Health Promotion: [See Health Promotion, page 1033] (DRSHC)
  • Building Health public policy
  • Creating healthy environments
  • Strengthening community action – power and control to communities to identify and solve their problems
  • Developing personal skills
  • Reorientating the health system: balance between preventative vs curative services

• Jakarta Declaration on Health Promotion in the 21st Century:
  • Comprehensive approaches (using all 5 Ottawa charter principles) are the most effective
  • Settings offer practical opportunities for the implementation of comprehensive strategies
  • Participation by the community is essential
  • Health learning fosters participation

• Declaration of Children’s rights 1959
  • United Nations Convention on the Rights of the Child (UNCROC):
    • Principles and standards by which governments, organisations and families can be measured
    • Ratified by NZ in 1993
    • Rights:
      o Provision
      o Protection
      o Participation
    • Key principles:
      o Actions in their best interests
      o Right to life and maximal development
      o Non-discrimination
      o Right to participation
    • Ongoing concerns in NZ about living standards, health, protection from violence, education and participation

Action

• Recognise:
  • The special rights of Maori
  • The Treaty of Waitangi
  • The impact of racism on health (through impact on determinants of health, exposure to risk + protective factors, and access to and quality of treatment)

• Actions:
  • Work with communities, shared-decision making
  • Effective, evidence based intervention
  • Effective leadership
  • Good data collection

• Conceptualising prevention:
  • Primordial (underlying conditions)
Paediatric Ethics

Important Concepts

- **Autonomy:**
  - Autonomy = self-rule; in medical ethics refers to the right of competent patients to consent to or refuse medical treatment
  - Babies and young children are clearly not autonomous
  - Autonomy is a capacity that typically develops from childhood to adulthood, diminishing again at the end of life, and often waning during periods of distress, intoxication, mental illness or other stressful events
  - Older children and adolescents may be able to provide consent or assent to treatment, depending on the severity of the condition and the nature of the treatment

- **Competence and consent:**
  - On a case by case basis, children can consent to or refuse treatment if under the age of 16 IF they are deemed competent
  - Competence is determined if an individual can answer yes to the following questions:
    1. Are they capable of expressing their wishes?
    2. Do they understand what is involved in respect to the proposed treatment?
    3. Do they understand the consequences of accepting or refusing treatment?
    4. Are they capable of rationalising/weighing the decision/manipulating the information (i.e. follow a logical sequence of thought in order to reach a decision)?
  - Even though a youth under the age of 16 can consent to treatment, parents have a legal right to know what this treatment is unless it pertains to contraception/STIs/abortions/emergency treatment

- **Best interests:**
  - It is usually parents who are asked to give proxy/surrogate consent to medical treatment on behalf of their child
  - Parents have this role and responsibility because it is generally assumed that parents are best placed to judge what would be in the best interests of the child
  - The law generally provides parents with wide discretionary authority in raising their children
  - However, health practitioners also have a duty of care towards their paediatric patients and they have a duty to intervene if they judge that parents' decisions are not in the child's best interests

- **Assent:**
  - This basically means that the child agrees with or endorses their parents’ and health providers’ decision about treatment
  - Assent should include at least the following elements:
    1. Helping the patient achieve a developmentally appropriate awareness of the nature of his or her condition
    2. Telling the patient what he or she can expect with tests and treatment(s)
    3. Making a clinical assessment of the patients understanding of the situation and the factors influencing how he or she is responding (including whether there is inappropriate pressure to accept testing or therapy)
    4. Soliciting an expression of the patient’s willingness to accept the proposed care

Relevant Sections of Law

- **HDC Code of Health and Disability Services Consumers’ Rights Regulation 1996**
  - RIGHT 7: Right to Make an Informed Choice and Give Informed Consent
  - Where a consumer is not competent to make an informed choice and give informed consent, and no person entitled to consent on behalf of the consumer is available, the provider may provide services where - a) It is in the best interests of the consumer

- **Care of Children Act 2004 No 90 (as at 29 November 2010), Public Act**
  - Section 36. Consent to procedures generally
  - If a child is 16 years or older, can consent to procedures

- **NB. Gillick precedent case, accepted in NZ = Prescription of contraception was a matter for the doctor's discretion, and that contraception could be prescribed to under-16s without parental consent**
  - Key conclusion: Minors are not incapable of consenting to medical procedures by reason of their age alone
See competence above for criteria that must be met when considering whether individuals are fit to make decisions

**Immunisation**

**National Immunisation Schedule (see immunisation section)**

<table>
<thead>
<tr>
<th>Age</th>
<th>DTaP-IPV-HepB/Hib</th>
<th>PCV7</th>
<th>Hib</th>
<th>MMR</th>
<th>DTaP-IPV</th>
<th>dTap</th>
<th>HPV</th>
</tr>
</thead>
<tbody>
<tr>
<td>6 weeks</td>
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<td>✓</td>
<td></td>
<td></td>
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<tr>
<td>3 months</td>
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<td>✓</td>
<td>✓</td>
<td></td>
<td></td>
<td></td>
<td>✓</td>
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<tr>
<td>5 months</td>
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<td>✓</td>
<td>✓</td>
<td></td>
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<tr>
<td>15 months</td>
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</tr>
<tr>
<td>4 years</td>
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<td>✓</td>
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<tr>
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<td>12 years – girls only</td>
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<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
</tbody>
</table>

- D = diphtheria; T = tetanus; aP = acellular pertussis; IPV = inactivated polio vaccine; Hib = haemophilus flu type b; PCV7 = 7-valent pneumococcal conjugate vaccine; d = adult dose diphtheria; ap = adult dose acellular pertussis
- For information about vaccine preventable diseases, see immunisation section
- For information re advice, risks, and FAQs re immunisation, see vaccination practice

**History and Examination**

**Difference Between Adult and Child History Taking**

- Kids may not be able to tell you, teens may not want to
- Concerned with **nutrition**: what normal and current feeding practices are, micro-nutrients
- **Growth**: weight, height and head circumference (**NEVER** forget this!)
- **Developmental** perspective:
  - **Gross motor**: rolling, sitting, crawling, walking, running, stairs, sports
  - **Fine motor**: hand skills, co-ordination (assessed through play → art → writing)
  - Vision
  - Hearing
  - Speech/language (receptive/expressive)
  - **Social development**: bonding → parents vs strangers → peers
- **Immunisation**: 'Are your immunisations up to date' – usually meaningless. Need to be more specific
- **Family history:**
  - Congenital abnormalities
  - Genetic factors
  - Parental age and experience
  - Impact of chronic illness on family
- **Social history:**
  - Abuse and neglect
  - Living circumstances – overcrowding, smoke exposure
  - Education settings, eg day care
  - Peer support for kids (eg in adolescence)
  - Adolescence: HEADSS Assessment (see page 1009)

**History Outline**

- **General data**: name, DOB, ethnicity, where they live
- Presenting Complaint
- History of presenting complaint:
  - Chronological and including symptoms across all systems
  - Treatments so far
  - Contact history
  - Family history of the complaint
- Paediatric Past Medical History (HABE-WIMP-MAFS-ROSE [review of systems, examination]):

- HPC
- Antenatal: normal scans? Smoking/EtOH/drugs/infections?
- Birth/perinatal: gestation, delivery, weight, APGAR, any inpatient care, complications, guthrie, MECONIUM
- Eating/feeding (breast, formula, solids): detailed if relevant (eg which formula, which solids, how much)
- Weight: growth history, where relevant growth and puberty in family members
- Immunisations
- Milestones: “tell me about their development” including relevant milestones for the child now: cover gross + fine motor, language, social, play and self care skills + vision + hearing
- Past medical history: any admissions, any surgeries?
  - Medications
  - Allergies
  - Family history: ages and health of parents and grandparents. Ages, names and health of siblings
  - Social history:
- Parent’s occupations
- Who cares for the child
- Schooling/childcare, performance at school
- Behaviour at home/school
- Sleeping arrangements and home circumstances
- Financial circumstances
- Alcohol, smoking
- Pets
- Problems/stresses at home
- Access to car/phone?
- **Systems enquiry** (OHCS, p 173):

<table>
<thead>
<tr>
<th></th>
<th>Neonate</th>
<th>Toddler</th>
<th>Older Child</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cardiorespiratory</strong></td>
<td>Tachypnoea, grunts, wheeze, cyanosis</td>
<td>Cough, exertional dyspnoea</td>
<td>Cough, wheeze, sputum, chest pain</td>
</tr>
<tr>
<td><strong>Gastrointestinal</strong></td>
<td>D&amp;V, jaundice, stool frequency</td>
<td>D&amp;V, stool frequency</td>
<td>D&amp;V, abdominal pain, stool frequency</td>
</tr>
<tr>
<td><strong>Genitourinary</strong></td>
<td>Wet nappies (how often?)</td>
<td>Wet nappies (how often?)</td>
<td>Haematuria, dysuria, sexual development</td>
</tr>
<tr>
<td><strong>Neuromuscular</strong></td>
<td>Fits, odd attacks, jitters, feeding ability</td>
<td>Fits, drowsiness, hyperactive, vision, hearing, gait</td>
<td>Headaches, fits, odd sensations, drowsiness, academic ability, vision, hearing, co-ordination</td>
</tr>
<tr>
<td><strong>ENT and teeth</strong></td>
<td>Noisy breathing</td>
<td>Ear discharge, teeth eruption</td>
<td>Earache/discharge, sore throat</td>
</tr>
</tbody>
</table>

- **General questions**: eating + drinking, rash, fatigue, lumps, itch, fevers, bleeding tendency, family interaction
- **General viral-type illness questions**: runny nose, pulling at ears, wheeze, cough, photophobia, stiff neck, rash, feeling hot, shaking, vomiting, diarrhoea, sick contacts
- **Is this child very unwell?**: floppy, cyanosed, breathing fast/slow, fitting, rash, vomiting bile, not eating/drinking, ↓UO

**Examination**

- **Principles:**
  - Leave nasty things till last
  - Observe
  - Get on floor and use games
  - Wait until child familiar with environment but start before bored
  - Don’t touch child until rapport established
  - Use your own toys – they’re novel
  - Get parents to undress them (or do anything else that is nasty)
  - Get them to draw pictures while taking the history
- They’re likely to be scared (depending on previous experience). Build rapport, play games, talk with child not through parent. Don’t wear stethoscope around neck
- Show them what you want rather than telling them
- **Blood pressure:**
  - Is important – **always do it**
  - Getting them calm is hard – usually anxious → artefacts common

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*Paediatrics* 889
- **Cuff**: Bladder should nearly encircle the arm. Width is 2/3 length from shoulder to elbow.

- **Chest exam**:
  - Percussion more sensitive than auscultation (won’t show anything in the absence of respiratory signs/symptoms)
  - Percussion will tell you about hyperinflation, fluid, mediastinal shift
  - Auscultate heart early in the exam – but not first

- **Abdominal exam**: Get child to suck in and push out tummy to check for tenderness – then you won’t have to hurt them yourself.

- **Differences in a baby**:
  - *More liver in the abdomen* (2 finger breaths is normal). Don’t press too hard – moves with respiration
  - Pelvic organs higher (eg bladder)
  - Pulses: Radial/Brachial – take both sides. *Must palpate femoral pulse*. If feet aren’t white don’t take peripheral pulses

- **Teenage girls**: examine chest underneath clothes

### Normal Values

<table>
<thead>
<tr>
<th>Age</th>
<th>Breathing</th>
<th>Pulse</th>
<th>Systolic BP</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 1 yr</td>
<td>30 – 40</td>
<td>110 – 160</td>
<td>70 – 90</td>
</tr>
<tr>
<td>2 – 5 yr</td>
<td>20 – 30</td>
<td>95 – 140</td>
<td>80 – 100</td>
</tr>
<tr>
<td>5 – 12 yr</td>
<td>15 – 20</td>
<td>80 – 120</td>
<td>90 – 110</td>
</tr>
<tr>
<td>&gt; 12 yr</td>
<td>12 - 16</td>
<td>60 - 100</td>
<td>100 - 120</td>
</tr>
</tbody>
</table>

- Stethoscope around your neck adds 10!

- Haemoglobin: at birth: 170, day 5: 200, 12 weeks: 120 (lower limit of normal is 90 – 100)

### Examination Outline

- **Growth**: height, weight and head circumference (and plot them)

- **General**:
  - Sick or well
  - Dysmorphic features
  - Obvious distress
  - Temperature
  - Colour/rashes/anaemia/cyanosis/jaundice
  - **Lymph nodes**: check anterior and posterior cervical chains, subhyoid, sub-occipital, sub-mandibular, sub-lingual, axillary, inguinal and epitrochlear
  - Hydration/perfusion

- **Cardiovascular**:
  - Pulses: radial (but use brachial in baby/toddler), **femoral** (always do this), synchrony, sinus arrhythmia (normal in all children)
  - Blood pressure (NB use correct cuff size)
  - JVP: often hard to see
  - Peripheral oedema (*peri orbital* in babies)
  - Liver enlargement → right ventricular failure
  - Feel the cardiac impulse: apex may be more lateral in children. Thrills
  - Auscultation

- **Respiratory**:
  - Ears, nose, throat, sinuses
  - Lymph nodes
  - Clubbing
  - Chest deformity
  - **Respiratory rate**, effort and accessory muscle use, grunting, ability to talk in sentences
  - Intercostal, sub-sternal and supraclavicular indrawing, hyperinflation, Harrison’s sulcus (lower ribs pulled in →chronic airways disease), pigeon chest (⇒ chronic ↑ in AP diameter), tracheal tug, nasal flaring
  - Auscultation, including cardiac dullness (⇒ hyperinflation). Tracheal position rarely of value
  - Percussion

- **Abdominal**:
  - Inspection, movements, scars, **herniae**
  - Liver, spleen and kidneys
  - Bladder
  - Masses
Tenderness
- External genitalia
- Examine anus (PR rarely required)

**Neurological:**
- **Developmental assessment:** See Child Development, page 899
- **Neurological Exam:** See Neurological Exam in Children, page 953

- **Joints**
- **Skin**

**When is a Child Really Sick?**

**Normal Vital Signs in Children**

<table>
<thead>
<tr>
<th>Age</th>
<th>Pulse rate</th>
<th>RR</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;3/12</td>
<td>160</td>
<td>60</td>
</tr>
<tr>
<td>3-12/12</td>
<td>160</td>
<td>50</td>
</tr>
<tr>
<td>1-5 yrs</td>
<td>140</td>
<td>30</td>
</tr>
<tr>
<td>6-11 yrs</td>
<td>120</td>
<td>25</td>
</tr>
<tr>
<td>&gt;12 yrs</td>
<td>100</td>
<td>20</td>
</tr>
</tbody>
</table>

- Factors which are not on their own discriminating between mild and severe:
  - **Temperature:** spikes easily
  - **Pulse:** variable, eg ↑↑ if crying
  - **Blood pressure:** hard to measure, and if shocked is still maintained till very late. As soon as they have any hypotension they’re the same as an adult with no recordable BP (i.e. VERY sick)
  - WCC
- **NB.** dysuria and pale extremities may be the only warning signs before they crash
- Agitation can be a sign of hypoxia
- Na is often low as septic illness/other severe illness leads to ADH release (stress hormone) and therefore H2O is retained

**Factors From History Which Discriminate**

- **Intake:**
  - Refusal to feed ⇒ more severe
  - Refusal to take solids but still taking liquids ⇒ not so bad
- **Losses:**
  - Vomiting:
    - **Frequency and amount:** if vomiting their whole feed then bad (vs a small spill)
    - **Colour:** Bile is bad. Yellow (from gallbladder), green (after bile has been in the stomach) or orange. Due to obstruction (anywhere distal to duodenum) or ↑↑ sympathetic discharge, eg due to pain (not necessarily abdominal – could be a torted testicle)
  - ↓ urine output (wet nappies < 4 per day)
  - Diarrhoeal losses

**Factors Which Discriminate on Exam**

- **Floppiness:** ↓ tone (can indicate acidosis)
- **Perfusion:** pale, mottled or blue, cold (feel calves). **Capillary refill > 2 secs.** (ie peripheral vasoconstriction)
  (check central by pressing with finger for 5s on skin of chest)
- **Fitting** (not febrile convulsions though, rather rigors)
- **Cyanosis** (central)
- **Respiratory rate:** quality as important as rate (either respiratory or central problem; central = sick ⇒ shock ⇒ hypoxia ⇒ anaerobic metabolism ⇒ lactic acidosis ⇒ act on chemoreceptors ⇒ ↑RR)
- **Rash** if petechial/purpuric (meningococcal septicaemia; NB. Rash can occur ANYWHERE, therefore need to look everywhere)
- ↓**Weight** (dehydration)

**Toxic Appearance**

- Decreased level of arousal
- Poor perfusion/circulatory compromise: pallor, tachycardia, cool + mottled limbs, hypotension
- Respiratory impairment:
  - Tachypnoea, grunting respirations, recession, cyanosis
Due to ↑ O2 requirements + trying to blow off CO2 from acidosis + pulmonary oedema from capillary leak

**Shock**
- Clinical diagnosis of failure of the circulatory system to deliver sufficient O2
- Look for compensatory mechanisms which try to maintain perfusion of vital organs (↑HR, peripheral vasoconstriction)
- Causes of shock:
  - Capillary leak → ↓ cardiac output
  - Changed vascular tone
  - Impaired myocardial function
- Progression: Toxic → Septic → Shock
- Specific signs:
  - Meningism: bulging fontanelle, rash, stiff neck
  - Pneumonia: chest sounds (not very sensitive)
  - Distended abdomen and guarding: obstruction, appendicitis
  - Lumps in the inguinal region (seen or felt): hernia → obstruction → acidotic
  - Blood in faeces: intussusception

**Resuscitation**
- 1. O2
- 2. IV fluids (~20ml/kg) – don’t waste time trying for an IVL, go to IO after a couple of failed attempts
- 3. Warm the child (unless raging temperature)

**Septic Screen**
- 1. Bloods: FBC, electrolytes, **culture**, ABG, (cross match)
- 2. X-rays: chest, abdomen if distended
- 3. Urine culture (bladder stab)
- 4. Maybe lumbar puncture

**Neonates**
- Check list for a neonate (clinical acumen less reliable):
  - Fever: consider full sepsis evaluation for any child > 38 C
  - Feeding: if intake < 50% normal
  - Urine output: < 4 wet nappies in 24 hours
  - Peripheral circulation: pallor of recent onset, mottling, cold periphery, slow capillary return
  - Responsiveness: poor response to stimulation and a weak cry
  - Activity: ↓ movement, ↑ sleepiness
  - Breathing difficulty: signs of distress, cyanosis, RR > 60
  - Apnoea: pause in respiration > 20 secs. Central (eg premature) or obstructive (eg URTI) or mixed
  - Vomiting: treat any vomiting in neonate seriously. Look for bile staining
  - Cyanosis
  - Seizures
  - Severe jaundice: risk of bilirubin encephalopathy

**Dealing with Children and Families**

**Talking with Children**
- Do:
  - Engage them
  - Explain who you are and why you are seeing them
  - Use language and concepts that are age appropriate
  - Reassure if seeing separate from parents
  - Outline confidentiality issues with older children or adolescents
- Don’t threaten:
  - The child’s sense of loyalty to their family
  - Their defences against unbearable emotional pain
- Interviewing preschoolers (3 – 5 years):
  - Get down to their level, use simple language
  - Take things at their pace
- Can use play, drawings and stories
- Ask about everyday world
- Watch verbal and non-verbal communication
- See with parent

**School age children (6 - 11 years):**
- Can be structured
- Ask about feelings (sadness, anger, etc) as well as daily life
- Ask about family, school, friends, problems, worries
- Wishes, hopes for the future
- Very abstract, open-ended questions can be confusing

For adolescents see Talking with Adolescents, page 1008

### Parent and Adolescent Education

- **Aim** is to change behaviour. Changing behaviour requires:
  - **Knowledge**: necessary but not sufficient
  - **Skills**: to manage the change
  - **Motivation**: involves striving towards a goal, not just ‘trying’. The goal must be:
    - Important to the person – ‘I want this’. Make it attractive. May need their goals to come before yours.
    - Achievable – ‘I can do this’. Believe in them
    - Not too unpleasant. ‘I don’t mind doing this’. Make it easy

- **Good counselling technique:**
  - Open-ended questions: “tell me about....”
  - Active listening: “Hmm, I see...”
  - Reflection: reflect facts and emotions
  - Summarising: “Let me see if I’ve got this straight....”
  - *Don’t* ask leading questions: eg “You don’t do that, do you?”

- **Take a history using open-ended questions, reflecting, summarising:**
  - Help parent or adolescent clarify exactly what it is they want to know
  - **Knowledge**: what do you understand about...? Where did you find that out? How convinced are you?
  - **Attitudes/fears**: are you worried about anything in particular?
  - **Practices**: What have you actually done so far?
  - **Barriers**: What’s stopping you from doing this?

- **Then:**
  - **Validate/reinforce** knowledge they already have: “That’s terrific – you already understand a lot....”
  - **Education** to correct incorrect beliefs/address fears
  - **Encourage** them to find their *own solutions*: “So, what do you think you could do?”
  - **Reinforce** safe practices and responses

- See also Neonatal and Infant Anticipatory Guidance (Parent Education), page 919

### Families

- **Ref:** notes from Lorraine Christie, Clinical Psychologist

- **The task of childhood is development of:**
  - Social relationships
  - Emotional maturity
  - Sound set of values and beliefs
  - Sound thinking patterns
  - Knowledge of body and skills

- **Self esteem and self respect laid down in the first 7 years are influenced by:** Gender, race, culture, sexuality, temperament, ordinal position, IQ, physical characteristics, creativity, did you arrive in the family at an okay time

- **Families are systems with:**
  - Structure
  - Various roles
  - Authority
  - Channels of communication

- **System theory:**
  - Families are systems
  - Systems have sub-systems (i.e. relationships between individuals) and subsystems have units (individuals)
External influences (environmental, extended family, wider societal) can disrupt/change the relationships within the family system

Stressors (e.g. illness) also can disrupt/change the relationships (i.e. strengthen or weaken) within families

Five characteristics of healthy families:

- The marital relationship is the strongest relationship and the greatest focus of power
- Communication is open and honest and permits spontaneous interruption
- Warmth and caring predominates over anger and hostility
- There are known problem solving techniques which can be instigated quickly
- Movement towards independence for all members of the family

The family life cycle: constant reorganisation and change

- Two form a couple:
  - Take on husband/wife/partner roles
  - Substantial reorganisation of boundaries: family, friends, togetherness vs autonomy
  - Work through differences
  - Structuring a relationship: complimentary vs symmetrical
- First baby:
  - Parenting roles
  - Ensure spouse relationship remains the strongest
  - Reorganised boundaries to allow for grandparents, friends, interests
- Preschoolers:
  - Protect spouse relationship: contact, support, being together
  - Parent/child subsystem: affection, encouragement of appropriate autonomy, boundaries for child, individuating siblings from each other
  - Continued reorganising of boundaries: grandparents, outside world, work
- School age children:
  - Integrating school and family systems
  - Allowing age appropriate autonomy
  - Children less egocentric, more sensitive to other’s needs, develop sense of fairness and gender awareness
- Adolescence:
  - Issues of proximity and distance
  - Extending boundaries to allow independence
  - Continual renegotiation – autonomy vs control
  - Sibling individuation from each other
- Young Adult: between families
  - Differentiating self from family of origin
  - Leaving home, career development
  - Intimate peer relationships, courtship
  - Parents: at height of careers, retirement looming
  - Grandparents: needy, mobility, loss of sight, death
  - Parents take on grandparent roles

Preparing a Child for Surgery

- Talk to the child about what is going to happen and why. Read books about hospital
- Reassure your child that you will be there too
- Answer your child’s questions
- Use simple terms that the child can understand
- Take a favourite toy. It can have bandages too
- Be honest without scaring: ‘It will hurt for a bit – but we’ll try and make it better”
- Tell the child he/she will be going home with you when it’s finished
- Don’t be surprised if the child gets angry with you: this is normal

The Dying Child

- Anticipated: preterm infants, congenital abnormalities, metabolic disease, etc
- Unanticipated: often older, trauma, SIDS
- Issues:
  - Relief of child’s pain → pain management, including neonates
  - Clear and simple information: check their understanding, explain prognosis, explain disease process, avoid information overload or jargon, respect silence
- Decisions about when to withdraw treatment
- Before death: time and space, preparation of child
- After death: viewing the body, coroner, funeral options, surviving siblings, other families, availability of health care team

- See also Children’s Grief, page 771

**Autopsy of a Child**

- Family concerns:
  - What is an autopsy – like a major operation
  - Will my child be cut – yes
  - When will it be done – soon
  - How long will it take – max 3 hours
  - What will my baby look like afterwards – won’t see chest incision if dressed. Vertical cut down back of head
  - Can I take my baby home afterwards – yes

- Autopsy may provide:
  - A cause of death – but may take time
  - Identify unacceptable iatrogenic lesions
  - Quality control for a neonatal unit
  - Assist medical knowledge
  - Information that may help other babies

- Common reasons for refusal:
  - Concerns about disfigurement and further suffering
  - Lack of information
  - Objections from family members
  - Religious beliefs
  - Interference with funeral arrangements

- Must refer to the coroner:
  - Where death certificates cannot be signed
  - Thought to be related to an invasive procedure
  - ?Birth asphyxia
  - Deaths thought to be related to an instrumental delivery

**Behavioural Issues**

- Behaviour doesn’t exist outside an environmental context

**Behaviour Management**

- History Taking:
  - Antecedent: what sets him off?
  - Behaviour: describe exactly what he does?
  - Consequence: What do you do about this?

- Principles:
  - Remove (time out). Somewhere safe and boring, and where you don’t mind the child disliking (ie not the toilet if toilet training or bedroom if sleep training). Leave a minute for every year of age. Be specific about what they’re going in for. At the end, remind of the behaviour you want, and then forget the incident.
  - Anticipate/avoid situations where conflict is likely
  - Ignore minor things, particularly tantrums
  - Distract
  - Example (set a good one)
  - Reward acceptable/wanted behaviour

- Reward Systems:
  - Star chart if young, more sophisticated and discrete if older
  - Agreed between parents and child. Child has to own it (can they help make it?)
  - Planned: don’t have to make a decision when the time comes
  - Anticipated: known about in advance – **When** you this, **then** you will have …
  - Consistently applied: no matter where he is or who he is with
  - Immediate: not at the end of the week or when dad gets home from work
  - **Strong reward** component
Meaningful to child:
- Young child: cuddles, praise and attention
- 8+ years: if you ... you can choose what we have for dessert/which video, etc (choice is powerful)
- 10+: money

Referral options:
- Special Education Service (SES): Resource teacher for learning and behaviour (RTLB) or Behaviour Support Team through SES
- Child psychiatry service (CAFS) if severe psychiatric symptoms (anxiety, depression, OCD, PTSD, sexually abused, ADD), persistent family dysfunction or resistant to simple management strategies
- Paediatrician if medical issues
- CYFS if abuse

Risk and Resilience

<table>
<thead>
<tr>
<th>Good</th>
<th>Bad</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Internal</strong> (child factors)</td>
<td>Resiliency: High self esteem, happy temperament, high IQ, problem-solving skills, coping strategies, humour</td>
</tr>
<tr>
<td><strong>External</strong> (factors in the environment)</td>
<td>Protective: caring and supportive adult, reasonable structure and limits, being believed in</td>
</tr>
</tbody>
</table>

- Attribution theory: Are their successes and failures due to an internal locus of control (‘I passed the test cause I did the work’ → high self-esteem) or an external locus of control (‘It doesn’t matter if I study or not, it won’t make any difference’ → low self esteem)
- Individual traits that build resiliency:
  - Insight: recognition of one’s distressed condition with subsequent action to overcome barriers
  - Independence: gaining emotional distance and autonomy amid chaos
  - Initiative: achievements that foster self confidence and constructive activity
  - Relationship building: Protective and nurturing connections with at least one supportive adult
  - Creativity: facilities healing and positive activity in a difficult environment
  - Humour: focuses on hope not harsh realities
  - Morality: commitment to fairness and compassion
- Family traits that build resiliency:
  - Commitment: loyalty, determination to work things out, sacrifice for mutual benefit
  - Cohesion: togetherness, respect for the individual, interdependence
  - Adaptability: flexible, stress coping skills
  - Communication: listening and speaking skills
  - Spirituality: shared purpose and values
  - Connectedness: Support within and beyond family, attitude of service
  - Effective resource management: Competent use of money, time, etc
  - Coherence: Optimism and self reliance
- Intervention strategies:
  - Provide opportunity for and encourage contributions
  - Enhance decision making skills → ↑ feeling of control
  - Encourage and give positive feedback
  - Develop self discipline: involve child in setting the rules and consequences

Toddler Behaviour

- Approach:
  - History, including:
    - Antecedents, behaviours and consequences
    - Social context
    - Collaborative history if necessary
    - Psychiatric history from mother (is the child the problem?)
    - PMH: ABFWIMPS
  - Exam: especially developmental
  - Education
- Most difficult behaviour does not indicate a serious disturbance. Indicators of serious disturbance include:
  - Deliberate self harm or messing
  - Wandering off
  - Running away
  - Age inappropriate sexual behaviour
- Developmental sequence of everyday habits:
  - Feeding
  - Sleeping
  - Eating
  - Toilet
  - Going to bed and getting up
  - Dressing and undressing
  - Washing and cleaning teeth
- Aim is to achieve regular habits and routines:
  - To start with need to insist on regular routine and time schedule. Once achieved can be more flexible
  - Failure to achieve routine: daily hassle and distress
  - Regular routines $\Rightarrow$ $\uparrow$ security of child, $\downarrow$ argument with parents
- Factors which $\downarrow$ behaviour problems:
  - Routine and regularity
  - Clear limit setting
  - Unconditional love and affection
  - High level of supervision
  - Consistent care and protection
  - Age appropriate disciplines and rewards
- Tantrums:
  - Want their way. Purpose of tantrum is to get their way. Giving in reinforces the behaviour
  - Must be consistent. If you say no, will have to stick with it choose your battles
  - Options for managing a tantrum (see Behaviour Management, page 895)
    - Ignore it: eg leave the room
    - Time out
    - Distract
    - Avoid problem areas (eg supermarkets)
  - Things will get worse before they get better. Once they realise the boundaries are consistent they will stop testing them
- Sleep Management: Sleep Management, page 923
- Other points:
  - Check parent’s are not expecting too much of the child (eg 3 year old boy not wetting at night)
  - Keep no for important things
  - All parents make mistakes

**Problems at School**
- For ADHD see Attention Deficit/Hyperactivity Disorder (ADHD), page 1001
- Symptoms:
  - Normal IQ, no disabilities, but fail to develop academic potential
  - Difficulty with peer relationships, loners, act out, difficult behaviour
  - Develop associated problems: psycho-somatic, $\downarrow$ self-esteem
- Usually multifactorial:
  - Constitutional factors: May have subtle defects in:
    - Receptive or expressive language
    - Auditory sequencing: can’t remember verbal sequence (eg instructions). Can have a pervasive effect on schooling
    - Visual sequencing: difficulty reading/spelling
    - Motor problems (eg clumsy)
    - $\downarrow$ Attention (may be secondary to the above)
    - Health, hearing, vision, etc
  - Environment: cultural, socio-economic status, family disruption, nutrition, etc
  - School related factors:
    - School factors associated with $\uparrow$ antisocial behaviour: poor morale, high turnover, inconsistent standards, undervaluing children’s work, bullying
- Kids spend 15,000 hours at school – so can have a big impact (just as family does)

- **Assessment:**
  - History: parents
  - Information from teachers
  - Physical and neuro exam
  - Sensory exam: vision and hearing
  - Neuro-developmental, educational and psychological assessment

- **For School refusal, see Separation Anxiety Disorder, page 1004**

- **Management of Truancy:**
  - Educational programme appropriate for the child’s needs
  - Monitoring child through the day
  - Assist with the learning process

**Child in Trouble with the Authorities**

- **History:**
  - Interview child and caregiver separately
  - Presenting complaint
  - History of presenting complaint:
    - Describe behaviour: Antecedents, Behaviours, Consequences
    - Social Context in which behaviour occurs: Relationships within family, school, and peers. Physical or sexual abuse
    - Collaborative history: parents, teachers, sports coaches – this is important
    - Psychiatric history: look for depression, anxiety, attentional problems
    - Formal assessment of learning if academic problems

- **Exam:** especially dysmorphisms, stature, neurocutaneous lesions, observations of reading, writing and relationship with parents, vision and hearing

- **Development of antisocial behaviour:**

- **Possible differentials:**
  - Attachment disorder
  - Developmental delay
  - Behaviour conduct disorder
  - Psychiatric illness: Depression, ADHD, PTSD (may appear to be daydreaming)
  - School refusal/Truancy
  - Neglect or other abuse
  - Domestic violence

- **Management plan:**
  - Keep in him school if at all possible: prognosis plummets if expelled or regularly truant
  - Ensure a thorough developmental assessment
  - Referral for psych assessment and counselling
  - Management: accentuate the positive, minimise the negative
  - Referral to other services

**Attachment Disorder**

- See also Anxiety Disorders, page 1004

- **Attachment:**
  - Starts in utero and is an ongoing process
  - Securely attached infants:
    - Are able to seek and obtain comfort from familiar caretakers
    - Are willing to explore and master their environment
  - **Insecurely attached** infants (eg due to long separation from parents and multiple carer-givers in hospital) appear:
    - Anxious: clingy without obvious stress
    - Avoidant: angry, distrustful of parents, won’t be comforted after brief separations
    - Indiscriminately affectionate: won’t show preference for parents

- **Concepts:**
  - **Separation:** the process by which a child develops an identity separate from their parents. Promoted by secure attachment. At risk when the parents perceive the child is ‘vulnerable’
  - **Autonomy:** Development of independence (→social competence)
  - **Mastery:** ↑ sense of competence over the physical environment
Together autonomy and mastery lead to an internal locus of control. Struggles for autonomy and mastery produce normal tantrums

Types of Attachment Disorder:
- **Disinhibited** type: will go to anyone. No stranger awareness and constant, insatiable need for attention. Likely to be due to neglect. Also see it in chronic hospitalisation
- **Withdrawn**: frozen watchfulness, fearful. Likely to be due to abuse

Test by observing child when parent leaves (separation), when a stranger comes in, and when parent returns (reunion)

**Domestic Violence**
- Has significant health consequences: injury, psychiatric, chronic pain, drug and alcohol abuse
- Is common (some studies report up to 20% of women being hit in the last year), but often missed by doctors
- Domestic violence starts with a cycle of ↑ control and disempowerment. Violence is used to reinforce this

Screening questions:
- ‘I have seen many people who come to see me with problems like yours. In my experience, many of these women are being hurt in some way by their partner. Is that happening to you?’
- ‘A lot of tension and violence can be due to relationships within the family – often with a partner. Is your partner being violent toward you?’

Management:
- Ensure mum and the children are safe. If not, refer to police/CYFS
- Refer to Women’s refuge – be aware of the local services available
- Educate: eg the cycle or violence, it won’t stop without help
- Avoid victim blaming (‘it’s not your fault’)
- Take careful notes (explain to the women why you are going this)
- Display information in your waiting room – signals a willingness to discuss it

**When Parents Separate**
- Responses to parent’s separation – all signs of distress:
  - Withdrawn
  - Clingy
  - Regression
  - Difficult behaviour
- Helping the child:
  - Accept the separation – then the child will too
  - Make sure the child knows you love them
  - Avoid conflict in front of the child
  - Allow them to express their feelings
  - Rely on other adults not the child for support
  - Tell the kids they’re not to blame
- Things to avoid:
  - Don’t abuse their loyalty and trust
  - Don’t use them as messengers
  - Don’t use them to spy on other parent
  - Don’t continue to be angry at partner in front of them
  - Don’t let outings/gifts take the place of normal parenting
  - Don’t force kids to take sides
  - Don’t force a clash of loyalties

**Growth and Development**

**Child Development**
- Represents the interaction of genes and the environment:
  - **Genes**: potential of the child
  - **Environment**: extent to which potential is achieved. Requires:
    - **Physical needs**: warmth, clothing, shelter, food, health, activity with rest
    - **Psychological needs**: security, personal identity, self-respect, independence, opportunity to learn, play, affection
- **Areas of child development**:
  - Gross motor
- Fine motor
- Language (expressive, receptive, non-verbal)
- Social (interaction, play, self-care)
- Cognitive: all of the above
- Vision and hearing

- Requirements for development (need all of them):
  - Hardware (neurons, muscles, etc)
  - Motivation (often driven by frustration – a child can’t do what it wants to)
  - Nurturing environment

- Types of assessment:
  - Developmental screening: point in time snapshot
  - Developmental surveillance: following over time
  - A formal assessment will yield a Developmental Quotient < 100 ⇒ delay. 100 ⇒ advanced.

- Principles of development:
  - Most children show unevenness between and within domains
  - The rate of development is more important than a single assessment

**Developmental Assessment**

- Indirect assessment of the acquisition of life skills
- Establish rapport: use names a lot, ‘thanks for coming’, etc → more valid assessment
- Factors to consider:
  - Prematurity – need to adjust age
  - Environmental/social factors
  - Factors affecting performance on the day (tired, unhappy, hungry etc)
- History:
  - Current development and time course of development
  - Order of questions should be:
    - When asking about milestones, start with things he is likely to be able to do and work up. Get better rapport than starting at the upper limit and working down
    - Hearing:
      - What things can he hear?
      - Have you been concerned about his hearing?
      - What makes you confident of that?
    - Vision:
      - What small things does he see?
      - Have you been concerned?
      - What makes you confident of that?
    - Gross motor:
      - Head up prone → up on elbows → up on hands → rolls front to back (then back to front) → sit → crawl → pull to stand → cruises → walk → run → scoot → pedal (progression: head → trunk → limbs)
    - Fine motor:
      - Hands to midline → transfer hand to hand → radial grasp → pincer → feeding self → spoon → marks paper with pen → vigorous straight scribble → circular scribble → circle/cross → 3 part man → 6 part man → triangle
    - Expressive language:
      - Coo → reciprocal vocalisation → babble → words with meaning → combinations (most common area of delay – usually focal not global)
    - Receptive language:
      - Turns to voice → to own name/understands no → understands object names → points to parts on body → follows one or two step instruction → knows name, gender, address, prepositions, pronouns
    - Social:
      - Social smile → lifts arms for pick-up → single step symbolic play → imitates play → parallel play → imaginative play → play with peers → name friend
    - Self-care:
      - Manage cup → spoon → undress → toilet → dress → laces
  - Get history of influences on development:
    - Miscarriages, still births
• Pregnancy: toxins, alcohol, infections
• Birth: APGAR (usually means brain was vulnerable before birth), gestation, birthweight
• Neonatal congenital abnormalities, feeding, jaundice, infections
• Early milestones (smiling, sitting, walking, first words)
• Illness (e.g. CF, heart/renal disease, epilepsy)
• Hearing (→ speech delay), vision (→ good verbal, poor motor)
• Nutrition, constipation (especially if mobility problems)
• Current development, especially social, self-care
• Behaviour problems (sleep, tantrums)
• Family stress
• Family history, especially of development
  ➢ History from other sources (e.g. kindy teacher)
  ➢ Review previous rate of development: may get slowing before loss
  ➢ Past Medical History: HABE WIMP MAFS
• Observation: Look systematically across each of the 6 areas. Use toys as tools.
• Examination:
  ➢ On lap first (stranger shyness from 8 months)
  ➢ Dysmorphism: eyes, head shape, body proportions
  ➢ Growth! Height, weight, head circumference – plot them
  ➢ Vision (do first, affects motor): following, hundreds and thousands
  ➢ Localise to noise (do before language): if concerned then formal testing
  ➢ For each of gross motor, fine motor, expressive and receptive language, social and self-care on the table below:
    o Ask open-ended questions to establish the floor (e.g. I notice he's walking, what other clever things is he doing)
    o Then use closed questions to establish a ceiling (e.g. can he walk backwards, throw over arm)
    o Then summarise: So he can .... but is not yet .... Have I got that right?... Therefore he is at age X for that domain
  ➢ Summary: age for each domain is X, Y, X. Therefore, overall, he's developmentally around age [Average for X, Y, Z]
  ➢ Other:
    o Skin pigmentation (e.g. tuberous sclerosis – seen under Woods lamp)
    o Ears, eyes, heart, abdomen, puberty
    o Neurologic exam
    o Relationship with parents
• Plan: for areas of weakness
  ➢ If significant delay then early intervention
  ➢ If some delay then anticipatory guidance – 'what could you do to help' – use Knowledge, attitudes/fears, practices, barriers framework
  ➢ Always pitch safety advice at the level of gross motor skills

*Development Chart: normal development from 0-60 months*
• Ref: Dr Russell Wills
• Red flags:
  ➢ Not smiling by 2 months
  ➢ No eye contact by 3 months
  ➢ Not reaching for objects by 5 months
  ➢ Not sitting unaided by 9 months
  ➢ Not walking unaided by 18 months
  ➢ Not using words by 18 months
  ➢ No 2 – 3 word sentences by 30 months
<table>
<thead>
<tr>
<th>Gross Motor</th>
<th>Fine motor-adaptive</th>
<th>Expressive language</th>
<th>Receptive Language</th>
<th>Personal-Social/Play</th>
<th>Self Care</th>
</tr>
</thead>
<tbody>
<tr>
<td>6 wk</td>
<td>Holds head up when prone Follow 180</td>
<td></td>
<td></td>
<td>Smiles spontaneously</td>
<td></td>
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<tr>
<td></td>
<td>horizontal (i.e. across midline)</td>
<td>Cry, coo (vowels)</td>
<td>Quiets to voice</td>
<td>Reciprocal smiles (TVS says this</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Follow 0 vertically</td>
<td></td>
<td></td>
<td>is 6/52, others say 12/52)</td>
<td></td>
</tr>
<tr>
<td>3 m</td>
<td>Up on elbows.</td>
<td>Radial grasp</td>
<td>Reciprocal vocalisation,</td>
<td>Turn head to voice</td>
<td></td>
</tr>
<tr>
<td></td>
<td>No head lag on pulling up</td>
<td>Retain 1 block</td>
<td>laugh</td>
<td>Localise bell/keys (horiz)</td>
<td></td>
</tr>
<tr>
<td>6 m</td>
<td>Up on hands</td>
<td>Take 2 blocks</td>
<td>Consonants - babbling</td>
<td>Localise bell/keys (vert)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Sit supported</td>
<td>Transfer hand to hand</td>
<td>Mono-syllabic babble</td>
<td>Lifts arms for pick up</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Rolls back-tummy</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>9 m</td>
<td>Sit stable</td>
<td>Object permanence: Take 3</td>
<td>Vocalise to communicate</td>
<td>Understands no, ta</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Pull to stand</td>
<td>blocks 1 at a time and hold</td>
<td>Poly-syllabic babble</td>
<td>Localise bell/keys (diag)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Crawl</td>
<td>onto them Bang, index point</td>
<td>Jargon</td>
<td>Peekaboo – requires object</td>
<td></td>
</tr>
<tr>
<td>12 m</td>
<td>Move around furniture</td>
<td>Good pincer</td>
<td></td>
<td>permanence</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>Few words with meaning</td>
<td></td>
<td>Cooperate with dressing</td>
<td></td>
</tr>
<tr>
<td>15 m</td>
<td>Walk independent</td>
<td>Stack 2 blocks</td>
<td>Several words</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Mark paper with pencil, fist</td>
<td></td>
<td>Push large wheeled toy</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>grip</td>
<td></td>
<td>Casting prom.</td>
<td></td>
</tr>
<tr>
<td>18 m</td>
<td>Walk backward</td>
<td>Stack 3 blocks</td>
<td>6-20 words; two wants</td>
<td>Few body parts</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Kick</td>
<td>Vigorous straight scribble</td>
<td>Many common objects</td>
<td>Hands familiar named object on</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Throw over arm</td>
<td>3 shape board</td>
<td>Family names, own name</td>
<td>request</td>
<td></td>
</tr>
<tr>
<td>2 yrs</td>
<td>Run</td>
<td>Imitate vertical line, then</td>
<td>2 word combo; Echolalia;</td>
<td>Few body parts</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Throw ball in bin</td>
<td>horizontal; dagger grip for</td>
<td>Songs/rhymes</td>
<td>Hands familiar named object on</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Seat self at table</td>
<td>pen</td>
<td>30 mo: Questions: what,</td>
<td>request</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Stack 6, train 3</td>
<td>who, who?</td>
<td>understands pointing</td>
<td></td>
</tr>
<tr>
<td>3 yrs</td>
<td>Walking:</td>
<td>3 shape board rotated</td>
<td>3-5 word comb; I, we, you</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>tandem, heels, toes</td>
<td></td>
<td>Verbs: eat, kick, gone</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Jump feet together Pedal; Up stairs</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>adult</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4 yrs</td>
<td>Hop 3 steps/ Jump off 2</td>
<td>Stack 9, 3 stairs/bridge</td>
<td>Echolalia resolved</td>
<td>Imagine play seq</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Catch big ball</td>
<td>Imitate circle, cross, tripod</td>
<td>Full name</td>
<td>T-shirt</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Down stairs like adult</td>
<td>grip 42 mo. Count bricks</td>
<td>Plurals</td>
<td>Shoes and socks</td>
<td></td>
</tr>
<tr>
<td>5 yrs</td>
<td>Run up stairs</td>
<td>5 brick gate</td>
<td>Intelligible to strangers</td>
<td>Gives age</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Gallop</td>
<td>4 part man, ladder, square.</td>
<td>Tenses</td>
<td>Co-op play, hide n seek, snap</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Bounce and catch</td>
<td>Cut with scissors; Higher,</td>
<td>Constant Qs: where, why...</td>
<td>Dressups, pretend</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>longer</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>6 part man, triangle, pencil</td>
<td>Prepositions: between</td>
<td>Undress indep.</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>grip 6 brick stair, castle</td>
<td>Opposites: big/little</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Count 15 bricks</td>
<td>What would you do if?;</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>Comparisons</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- Few key milestones to have in your mind are highlighted and NB. milestones develop sequentially (i.e. do not skip stages)
• Older kids:
  ➢ Gross motor: bike (can ride without trainer wheels at 5), sport (running, kicking), clumsiness
  ➢ Fine motor: computer, play station
  ➢ Cognitive: don’t ask if does OK at school – everyone does OK these days! Instead, does he do age appropriate work, need extra tuition, etc

Cognitive Development

• Overall process:
  ➢ Autonomy: dependent on parents → peers → independent
  ➢ Abstract thinking (what if?): concrete → mature
  ➢ Future consequences of present actions
  ➢ Gratification: immediate → delayed
  ➢ Satisfaction with body image
  ➢ Black and white → comfort with shades of grey

• Infancy (birth – 2 years): Developmental issues:
  ➢ Later develop goal directed activity
  ➢ Learn to distinguish between self and surroundings
  ➢ Develop object permanence
  ➢ Need secure attachment relationship with parents
  ➢ Separation, individuation in toddler years
  ➢ At 2: trial and error problem solving, planned and purposeful play but limited content, egocentric, parallel play

• Preoperational (3 – 5 years):
  ➢ Egocentric world view (I made it happen, so it’s my fault)
  ➢ Use of magical thinking, difficulty distinguishing real from symbolic (if I wish it, it will come true)
  ➢ Trial and error problem solving only
  ➢ One aspect of a problem at a time
  ➢ Cannot order a series of events
  ➢ Cause and effect thinking: I did X, then Y happened, therefore X → Y
  ➢ Imaginative play
  ➢ Gradually move from parallel play to interactive play with peers
  ➢ Separation and autonomy
  ➢ At 5: symbolic thought (imagination), classify by colour/shape, curiosity, magical thinking, social values, rules internalised but fixed, turn-taking, cooperative plan, other’s perspective, ↑ independence

• Concrete Operational (6 – 10 years):
  ➢ Black and white thinking, right and wrong
  ➢ Capable of simple logic and problem solving
  ➢ Can order things in a chronological sequence
  ➢ May have difficulties with multiple perspectives
  ➢ Peer relationships ↑ ly important
  ➢ Sharing games, competition
  ➢ Analogy, metaphor, figures of speech being
  ➢ Able to concentrate for longer, delay gratification, predict personal and social consequences of actions, plan ahead

• Formal Operations (10 – 13 years):
  ➢ Better memory, concentration, forward planning
  ➢ Social skills refined
  ➢ Still concrete and literal (black/white, good/bad, right/wrong)
  ➢ Limited abstraction: eg what if I didn’t do this? (Contrary-to-fact abstraction)
  ➢ Dramatic changes to body → constant comparisons and normal anxieties
  ➢ Need to conform with peer norms
  ➢ Difficult to take others perspectives
  ➢ Difficult to understand complexity
  ➢ Difficult to apply rules to own situation
  ➢ Lack future orientation/forward thinking
  ➢ Clear consequences

• Middle Adolescence (14 – 16 years):
  ➢ Developing abstract and complex thought
  ➢ Beginning to see other’s perspectives, starting to cope with shades of grey
- Increased self consciousness
- Easily swayed – not certain of own view
- Still difficult to integrate conflicting ideas
- Narcissistic (feels good/what I want → therefore its right → impulsiveness)
- Less need to conform to peer norms, try alternative beliefs and philosophies
- Need limits to be secure, limit testing

**Late adolescence**
- Adult memory and concentration
- Mature abstractions, problem-solving, self reflection and long range planning
- Weigh up multiple information
- See multiple meanings, complex relationships, different points of view, tolerant of shades of grey
- Able to think hypothetically and plan for possible events
- Remains more difficult to use new abilities in challenging situations
- Autonomous: able to leave home and return for counsel, rely on own opinion

**Developmental Delay**
- Constant slow development leads to widening gap
- Investigations:
  - 1. Hearing, vision
  - 2. Chromosomes, DNA screen/micro-array (eg Fragile X, Angelman, Prader-Willi)
  - 3. Thyroid, metabolic, mucopolysaccharide screen, CK (Duchenne’s)
  - 4. Brain imaging, EEG
- Type of Diagnosis:
  - Functional Diagnosis:
    - Mobility, communication, learning, self-care, socialising, etc
    - What does the child need to achieve age-appropriate function
  - Pattern diagnosis:
    - Autism: see Autism, page 907
    - Cerebral palsy: see page 963
    - Other syndromes
- Biological diagnoses: DNA disorders, brain injury
- IQ scores:
  - < 20 profound intellectual disability
  - 20 – 35 severe
  - 35 – 50 moderate
  - 50 – 70 mild
  - 70 – 85 borderline
  - Definite or highly probable cause in majority < 50. Cause in about half < 70
- Management:
  - Objectives:
    - Maximising function
    - Preventing and treating secondary problems
    - Supporting carers
  - Referral: paediatrician, geneticist, psychologist (eg cognitive testing), SLT (speech, swallowing, play), physiotherapist (gross motor problems), OT (fine motor, self care, aids and equipment), early intervention groups, VNDT (visiting neurodevelopmental therapist), support groups
  - Medical assessment of a diagnosed disabled child
    - Always consider new illnesses
    - Look for syndrome specific health problems
    - Feeding difficulties, nutrition
    - Constipation
    - Medication
    - Carer Stress
    - Access to services and allowances

**Tamariki Ora (Well Child) National Schedule**
- Covers:
  - Health education and promotion (e.g. breastfeeding, imms, preventing SUDI, parenting for child age/stage)
Clinical assessment + health protection (e.g. growth + development, vision + hearing, oral health etc)
Interventions (e.g. smoking cessation, family violence screen/respond, PND screen/respond etc)
Family/whanau care and support

Prevention:
- Types:
  - Primary: shifting the whole population curve → improves the overall standard
  - Secondary: identifying risk factors → early or targeted intervention
  - Tertiary: minimising impact of established disease
- Benefits of prevention: ↓ adult sequelae: injury, child abuse, delinquency and arrest rates

PPV of parental concerns about delay is about 80 –90%. Must act or refer on parental concern

Causes of Developmental Delay
- Warning signs:
  - Parental concern
  - Regression
  - No word combinations by 2 years
  - Irritable or difficult child
  - Abnormal neurology (hand dominance before 18/12, persistent primitive reflexes beyond 4/12)
- Causes of abnormal development:
  - Environmental (e.g. neglect, other forms of abuse)
  - Genetic (eg chromosomal, metabolic)
  - Disability (vision, hearing, motor)
  - Brain injury (hypoxia, trauma, toxins, infection, prenatal & post-natal)
  - Illness, nutrition
  - Unknown

Hearing
- See Hearing Loss in Hearing Loss, page 226
- 1 in 500 has significant permanent hearing loss → receptive and/or expressive language delay
- All infants babble, even hearing impaired
- Suspect deafness when:
  - Parental concern
  - At risk babies (should be routinely screened):
    - Family history
    - Intrauterine infection: rubella, CMV
    - Defects of ENT: cleft palate, external ear
    - Low birth weight
    - Neonatal distress
  - Poor response to sound
  - Not using words by 15 months
  - General developmental delay
  - Poor speech, comprehension and hearing failure
  - Following brain trauma, infection, neurotoxic drugs
  - Recurrent or persistent ear infections
- Normal development: See Development Chart: normal development from 0-60 months, page 901
- History:
  - Can he hear – how do you know?
  - Previous development: first word, use of consonants, etc. Check Well Child Book
  - Ear infections
  - Antenatal: rubella, prematurity, jaundice, drugs
  - Family history of hearing problems, developmental delay, neuro problems
- Exam:
  - Dysmorphic features: cleft palate, external ear, skin, heart murmurs, liver enlargement, normal genitalia
  - Basic neuro exam, gait, symmetry of movement (including face), eye movement
- Investigations:
  - Tympanogram
  - Don’t do distraction testing – hard unless you’re well trained. Send straight for audiology
  - Others depending on clinical findings: eg if regression then EEG, brain scan, check stressors, chromosome problems, CK for Duchenne’s
• Differential of language delay:
  ➢ End of normal range
  ➢ Deafness
  ➢ Isolated language delay (usually expressive more delayed than receptive – but not necessarily)
  ➢ General delay or mild intellectual handicap → formal cognitive testing
  ➢ Autism
  ➢ Epilepsy: absence seizures – especially if fluctuates or regressive
  ➢ Possibly poor environment with little stimulation – but would also expect ↓socialisation and ↓self care
  ➢ Congenital problems: cleft palate, macroglossia (eg Down’s)
  ➢ Rare isolated CNS or motor problems

• Management: Speech language therapist, early intervention service, multidisciplinary team if problems over other domains. GP to support and co-ordinate, anticipate problems – especially at transitions (eg school, moving) and checking for comorbidity (eg behavioural problems, ↓self esteem)

• Prognosis: Good if early intervention – but maybe problems with higher language function (eg essay writing)

**Down Syndrome**

• Trisomy 21: 47XY + 21
  ➢ Accounts for 95% of presentations of Down Syndrome. Usually (80%) non-disjunction at first meiotic division
  ➢ 5% have different karyotypes:
    o Mosaic Down: 3 %
    o Robertsonian translocation t14:21: 4.8%

• Epidemiology:
  ➢ Overall incidence is 1 in 700
  ➢ At least 20% still born
  ➢ Incidence increases with ↑maternal age: at 16/40 gestation, 1 in 300 at 35 years, 1 in 22 at 45 years
  ➢ Accounts for 25% of children with IQ < 50
  ➢ ¾ of all chromosomal abnormalities. Chromosomal anomalies represent 15% of congenital anomalies
  ➢ Risk:

<table>
<thead>
<tr>
<th>Maternal age at birth</th>
<th>Down in live births</th>
</tr>
</thead>
<tbody>
<tr>
<td>25 - 29</td>
<td>1:1100</td>
</tr>
<tr>
<td>30</td>
<td>1: 900</td>
</tr>
<tr>
<td>35</td>
<td>1:350</td>
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<tr>
<td>37</td>
<td>1:200</td>
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<tr>
<td>40</td>
<td>1:100</td>
</tr>
<tr>
<td>43</td>
<td>1:50</td>
</tr>
<tr>
<td>45 and over</td>
<td>1:25</td>
</tr>
</tbody>
</table>

• See Prenatal Testing/Diagnosis, page 610

• Neonatal signs:
  ➢ Hypotonia
  ➢ ↓Moro reflex
  ➢ Joint hyper-extensibility
  ➢ Excess skin at the back of the neck
  ➢ Flat facial profile
  ➢ Misshapen low set ears
  ➢ Protruding tongue
  ➢ Blunt inner eye angle
  ➢ Single palmar crease in 50%
  ➢ Clinodactyly (incurving) of little fingers in 50%
  ➢ Big ‘saddle’ gap between big and 2nd toe

• Complications:
  ➢ IQ generally from 45 – 55
  ➢ Congenital heart malformations in ~50%: VSD, ASD, patent ductus
  ➢ Susceptible to respiratory infections
  ➢ Duodenal atresia
  ➢ Also cataracts (2%), epilepsy (10%), hypothyroidism (3%), acute leukaemia (1%)

• Development:
  ➢ Most will walk and develop simple language
  ➢ Puberty is often delayed and incomplete
Average adult height is 150 cm

Pre-senile dementia (similar to Alzheimer’s disease) supervenes after age 40

8% live past 40 years

**Autism/Autism Spectrum Disorder**

- Onset **before age 3** of a triad of symptoms (SLR: social, language, restrictive/repetitive):
  - **1. Impaired social interaction:** slow to smile, don’t enjoy being cuddled, don’t pick up on emotions, ↓eye contact
  - **2. ↓language:** use of both verbal and non-verbal communication – slow onset, echolalia, no use of gesture, poor pragmatics (eg turn taking and eye contact in conversation). If it was isolated language delay you would expect compensation in other areas (eg social) but here that’s affected as well
  - **3. Restrictive and repetitive behaviours:** dislike change

- May start from birth, or **regress** after normal development

- **Other behavioural problems:** outbursts, sleep problems, distractibility, poor toileting

- Rare: 2 – 4/10,000. Boys = 3 x girls

- 75% show some degree of general intellectual impairment

**Asperger’s Syndrome**:

- Symptoms overlap with autism
- Social interaction and behavioural problems similar to autism but not associated with significant language or intellectual delay

- **Hx:**
  - Antenatal: drugs, ETOH, smoking, infections
  - Questions around the triad of symptoms
  - Regression
  - FHx
  - HI/meningitis/neglect/abuse questions

- **DDx:**
  - Hearing problems
  - Global developmental delay
  - Chromosomal abnormalities (e.g. fragile x)
  - Hypothyroidism

- **Examination/Ix:**
  - Growth parameters
  - Full developmental assessment
  - Audiology (and vision) assessment
  - ?Chromosomal microarray + karyotype
  - ?TFTs

- **Management:**
  - Multi-disciplinary approach (e.g. child development team, special education, therapists – SLT, ?OT, paediatrician)
  - Education: early intervention service
  - Social: child disability allowance, disability allowance, support groups

**Effect of Chronic Disease on Development**

- See also Chronic Illness and Disability in Adolescents, page 1012

- 10 – 15 % of children have some chronic health condition. 1 – 2% are severe enough to interfere with their ability to take part in normal activities

- Chronic illness can effect development by:
  - Direct effect: eg deafness → language delay
  - Effect of treatment: eg neuro-radiation
  - Indirect effect: reduced energy in cystic fibrosis
  - Social environment: sense of differentness → withdrawal or bullying
  - Transaction: impact on parents (eg maternal depression) → affects child’s adaptation

- May lead to failure to develop independence (self control) and competence (control over their environment), leading to self-doubt or indecision.

- **Issues to consider:**
  - Burden of care: don’t give them more helpful ideas if they’re already over-stretched!
  - Unpredictable future: Clear idea for the parent and child of what the future might hold
Cost: check relevant benefits received
Respite care: do parents need a break? Deal with feelings of guilt and indispensability
Activities of daily living: the daily routine will be revealing
Multiple professions: check these are co-ordinated and organised around the family’s needs
Psychological: consider impaired attachment, depression, stress, family dysfunction

Also ensure:
- Information for child and parents
- Access to services
- Access to consumer groups
- Equipment and transport needs
- Environmental modification
- Vocational training for an adolescent

**Infants**

- Effect on parents of congenital malformation:
  - Shock, disbelief, upset, problem solving processes slowed
  - Adaptation over time
  - Grief reaction similar to death of a child (must mourn the loss of a ‘normal’ child) – but parent must also attach to the living child

- Management:
  - Support good bond-enhancing practices before and immediately after birth:
    - Normal preparation for birth (learn about routines, processes, options, etc)
    - Time to establish rapport with paediatrician and visit NICU
    - Long periods together in first few days and breast-feed if possible. Is any separation really necessary?
    - Avoid criticism – a very sensitive time
    - Watch for signs poor attachment. See Attachment Disorder, page 898
  - For the toddler:
    - Watch for ‘vulnerable child syndrome’: continued parental concern after child has recovered → adverse affects on child. Problem is parents’ expectations, not attachment. More complicated when some ongoing vigilance is required
    - Support appropriate attitudes and plans
    - Mobilise family support
    - Remain optimistic
    - If in hospital, use separations to reinforce that parents will return. Limited number and consistency in nursing staff

**Pre-schooler**

- Social and emotional development may be limited through lack of opportunity to achieve goals in play and by limited peer interactions

- Management:
  - Refer for early intervention, especially low socio-economic and disabled children
  - Promote normal development: separation, appropriate discipline
  - In hospital: encourage rooming in, maximum contact with families
  - Warn parents to anticipate behavioural problems especially if hospitalisation is prolonged or frequent

**Head injured child**

- Initial crisis: grieving put on hold, waiting to see if things improve, child still looks the same, swinging between hope, despair and disbelief

- Restructuring:
  - Reassign tasks in the family
  - Move out of crisis reorganisation into long term reorganisation
  - Inclusion of outside help into family
  - Appropriate time for husband/wife/other children
  - Time for self

- Grieving:
  - Allow for grief and acknowledge the loss
  - Avoid dichotomy of one person (eg mother) taking hope position and others despair
  - Promote openness. Devastation of silence
  - Denial can also be a coping mechanism
• Develop an acceptance of a new identity through the crisis:
  ➢ Seeing how the child is different
  ➢ Finding positives in this new identity and helping the family value these
  ➢ Achieve a sense of movement through the crisis. Mark positives and achievements of the family

• Encouraging compliance:
  ➢ For the highly compliant: teaching, directions
  ➢ For the non-compliant (those who respond ‘yes – but….’): general indirect messages, metaphor/story telling

• Subsequent learning disabilities: may have problems with learning from then on – but may not show up till those skills are needed (eg trouble reading when they start school)

**Learning Disability**

• History:
  ➢ Start with things he is likely to be able to do and work up
  ➢ Questions over traditional domains for learning:
  ➢ Reading: ‘what is she reading now’, ‘can she read three letter words’
  ➢ Spelling
  ➢ Numeracy
  ➢ Writing
  ➢ Drawing, art, craft
  ➢ Social skills
  ➢ Strengths
  ➢ Collaborative history:
    o Previous assessments, IQ tests
    o Talk to the teacher
  ➢ Comorbidity screen:
    o Is the norm in developmental paediatrics
    o Can be:
      ➢ Primary: eg biological morbidity such as learning and co-ordination difficulties, ADHD and clumsiness
      ➢ Secondary: eg acquired psychological and behavioural problems such as loss of self-esteem, non-compliance, etc
    o Differential:
      ➢ Behaviour: aggression, attention seeking, school refusal
      ➢ Mood, anxiety, attention
      ➢ Relationship with peers, teasing, bullying
      ➢ Family issues – get good social history
      ➢ If adolescent then HEADDSS assessment (See page 1009)
  ➢ School factors: teacher skills, interest/ability to manage the child’s needs, available skills
  ➢ Parental insight: are they helping or hindering
  ➢ Use questionnaires: eg Child Behaviour Checklist (screen for anxiety, depression, etc) or Connor’s (specific for ADHD) to provide diagnostic information and provide a pre-treatment baseline

• Exam:
  ➢ Screen for gross and fine motor delay
  ➢ Refer for vision and hearing tests

• Possible differentials:
  ➢ Hearing and vision
  ➢ Medical: hypothyroid
  ➢ Intellectual disability
  ➢ Specific learning disabilities
  ➢ Head Injury
  ➢ Psycho-social: Abuse, stress, etc
  ➢ Psychological: depression, anxiety, ADHD

• Principles for management:
  ➢ Review and follow-up (eg 3 monthly), especially at times of transition (eg changing schools)
  ➢ Multidisciplinary approach: OT, Physiotherapist, SLT, VNDT, Educational Psychologist
  ➢ Excellent communication between professionals
  ➢ Helping parents to create realistic goals
  ➢ Dealing with normal parent grief
• Strategies for management:
  ➢ Demystify: Explain strengths and weaknesses to the child, parents and teacher. Removes guilt, pejorative labels (eg lazy), gives optimism
  ➢ Bypass strategies: adjust rate, volume, complexity, format or use devices to make the task easier
  ➢ Remediation of skills: focus on study skills, organisation, use strengths to remediate weaknesses
  ➢ Developmental therapies: Eg speech therapy, gross and fine motor, etc. More effective when skill deficits reflect lack of opportunity, and when instituted earlier
  ➢ Modify the curriculum: Eg drop subjects they’re not succeeding in
  ➢ Strengthen strengths: sport, art, mechanics, etc
  ➢ Individual/family counselling: especially with behaviour management, family dysfunction
  ➢ Advocacy
  ➢ Medication
  ➢ Longitudinal case management
• Check whether parents get the child disability allowance. Can get a needs assessment done for respite care, home help, etc

**Child Development Team**

• For children with:
  ➢ An identified disability
  ➢ Developmental delay
  ➢ At risk of developmental delay/difficulties
• Involves multi-disciplinary assessment and intervention

**Social worker:**
  ➢ Conducts individual, marital and family social assessments
  ➢ Liases with other community services (CYFS, WINZ, etc) and facilitates brokerage of services
  ➢ Provides emotional support
  ➢ Teaching parenting skills
  ➢ Advocacy

**Psychologist:**
  ➢ Assessment: neuropsychological, development, behaviour/emotion, family function
  ➢ Intervention: For individual, skills for parents, family relationships

**Physiotherapist:**
  ➢ Functional assessment of gross motor skills: delay, abnormal muscle tone, loss of range of movement, gait abnormalities, mobility, co-ordination
  ➢ Therapy (including hydrotherapy) and home/school exercise programmes
  ➢ Assessing for standing frames, walking aides and wheelchairs (with OT)

**Occupational therapist:**
  ➢ Assessment of fine-motor skills (use of hands):
    o Tool manipulation: grasp and grip, bilateral hand use, release, eye-hand co-ordination (eg stacking)
    o Pre-writing: lines, circles, picture of a person
    o Handwriting: grip, control, sizing, closure, hand dominance, speed
    o Cutting with scissors: accuracy and co-ordination
  ➢ Assessment of self-care skills:
    o Undress/dress, buttons, zips, shoelaces, etc
    o Feed themselves
    o Sit unsupported in the bath
    o Toileting, including sitting on toilet, pulling pants down, wiping
    o Clean teeth, brush hair, wipe face
  ➢ Assess for equipment to help with the above

**Speech language therapist:** assesses and assists with:
  ➢ Receptive language: understanding
  ➢ Expressive language: including gesture and facial expression
  ➢ Phonology: sound system
  ➢ Pragmatics: social rules – sharing, turn taking, eye contact (biggest problem in autism)
  ➢ Feeding: transition from tube to oral feeding, behavioural feeding issues
  ➢ Voice: vocal nodules due to abuse (eg screaming)
  ➢ Fluency: stammering

**Visiting neurodevelopmental therapist:**
  ➢ Home based assessment
Family support
Liaison with other health professionals and community agencies
Assessment for equipment

Developmental paediatrician:
Developmental assessments/examination for suspected delay
Investigates cause
Review of developmental progress

Growth

- Growth velocity = change in height over time. Declines till about 4, levels out, spikes at puberty then zero
- Factors influencing growth:
  - Genetic potential (can be influenced by chromosomal abnormalities)
  - Psychosocial factors (eg psychosocial dwarfism)
  - Nutrition (including in utero): adequate kj, balance of nutrition
  - Diseases in major systems: uses energy (eg ↑ respiratory effort) and nutritional effects (eg GL)
  - Hormones (GH, TH, sex, adrenal steroids, PTH, vit D, insulin)
  - Growth factors

Measurement:
- Method: Use stadiometer, fixed to wall, feet together, knees straight, lift mastoid processes
- Accuracy and reliability:
  - SD of a single measurement ~ 0.25 cm. In a 5 year old this can cause a range in growth velocity from 10th to 50th centile
  - Taller in morning than at night
- Minimising error: Same measurer, calibrate regularly, careful measurement, don’t look at last measurement, measure at beginning and at end of exam

Short Stature

- Definition:
  - > 2 standard deviations below the mean = < 5th centile
  - Reduced growth velocity
- Exclude failure to thrive
- Growth pattern is more important than height
- Normal variants:
  - Familial (genetic) short stature
  - Constitutional delay of growth and development. Presents mid to late childhood. Is global delay in development affecting every organ system. Can be inherited via various different modes of inheritance.

<table>
<thead>
<tr>
<th></th>
<th>Familial (genetic) short stature</th>
<th>Constitutional Delay</th>
</tr>
</thead>
<tbody>
<tr>
<td>Height</td>
<td>&lt; -2 SDs</td>
<td>&lt; -2 SDs</td>
</tr>
<tr>
<td>Bone age (hand xray)</td>
<td>= Chronological</td>
<td>&lt; Chronological. Delayed through childhood, accentuated when peers reach puberty</td>
</tr>
<tr>
<td>Puberty</td>
<td>Normal</td>
<td>Delayed</td>
</tr>
<tr>
<td>Growth velocity</td>
<td>Normal</td>
<td>Normal</td>
</tr>
<tr>
<td>Final height</td>
<td>Short</td>
<td>Normal/Tall (keep growing for longer)</td>
</tr>
<tr>
<td>Parents</td>
<td>Short</td>
<td>Normal</td>
</tr>
<tr>
<td>Family History</td>
<td>Positive (for short stature)</td>
<td>Positive (for constitutional)</td>
</tr>
</tbody>
</table>

- Pathological causes:
  - Systems: eg subclinical GI or renal disease (reflux, coeliac, malabsorption, CF, etc)
  - Psychosocial dwarfism (extreme stress eg neglect → ↓GH)
  - Genes:
    a. Turner syndrome: webbed neck, wide nipples, wide carrying angle
    b. Skeletal dysplasia: eg achondroplasia
    c. Syndromes
  - Hormones: thyroid or GH deficiency, glucocorticoid excess, combinations (e.g. pituitary – congenital: septo-optic dysplasia [hypoplasia of optic nerve + absence of septum pellucidum + hypopituitarism]; acquired: tumour, irradiation, head injury)
  - Drugs: steroids
- Assessment:
History:
- Height: measured accurately and over time
- **Mid-parental height**: assessment of genetic potential (adjusted so both parents are same sex as child.
  Male: add 13 to mum’s ht then ave w dad; female: subtract 13 from dad’s ht then ave w mum)
- Family history: eg constitutional delay
- Systems
- Psychosocial
- Development

Examination:
- Growth parameters: ht, wt, BP
- Dysmorphic features → ?syndrome
- Proportions: limbs vs trunk, eg arm span vs height, or upper segment (head to pubic bone) vs lower segment (pubic bone to floor)
- Blood pressure (?renal disease)
- Fundi and visual fields (?pituitary tumour)
- Thyroid: goitre, hypothyroidism
- General (chronic disease with limited symptoms)

Investigations:
- Bone age: accurate to about 3 months
- Specific depending on history/exam, eg renal → creatinine, coeliac → antibodies
- Karyotype in girls (if <5th centile)

Treatment:
- Treat cause
- Growth hormone:
  - Effective in GH deficiency and Turner’s syndrome
  - May help in chronic renal failure, intrauterine growth retardation and severe idiopathic short stature
- Androgens: consider in constitutional delay – won’t influence final height but get there faster.

**Tall Stature**
- Arbitrary definition (>2SDs)
- Associated stigma (females more often seek help)

Causes:
- Familial/genetic
- Over-nutrition
- Syndromes (eg XXY – Klinefelter, Marfan’s, Homocystinuria)
- Precocious puberty (tall early, but stop growing → eventually short)
- Growth hormone excess is extremely rare

Treatment:
- Treat the underlying cause
- High dose oestrogens/androgens

**Growing Pains**
- Occurs frequently: 15% of children with peak age of 11
- **Diagnosis of exclusion** – no organic pathology usually found. ?Child more vulnerable to pain and stress-induced exacerbations
- Occurs at least monthly and often at night for a ~ three-month period. Between times the child is well

Differential:
- Orthopaedic disorders
- Collagen vascular disease
- Infection
- Neoplastic disorders

Management:
- Reassure, even if you can’t find a cause
- Symptom diary (also check for psycho-social stressors)
- Symptomatic relief

**Childhood Obesity**

*Definition + Epidemiology*
- = Excess adiposity, not just ↑ BMI
- Now an epidemic and incidence ↑ (10% obese, further 20% overweight)
- **Maori + Pacific** have higher rates of obesity
- Practically, **BMI +/- WC +/- skin fold thickness** used to screen for obesity in children
- **BMI changes with age, gender and maturation** and thus needs to be calculated and plotted on **child-specific BMI charts**
- We live in an **obesogenic environment** (energy dense, nutrition poor food + sedentary lifestyle, wider societal factors e.g. marketing, expensive vegetables etc) which makes positive individual choice on behalf of the child very difficult

**Risk Factors**
- Genetic factors e.g. parents, ethnicity
- **Lifestyle** factors e.g. food choice (energy dense foods), sedentary lifestyle (TV watching a/w obesity)

**Contributory/Prognostic Factors**
- Positive = ↑SES – allowing finances for healthy food etc; motivated + supportive family; educated parents
- Negative = the opposite to the above; family/cultural beliefs re weight

**Complications/Natural History**
- ↑ in CV risk factors
- T2DM
- NAFLD (non-alcoholic fatty liver disease)
- OSA
- Psychological issues
- Adult obesity (risk depends on age of obesity onset - ~ 20% chance of adult obesity if obese at age 4; ~ 80% chance at age 13)

**Role of the GP**
- Identify obesity and engage with child and family
- Manage co-morbidities
- Behavioural intervention (motivational interviewing) and lifestyle advice
- Consider referral

**Initial Assessment**
- Determine risk:
  - Age
  - Parental obesity
  - FHx early CVD
  - Weight related problems
- If BMI >85th percentile, do full hx and exam
- If BMI >95th percentile, do investigations and refer

**History**
- Lifestyle (exercise, how they get to school etc)
- Diet
- HEEADSSSSSS
- Full system review
- Complications (DM, OSA, joint pain)
- FHx (early onset CVD)
- Puberty onset

**Investigations**
- When?
  - If **high-risk FHx** (e.g. of CVD), **severe obesity** (>99th centile), acanthosis nigricans, or if child is an adolescent
- What?
  - First-line: fasting lipids, LFTs, glucose
  - Second-line: OGTT, liver US, sex hormones, sleep study (if appropriate)

**DDx**
- In a **short and fat** child (obese children are normally tall as obesity drives growth), should consider:
Endocrine causes (e.g. hypothyroid, cushing’s, ↓GH)
Medications (e.g. steroids)
Specific syndromes (e.g. PWS, down)

Management
- Should be a multifaceted, multi-disciplinary-team, incremental, sustainable approach (not all at once – not achievable)
- Education and motivational interviewing (precontemplation, contemplation, planning, action, maintenance)
- Support for behavioural change
- **Whole family lifestyle change** e.g. eating together, 1 hr outside every day, water as main drink, 1hr TV/d
- Therapist/dietician involvement
- Clarify goals (e.g. improvement in self-esteem or weight loss)
- **Green prescription** (“Active Families”: there are specific SPARC funded exercise programmes)

Addressing the Obesogenic Environment
- **Home**: set aside time for healthy meals/physical activity together; limit TV
- **School**: PE, eliminate unhealthy foods, education
- **Urban design**: parks, pavements, cycleways
- **Media/marketing**: remove tax from healthy food, nutrition labelling, prohibit advertising of unhealthy foods, ↑ funding for PH campaigns
- **Political**: regulate contributions from food industry

Sleep Disorders in Childhood
- Taking a sleep history:
  - **BEARS** (bedtime, excessive daytime sleepiness, awakenings: night/early morning, regularity and duration, snoring)
  - Bedtime: time to sleep; assistance to sleep
  - Night-waking: setting; what is required?
  - OSA symptoms: sweating, snoring, observed apnoea, restless sleep, enuresis, mouth breathing
  - Morning: time up; refreshed or not; dry mouth
  - Daytime behaviour: sleepiness; concentration; school issues
- Things that might wake a child:
  - Parasomnias (see below)
  - OSA
  - Other medical problems eg asthma
  - Toilet!
- OSA in childhood:
  - **Primary snoring (i.e. not OSA)**: occurs in 10-15% of children; only 10% of these will have OSA
  - Peak age = 2-6yrs; affects 2-3%; may be FHx
  - Associations with childhood disorders (cranio-facial abnormalities; neuromuscular conditions [MD, CP]; genetic conditions [PWS – obesity, Down syndrome; achondroplasia] etc)
  - Most commonly due to **adenoid/tonsillar hyperplasia** → T & A
  - Symptoms:
    - Snoring, apnoea, sweating, restlessness, tiredness
    - Mouth breathing, difficulty swallowing, bad breath
    - Learning difficulties
    - FTT
    - Night terrors
  - Signs:
    - Odd shaped head/face
    - Nasal obstruction (check can breathe through each nostril)
    - Big tonsils
    - Signs of chronic upper airway obstruction (e.g. harrison’s sulcus)
- **Parasomnias** = disorders characterised by undesirable motor, verbal, or experiential phenomenon occurring in association with sleep:
  - Sleep walking
Sleep/night terrors:
- Associated with sleep deprivation, OSA, medicines, genetic component
- Non-REM sleep, disoriented on waking + not consolable (as cf nightmares), usually return to sleep quickly

- Sleep talking
- Sleep-related enuresis
- Bruxism (teeth grinding)

- Sleep:
  - REM + non-REM (stages 1-4 from 6/12)
  - <6/12 = active sleep (equivalent of REM) + quiet sleep (equivalent of non-REM) + intermediate sleep
  - Sleep architecture = the progression of sleep stages across a night’s sleep – REM + non-REM alternate throughout the night (sleep cycles)

- Measurement of sleep:
  - Polysomnography:
    - Records sleep state (EEG, EOG – electro-oculogram, EMG), RR + effort (chest + abdo sensors + diaphragm EMG), HR (ECG), O2 sats, vent airflow (nasal pressure), continuous observation by technician
  - History
  - Sleep diary
  - Actigraphy (detects movement)

- Behavioural sleep problems in infants:
  - Night wakings ↓ from 35% (at 2.5yrs) to 7% (age 6)
  - Main cause = behavioural insomnia of childhood (sleep onset association disorder)
  - Key features = infants need a parent to be with them to get to sleep and if they wake versus ‘self-soothers’
  - Need to ask bedtime habits/routines, how parents respond to waking etc, drinks before bedtime (caffeine)
  - Treatment aim = facilitate infant autonomy in sleep
  - Information for parents = normal sleep patterns for infants, waking is normal, infants should be put to bed awake, need to learn to sleep on their own, if feeding at night, decrease this

  - Management:
    - Make sure no organic cause for waking
    - Balance day and nighttime naps
    - Encourage use of a security item eg teddy bear/blanket
    - Encourage a bedtime routine
    - Controlled comforting = leave child to cry for a period, if checking, only talk, don’t pick up
    - Be consistent!
    - Gradual withdrawal if having to be present during going to sleep – move further away each night etc

- Behavioural sleep problems in older children:
  - Insufficient sleep time (not going to bed early enough, problems going to sleep, night waking etc)

  - Management:
    - Routine
    - Nightlight, ?music, “monster checking”, “worry box”
    - Reward system

- Investigations:
  - Healthy children without parasomnias such as sleep terrors = not required – refer to ENT for T & A
  - Those with co-morbidities (eg Down syndrome) = refer to paediatrician, ?needs sleep study, ? T & A

Neonatal and Infants
- Neonatal is < 4 weeks

Examination of the Newborn

History
- Maternal history:
  - General health and well-being: past medical history and social history (partner, planned pregnancy, etc)
  - Pregnancy: medications, alcohol and other drugs, complications, infectious illness (toxoplasmosis, rubella, etc), EDD, scan findings, parental blood groups
- **Family history**: perinatal deaths, paediatric deaths, congenital problems (especially congenital dislocated hip)
- **Delivery history**: length of labour, infection, resuscitation, APGAR, any concerns
- **Post-natal history**: feeding, colour changes (blue, jaundice), behaviour, stools, urine
- **Have you any concerns about your baby?**

**Examination**

- Initial assessment immediately after birth to check adaptation to extra-uterine life (eg APGAR) and to look for major congenital anomalies, especially:
  - Dysmorphic features
  - **Choanal atresia** (narrow/block nasal airway)
  - Major limb defects
  - Spina bifida
  - Anal atresia
  - Genital abnormalities
  - Birth trauma: bruising, cephalhaematoma
- Examine on *Resuscitaire*. Check all equipment carefully first.
- **APGAR** (appearance, pulse, grimace, activity, respiration) assessment – at **one minute, then 5 minutes then every 5 minutes** till a score of 10:
  - **Pulse/Heart rate**: 2 for > 100, 1 for < 100, 0 for not present
  - **Appearance/Colour**: 2 for pink, 1 for blue, 0 for pale
  - **Respiration**: 2 for regular or strong cry, 1 gasping intermittently (may be bad sign – secondary hypoxia), 0 for none. May slow due to maternal drugs (eg pethidine)
  - **Activity/Tone**: 2 for active movement with flexed limbs, 1 for some limb flexion
  - **Grimace/Reflex irritability**: 2 for cry/pull away when stimulated, 1 for grimace/feeble cry when stimulated
  - **NB. HRITC** (how ready is this child: HR, respiration, irritability, tone and colour) can be used

- **Apnoea**:
  - Primary apnoea: pulse < 60 and cyanosis. Give O2 and wait a minute
  - Secondary apnoea: pulse < 60, pallor and floppiness: suction, ventilate, intubate

- General inspection:
  - **Dysmorphisms**: eyes, ears, mouth, cry
  - **Colour**: central, peripheral
  - **Respiratory effort**: grunting, indrawing, flaring nostrils, accessory muscle use
  - Posture and movements:
    - Normal: hips abducted, partially flexed, knees flexed, arms adducted, flexed at elbow, hands closed (not tightly), fingers over thumb
    - Abnormal: hypotonia, irritability
  - **Skin**: colour, rashes (e.g. erythema toxicum)

- Systematic examination:
  - **Head**:
    - Skull: fontanelles, sutures, birth trauma
    - Eyes: red reflex, opacities, conjunctivitis
    - Nose: patency
    - Mouth: palate and suck
    - Ears: hearing, tags
  - **Neck**: upper airway
  - **Chest**: shape, deformities, respiratory distress, cardiac auscultation, peripheral pulses (femoral), respiratory auscultation
  - **Abdomen**: cord, 3 vessels (2 arteries and a vein), shape, liver, spleen, kidneys, bladder, genitalia, urine stream, anus, passage of meconium, femoral pulses
  - **Limbs and other bones**: upper limbs, digits, palmar creases, clinodactyly, grasp, lower limbs, digits, hips, talipes equinovarus (club foot), spine
  - **Neurological status**: cry, jittery, spastic, grasping, activity, irritability, symmetry of movement, tone, neonatal reflexes
  - **Neonatal reflexes**: stepping, walking, Moro, grasp, rooting, suckling

- Also:
  - **Growth**: weight, length, OFC → plot
- Offer vitamin K IM as prophylaxis against **haemorrhagic disease of the newborn** (any bleeding due to vitamin K def – hard to prove! e.g. intraventricular haemorrhage)
- Cord blood for blood typing and Rhesus-ive, and also measure Cord pH (from artery) – measure of hypoxia
- If baby has patches of yellow ⇒ sitting in meconium for a while → stain
- If uncertainty about gestational age then formal assessment
- Re-examine at end of the first week of life, especially for signs of congenital heart disease. Takes ~ 48 hours for ductus to close

- Other observations:
  - Micturition: usually soon after birth, infrequent for first 24 hours
  - Bowel: 99.9% passed meconium by 48 hours; if not ?CF, ?Hirschprungs
  - Jaundice: 40% develop it, but transient, resolves by day 5
  - Vomiting: a little is common. Green/orange/yellow is bad (= bile)
  - Temperature: rectal best. **Same range as adults** when dressed appropriately
  - Weight: 1st 3 – 5 days may lose 5 – 10% of birth weight. Should regain it in 7 – 10 days

- In first week:
  - Immunisations: if mother HBsAg +ive then Hep B Vaccine and HBIG
  - Guthrie card (**around 48hrs**). See Genetic Testing, page 777

### Outcome after Preterm Birth

- At 27 weeks, 90% survive to discharge

- Definitions:
  - Term = 37-41/40
  - Prematurity = <37/40; Very premature = <32/40; Extremely prem = ≤28/40
  - Weight = Low BW = <2500g; Very low = <1500g; Extremely low = <1000g
  - Small for dates (SFD) = <10th centile

- Factors affecting prognosis:
  - Prenatal: Socio-economic, maternal smoking, infertility
  - Antenatal: multiple birth, IUGR, maternal illness, smoking, steroids before delivery
  - Birth: time of transfer, method of delivery, APGAR, resuscitation
  - Postnatal:
    - Size of NICU, surfactant, breast feeding
    - **Hypoxic-ischaemic Encephalopathy** (HIE): ↓O2 delivery to brain → becomes oedematous over next 24 – 48 hours
  - Assessment of outcome: lots of problems with cohort studies: which population, admission, length of follow-up, what’s measured, etc

- Issues for mothers of NICU babies:
  - How they perceive health workers
  - Postnatal Depression
  - Visiting family commitments
  - Breast feeding: often expressing

- History to take for preterm infants when readmitted:
  - How long ventilated for/time on other respiratory support (CPAP, O2)
  - Time acquired feeding skills
  - Concern about apnoea
  - Time discharged home
  - Other complications eg NEC, PDA etc

### Complications of Preterm Birth

- Preterm infants – 32-36/40:
  - Temperature instability
  - Feeding problems
  - Apnoea
  - Hypoglycaemia
  - Jaundice
  - Higher risk of **TTN** (transient tachypnoea of the newborn)
  - RDS
  - Anaemia of prematurity

- Preterm infants – 32-36/40 – **long-term outcomes:**

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*Health Care of the Elderly*
May be home by 35-36/40
Apoena should be resolved
Follow-up may not be required unless particular reason, e.g. ventilated for RDS
Should have normal developmental outcome, albeit delayed a few weeks (expect milestones at corrected age)
?Some increased risk of SUDI therefore need to advise re safe sleep at home
Will have caught up with chronological age by 6-12/12

• Morbidity – preterm infants <32/40:
  Worsens with ↓gestation
  Developmental outcomes: physical, cognitive disabilities, learning difficulties, vision + hearing problems
  Poorer respiratory outcomes
  Physical scars

• Anaemia:
  Miss out on the ‘iron loading’ that happens through 3rd trimester
  Haemorrhage: feto-maternal, twin to twin, placental, cephalhaematoma, etc
  Haemolysis: Rhesus disease, ABO incompatibility, spherocytosis, G6PD deficiency (req for glu in RBC)
  Infection: CMV, rubella, septicaemia, UTI
  Bleeding disorder: haemorrhagic disease of the newborn

• Respiratory Distress Syndrome:
  =Hyaline Membrane Disease
  Inversely proportional to gestational age and birth weight, also diabetic mothers, asphyxia, cold stress, etc
  Surfactant deficiency → alveolar collapse → haemorrhage/protein leaking → hyaline membranes
  Signs: indrawing and expiratory grunt
  Treat with surfactant (antenatally with steroids)
  CXR: ground glass appearance with air bronchogram. See Chest Radiology, page 937

• Chronic Lung Disease of Prematurity (CLD)/Broncho-Pulmonary Dysplasia (BPD):
  Follows ventilation for respiratory distress and O2 toxicity
  Histology: necrotising bronchiolitis and alveolar fibrosis
  Mortality 40%
  Long term: airways obstruction, airways hyper-reactivity and hyper-inflation
  CXR: patchy collapse and fibrosis with areas of cystic change and over-distension

• Pulmonary interstitial emphysema:
  Complication of the treatment of RDS
  Collection of gases outside the normal air passages+ inside the connective tissue of airways secondary to alveolar rupture
  PIE is more frequent in premature infants who require mechanical ventilation for severe lung disease
  Can see pneumothoraces/pneumomediastinum

• Intraventricular Haemorrhage (IVH):
  Small haemorrhages into the germinal layer lining the lateral ventricles with hypoxia. May → hydrocephalus.
  Most have no serious long term sequelae

• Parenchymal Haemorrhage:
  Into brain, not IVH
  Incidence 1 – 2 % of preterms
  Most are unilateral
  Outcome depends on site
  Varies from nil to severe hemiplegia

• Periventricular Leukomalacia:
  Incidence 4% of preterms
  ?associated with maternal infection
  Frontal, usually watershed lesion
  Cysts long term → spastic diplegia (legs worse than arm)

• Retinopathy of Prematurity:
  Abnormal vascularisation of retina following exposure to high O2 concentrations (toxicity) – may lead to blindness
  Screen all babies < 31 weeks or 1500g

• Necrotising Enterocolitis:
  During first 3 weeks (up to 3 months in VLBW infants). Rare in term babies
  Aetiology uncertain:
o **Hypoxic damage** to bowel wall (umbilical catheterisation, apnoeic spells, septicaemia)
  o **Colonisation** with certain bacteria: *Clostridium perfringens*, *E Coli*, *S Epidermidis*, *Rotavirus*
  o Necrotic segment of intestine with **pneumatosis intestinalis** (*string of pearls’ sign on X-ray plus portal gas seen in liver*) → perforation, sepsis, etc

- Presentation: sepsis, bloody stools, bile stained vomiting
- Pathogenesis:
  o Necrotising inflammation of the small and large intestine
  o Mucosal oedema → necrosis → gangrene, perforation, peritonitis
- Sequeluas: malabsorption, strictures, short gut syndrome

- **Skin:**
  o Easily irritated (eg alcohol, tape, drips) → long term scars
- Also:
  - **Jaundice** more common
  - **Hypoglycaemia** more common
  - **Failure of closure of patent ductus** (give anti-PGs - NSAIDs, eg indomethacin)

- **Problems associated with Intrauterine Growth Restriction:**
  - Immediate:
    o **Hypoglycaemia** (see Hypoglycaemia of the Newborn, page 924)
    o **Polycythaemia** (eg due to placental insufficiency) → **heart failure** (due to ↑viscosity), pulmonary hypertension, NEC. Treat with exchange transfusion (eg or saline) → ↓Hb
    o **Hypocalcaemia** (test ALP)
    o **Jaundice**
    o Plus others (eg **Cerebral Palsy**)

**Neonatal and Infant Anticipatory Guidance (Parent Education)**

- **See** Parent and Adolescent Education, page 893
- Consider the topics for discussion about a neonate:
  - **Vision and hearing:** Can your baby hear and see (how do you know?)
  - **SUDI prevention:** sleep on back, ↓ smoke exposure, breast feeding, nothing over head when sleeping (see SUDI, page 923)
  - **Immunisation:** the schedule, genuine and non-genuine contra-indications, common myths, benefits and risks (see Vaccination Practice, page 840)
  - **Maternal mental health:** screening and assessing for post-natal depression (See Perinatal and Postpartum Mood Disorders, page 717)
  - **6 week screening:** dysmorphic features, cleft lip and palate, growth, eyes, heart, hips (see Six-Week Check, page 658)
  - **Contraceptive advice**
  - **Smoking** cessation
  - Always ask why has the mother really presented

- When neonatal and/or later, consider the following:
  - Recognition of illness, emergency contacts
  - Feeding: breast feeding and maternal nutrition, introducing solids, nutrition
  - CPR
  - **Parenting skills:** eg management strategies for sleep and toddler behaviour, toileting, eating
  - **Injury prevention:** seat belts, fire safety, falls, hot water, sun exposure, poisoning, safe child care, pools, playgrounds, road
  - When to expect which developmental milestones. Reassure for parents. Also early identification → early intervention
  - **Developmental** needs of kids: play, language, nutrition, social etc

**Breast-feeding**

- See also Pharmacology of Pregnancy and Breast Feeding, page 852
- See also Breast in Pregnancy and Breastfeeding, page 663
- **Advantages** of breast milk:
  - **Cheap and convenient** (available, portable, sterile – cf bottle feeding, especially in 3rd world)
  - **Contents vary** with babies needs + circumstances (foremilk [first part] has ↑ water content + ↓ calories; hindmilk has ↓ water + ↑ calorie content therefore babies who are thirsty drink often and babies who are hungry drink longer)
Health Care of the Elderly

- Prevention of disease: passive immunity against gastro-enteritis (eg rotavirus) and ↓ otitis media due to better Eustachian tube drainage
- Supply matches demand (NB. Suckling is effort dependent – when the babe has had its fill, whilst still suckling, the effort will disappear and babe will get no milk; cf bottle feeding, will still receive milk and potentially be overfed)
- Natural contraception (important in 3rd world)
- Bonding
- ↓ PPH
- ↓ SUDI
- No constipation (NB. Babies change their pattern of pooing from ~ 6-8/d in the first 6/52ish to something entirely different e.g. 1 every 3d or even much longer – in a BF baby, this is not constipation as cf formula fed babes – would be considered const)
- Less spilling, less irritating than bottle feeding
- Smells nicer at both ends
- ? Higher IQ
- Males can’t do it!

**Disadvantages** of breast milk:
- Limited iron and phosphate, Vit D and C (esp if small as small babies grow rapidly and outstrip their supplies of these nutrients; also potential for Vit D deficiency and rickets in dark-skinned babies)
- Discomfort establishing
- Can’t easily measure intake
- Modesty issues e.g. leaking
- Maternal drugs are included (eg lithium)
- Potential virus transmission esp HIV
- Breast milk jaundice

Establishing breast feeding:
- Babies don’t feed much for 1st 48 hours
- Breast milk comes in around day 3 (especially 1st baby) ⇒ baby’s hungry on day 1 (colostrum first)
- Can hurt – usually uncomfortable
- Baby and mother must learn each other’s supply, demand and preferences
- Growth is best way of proving adequacy
- Very hard to overfeed compared with bottle feeding (sucking is a reflex → will keep bottle feeding even if they don’t want the feed)

**Bottle feeding advantages:**
- Higher Vit D, C, Fe and phosphate
- Measurable intake
- No added drugs/viruses (unless water unclean)
- Easier to establish
- Males can do it

**Bottle feeding disadvantages:**
- Major problems in third world (water, sterility, cost)
- Difficulty in storage, portability
- More vomiting, irritation
- Constipation common
- Easy to overfeed
- Does not vary with need or circumstance
- Males can do it!

**Ongoing issues:**
- If feeding too regularly then baby will be getting CHO-rich foremilk but not fat-rich hind milk → hungry
- Attachment to the breast is key: Is the baby nipple-feeding or breast-feeding. If nipple then repeated trauma → pain, cracked nipples, etc
- Mastitis or blocked duct → express lots (try it in the bath)

**Establishing bottle feeding:**
- Day 1: average intake 60 ml/kg (= 40 calories/kg)
- ↑ by 15 ml/kg/day until average of 150 ml/kg/day (this is the key figure to remember)
- If too much then ↑ stools, ↑ vomiting, ↑ misery
- Alternatives to cow’s milk: goat (but no folate), soy, hydrolysed (if allergic to everything else)
- Allergy: eczema reaction mainly to casein proteins, but can also be allergic to whey protein
- Can be intolerant (ie non allergic reaction to):
Lactose (galactose + glucose): ↓lactase → osmotic diarrhoea + ↑fermentation by bacteria → ↑gas → frothy acid stools → acid burns round perianal skin. *More common as secondary intolerance (eg following Rotavirus).* Breast milk has lactose too.

- Fructose (eg fruits)
- Sorbitol (artificial sweeteners)

### Average Growth Parameters

- From Toronto Notes:

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Birth</th>
<th>Normal Growth</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Weight</strong></td>
<td>3.5kg</td>
<td>2 x BW by 4-5/12&lt;br&gt;3 x BW by 12/12&lt;br&gt;4 x BW by 24/12</td>
<td>→ Wt loss (up to 10% of BW) in first few days of life = normal&lt;br&gt;→ Should regain wt by 10d</td>
</tr>
<tr>
<td><strong>Height</strong></td>
<td>50cm</td>
<td>25cm in 1st yr&lt;br&gt;12cm in 2nd yr&lt;br&gt;8cm in 3rd yr&lt;br&gt;4-7cm /yr until puberty&lt;br&gt;½ adult height at 2 years</td>
<td>→ Measure supine length until 2yrs, then measure standing</td>
</tr>
<tr>
<td><strong>HC</strong></td>
<td>35cm</td>
<td>2cm/month for 1st 3 months&lt;br&gt;1cm/month at 3-6/12&lt;br&gt;0.5cm/month at 6-12/12</td>
<td>→ Measure around occipital, parietal, frontal prominences for greatest circumference</td>
</tr>
</tbody>
</table>

### Failure to Thrive (FTT)

- = Failure to gain weight normally (< 3rd percentile, or crossing 2 centiles) [cf stunted growth = failure to gain height]
- If also failure of linear growth ⇒ longstanding problem (weight always falls first, then length, then head circumference falls last)
- History:
  - What goes in (diet):
    - What and how much (and does it actually go in, or is it just offered?). Milk, other drinks, meat, fruit and vegetables, cereals and breads, lollies
    - Assess parents knowledge base
    - Feeding difficulties: appetite, behavioural, structural, swallowing
  - *What comes out* (poos) – especially steatorrhoea. People usually overestimate vomit
  - Chronic illness: cardiac, renal, neurological
  - HABE WIMP MAFS ROSE (remember Guthrie – e.g. CF)
  - Development
  - Social history: especially PND, other psych stresses, violence, drugs and alcohol

- Examination:
  - End of bed: fat, thin, energy, pallor, well/sick, dysmorphisms
  - Muscle and fat stores – look for scraggy buttocks
  - Signs of abuse and injury
  - Signs of chronic disease:
    - Cyanosis due to heart: L → R shunt and heart failure or cyanotic lesion (R → L shunt)
    - Respiratory: clubbing, nasal polyps (CF, asthma)
    - Gut: coeliac (not if breast feed) – distended abdomen and thin legs
    - Renal: blood pressure
  - Assess suck, chew, swallow
  - Rickets (↓vitamin D), anaemia (↓Fe), bruising (↓vitamin K), dermatitis & neuropathy (↓Vitamin B) (all late signs)
  - Differential:
    - Parent’s expectations: In the 2nd year of life: ↓appetite, ↓rate of growth, ↑activity are all normal. Parents may need reassurance
    - Non-organic failure to thrive:
      - *Inadequate parenting/poor nutrition* the most common cause (will feed and gain weight well while in hospital).
Usually complex situation: eg young mum, unwanted pregnancy, obstetric problems, poor bonding, bottle feed, maternal depression, etc.

Is the milk being made up properly, any strange stuff (eg tea, Milo, etc)

**Check for attachment:** observe mum chatting to baby while they dress – is she talking to the baby

### Organic causes:

- **↓ Intake** secondary to:
  - Underfeeding (eg engorged breasts → poor latching, inverted nipples)
  - Congenital abnormalities (eg cleft palate)
  - Dyspnoea (eg chronic heart failure, CF, chronic URTIs)
  - Neurological lesions (eg pseudobulbar palsy)
  - Behavioural factors (eg alert, restless)

- **Abnormal losses:**
  - Vomiting: need to be severe and persistent to → FTT. Eg pyloric stenosis, chronic UTIs, renal disorders
  - Stools: diarrhoea, steatorrhoea
  - Urine: eg diabetes, renal failure, diabetes insipidus, adrenal insufficiency

- **Failure of utilisation:**
  - Chronic infection (eg Tb, UTIs, immune disorders)
  - Metabolic disorders (eg phenylketonurea)
  - Endocrine disorders (eg hypothyroidism)

- **Constitutional and genetic abnormalities:** Short stature, Down’s, Turner’s, Achondroplasia

- **Increased requirements:** chronic lung disease, heart failure, etc

- Macrosomic babies (ie mum diabetic) will lose excess weight after birth → looks like failure to thrive

### Management:

- If non-organic failure to thrive, then educate regarding a baby’s dietary needs. See Parent and Adolescent Education, page 893
- Investigations: rarely necessary. Maybe Fe for anaemia

### The Crying Baby

- **A multifactorial problem**

- **Normal crying**:
  - Babies cry their most at 6 weeks – just when the honeymoon period is over and all the supports have gone back to work/gone home
  - Range from ½ to 7 hours per day
  - It’s their only means of communication
  - May be hungry, overfed, tired, pain, bored, hot, cold, inadequate burping, switching breasts too soon (→ low fat feeds), solids before 3 months.
  - Note especially babies cry when they’re tired – common mistake is to stimulate and soothe them when they need to sleep
  - **Not due to parental stress. Crying leads to stress not the other way round.** Harder for older women and professional who worked up to delivery to cope with (→ ↑ sense of isolation post delivery)

- **Colic**:
  - Definition varies from crying lots to “well thriving baby who develops muscle spasms, flushing face, pulls up legs, screams on and off every few minutes for several hours, loud tummy rumbles, relieved by flatus or passage of stool”
  - Theories:
    - Gut immaturity → disordered intestinal motility → GI pain
    - CNS immaturity → immature, disorganised response to stimuli → response to most things is to cry
    - Very unlikely to be lactose intolerance (rare before 3 months) or maternal cow’s milk consumption

- **History**:
  - Clarify what the parent wants to know – address their issues
  - HPC: How often, when, associated behaviours, timing, pattern
  - Vomiting and bowel patterns
  - Feeding and sleep patterns
  - PMH: ABFWIMPS
  - Maternal social history: attitude to baby, supports, PND, drugs and alcohol

- **Exam and investigations**:
  - Check growth
  - Exclude physical causes:
Acute: otitis media, intestinal cramping/diarrhoea, corneal abrasion, incarcerated hernia
Chronic: gastro-oesophageal reflux
Nutritional intolerances from mother’s diet (rare)

Issues:
- Baby’s safety: Is mum at breaking point?
- Feeding problems: sore nipples, nipple infection (eg thrush)
- Maternal mental state: depression, lacking support, sleep deprived, anxious
- Maternal nutrition: is she eating well?

Management:
- Acknowledge strain
- Reassurance: “I have looked carefully for physical causes and there are none that I can see”. “Baby is growing well so is getting the food they need”
- Things to try: rocking, pram, vacuum cleaner, ride in car, dummy, massage, warm bath
- Feeding: not too often, burp well, having enough?, no solids till 4 – 6 months, maternal diet (↓ caffeine, cabbage, onions, experiment with what causes baby to cry)
- Optimistic outlook: from 6 weeks to 3 – 4 months amount of crying normally reduces significantly
- Active advice: plan what mum can do to make it easier
  - Referral to Plunket nurse or Plunket Karitane centre and/or lactation consultant

Sleep Management

- Principles:
  - Sleep is a learned process – you train your baby to do it
  - After 6 months a night feed becomes a reward for waking up → trained night waker
  - Parents also need time for themselves
- For babies:
  - Night feeds: quick, quiet, dim light
  - Leave the baby to cry for a while
  - Wrap them well, then not woken by their own reflexes (eg startle reflex when lightly asleep)
- Toddlers:
  - Evening routine: won’t harm toddler if you’re firm with bedtime routines. No energetic games beforehand
  - Approach to Sleep Training:
    - Agree with partner/family what you are going to do
    - Plan in advance (eg start on a long weekend). Warn neighbours
    - Tell the child how it is going to be and why
    - Quiet bedtime routine every night
    - Put in bed, say good night, walk out
    - If they come out, return them to bed with no reinforcement or eye contact
    - If they cry, wait 5 minutes, then 7 minutes, then 9 minutes, etc. When going in, no reinforcement
    - Stick with it. May get worse before it gets better. Should see improvement by 5th night

Sudden Unexplained Death in an Infant (SUDI)

- Defn: death < 1 year, and still unexplained after autopsy, review of clinical history and examination of the death scene (in practice none of these are usually done well)

- Epidemiology:
  - 1990: approx 4.5 per 1000 live births
  - 2000: approx 1 per 1000 live births (about 70 per year). Pakeha lower, Maori about 4 per 1000

- Epidemiological risk factors:
  - Age (3 – 5 months)
  - Maternal smoking – now greatest modifiable risk factor given sleeping on back well established
  - Prone sleeping position
  - ?Bed sharing
  - Seasonal (winter worse)
  - Previously well
  - Race (eg higher in indigenous minorities)
  - Male
  - Low birth weight
  - Low maternal age
  - Low socio-economic status
Theories:
- Re-breathing of expired gases (e.g., prone or bed sharing)
- Hyperthermia
- Co-sleeping (bed sharing)

Differential diagnosis:
- Child abuse (e.g., shaking injury, suffocation)
- Metabolic disease
- Cardiac disease (congenital or acquired)
- Overwhelming sepsis
- Accidental asphyxia (e.g., in bed) — requires good death scene exam and history

S U D I follow-up:
- Explanation of death
- Explanation of grieving process
- Follow up with next child
- Screen for risk factors
- Role of monitoring (no evidence of effectiveness but reassuring for parents)

Prevention:
- Supine sleep position
- No smoking
- Own cot
- Avoid bed sharing or sofa if tired or smoker or alcohol intake or pillows
- *Dress for room temperature* (i.e., don’t let them get too hot, no hat in bed)
- Make up bed so they can’t slip under the covers (i.e., short-sheet the bed)

Complications of supine position: Plagiocephaly (flat spot on skull). Prevent by varying position of the head when lying

Neonatal Acute Airway Problems
- NB. DDx of a newborn gasping for air, blue, bradycardic =
  - 1. Diaphragmatic hernia
  - 2. Pneumothorax
  - 3. Upper airway problems (see below)
  - 4. Maybe meconium aspiration if traumatic birth

Choanal atresia:
- Failure of formation of nasal passages
- Baby goes blue until someone opens the mouth (obligate nose breathers)
- Can’t pass NG tube. Can be unilateral

Congenital masses:
- Nasal encephalocele and nasal dermoid
- Care with nasal intubation
- Beware the midline lesion as may extend into cranial cavity

Pierre Robin Sequence:
- Short jaw, cleft palate and glossoptosis — tongue falls back and obstructs if supine (due to hyper-flexed jaw in-utero)
- Nurse the baby prone
- Associated with oligohydramnios

Subglottic Stenosis:
- Due to intubation trauma in a preterm baby

Hypoglycaemia of the Newborn
- Needs to be recognised and managed
- Causes (either big babies or small babies):
  - ↑ insulin:
    - Child of poorly controlled diabetic mother → ↑ maternal glucose → ↑ foetal glucose → ↑ foetal insulin (important growth factor in utero) → fatter and larger baby
    - NB. Also see ↑ haemoglobin (as insulin is a growth factor + chronic hypoxaemia – complicated reasons)
  - ↓ substrate:
    - Small babies: lack of substrate (glucose stores e.g., glycogen, fat)
NB. Small babies – need to know w, h, HC, gestation (prem vs IUGR); IUGR can be symmetric (globally small) or asymmetric (big head, small body i.e. lost weight). **Asymmetric babies at higher risk of hypoglycaemia**

- **↑requirements:**
  - If septic or otherwise sick (may also become hyperglycaemic due to cortisol and adrenaline)
  - Poor thermoregulation therefore **cold baby**

### Symptoms:
- Usually none. Can be asymptomatic at < 1 mmol/L of glucose [would cause convulsions in adult]
  - [ABC] DEFG = don’t ever forget glucose!
  - May be jittery (but most common cause of jitteriness is hypoxaemia due to birthing process)
  - Convulsions or floppy – late signs

### Complications:
- can lead to **blindness and epilepsy**

### Prevention:
- Identify at risk babies and monitor blood glucose
- **Feeding** is usually required (normal babies can go 48 hours without a feed)
- May need IV glucose
- **Prevent hypothermia.** If they’re small and get cold they will become hypoglycaemic

### Jaundice

- Key question is why, not how much (although this is important too)
- Two types of bilirubin:
  - **Unconjugated:**
    - If ↑ unconjugated, can lead to **kernicterus** ("yellow basal ganglia"): cerebral palsy, deafness, ↓ IQ
    - Can die acutely (seizures, bilirubin encephalopathy)
    - If survive: deaf, athetoid cerebral palsy (snake-like movements – the harder they try to move the harder it becomes), normally intelligent
  - **Conjugated:** water soluble, conjugated in liver by glucuronyl transferase

#### Types of Jaundice

- **Early onset** (in 1st 24 hours):
  - Always pathological
  - **Causes:**
    - 1. **Haemolysis** of any cause (eg Rhesus, ABO blood incompatibility, spherocytosis, G6PD deficiency etc)
      - ABO incompatibility (mother is O, baby is type A or B – cannot be AB!) = can have problems with 1st birth (cf rhesus disease); test cord blood (**DAT** – direct antiglobulin test) if mother is O; generally is not severe
      - Rhesus incompatibility = only problem with 2nd babe; **can also develop Ab after miscarriage**
    - 2. Sepsis:
      - Not a common cause of jaundice, but a **serious one**
      - Will also see an ↑ work of breathing
      - If jaundice + ↑ WOB, give antibiotics + admit to NICU
      - Often **GBS** (group B strep) implicated therefore vaginal swabs taken at 36/40 – if positive, AB given during labour
  - **Prevention:**
    - Expect ABO if they’ve had it before
    - Check for Rhesus disease
- **Jaundice in 1st week:**
  - Emphasis on extent of the jaundice (as well as consideration of the cause) to prevent kernicterus
  - Could be due to haemolysis or any of the other causes
- **Persistent jaundice:**
  - If it doesn’t get away by 10 – 14 days then revisit
  - **Causes:**
    - ↑ conjugated bilirubin (skin goes green) – needs treatment (but not with phototherapy)
    - Liver obstruction abnormalities (eg biliary atresia; liver damage from infection; toxins, etc)
    - Hepatitis/liver inflammation
    - Unconjugated (skin goes yellow) – needs treatment if high. E.g. **breast milk jaundice** (most common) – progesterone in breast milk delays switching on of glucaronyl transferase therefore ↑ unconjugated bili
Other causes = hypothyroidism, CF, galactosemia

Treatment
- Phototherapy (visible light at the blue end of the spectrum – not UV)
- Exchange transfusion
- IV immunoglobulin

Diseases Picked Up on Guthrie Card Causing Jaundice
- Hypothyroidism
- Galactosaemia
- Cystic fibrosis

Aside: ABO Blood Incompatibility
- Maternal antibodies from mother with type O blood attack fetal blood cells if type A, B, or AB. Not isoimmunisation – it’s an existing immune response. Doesn’t get worse with subsequent pregnancies
- Transfusion:
  - Transfuse type O RBCs – aren’t antigenic to anyone
  - Transfuse type AB plasma – won’t contain antibodies to either type A or B blood

Cardiac and Respiratory Conditions Presenting in the Neonatal Period

Respiratory Disorders
- Respiratory disorders presenting in the term newborn:
  - TTN (see below)
  - Congenital pneumonia (especially group B strep): can see maternal fever, tender uterus, fetal tachycardia, prolonged rupture of membranes
  - Aspiration pneumonia – meconium/blood/breast milk
  - Pneumothorax – can see after resuscitation or spontaneous (most common)
  - Upper airway obstruction (see neonatal acute airway problems)
  - Congenital anomalies of the lung e.g. diaphragmatic hernia
- Respiratory disorders presenting in the preterm newborn (see complications of preterm birth):
  - RDS
  - Chronic lung disease of prematurity
  - PIE
  - Pulmonary haemorrhage

Cardiac Disorders
- Cyanotic lesions:
  - TGA
  - Pulmonary atresia
  - Tricuspid atresia
  - Tetralogy of Fallot
- L → R shunts:
  - VSD
  - ASD
  - PDA
  - AVSD
- Left outflow tract obstruction:
  - Coarctation of the aorta
  - Hypoplastic left heart

Other Neonatal Problems

Infant Drug Withdrawal Syndrome
- For first 2 weeks after delivery if mother is abusing heroin, methadone, other narcotics:
  - Jitteriness
  - Sneezing
  - Yawning
  - Poor Feeding
  - Vomiting
Diarrhoea
Weight loss
Seizures

Child of Diabetic Mother
- Maternal complications: polyhydramnios, preterm labour, still birth near term
- Fetal: ↑malformations, macrosomic, growth retarded, shoulder dystocia
- After birth: hypoglycaemia, hypocalcaemia, respiratory distress (surfactant doesn’t ↑ till later in gestation), polycythaeMIC (venous hematocrit > 0.65, looks plethoric. May require exchange transfusion to remove RBCs)

Transient Tachypnoea of the Newborn
- Occurs in both term and prem babies
- Delayed absorption/expulsion of amniotic fluid from lungs
- Risk factors: C-section or rapid second stage (baby does not travel through the birth canal so fluids not pushed out of the lungs during delivery), perinatal asphyxia, excessive analgesia, hypothermia
- Presentation: subcostal recession, grunting, and cyanosis all seen but not prominent
- CXR: inflated lung fields, perihilar opacities, ↑vascular markings
- Treatment: O2 for several days, respiratory failure uncommon. Penicillin if ?congenital pneumonia

Meconium Aspiration
- Hypoxia during labour → gasp → aspiration meconium (+/- vernix, meconium, blood)
- Patchy lung collapse and hyperinflation (ball valve effect – i.e. can get air in but not out)
- Complications: pneumothorax and pneumomediastinum (→ angel wing appearance on CXR due to air under the thymus)
- Treatment: suction via ET tube

Heart Disease in Children

Innocent Murmur
Characteristics
- Soft
- Short
- Systolic
- Symptomless
- Standing/sitting (↓ on standing; most pathological murmurs will stay the same, except HOCM)

The Blue Baby
- Neonatal adaptation:
  - With first breath:
    o Alveolar oxygen tension increases
    o Pulmonary bed dilates
    o Ductus arteriosus starts to constrict
  - Cord clamp:
    o ↑ in LV and LA pressure
    o Functional closure of foramen ovale
  - Ductus: closes at 24 – 48 hours. Murmur may be normal. Can open/close with drugs (NSAIDS close, prostaglandins open)
  - Replacement of HbF with HbA from 24 weeks (90%) to birth (70%) to 6 months (trace)

Cardiovascular Changes at Birth
- Increasing uptake of oxygen by lungs (first and subsequent breaths) induces a vasoconstriction of ductus venosus and ductus arteriosus
- Aeration of the lungs at birth is associated with:
  1. a dramatic fall in pulmonary vascular resistance due to lung expansion.
  2. a marked increase in pulmonary blood flow (thus raising the left atrial pressure above that of IVC)
3. A progressive thinning of the walls of the pulmonary arteries (due to stretching as lungs increase in size with first few breaths)

- **The first breath:** ... the pulmonary alveoli open up:
  - Pressure in the pulmonary tissues decreases
  - Blood from the right heart rushes to fill the alveolar capillaries
  - Pressure in the right side of the heart decreases
  - Pressure in the left side of the heart increases as more blood is returned from the well-vascularized pulmonary tissue via the pulmonary veins to the left atrium

- **Resulting circulatory changes include:**
  - Blood pressure is now high in the aorta and systemic circulation is well established

**Clinical Signs of Heart Disease**

- Clinical warning signs:
  - Early murmurs in a clinically well baby
  - Newborn who becomes hypoxic

- Classifying:

<table>
<thead>
<tr>
<th></th>
<th>Cyanotic Heart Disease</th>
<th>Acyanotic Heart Disease</th>
<th>Respiratory Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cyanosis</td>
<td>Severe</td>
<td>Variable</td>
<td>Variable</td>
</tr>
<tr>
<td>Tachypnoea</td>
<td>Mild</td>
<td>Variable</td>
<td>Variable</td>
</tr>
<tr>
<td>Respiratory Effort</td>
<td>Not major</td>
<td>Variable</td>
<td>Variable</td>
</tr>
<tr>
<td>Heart Murmur</td>
<td>+/-</td>
<td>+/-</td>
<td>None</td>
</tr>
<tr>
<td>When</td>
<td>First 1 – 7 days</td>
<td>First 1 – 4 weeks (effect of failure – takes longer)</td>
<td>Often at birth</td>
</tr>
</tbody>
</table>

**Causes of Cyanosis**

- Respiratory Causes:
  - **Hypoventilation:** central apnoea from drugs, apnoea of prematurity, sepsis, metabolic (eg hypoglycaemia), seizures
  - **Mechanical interference** with lung function: airway obstruction, abdominal distension, pneumothorax, thoracic and sternal deformities, etc
  - **V-Q mismatch** with lung disease:
    - *Infection* (Gp B Strep, G – iv): pneumonia on X-ray hard to distinguish from wet-lung of early respiratory distress. Have high index of suspicion, low threshold for antibiotics
    - *Respiratory distress syndrome:* X-ray appearance: Ground glass + air bronchogram \(\Rightarrow\) \(\downarrow\) surfactant. If maternal diabetes, are deficient in surfactant until later in gestation
    - *Aspiration:* meconium, milk, blood
    - Pulmonary oedema, hydrops fetalis (\(\Rightarrow\) in heart failure before delivery. Used to be due to Rhesus negative disease prior to Anti-D treatment, now numerous other causes)
    - Lung haemorrhage: complication in premature
    - Primary lung disease

- Cardiac causes of cyanosis:
  - R to L shunt: cyanotic heart disease or pulmonary hypertension
  - L to R shunt and heart failure

- Differentiating Heart and Lung Disease:
  - History and exam:
    - When did it start?
    - Relationship of cyanosis to birth. *If heart, pink to start with then go blue as ductus closes* (blood gets to lungs via reverse flow through ductus if right heart not functioning well)
    - Check respiration:
      - If apnoea \(\Rightarrow\) heart. If heart problems, won’t work so hard at breathing
      - Respiratory distress and \(\uparrow\) effort \(\Rightarrow\) airway or lung problem
    - Exam: big heart or liver/murmur suggests cardiac problem; tachypnoea/grunting/recession/wheeze could be either!
  - Investigations:
    - CXR (heart size, lung fields)
    - ABG/O2 saturation monitoring. If lung disease, may have \(\uparrow\)CO2
    - ECG – only of help if dramatically abnormal
    - Hyperoxia test: give 100% O2 – if heart disease then PO2 won’t change as gas transfer is not the problem but if respiratory cause, will see an increase in PO2
    - Echocardiography – investigation of choice
• Also consider sepsis and anaemia

**Congenital Heart Disease**

**Summary**

• **Congenital:**
  - **Acyanotic:** ventricular septal defect (VSD), atrial septal defect (ASD), atrioventricular Septal Defect (AVSD) and patent ductus (PDA)
  - **Cyanotic:**
    - Decreased pulmonary flow (→ **dark lungs** on X-ray):
      - Critical pulmonary atresia/stenosis, critical aortic stenosis (if not critical then acyanotic)
      - Tricuspid atresia
      - Fallot’s Tetralogy (commonest congenital cyanotic problem, presents about 3 months of age, no murmur)
    - Increased pulmonary flow:
      - *Transposition of the great arteries* (TGA): fine till birth, goes blue as ductus closes
      - Total anomalous pulmonary venous drainage (TAPVD): very rare
      - Persistent pulmonary hypertension
  - **Other:** Coarctation

• **Acquired:** Rheumatic fever
• **Arrhythmia:** Long QT, SVT, Pre-excitation, VT
• **If chronic →** developmental delay and clubbing
• **Associated with:**
  - Chromosome disorders: **Trisomy 21** (40% have cardiac lesion – mainly **AVSD**), 18, 13 and **Turner’s coarctation**
  - Numerous syndromes

**Aetiology**

• **Genetic causes:**
  - 8/1000 live, full term births (higher in premature and still born). Second most common congenital malformation after brain
  - Chromosomal eg Down Syndrome
  - Single gene eg Marfan’s (prolapsing mitral valve)

• **Environmental:**
  - Infection (eg Rubella)
  - Maternal (eg Diabetes)
  - Substance abuse (eg alcohol)
  - Drugs (eg phenytoin, thalidamide)

• **Usually leads to an abnormality in tissue migration**

**Incidence** *(Pathology not Paediatrics’ numbers!)*

<table>
<thead>
<tr>
<th>Shunt Type</th>
<th>Condition</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acyanotic (L-R Shunt)</td>
<td>Ventricular Septal Defect</td>
<td>25 – 30%</td>
</tr>
<tr>
<td></td>
<td>Atrial Septal Defect</td>
<td>12 – 20%</td>
</tr>
<tr>
<td></td>
<td>Patent Ductus</td>
<td>10 – 15%</td>
</tr>
<tr>
<td>Cyanotic (R-L Shunt)</td>
<td>Tetralogy of Fallot</td>
<td>8 – 15%</td>
</tr>
<tr>
<td></td>
<td>Transposition of Great Vessels</td>
<td>8 – 10%</td>
</tr>
<tr>
<td>No Shunt</td>
<td>Coarctation of the Aorta</td>
<td>5 – 7%</td>
</tr>
<tr>
<td></td>
<td>Pulmonary Stenosis</td>
<td>5 – 7%</td>
</tr>
<tr>
<td></td>
<td>Aortic Stenosis</td>
<td>4 – 5%</td>
</tr>
</tbody>
</table>

**Ventricular Septal Defect**

• Epidemiology: 12/10,000
• Types are muscular, perimembranous and outlet (affects aortic valve)
• 90% involve **membranous septum** which grows down to meet muscular wall
• Wide range: from asymptomatic through life to fulminant heart failure in infancy
• **Signs:**
  - **Pansystolic murmur** (often with thrill). VSD murmurs are due to **left-to-right shunting** at the ventricular level. Small ventricular septal

*Health Care of the Elderly*
defects are typically louder than larger ones. The murmur of a VSD is heard best at the left lower sternal border.

- Features of heart failure
- Features of pulmonary hypertension if large: ↑JVP, sternal heave (↑RH work), loud P2

- Investigations:
  - ECG: LV hypertrophy (due to volume loading)
  - CXR: ↑heart size, ↑vascular markings in lungs
  - Echo: size and location of defect

- Management: treat only if large: surgical repair

- Prognosis dependent on size of defect:
  - Small defects often close over spontaneously. Remaining ones at small risk of infective endocarditis. Prophylaxis if dental work – this is controversial
  - Large defects → Eisenmenger’s syndrome (see below, pulmonary hypertension, shunt reversal and cyanosis)

Atrial Septal Defect (ASD)

- Epidemiology: 6 – 8/10,000 live full term births. F:M = 2:1. Higher in stillborn and premature births
- Aetiology unknown in > 90% of cases
- Pathogenesis/types:
  - Septum primum defect: Septum primum closes foramen primum at week 5. Failure to form completely results in a low ASD adjoining AV valve
  - Septum secundum defect (most common): Septum secundum closes over foramen secundum at week 4 – flap forms a one-way value. If it fails to reach far enough leads to fossa ovalis ASDs. Common in trisomy 21
  - Defects in primitive sinus venosus lead to ASD near vena cava ostia

- Clinical:
  - A L → R shunt increases pulmonary flow but if < 1 cm may be asymptomatic through life
  - Larger defects → arrhythmias and/or murmur in 3rd decade. Evaluate for corrective surgery to prevent pulmonary hypertension, heart failure or arrhythmia
  - Chronic pulmonary flow 2 – 4 times normal → pulmonary hypertension with R → L shunt (Eisenmenger’s) and heart failure in less then 10% of cases
  - Signs:
    - May have evidence of RH overload: ↑JVP, sternal heave, loud P2
    - Ejection systolic murmur in pulmonary region (flow murmur due to ↑flow through pulmonary outflow tract, not due to defect). This is not specific – many children have it, especially when ill ⇒ P2 important in differentiating benign from ASD. Potentially can have a diastolic murmur too as more blood flowing past tricuspid valve
    - In larger ASD an early diastolic murmur at the left lower sternal border, due to ↑ blood flow across the TV is heard
    - Fixed splitting of S2 (pathognomonic; no respiratory variation since the blood flow through the pulmonary valve is always ↑ due to the L → R shunting at the atrial level causing a delay in pulmonary valve closure throughout the respiratory cycle)

- Investigations:
  - ECG: RV hypertrophy and right axis deviation (due to RV volume loading) + RA hypertrophy (tall T waves – p pulmonale)
  - CXR: ↑heart size, prominent pulmonary arteries with ↑vascular markings (L → R shunting at the atrial level will cause ↑ blood volume in the RA+RV resulting in cardiomegaly, in addition the ↑ pulmonary blood flow causes the pulmonary vasculature to be more prominent)
  - Echo to confirm diagnosis

- Management: Surgical or percutaneous closure (amplatzer device) by age 5 (unless small and spontaneous closure)

Atrioventricular Septal Defect

- = endocardial cushion defect

Health Care of the Elderly
Commonly seen in **Down syndrome**
- Deficient atrioventricular septum

**Patent Ductus Arteriosus**
- NB. Physiological closure within 15hrs and anatomical closure in first few days
- **Aetiology:** Occurs as an isolated lesion or in combination with other abnormalities (eg Tetralogy of Fallot). Association with Rubella. 90% isolated defects. Incidence 1 in 2000
- **Pathogenesis:**
  - Connects aorta to left PA (acts as R → L shunt in foetus).
  - **↑Oxygenation at birth** → **↓PGs** (lungs metabolise them) → muscular contraction → functional closure at 2 days, anatomic closure at 2 – 3 months. Forms **ligamentum arteriosum**.
  - If hypoxia at birth then it can remain patent. A patent ductus allows up to 75% of LV output to flow from the aorta to the pulmonary artery (ie becomes a L → R shunt)
  - If persistent then → pulmonary hypertension → becomes a R → L shunt (Eisenmenger’s Syndrome), **deoxygenated blood flows more to legs than arms** → **clubbing in toes** not fingers
- In term infants: Delayed closure due to ↓PaO2: pulmonary disease (eg meconium aspiration), pulmonary hypertension, high altitude
- In preterm:
  - **↑Incidence with ↓birth weight**
  - **↓Sensitivity to PaO2 and ↑sensitivity to PGE2**
  - Haemodynamic effect of hypoperfusion and hypotension: associated with intraventricular haemorrhage and necrotising enterocolitis
- **Clinical:**
  - **Murmur at left sternal edge**, 2nd or 3rd intercostal space i.e. **pulmonary region: systolic and diastolic** but **systolic mostly only heard**. Silent if high pulmonary artery pressures (can be heard in first few hours in many infants)
  - Active praecordium with **bounding pulses due to ↑ pulse pressure** (collapsing pulse)
  - Hepatomegaly
  - LV failure: apnoea, bradycardia
  - → LV hypertrophy, RV hypertrophy secondary to pulmonary hypertension if persistent
- **Investigations:**
  - ECG usually normal. LV and/or RV hypertrophy if large and persistent
  - CXR: cardiomegaly and pulmonary plethora (↑flow)
  - Echo: diagnostic
- **Management:**
  - Requires closing:
    - **NSAIDs** (anti-PG – PG dilate) → promote closure
    - Surgical or device closure
  - Small risk of endocarditis if closed

**Persistent Pulmonary Hypertension**
- Failure of pulmonary capillary bed to dilate sufficiently after birth
- Return to fetal circulation (ie R → L shunt): ↓pulmonary flow
- **Causes:**
  - Aspiration, eg meconium
  - Hypoxia: asphyxia
  - Infection: Group B strep
  - Hyaline membrane disease
  - Lung hypoplasia
- Treat with **nitrous oxide** to dilate pulmonary vascular bed

**Coarctation of the Aorta**
- Preductal or infantile form:
  - Narrowing of the arch of the aorta between the left subclavian artery and ductus arteriosus.
  - Association with PDA and ASD (?due to low flow in this area after
birth) and with bicuspid aortic valves.

- Associated with Turner’s syndrome
- Severe consequences: LVF, cyanosis in lower half of body

- **Variety of presentations:**
  - Heart failure in infancy (LVH due to pumping against an ↑ afterload – can lead to RVH)
  - Hypertension in child/young adult
  - Asymptomatic murmur

- **Exam:**
  - ↓ Femoral pulses, radio-femoral delay
  - Upper limb hypertension
  - **Systolic murmur** heard anteriorly and posteriorly (in back). Continuous murmur if severe
  - Maybe cyanosis/clubbing in lower limbs

- **Investigations:**
  - ECG shows evidence of LV hypertrophy
  - CXR:
    - Rib notching due to collaterals (> 5 years of age)
    - Abnormal aortic arch contour: look for faint post stenotic dilatation below cardiac knuckle
      - Echo: shows lesion – harder to see descending aorta
      - **Cardiac catheter:** assess haemodynamics

- **Treatment:** surgery, balloon angioplasty and ongoing management (hypertension, risk of dissection, etc)

- **Postductal or adult form:** Less severe narrowing with possible post-stenotic aneurysm due to turbulence. Ductus is closed. May be asymptomatic. Possible LV hypertrophy. Left intercostal artery provides collateral flow. (NB Proximal aneurysms occur in Syphilis, Coarctation and Marfan’s)

- Left and right pulses may be different (left bounding)

**Hypoplastic Left Heart**

- The *mitral and aortic valves are stenotic or atretic* causing ↓ flow through the LV in utero → poor development → hypoplasia
- Very poor prognosis

**Tetralogy of Fallot**

- Malformation during closure of the interventricular septum leads to:
  - 1. Transposition/over-riding aorta
  - 2. High VSD
  - 3. RVOT obstruction: pulmonary valve stenosis/atresia
  - 4. RVH (giving a boot shaped heart – diagnose on X-ray)

- Survival requires a PDA

- **Clinical:**
  - Right ventricular impulse
  - **Systolic ejection murmur at left sternal edge.** Right-to-left shunting at the VSD is not audible due to a small amount of pressure difference between the RV + LV. This is the reason why a VSD murmur is not present, but rather a harsh systolic ejection murmur *due to RVOT obstruction*
  - ↓ lung volume (oligaeic on CXR) as harder to pump blood through RVOT obstruction
  - Cyanosis after several weeks or months (R → L shunt as aorta opens over VSD and RVOT obstruction therefore as RV contracts, deoxygenated blood preferentially goes up aorta)
  - RH failure (boot shape on CXR)
  - Can see endocarditis with subsequent brain abscess
  - Death likely at puberty if not corrected
  - Can see arrhythmias post repair

- Repair by patching VSD and opening out RVOT (+/- patching this too)

**Transposition of the Great Arteries (TGA)**

- Aortic and pulmonary arteries transposed → 2 separate circuits
- **Requires a patent ductus** +/- VSD (if VSD then cyanosis not as marked)
- OK until birth. *Cyanosis as ductus closes* (normally 24-48 hrs)
• CXR = egg shaped heart
• Dx with echo
• Maintain PDA patency with PG
• Surgery with arterial switch (care with position of coronary arteries)

**Pulmonary Valve Stenosis**

- Similar effect to pulmonary atresia
- \( \rightarrow \downarrow \) Right heart development. Blood has always got to LA via foramen ovale, rather than through lungs
- Ejection systolic murmur, radiates to back

**Truncus Arteriosus**

- Congenital malformation in which the pulmonary artery and aorta have failed to separate from their common precursor truncus

**Arrhythmias in Children**

- Relatively uncommon in paediatric population
- Often not associated with other heart disease (cf adults, associated with structural disease)

**Clinical:**
- Asymptomatic or palpitations
- If prolonged may \( \rightarrow \) growth retardation, heart failure, arrest, etc

**Classification:**
- **Bradycardias:**
  - AV Block:
    - 1\(^{st}\) and 2\(^{nd}\) degree: normal variant
    - 3\(^{rd}\) degree: Associated with AVSD, post-surgical, Rheumatic fever, myocarditis, maternal mumps, etc.
      - Acute treatment: Isoprenaline/Atropine \( \rightarrow \) \( \uparrow \) HR. Long term: pacemaker.
    - Sinus node dysfunction
- **Tachycardias:**
  - Supra-ventricular tachycardia (SVT): due to re-entrant pathway associated with A-V node.
    - Management: Terminate tachycardia: **vagal manoeuvres** (ice on face, valsalva – blowing against closed glottis), IV adenosine (AV node blocker), \( \beta \)-blockers, DC cardioversion. Prevent recurrences with \( \beta \)-blockers, CCBs or ablation of re-entry pathway
  - Pre-excitation syndromes:
    - **Wolfe-Parkinson White.** Accessory pathway from atria to ventricle \( \rightarrow \) short PR interval, wide QRS and delta wave (upslanting at the start of the QRS complex). Risk of cardiac arrest and sudden death via VF. Treatment: ablation
  - **Long QT syndrome:**
    - General rule = QT segment should be less than \( \frac{1}{2} \) the R-R interval
    - Congenital (K+ channel abnormality) or acquired (drugs, hypocalcaemia).
    - Susceptible to arrest, torsades (twisting of the points) and bradycardias.
    - Consider in unexplained syncope or convulsions.
    - Treatment: cardiovert if arrhythmia, \( \beta \)-blockers or ICD to prevent

**Complications of Congenital Heart Disease**

**Heart Disease with Failure**

- Definition: inability of myocardium to meet metabolic needs of the body
- Causes:
  - Congenital heart disease:
    - Lesions with left to right shunt: Large VSD (\( \rightarrow \) \( \uparrow \) blood to pump \( \rightarrow \) overloaded heart), AV canal defect, patent ductus
    - Left outflow obstruction: Hypoplastic left heart, coarctation of the aorta, aortic stenosis
Arrhythmia: usually SVT
Cardiomyopathy: Usually ischaemic, due to birth asphyxia

Incidence by age:
- Infants: congenital heart lesions, rarely arrhythmias (eg SVT)
- > 1 year: cardiomyopathy, right heart disease, dysrhythmias

Symptoms of heart failure:
- ↑respiratory effort
- Sweating (important sign)
- Poor feeding (no energy to suck)
- Failure to thrive (hypermetabolic state and poor feeding due to breathlessness)

Signs of heart failure:
- Tachycardia (↑160 in infants)
- Tachypnoea (intercostal indrawing, wheeze)
- Gallop rhythm
- Hepatomegaly
- Cyanosis

Features not found in children:
- ↑JVP
- Peripheral oedema
- Crepitations in lung fields

Key differential to acute onset is sepsis

Treatment:
- Rest
- Diuretics
- Digoxin +/- ACEi
- O2
- Adequate calories: fortified feeds
- Treatment of underlying cause (arrhythmias, infections, anaemia, etc)

Eisenmenger’s Syndrome (Pulmonary Hypertension)

- Sequelae of large L → R shunt with untreated VSD, PDA or ASD
- Rare – as they are usually corrected
- Usually present in 3rd to 4th decade (but can present in childhood)
- L → R shunt → ↑pulmonary flow → oversupply of blood → pulmonary capillary hypertrophy → ↑resistance → pulmonary hypertension:
  - Reversal of shunt (now R → L) → development of cyanosis
  - RV hypertrophy and failure
- Also abnormal flow → mural thrombosis → endocarditis (as in most congenital defects)

Clinical:
- Signs of pulmonary hypertension:
  - 1. RV heave (as hypertrophied RV swings round and strikes chest)
  - 2. Loud P2
  - 3. Hepatomegaly
  - 4. Can lead to LVH
  - 5. Cyanosis, clubbing
- Little or no murmur

Prognosis:
- Arrhythmias and sudden cardiac death
- ↑Hb due to cyanosis (polycythaemia) → ↑viscosity → clotting problems
- ↑risk of systemic emboli (lungs don’t act as a filter for emboli)
- Haemoptysis due to pulmonary infarct/haemorrhage

Treatment: Supportive or heart-lung transplant (NB. If try to reverse VSD/ASD then rapid RVF and death)

Rheumatic Fever

Incidence:
- Incidence has declined over last 50 years worldwide, but not to the same extent in NZ
- 1 per 1000 people in NZ (highest rate in western world).
- Maori 50 – 100 times, Pacific island 100-200 times rates of non-Maori – widening ethnic disparities
- Intensely concentrated in 5-14 yr olds, Maori + PI, and upper north island
Acute attacks occur mainly between 5 – 15 years of age. Peak 10 – 11 years.

**Aetiology:**
- Incidence following strep throat is 0.3 % (sore throat for 1 week) to 3% (sore throat for 3 weeks)
- ?Some at ↑ risk due to longer carriage of strep → ↑ antibody response

**Pathogenesis:**
- Group A β-haemolytic streptococci infection (eg Streptococcus Pyogenes) → antibodies formed that cross-react with substances in myocardium (M protein in strep and myosin contain identical amino acid sequences) similar to strep antigens → carditis → acute rheumatic fever 1 – 5 weeks following infection (average 19 day latent period).
- Also see anti-neuronal antibodies (chorea)
- Damaged myocardium contains complement, IgG, IgM, IgA

**Clinical features:**
- JONES criteria (joints, o = heart, nodules, erythema marginatum, sydenham’s chorea)
  - Carditis:
    - Endo +/- myo +/- peri
    - Usually mild in first attack
    - New left sided murmur: mitral and/or aortic regurgitation
    - Tachycardia
    - ECG changes: PR prolongation (may be buried in T wave)
    - Cardiomegaly: due to valve dysfunction (→ dilation) or myocarditis
  - Arthritis:
    - Migratory polyarthritis – as one joint starts to recover another flares
    - Usually large joints. Can be red and swollen
    - Dramatic response to aspirin
    - Never permanent joint damage
- Sydenham’s chorea (St Vitus’ Dance):
  - Sudden or gradual onset. Acute onset chorea in a child only occurs in RF
  - Usually generalised, although can be focal
  - Deterioration at school, eg writing
  - Stops during sleep
  - Increased by anxiety/stress
  - Rare symptom. Always resolves, after 2 – 3 weeks
- Erythema marginatum:
  = Red rash around edge, centre normalises as it expands
  - Evanescent (comes and goes quickly)
  - Not itchy, blanches with pressure, mainly on trunk and proximal limbs

**Subcutaneous nodules:** small, painless, over bony prominences, RARE

**Investigations:**
- Throat swab: +ve for strep in 15%
- Streptococcal titres
- ESR usually > 100 (not if chorea or CHF)
- CXR: looking for cardiomegaly
- ECG: prolonged PR in 14%
- Echocardiogram

**Diagnosis:**
- Acute Phase: Jones’ criteria: evidence of strep throat (↑serum titres) plus 2 major or 1 major/2 minor:
  - Major criteria: as above: carditis, migratory polyarthritis of major joints (75%), erythema marginatum (non pruritic, non painful), subcutaneous nodules, and chorea (later)
  - Minor criteria: fever, arthralgia, ↑acute phase proteins, c-reactive protein, ESR, ↑PR interval
  - Also watch out for murmurs, arrhythmias (from focal fibrosis)
  - Very difficult to diagnose. Always consider as differential in pyrexia of unknown origin
- Chronic Phase: recurring attacks magnify cardiac injury. Mitral and/or aortic stenosis progresses to congestive heart failure. Recurrent attacks make it worse → ?long-term prophylaxis

**Treatment:**
- Eradicate streptococcus (antibiotic therapy, given within 5 to 7 days, reduces risk of developing ARF by 70% - 80%)
- Aspirin: 75 mg/kg/day (∧inflammation)
- Bed rest if cardiomegaly or CHF, others should avoid rigorous exercise
- Steroids for acute treatment – but doesn’t affect long term prognosis
Diazepam for chorea

Is it worth treating sore throats in children?

- Of children aged 5 to 15 years presenting with a sore throat 15-20% will have GAS (NZ guidelines strongly advocate antibiotics in “high risk” group)
- Clinical accuracy in diagnosing streptococcal infection versus viral infection is poor:
  - tender, enlarged cervical nodes
  - high fever
  - no URTI/cough
  - headache
  - exudate
- If all present probability of strep infection 50-70%
- 1 in 6 will have strep, 1 in 50 of those may get rheumatic fever
- 300 need to be carefully assessed and treated to prevent one case of rheumatic fever
- 50% of children with RF have no history of sore throat

Course:
- Acute phase lasts 6 – 8 weeks, monitored by ESR
- Dental check
- Ongoing management:
  - Will get it again if they get another strep infection, and more severe
  - Penicillin prophylaxis: 4 weekly IM benzathine penicillin until 18 or 21 if no cardiac damage (for life if damaged).
  - Regular dental care. Prophylaxis for deep dental work (erythromycin or clindomycin – won’t have any penicillin sensitive organisms on board)
- Acutely damaged valves can recover

Pathology

- GAS cross reactivity (strept Ag + myocardial Ag)
- Acute = pancarditis (aschoff bodies, vegetations), can see arrhythmias
- Chronic = valve fibrosis (esp mitral; see commissural fusion – fishmouth deformity, thickening and shortening of chordae tendoniae), regurg
- Aschoff bodies = degenerative material, large histiocytes
- Macroscopic appearance:
  - Acute (exudative and proliferative) phase: Pancarditis grossly visible in valves and pericardium. Valve leaflets have evenly spaced small 1 – 2 mm sterile/inflammatory (not infective) ‘verrucae’ – small vegetations resulting from deposition of fibrin along edges of value. Verrucae resolve but Aschoff bodies (areas of necrosis surrounded by macrophages) organise and fibrose. Mitral valve always involved. Pericardium shows non-specific serofibrinous (bread and butter) pericarditis similar to uraemia or acute MI
  - Chronic (healed) phase: Heals with organised fibrosis → deformed valves (50% mitral, 50% mitral and aortic) and/or shortening/thickening/fusion of chordae tendineae.
    - Subendocardial fibrosis → fibrous plaque (McCallum’s patch). Characteristic “fish mouth” stenosis → atrial hypertrophy and LV atrophy. Aortic stenosis → LV hypertrophy. May lead to murmurs or arrhythmias
- Microscopic appearance:
  - Exudative phase: fibrinoid necrosis with neutrophils, lymphocytes, plasma cells and macrophages
  - Proliferative phase: Aschoff body in the myocardium is pathognomonic. Consists of central fibrinoid exudate/necrosis with aggregates of large mononuclear or multinuclear cells (Aschoff giant cells), fibroblasts, plasma cells, lymphocytes and oedema. Aschoff bodies may also be seen in perivascular spaces, joint capsules, tendons, subcutaneous tissues
- Susceptible to later valvular infection
- Treatment: Possible surgical replacement of deformed valves

Respiratory Illness

- See Allergic Rhinitis, page 86

Symptoms

- Differential of dyspnoea:
  - 1. Heart failure
2. Cerebral hypoxia
3. Metabolic acidosis
4. Respiratory causes

Differential of stridor:
- Retropharyngeal abscess: lymph nodes in midline behind pharynx, usually under 4 years, mainly strep, maybe staph aureus. Acute toxicity, hyper-extended, quiet stridor, CT diagnostic
- Croup
- Epiglottitis
- Foreign body
- Angio-oedema
- Peritonsillar abscess
- Laryngomalacia: noisy breathing due to floppy larynx from birth, especially inspiratory, crying or exertion
- Tracheomalacia: soft tracheal cartilages: Brassy cough (honking). May get severe obstruction
- Adenoid and tonsillar hypertrophy: reaches peak at 8–10 years, but relatively largest at 5–6. Snoring and obstructive sleep apnoea. Acutely enlarged → stridor (eg in EBV – treat with steroids)

Chest Radiology

- View Jean’s handouts
- Initially:
  - Name, date, and view
  - Orientation: L & R
  - Check exposure: lung fields and intervertebral discs
  - Centering: check rib length on each side for rotation (clavicles unreliable)
  - Lung field size:
    - 5–7 anterior ribs to the midline of the right diaphragm
    - 7–9 posterior ribs to the spine
    - If too many, then hyperinflated: asthma, CF
    - If too few, then expiratory film: hard to interpret
- Middle right lobe is against RH border – consolidation there will obscure border. No other consolidation will
- Staph pneumonia → pneumatocele (air filled cysts). Generally resolve
- Pneumo-mediastinum → ‘angel wing’ appearance as air lifts up thymus
- Chylothorax: lymph surrounding lung in the newborn → ?thoracic duct dysfunction
- Trachea: in an infant is floppy, so in an expiratory film can have a kink
- Lateral CXR:
  - Vertebrae should get blacker as go down
  - Retrosternal clear space: in infant whiter due to thymus
- Thymus on AP CXR:
  - Lots of variation – can look like large heart (lots of fatty tissue so moulds easily)
  - Thymic notch: lower right or left edge as it abuts the heart
  - Thymic wave sign: contour down the side of the thymus
  - Thymic sail sign: sail-like shape sticking into the lung fields
- Respiratory Distress Syndrome:
  - Alveolar collapse (not bronchi)
  - Xray: diffuse opacity (ground glass), air bronchograms and small lung volume
  - Severity assessed by blurring of heart borders and diaphragm
  - Group B Strep infections in full term babies can look a bit like it
- Transient Tachypnoea of the Newborn:
  - Xray: Retained lung fluid, lung volumes normal to large, and pleural effusions
  - Mild → recover
- Meconium Aspiration:
  - Xray: Diffuse, coarse lung field opacity (fluffy), hyperinflated (airway pathology not air space pathology → plugging and ball/value effect)
  - Can get pneumothorax, pleural effusions due to the work of breathing
  - Mainly in term babies – they have the grunt to suck it down. Also, pre-term babies less likely to pass meconium when stressed

Respiratory Tract Infections in Children

- Reference: Mainly from Prof Grimwood’s extensive infectious diseases handout
- Epidemiology:
Health Care of the Elderly

- Common: During the first 3 years of life, a child may have up to 6 episodes of otitis media, 2 episodes of gastro-enteritis and 4-8 respiratory infections per year. 10 – 15% have 12 colds per year.

- Risk factors:
  - Breast feeding is protective
  - Passive smoking
  - Exposure to infection: older siblings, day care, etc
  - Socio-economic status (multifactorial)

- 95% of respiratory infections involve the upper respiratory tract and 90% are viral

- But antibiotics prescribed in 70% of cases. Leads to:
  - Unnecessary adverse effects: rashes, diarrhoea, thrush, plus more serious ADRs
  - ↑cost
  - Antibiotic resistance → major increases in cost. Especially S pneumoniae and S. aureus
  - Reduce unnecessary prescribing by developing guidelines, practitioner education, public relations and ↓OTC antibiotic sales (eg mupirocin)

**Pathogenesis:** 60% due to rhinoviruses and coronaviruses, then RSV, parainfluenza viruses, influenza and adenovirus

**Common Cold**

- Starts with nasal congestion, throat irritation → sneezing, watery nasal discharge
- Low grade fever, malaise, cough, headache
- After 1 – 3 days nasal discharge becomes thicker and mucopurulent. This is part of the natural history of URTI and does not indicate a bacterial super-infection
- Generally improved by day 10, although cough (in 30%) and nasal discharge (in 40%) may persist for > 2 weeks
- Numerous RCTs have consistently failed to show that antibiotics alter the course of the common cold

**Acute Otitis Media**

- = Infection of the middle ear cleft
- Presentation:
  - Eardrum opaque (not semitransparent), red, normal landmarks lost, bulging. But if kid is screaming, ear will be red regardless
  - Otalgia, otorrhoea, hearing loss
  - Systemic signs: fever, irritability
  - If it ruptures, child will be instantly better (but parents will panic!). Acutely ruptured eardrum will heal in 24 hours

- Pathogens:
  - **S pneumoniae** (30 – 50%), Non-typeable strains of **H influenzae** (20 – 30%), **M Catarrhalis** (10 – 20%)
  - **Viral** (10 – 20%) especially RSV
  - Mixed bacterial/viral infections account for 50% of antibiotic failures

- Treatment:
  - Without treatment, 70 – 90% of infections resolve spontaneously
  - Those least likely to respond are:
    - Aged < 2 years
    - Those with constitutional disturbance (eg > 39 C)
    - Where S pneumoniae is the pathogen

- Antibiotics:
  - For the 90 – 95% of otitis media that responds to antibiotics, 90% are due to spontaneous resolution
  - If < 2 years, constitutional disturbance and persistent symptoms > 48 hours:
    - **Amoxycillin** 15 – 30 mg/kg TID for 10 days (ie high dose).
    - If no improvement after 48 – 72 hours try Augmentin (cover H influenzae and Moraxella)
  - Main aim is to reduce the very small chance of suppurative complications

- Treatment for AOM in children (NZ Guideline for AOM):
  - Main benefit from antibiotics is less pain on the 2nd or 3rd day in 1 in 17 kids, and failure to spread to other side in 1 in 17. No effect on pain on first day, prevention of recurrence or build up of middle ear fluid
  - Side effects of skin rash, vomiting or diarrhoea are as common as benefits
  - Recommendation: use Paracetamol, return to doctor if symptoms persist beyond 48 hours, and have ears checked in a month for persisting fluid (common in first several weeks) – this occurs in about 1 in 10
Oral cephalosporins and 2nd generation macrolides don’t penetrate the middle ear and/or have poor activity against S. pneu

Complications:
- Mastoiditis in 0.1%. Incidence is not increased by delayed treatment
- Little evidence to suggest that untreated otitis media causes mastoiditis
- Very rare: petrositis, labyrinthitis, facial palsy, subdural/epidural/brain abscess

Recurrent Acute Otitis Media
- **Risk factors** for recurrent acute otitis media: childcare centres, passive smoking, family history, reflux
- **Management:**
  - Ensure correct diagnosis
  - Reassure: spontaneous improvement in many after age 2 – 3 years and during summer
  - Limit passive smoking, discourage pacifier use
  - Encourage breast feeding in infancy
  - Antibiotic prophylaxis generally ineffective
  - Avoid unproven therapies: antihistamines, decongestants, chiropractic, homeopathy and naturopathy
- **Refer to** paediatrician/ENT surgeon (grommets) if febrile seizures, antibiotic intolerance, hearing loss/speech problems, underlying craniofacial abnormalities
- **In the future, conjugate pneumococcal vaccines are likely to play an important role**

Chronic Otitis Media with Effusion
- Presence of sterile or infected fluid in middle ear
- Chronic OME (= glue ear) if > 3 months. If it hasn’t cleared by then, less likely to clear spontaneously
- Common up to age 5 or 6
- **Symptoms:**
  - Incidental finding in asymptomatic child
  - Hearing loss and its effects: speech delay, slurred speech, failing at school, irritable, poor balance, falling over. But delayed language and cognitive problems related more to genetic and SES than previous otitis media
- **Pathogenesis:** eustachian tube dysfunction (not just blockage)
- **Sequalae** of otitis media:
  - In 70% after 2 weeks
  - In 50% after 1 month
  - In 20% at 2 months
  - In 5 – 10% after 3 months
  - Associated with mild hearing loss.
- **Treatment:**
  - Effusion common after an ear infection. Watch and wait
  - If bubbles behind ear drum then it’s resolving itself
  - Drugs: antibiotics and decongestants not very effective
  - If persisting > 3 – 6 months:
    - Test hearing
    - Limit passive smoke exposure
    - Treat underlying allergic rhinitis/adenoidal enlargement with intra-nasal steroids
  - Refer after 3 – 6 months if hearing loss and:
    - Failure to respond to antibiotics
    - Recurrent acute otitis media
    - Persistent otalgia
    - Retraction pockets
    - Expressive/receptive language delay
    - Underlying cranio-facial abnormalities (eg Down syndrome)
  - ENTs say grommets are the treatment of choice: Aerate middle air (\( \rightarrow \downarrow \text{CO}_2 \rightarrow \downarrow \text{squamous metaplasia} \rightarrow \downarrow \text{goblet cells} \rightarrow \downarrow \text{effusion} \)). Extrude over 18 months – 2 years. Take out if still there 5 yrs later. May take out adenoids at same time \( \rightarrow \uparrow \text{eustachian tube function} \) (paediatricians say adenoidectomy is treatment of choice).
  - Precautions with grommets:
    - Plug ears when washing hair and bathing
    - Can swim in clean fresh water but no diving below the surface
- **Chronic Suppurative Otitis Media** – with hole in drum. Treatment: get rid of infection then surgical repair
Pharyngitis

- See Acute Pharyngitis, page 86
- Almost 100% given broad-spectrum antibiotics. Inappropriate in 90% of cases

Pathogens:
- Viruses: Adenovirus, also rhinovirus, coronaviruses, RSV, Parainfluenza virus, influenza, enteroviruses, EBV
- Bacteria: S Pyogenes (GABHS = Group A Beta-Haemolytic Strep) in about 20 – 30% of cases, predominantly in those over 4 years

Differentiating (at best 70% predictive accuracy):
- Exudative tonsillitis: Adenovirus, GABHS, EBV
- > 4 years, enlarged tender anterior cervical lymph nodes and diffusely inflamed pharyngeal structures (+ exudates) and absence of cough suggests S Pyogenes
- Diffuse, sandpaper-like red rash, accentuated in skin creases (Pastia lines) suggest Scarlet Fever.  See Streptococcal Skin Infections

<table>
<thead>
<tr>
<th>Streptococcus pyogenes skin conditions</th>
<th>Rx</th>
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<tbody>
<tr>
<td>Impetigo</td>
<td>Superficial pyoderma (pus of the skin) characterised by vesicular + crusted lesions</td>
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<tr>
<td>Cellulitis</td>
<td>Acute spreading subcutaneous tissue skin infection</td>
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<tr>
<td>Erysipelas</td>
<td>Distinctive superficial cellulitis (usually on the face) with lymphatic involvement</td>
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<tr>
<td>Necrotising fasciitis</td>
<td>Severe + spreading infection of SC tissues involving both superficial + deep fascia – toxic shock can ensue</td>
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- Streptococcus Pyogenes (Group A, β -Haemolytic), page 814
- Nasal discharge, cough, hoarseness, conjunctivitis or diarrhoea +/- fever +/- tonsillar exudates suggests virus
- Throat swabs: usually identify organism, but 10 – 50% are carriers

Treatment:
- Aim: prevent acute rheumatic fever, suppurative complications (peri- or para tonsillar abscess) and hasten recovery
- But:
  - Only benzathine penicillin has been shown to reduce RF – and this was in military personnel
  - No convincing data which shows antibiotics reduce the risk of rare suppurative complications
  - Antibiotics reduce symptoms by 8 hours only
  - Reinforces the notion that antibiotics are effective and increases the likelihood of their future use for trivial illnesses
- If high risk for RF (eg Maori, PI, > 4 years of age) take swabs or treat empirically. However, prescribing penicillin for sore throat hasn’t altered the rates of RF, and many children with RF haven’t consulted their doctor
- S Pyogenes: penicillin, 500 – 1000 mg BID for 10 days (Allergy: erythromycin)

Acute Sinusitis

- Uncommon. Bacterial sinusitis complicates 0.5 – 5% of viral upper respiratory tract infections
- With most colds, nasal discharge and obstruction are improving after 2 weeks. Children with acute sinusitis will not be improving
- A minority present with high and persistent fever, periorbital swelling, facial and dental pain
- Imaging:
  - Plain x-rays don’t differentiate well between common cold and sinusitis
  - CT more useful. Air-fluid levels, opacification, mucosal thickening > 4 mm
- Maxillary and ethmoid sinuses present at birth (although small). Frontal and sphenoid sinuses aerate at 4 – 6 years of age
- Pathogens: S pneumoniae (30 – 70%), H influenzae (20%), M Catarrhalis (20%), virus alone (10%)
- Treatment:
  - High spontaneous cure (60% by 10 days vs 85% with amoxycillin)
  - Treat for S Pneumoniae in children with persisting symptoms which are not improving
  - Amoxycillin 15 – 30 mg/kg TID for 5 days. Higher limit if < 2 years, attend child-care, or have received antibiotics in the last month in areas with > 10% penicillin resistance
  - Consider Augmentin, co-trimoxazole, cefuroxime or ceftriaxone if no improvement after 48 – 72 hours
**Bronchitis**
- Inflammation in bronchial mucosa → productive cough
- Most cases are from viruses (eg RSV)
- Numerous studies have not found any evidence to support antibiotic treatment (but they’re usually prescribed…)
- Production, colour or culture or sputum does NOT predict aetiology
- Consider treatment if:
  - Prolonged cough in older child: ?M pneumoniae → erythromycin
  - Pertussis and cough < 4 weeks: erythromycin (or co-trimoxazole) reduces infectivity
  - Cystic fibrosis/other chronic lung disease: tailored antibiotics
  - Prolonged cough (> 8 – 12 weeks and not from URTI): investigate for asthma, Tb, pertussis, CF, foreign body, subacute-sinusitis, psychogenic cough

**Croup**
- = Laryngotraceobronchitis
- **Pathogens:** Usually viral: Parainfluenza 1 and 2 are the most common. Measles and influenza are the most severe. Don’t give ABs
- **Presentation:**
  - Child < 5 years (peak 12-24/12)
  - Coryza and fever over 1 – 2 days
  - Then characteristic harsh “barking” cough, hoarseness +/- signs of upper airway obstruction (stridor, respiratory distress), inspiratory stridor
  - Worse at night, and peak on 2nd or 3rd night. Varies hour to hour (i.e. don’t send them home just yet…)
  - Lasts 3 – 4 days then changes to sound productive. May last for another 2 weeks
- **Differential:**
  - Epiglottitis: absent/minimal cough, low-pitched expiratory snore
  - Bacterial tracheitis: toxic appearing, older child, high fever, brassy cough, stridor, tender trachea
  - Laryngeal foreign body: sudden onset, unable to vocalise
  - Angioneurotic oedema: associated signs usually present
  - Retropharyngeal abscess: high fever, dysphagia, hyperextension of neck
- **Assessment:**
  - Severe if restless, anxious, pallor, lethargy, tachycardia, tachypnoea, indrawing, cyanosis or ↓breath sounds
  - Loudness of stridor is not a reliable guide to severity of obstruction
  - ↑Risk of obstruction if: pre-existing upper airway narrowing (eg sub-glottic stenosis) or Down Syndrome
- **Management:**
  - Avoid distressing the child, settle them on parent’s lap
  - Blood tests, pulse oximetry, O2 masks and nebulisers rarely needed
  - Mild:
    - Not distressed, no stridor at rest
    - No treatment, management at home, return if signs of ↑obstruction, lots of comfort
    - Paracetamol
  - Moderate:
    - Frequent barking cough, distressed, persistent inspiratory stridor, tracheal tug or sternal retraction at rest, but no signs of hypoxia
    - Observe or admit
    - Steroids (dexamethasone or betamethasone 0.6 mg/kg orally or im, prednisolone 1 mg/kg) orally. May be repeated 12 – 24 hours later (but consider alternative diagnoses first)
    - Disturb child as little as possible
  - Severe:
    - Signs of obstruction, hypoxia (restless, irritable, anxious, cyanosis), ↓breath sounds
    - ?ICU admission
    - Nebulised adrenaline + steroids (Prednisolone 1 mg/kg/day)
    - Monitor closely

**Epiglottitis**
- Caused by Haemophilus influenza type B (Hib)
- Incidence ~ 20 cases pa (dropped from 160 in 1992 prior to vaccination)
- Presentation:
Incubation 2 – 4 days
Acute, febrile illness, toxic looking child
Snore, mouth always open, drooling, prefers to sit upright. Soft inspiratory stridor, louder expiratory stridor
No cough (cf croup)

Management:
- Intubate first, then give iv antibiotics (if given first, pain → panic → respiratory arrest)
- Blood cultures
- Cefotaxime 25 – 50 mg/kg/8hr iv (max 2g) due to ↑penicillin resistance
- Amoxycillin 50 mg/kg/4 hr iv (max 2g) if penicillin sensitive
- Other illnesses caused by Hib:
  - Meningitis: 5% mortality, 10% with sequelae (retardation, seizures, hearing loss, etc), 20 – 30% have functional disabilities (eg learning difficulties)
  - Also pneumonia, empyema, septic arthritis, periorbital or facial cellulitis
- Vaccination:
  - Prior to immunisation was the most common cause of life threatening bacterial infection < 5 years of age.
  - Herd immunity now works well
  - Subunit vaccine is 95% effective. Few side effects (< 5% with local reactions)
  - Notifiable disease

Pertussis
- Bordetella pertussis (bacteria) = whooping cough
- Epidemiology:
  - Highly contagious. Regular epidemics every 3 – 5 years in NZ
  - Incidence: up to 5000 cases a year (only a small proportion notified)
  - In first year of life 80% are hospitalised and 0.2% die
- Risk factors: <1 yr, low SES, no immunisation, prematurity
- Presentation:
  - Phases:
  - Incubation 2 – 3 weeks
  - Catarhal phase: ~ 1-2 weeks, runny nose, malaise, sneezing, low-grade fever, mild cough, most infective stage
  - Paroxysmal phase: ~ 1-6 weeks, up to 12 weeks
    - Develops into paroxysmal bouts: unprovoked cough followed by inspiratory gasp (whoop), apnoea, vomiting.
    - Thick sputum → can’t clear → coughing spasm. Whoop may be absent in infant. If severe may need suction
    - In between paroxysms looks well, is afebrile and has no chest signs
    - Infectious for 2 – 3 weeks of paroxysmal phase
  - Convalescent phase: persistent cough for 3 – 4 months
- Diagnosis: WHO = cough > 2/52 + either paroxysms of coughing, inspiratory whoop or post-tussive vomiting; can do PCR, cultures
- Treatment:
  - If < 4 weeks duration: erythromycin (14d). Doesn’t impact illness after paroxysmal phase is established, but will ↓infectivity
  - Admit if under 6 months and/or cyanosis or apnoea in paroxysms
  - Corticosteroids, anti-tussives and anti-histamines not recommended
- Complications:
  - Anoxic seizures in 1 – 3%
  - Encephalopathy in 0.1 – 0.3% → retardation, spasticity and seizure disorders. Rate of severe neurological complications of immunisation negligible compared with the risk of encephalitis from whooping cough
- Vaccine:
  - Whole cell vaccine effective in 60 – 90%, has higher efficacy for more severe outcomes, local reactions or fever in 50%. 1 in 1 million are associated with an encephalopathy (? No causal relationship established)
  - Acellular pertussis has higher efficacy and is better tolerated (< 10 – 15% adverse reactions) – now being introduced

Bronchiolitis
- Epidemiology:
Classically RSV
Highly infectious acute viral respiratory illness in kids (2/52 to 12 months) of airways < 1 mm diameter
Epidemics every winter with RSV, also parainfluenza, influenza and adenoviruses
Major cause of URTI in kids: up to 50% of 1 year olds have had RSV infection
Seasonal in winter/spring

• Presentation:
  - Short incubation: 3 – 4 days
  - Contacts: older siblings will have had nothing more than a snotty nose
  - Difficulty with/prolongation of expiration (cf croup – inspiratory)
  - Low-grade fever, non-toxic, cough, wheezy, difficulty feeding, hyperinflated chest, diffuse fine inspiratory crackles and expiratory wheeze
  - If more severe then ↑ irritability, cyanosis, pallor, pulse > 160/min, respiratory rate 50 – 70/min, expiratory grunt (not stridor), head bobbing, more marked retractions, apnoea in young infants
  - Respiratory failure in 1 – 2%: pallor, sweating, drowsiness, ↓resp effort, ↓breath sounds, apnoea. Cyanosis = late sign
  - Feeding a good indicator of respiratory distress (and one which parents can monitor at home)
  - Recurrence common (?hypoplastic airways and smoke exposure)
  - Usual recovery is 7 – 10 days
  - Can get repeat viral illness – in which history suggests fluctuation – getting better, then got worse again, etc

• Natural history:
  - Starts as URTI - 1 day of runny nose → 1 day of cough → then wheeze
  - Illness/breathlessness worst on 4th day of wheeze (6th or 7th day of illness)
  - Runny nose lasts around 5-7 days, cough for 3-4/52, wheeze for 2/52

• Pathophysiology:
  - Mucous + oedema = narrowing/obstruction of small airways + V/Q mismatch therefore hypoxia + ↑ WOB (no bronchospasm, therefore not bronchodilator responsive, this differentiates from asthma)

• Distribution of LRTI from RSV:
  - Bronchiolitis: 40 – 90%
  - Pneumonia: 5 – 40%
  - Tracheobronchitis: 10 – 30%

• Risk factors for severe presentation:
  - < 6 weeks old
  - Older siblings
  - Maternal smoking
  - Preterm delivery
  - Underlying conditions: congenital heart disease, chronic lung disease of infancy, congenital abnormalities, immunodeficiency

• Differential:
  - Recurrent bronchiolitis, history of eczema, strong family history of atopy ⇒ ?asthma. Trial of nebulised salbutamol.
  - Persistent cough, failure to thrive ⇒ cardiac disease, cystic fibrosis, structural lung disease, aspiration, immunodeficiency

• Investigations:
  - Nasopharyngeal aspirate for culture and viral immunofluorescence
  - Bloods for culture and serology
  - Imaging (not normally required): CXR shows hyperinflation, peribronchial thickening, often patchy areas of consolidation and collapse. 

• Treatment:
  - Symptomatic treatment: O2, rehydration, minimal handling
  - Not bronchodilators, steroids, ribavirin or antibiotics
  - Can go home if they’re feeding OK and don’t need O2
  - Admit if respiratory distress, difficulty feeding, or adverse social circumstances. If sending home early in the illness, arrange for review within 24 hours
  - Put on NG feeds: not hungry ⇒↓distress
  - If respiratory rate > 70/min and feeding poorly then IV or NG fluid at 2/3 of maintenance requirements (risk of SIADH)
  - If oximetry < 92% then O2
  - If severe, monitor blood gases, consider CPAP or ventilation (especially chronic respiratory/heart disease)
May be wheezy for 2 weeks and a cough for 4 weeks

**Pneumonia**

- **Epidemiology:** Peak incidence in first 2 years, and in Maori and PI children
- **Presentation:**
  - Initial prodromal coryzal symptoms for a few days
  - Fever, cough, tachypnoea, signs of consolidation
  - Young children may present with predominantly systemic features: fever, lethargy, vomiting, abdominal pain
  - Older children may have headache, pleuritic chest pain, irritating cough, maybe **abdo pain** if lower lobe or even signs of meningism if upper lobe
  - Severe if:
    - Toxic: lethargy or ↓arousal, circulatory compromise, abnormal respiration (eg apnoea, cyanosis)
    - Respiratory distress: pallor, restless, agitated, nasal flaring, grunting, head bobbing, chest wall recession, paradoxical abdominal movement, difficulty feeding
- **Signs on exam:**
  - In infants: may be few signs, usually limited to a few focal crackles
  - Older children: ↓chest wall movement, ↓breath sounds, fine crackles, later dull to percussion and bronchial breath sounds
- **Pathogens:**
  - **Viruses** are the most common cause in infants and young children:
    - RSV and Parainfluenza 3 most common
    - Suggested by: infant or young child, coryzal prodrome, mild or moderate constitutional disturbance, hyperinflation and diffuse inspiratory crackles, *patchy consolidation on CXR*
    - Rarely, infections with influenza A, adenovirus 3, 7 or 21 can be severe, leading to death or severe lung damage
  - **Bacterial:**
    1. *S pneumoniae* most common bacteria (*see lobar pneumonia*)
    2. *M pneumoniae* common in school age children (>5), insidious onset (*walking pneumonia*) including anorexia, headache, scattered fine inspiratory crackles, bilateral
    3. *S aureus* uncommon but severe, *H influenzae* uncommon
    4. *S pyogenes*: typically follows Varicella, influenza A or measles, protracted course and often empyema
    5. *Chlamydia*: in 1st 2 months. Vertical transmission + eye infection in first 5 – 7 days. See Eye Disorders in Children, page 967
- **Investigations:**
  - Imaging: CXR to:
    1. Confirm diagnosis
    2. Detect complications: pleural effusion, pyopneumothorax, lung abscess
    3. Exclude other causes: congenital lung lesions, lung abscesses
  - **Blood cultures before** antibiotics
  - Nasopharyngeal aspirate for RSV detection
  - Serology for *M pneumoniae* or RSV
  - Aspiration of pleural fluid (assists diagnosis, and is therapeutic – antibiotics won’t penetrate a large effusion)
- **Treatment:**
  - **Penicillin G** is the treatment of choice for uncomplicated bacterial pneumonia (unless allergy). Despite 20% of *S pneumoniae*’s showing reduced sensitivity, concentrations in the serum and lung tissue exceed the MIC by several fold. More treatment failures are associated with erythromycin and co-trimoxazole
  - Admit if any of:
    1. < 2 years
    2. Signs of toxicity, hypoxia, respiratory distress
    3. Extensive consolidation or an effusion
    4. Clinical or x-ray signs of Tb
    5. Adverse social circumstances, no transport or no access to phone
    6. If sent home, then review within 12 – 24 hours
  - For uncomplicated bacterial pneumonia: Penicillin G 25 – 30 mg/kg/6hr iv (max 2.4g)
  - If not afebrile within 24 hours on penicillin G, then review microbiology results, repeat CXR, consider other causes and treatments. Treatment failure: consider Viral, Mycoplasma, *S aureus*, resistant *H influenzae*
Supportive therapy: **minimal handling**, careful fluid management (max 50% of maintenance fluids if IV), O2

Management of pleural effusion. Before antibiotics do diagnostic aspiration and urgent gram stain.

Discuss with paediatric surgeon:

1. Thin clear fluid: aspirate as much as possible
2. Thin purulent fluid: intercostal drain
3. Thick purulent fluid: loculates so drain won’t work ⇒ thoracotomy (consider fluclaxacillin +/- Cefotaxime)
4. Infected effusion = Empyema = pus in pleural cavity
5. Fibrous septae will form around empyema = loculated empyema

**Tb Pneumonia**

- Rarely presents as acute pneumonia
- Consider if:
  - Known exposure to Tb
  - Child or family born in an endemic area
  - > 4 week history of cough, especially if fever, sweats and weight loss
  - Refractory pneumonia
  - Suggestive CXR
- Nurse in respiratory isolation:
  - Virtually all child cases are primary and non-infectious with a small burden of disease
  - But adolescents, those with extensive or cavitating disease, or infected visiting family are infectious
- Investigations:
  - FBC, ESR, electrolytes, CR and LFT
  - Mantoux test
  - Specimen collection: sputum if available. Early morning gastric aspirates better than lavage. Also consider urines, pleural biopsy and LP
- **Empiric treatment**: isoniazid, rifampicin, pyrazinamide, ?ethambutol (RIPE)
- Notify to Medical Officer of Health

**Miscellaneous:**

- Bronchiolitis = generally <12/12. Inflammation + mucus plugging with no bronchospasm therefore not BDR responsive
- **Viral induced wheeze** = >12/12 coryzal prodrome (runny nose etc) + wheeze + no interval symptoms (inflammation + some bronchospasm component therefore BDR responsive to an extent)
- Viral pneumonia = coryzal prodome + wheeze + more unwell than the above (e.g. fever)
- Viral exacerbation of asthma = coryzal prodrome + wheeze + asthma background/interval symptoms (e.g. cough at night, with exercise etc)

**Asthma in Young Children**

- See also Asthma, page 107, especially for Medication and Spacer Use
- 3rd most common reason for admission (after bronchiolitis and URTI/otitis media)
- 2 components to asthma (useful in explanation):
  - Inflammation, causing narrowing of the breathing tubes (preventer works here)
  - Bronchospasm: muscular constriction, causing narrowing of the breathing tubes (reliever works here)
- Much much less common in < 1 years (bronchiolitis causes most wheezing in young). Peak 2 – 4 years
- Peak flow very unreliable under age 7 (and most bad asthmatics diagnosed from 2 – 5) ⇒ have to rely on history
- History:
  - Symptoms: waking at night with cough/wheeze, after exercise, how often are attacks, had time off school/kindy as a result, how long does preventer last, previous admissions (esp to ICU)
  - Environmental factors: smokers, pets, damp, obvious triggers
  - Current treatment: medicines, do the family understand the difference between reliever and preventer, assess technique and compliance, is spacer accepted by child and is it washed
- 2 patterns on history:
  - **Episodic** (intermittent): viral URTI ⇒ cough and wheeze. *No interval symptoms* + not atopic – acute event called viral induced exacerbation of asthma
  - **Persistent** (with exacerbations): *interval symptoms* (cough/wheeze at night or with exercise), exacerbations with viral infection, interferes with everyday life, tend to be atopic + positive FHx
• Asthma in a toddler:
  ➢ Cough, often worse at night
  ➢ May vomit with cough (NB exclude pertussis: cough → choke → vomit → OK for an hour. In asthma, cough again straight away)
  ➢ Usually wheezy with URTI
  ➢ Exercise induced sx less obvious until older age
  ➢ Diagnosis difficult in an infant (i.e. 1/12 – 12/12) unless recurrent, strong immediate family history or evidence of atopy

• Physical findings in a toddler:
  ➢ Usually normal chest exam
  ➢ If severe chronic symptoms:
    o *Hyperinflated chest* (↑ AP diameter) + liver and spleen ptosis
    o *Harrison’s sulcus*: dip in chest wall where diaphragm attaches
    o Eczema
    o Reduced growth (if severe)
  ➢ Stethoscope can be confusing
  ➢ Acute presentation:
    o Observation: tachypnoea, tachycardia, ↑WOB (intercostal, subcostal, supraclavicular, substernal recession)
    o Chest exam: wheeze, creps (these are common – may be due to mucous plugging/atelectasis), loss of cardiac dullness (hyperinflation)
    o Abdo exam: liver and spleen ptosis (downward displacement)

• Diagnosis:
  ➢ Cough is very common in kids (8 – 10 per year). But more during the day than at night. Won’t slow them down when running
  ➢ Is it asthma, bronchitis, bronchiolitis? (asthma will be bronchodilator responsive as cf other conditions as bronchospasm – muscle constriction – a major component)
  ➢ Positive response to trial of therapy (preventative as well as relievers) and review

• Criteria for admission/severity:
  ➢ Pulse rate > 1.5 * normal (>120 in >5yr olds or >130 in 2-5 yr olds)
  ➢ Respiratory rate > 60-70 minute (>30 in >5yr olds or >50 in 2-5yr olds)
  ➢ Marked accessory muscle use
  ➢ Agitation/restlessness/apathy/CNS depression or cyanosis/pallor [signs of hypoxia + exhaustion]
  ➢ Too breathless to *talk or feed*
  ➢ Saturation < 92%

• Severity assessment:

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<th>Critical</th>
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<td><em>Mental State</em></td>
<td>Normal</td>
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<td>Agitated</td>
<td>Confused/drowsy</td>
</tr>
<tr>
<td><em>Accessory Muscle use</em></td>
<td>Nil</td>
<td>Minor</td>
<td>Mod/marked</td>
<td>Maximal/exhaustion</td>
</tr>
</tbody>
</table>

• Treatment:
  ➢ Avoid triggers: passive smoking, pets, house dust mite (dehumidifiers don’t work), pollens, cold, exercise, damp houses, certain foods ( overstated)
  ➢ Bronchodilators:
    o < 6 yrs = 6 puffs via spacer (1 puff:6 breaths; repeat x 6)
    o 6+ yrs = 12 puffs via spacer (1 puff:6 breaths; repeat x 12)
  ➢ Episodic asthma:
    o Consider no therapy, avoid triggers
    o If distressed with attacks: use bronchodilators + spacer only. Start during URTI phase. No preventative
  ➢ Frequent episodic asthma (only get it with a cold):
    o Intervals between attacks < 6 weeks
    o Bronchodilator as needed with URTIs
    o Prophylaxis: inhaled steroids: if it makes no difference then stop
  ➢ Persistent Asthma:
    o i.e. interval symptoms
    o Male: female = 4:1
      1. Preventative:
        a. Inhaled corticosteroids– start with 4 puffs (i.e. 400ucg) per day (beclamethasone)
        b. No need to split dose between day and night
c. Takes 2 – 3 months for maximal effect therefore need to wait this length of time before introducing/↑ med.

d. Titrate back once controlled

e. Using a spacer, there are NO side-effects (virtually no medication is deposited in mouth)

f. NB. Prolonged oral steroids in children = short and fat children

g. For the first 3/12 when started CS, growth often slowed (height) – unknown as to why, but recovers entirely

2. Bronchodilators as required
3. Review after 2-3 months (CS effects take this long)

○ If symptoms persist:
  1. Check technique etc (as below)
  2. Either ↑ CS dose or add LABA (NB. Has different binding properties to SABA – prolonged effect) e.g. salmeterol (serevent) 2 puffs q2h
  3. Review after a few days (LABA acts quickly)

○ If symptoms still persist:  
  ➢ ↑ CS dose + change to fluticasone (at max dose, beclamethasone has no SE, but it can above this – fluticasone has less)
  ➢ Then add theophylline (PDES inhibitor ↓cAMP, and smooth muscle relaxation)

• If asthma control is poor, consider:
  ➢ Checking inhaler + spacer device and technique
  ➢ Poor compliance
  ➢ Environmental triggers eg smoking
  ➢ If not responding to acute treatment: consider mucous plugging causing atelectasis (i.e. less bronchospasm component therefore potentially little wheeze and poor response to BDR)

• Other treatment options:
  ➢ Long-acting β-agonists: salmeterol (Serevent), eformoterol (Foradil, Oxis)
  ➢ Theophylline (Nuelin, Theodur): 3rd line, gut ache →poor compliance and not overly effective
  ➢ If severe: alternate day oral prednisone treatment – reduced side effects (short and fat), and reasonable asthma control

• Protocol for an acute attack:
  ➢ Salbutamol dose: up to 5 years: 6 puffs via spacer. Over age 5: 12 puffs via spacer
  ➢ For severe, add (ipratropium (Atrovent; muscarinic receptor antagonist – blocks PSNS effects ↓ mucous secretion and bronchoconstriction)
  ➢ For moderate and severe, give doses at 0, 15, 30, 45 and 60 minutes and review at 75 minutes
  ➢ Oral steroid (redipred) for all except minor attacks: 1 mg/Kg/day → ↓relapse
  ➢ If not responding, give O2, IV salbutamol + Mg (can improve bronchodilation) and consider ICU admission

• Basic asthma plan:
  ➢ Upon d/c home, give asthma plan and advise salbutamol use q4h during the day for the first day at home, only at night if symptomatic and then re-assess the next day – if still symptomatic continue, if not, stop
  ➢ When getting a cold/cough/wheeze – give 6/12 puffs q4-6h for the first day or two then if asymptomatic → cease
  ➢ Can use up to q3h if necessary but if required q2h, need medical assessment

Differential of Wheezing in an Infant

• Common:
  ➢ Asthma:
    o NB. Cannot really make a dx of asthma until at least 8-9/12
    o Would see interval symptoms (eg night cough), recurrent episodes, BDR responsive, FHx, tendency to atopy
  ➢ ‘Happy wheezer’:
    o Diagnosis of exclusion
    o Usually < 12 months
    o Chronic daytime wheeze and no cough – wheeze during times of ↑ air flow eg crying, laughing
    o Child undistressed (ie feeding OK, not waking)
    o Less wheeze when asleep
    o Requires no therapy
    o Related to maternal smoking
    o Smaller airways? collapsible
    o Can become an ‘unhappy’ wheezer when they get a cold, in which case treat as for bronchiolitis
- **Bronchiolitis**: See 942

- **Uncommon**:
  - **Inhalated foreign body**:
    - Reflexes: inhalation → gag → vocal cord spasm (therefore stridor-type noises) → passage to bronchi/loes → wheeze/cough
    - If convincing episode of inhaling a foreign body (stridor, went blue, etc) should be bronchoscoped – even if they think they brought it all back up
    - Signs: unilateral wheeze or stridor. May present months or years later with haemoptysis.
    - CXR inspiration/expiration – will have hyperinflation (ball/valve) or collapse on side of inhaled object
  - **Cystic fibrosis**: [see Cystic Fibrosis (CF), page 948]
    - If breast fed can still thrive for a month or two
    - Respiratory symptoms often present with wheeze not cough
  - **Heart failure**:
    - Sweat when feeding + poor feeding/cyanosis
    - Wheezy – sounds like bronchiolitis
    - Look for enlarged liver (but beware, bronchiolitis → hyperinflation → liver lower)
    - HF at birth = TGA
    - HF in first 2/52 = coarctation, hypoplastic heart
    - HF between 2-8/52 = VSD
  - **Aspiration**:
    - If due to neurological problems, will cough and splutter when swallowing
    - Long vague history with unclear start
    - Gives acute onset of wheeze – eg OK when you put them to bed, but sudden coughing and wheezing later
    - If lying on back, most likely to aspirate into right upper lobe, but in practice they are wheezy everywhere
    - Hard to prove. Diagnosis of exclusion. Can do reflux probe to show they reflex often
  - **Immune deficiency**:
    - Rare. Only consider if lots of serious illnesses
    - Cilia dyskinesia: usually starts with ears (middle ear has respiratory epithelium with cilia), then lungs and sinuses. Associated with dextrocardia
    - Hypogammaglobulinaema
    - Can confuse wheezing with soft stridor: eg laryngomalacia. Inspiratory sound
  - Rare congenital causes: cysts, tumours, lobar emphysema, tracheomalacia/bronchomalacia (not properly formed → floppy)

- Smoking contributes to all the above:
  - Prenatally, maternally smoking → ↓airway size
  - Post-natal → inflammation/irritation

**Cystic Fibrosis (CF)**

- **Autosomal recessive**. 1 in 25 are carriers
- Disease of epithelial-lined organs:
  - **Lungs**: mucus plugging → chronic inflammation → necrosis, adjacent pneumonia, bronchiectasis. Leads to chronic infection, emphysema and pseudomonas colonisation. Eventually → cor pulmonale
  - **Pancreas**: fibrosis around ducts, dilated ducts, islets cells relatively preserved→ pancreatic insufficiency
  - **Gut**: meconium ileus, biliary cirrhosis, recurrent RLQ pain
  - Bile ducts obstructed
  - Middle ear problems + sinusitis
  - Congenital absence of vas deferens → infertility

- **Presentation**:
  - Newborn screening (80% will turn out to be carriers, not diseased). Guthrie card for **immunoreactive trypsin (IRT)**. Trypsin leaks into blood from pancreas if pancreatic duct blocked. Sensitivity high (~95%) but not at all specific. If positive then → gene screen then confirmatory sweat test
  - Neonates: meconium ileus:
    - > 90% with meconium ileus will have CF → obstruction at birth. Occurs in 15% of those with CF
    - Presentation: bilious vomiting, palpable bowel loops, distension if perforated
    - CXR: distended bowel loops with thickened walls
    - May also have associated volvulus, small bowel atresia, perforation, neonatal meconium peritonitis secondary to perforation
Treatment: enema + IV fluids or surgery

- Failure to thrive
- Sibling with CF

**Pathogenesis:**
- In 70% of the mutations, the protein is not glycosylated normally → not transported to site
- Abnormality of cAMP dependent chloride transport due to mutation of the CFTR protein
- Defective CFTR results in ↓secretion of chloride and ↑reabsorption of sodium and water across epithelial cells. Resultant ↓hydration of mucus results in mucus that is stickier to bacteria → which results in infection and inflammation
- Also, thicker mucus ⇒ obstruction and ↓ciliary clearance

**Testing:**
- Guthrie screening
  - Looking for IRT (as above); IRT will be *high as trypsin leeches into the blood* as is not excreted as well from pancreas
  - NB. 5-7% of CF cases not picked up on IRT
- Gene screen for *common CF mutations* (e.g. DF508/U) on chromosome 7
- Confirmatory sweat test (abnormal Cl channel → can’t reabsorb NaCl from isotonic secretions → salty sweat; test by applying current between electrodes on skin to induce sweating, then test NaCl concentration)
- Formal genetic testing for other rare CF mutations

**Advantages of early diagnosis:** ↑lung function, ↑nutrition, less traumatic diagnostic process

**Post-natal management:**
- *Good nutrition:* enzyme replacement, high calories, fat soluble vitamin supplements
- *Antibiotics* for URTI (staph infections common in babies, pseudomonas in older children/adults)
- *Grommets* at 2 years
- Multidisciplinary approach

**Possible monitoring tests:**
- CXR, lung function tests, sputum culture (esp pseudomonas lung infection – key prognostic indicator)
- FBC, electrolytes, total protein, albumin, Vit A, D, E, blood glucose
- Faecal elastase (testing pancreatic insufficiency)

**Complications include bronchiectasis (CF is commonest cause):** terminal bronchioles dilated and filled with purulent secretions

**Genetics of CF/Autosomal Recessive**
- Autosomal recessive
- 1/25 of general population are carriers
- *Unaffected* siblings of child with CF (implying carrier parents) have 2/3 chance of being carriers
- Siblings of parents of CF child have ½ chance of being a carrier
- Risk of CF in unborn child of CF parent and unknown carrier status parent = 1/25 x 1 x 1/2 = 1/50
- Risk of CF in unborn child of parent who is the sibling of a CF pt and an unknown carrier status parent = 2/3 x 1/25 x ¼ = 1/150

**Bronchiectasis**
- Bronchiolar dilatation +/- parenchymal damage with sputum retention
- Epidemiology: very high incidence cf other OECD countries
- ?due to undiagnosed pneumonia (in addition to CF)
- **Symptoms:** chronic sputum production + recurrent respiratory infections
- **Signs:**
  - Clubbing
  - Chest deformity
  - Persistent localised crackles
- **Prevention:**
  - Raise awareness, education, improved housing, improved access to health care for children
Infectious Diseases

- See also:
  - Respiratory Tract Infections in Children, page 937
  - Gastroenteritis, page 983
  - Epstein Barr Virus, page 820
  - Herpes Simplex Virus (HSV), page 818
  - Varicella Zoster, page 819
  - Streptococcus, page 814
  - Bacterial Meningitis, page 808
  - Polio and Rubella in Vaccine Preventable Diseases, page 841

Fever in Children

- Most fevers are caused by respiratory tract viral infection, are self-limiting, and require only symptomatic treatment
- Kids have 6 – 8 viral infections each year → they are common
- Role of doctor:
  - Identify source of infection
  - Counsel caregivers and child
  - Manage the illness
  - Identify and refer those with potentially serious illness
- If no focus found:
  - Consider UTI, occult pneumococcal bacteraemia, meningitis
  - Consider non-infectious causes: rheumatic fever, poisoning, drug fever, more rarely leukaemia and other autoimmune diseases (eg Kawasaki disease)
  - On exam, pay attention to:
    - General appearance: activity, perfusion, colour
    - Vital signs: pulse, respiration, blood pressure
    - Exclude: fontanelle, neck stiffness, respiratory distress, abnormal chest signs, ears, throat, lymphadenopathy, hepatosplenomegaly, abdominal distension, bone or joint tenderness/swelling, skin rashes
  - At greater risk: neonates, immunocompromised, congenital abnormalities, toxic appearance, epidemiological ↑ risk (eg Maori)
  - WBC are unreliable for detection of serious infection
  - Review within 24 hours and parent education
- Investigations (courtesy Starship hospital guidelines):
  - Full sepsis work up is necessary in the child <6/52 with t >38°C, including:
    - 1. CXR
    - 2. FBC
    - 3. Blood cultures
    - 4. LP
    - 5. Urine (dipstick and culture)
  - Decisions regarding investigation and management for children of other ages are based on the child’s hx and exam findings
- Treatment (Starship):
  - Infants who look unwell (lethargic, irritable) should have antibiotics commenced immediately, else should wait until Ix complete
- Advice for parents:
  - Light clothing
  - Small, frequent drinks of water or fruit juice diluted 1:4, 5 – 7 mls/kg/hr
  - Paracetamol, 15 mg/kg/6 hourly, max of 90 mg/kg/day for 2 days
  - Return to doctor if refusing drink, pale or floppy, difficulty breathing, headache/neck stiffness/photophobia, doesn’t improve in 48 hours
- Clues for predicting serious illness (even over the phone):
  - Responsiveness and activity
  - Feeding
  - Urine output
  - Breathing
  - Colour
Potentially Serious Infections

- See When is a Child Really Sick?, page 891
- Sepsis: leads to systemic inflammatory response syndrome (SIRS). Also get it in major trauma, pancreatitis, etc. Mass release of cytokines. (Cf bacteraemia: bugs in blood but no major systemic reaction)
- Sepsis + focus (pneumonia, kidneys, joints/bones):
  - Neonate: Gp B Strep (S agalactiae), E Coli, S aureus
  - Infant/older child: S Pneumoniae, N Meningitidis, S aureus (complication of skin infections), S pyogenes, [HIB]
- Meningitis: infection of CSF via choroid plexus
  - See Bacterial Meningitis, page 808
  - Neonate: Group B Strep, E Coli, Listeria

Common Paediatric Viruses

- Reference: Prof Grimwood’s Paediatric Infectious Diseases Handout (all 94 pages of it!)

Measles

- Highly contagious paramyxovirus spread by respiratory droplets
- Epidemiology:
  - Overall mortality 0.5%
  - Risk of infection 100% if not immunised
  - Epidemics occur every 7 years
  - Incidence up to 3000 notifications in epidemic years. Lab confirmations drop in epidemics as high incidence → high PPV of clinical diagnosis. Very few cases in non-epidemic years will actually be measles
- Presentation:
  - Incubation 10 – 14 days
  - Fever
  - ALWAYS a cough (“measles bronchiolitis”)
  - Coryza
  - Conjunctivitis
  - White spots on cherry-red buccal mucosa opposite molars for 24 hours before rash (Koplik’s spots) – pathognomonic
  - Then red maculo-papular rash beginning on face (often behind the ears) and spreading to rest of body
- Treatment: Supportive, antibiotics for 2ndary infection
- Complications:
  - Otitis media (10%)
  - Pneumonia (1 – 5%)
  - Encephalitis (0.1%): 15% die and 25% left severely disabled. 1 in 100,000 develop the fatal grey matter degenerative disorder Subacute Sclerosing Panencephalitis (SSPE)
  - Vaccine:
    - Live attenuated virus. Now MMR2 given at 4 years to ↑ time between epidemics and address 2 – 5% chance of primary vaccine failure in first dose
    - Mild fever, malaise or rash develops in about 1% 7 – 10 days after vaccination
    - 1 in 1 million develop encephalitis (1,000 fold less likely than if infected with wild virus)
    - Contraindicated during pregnancy and in immunocompromised hosts

Mumps

- Contagious paramyxovirus spread by respiratory droplets
- ~ 80 notified cases per annum. Used to be 3 – 4 year epidemics, now longer
- Presentation:
  - Incubation 2 – 3 weeks
  - 70% develop fever and swelling and tenderness of salivary glands
  - 15% have aseptic meningitis
  - 0.2% develop encephalitis
  - 20% of post-pubertal males have painful orchitis and can cause infertility
  - Case fatality is 0.02% → usually from encephalitis
• Infective 1 week before and after parotid swelling starts
• Vaccine: Live attenuated virus (contraindicated during pregnancy and immunosuppression). Efficacy 95%. Only introduced because it can piggyback other vaccinations

**Non-Polio Enteroviruses**

• Include Coxsackie A and B, echoviruses and enteroviruses
• **Cause:** non-specific febrile illnesses, pharyngitis, gastroenteritis, viral meningitis, encephalitis, pericarditis, myocarditis, hepatitis, haemorrhagic conjunctivitis, etc
• **Viral exanthem:** macular rashes, maculopapular, vesicular and petechial rashes
• Incubation for 3 – 6 days, infectious for at least 1 week after onset of symptoms
• Diagnosis: culture (including from faeces – if isolates persist for several weeks may be unrelated to illness), possible PCR for blood and CSF. Serology difficult

**Hand, Foot and Mouth Disease:**
- Coxsackie A16.
- Mild illness, low-grade fever and sore throat
- Scattered **vesicular lesions in the mouth** with similar lesions surrounded by erythematous areolae on the hands and feet.

**Human Herpes 6 and 7 (Roseola Infantum)**
- Acute febrile illness of young children for several days with **occipital lymphadenopathy**, then reduced fever and appearance of a **fine red maculo-papular rash** over the **trunk and arms** for 1 – 2 days (confused with antibiotic rash)
- 70% of 2 year olds are sero-positive. Serology and PCR problematic due to latent infection
- Incubation 5 – 15 days
- Rare complications: **encephalitis** or benign intracranial hypertension

**Erythrovirus (Parvovirus) B19**
- = Erythema Infectiosum or **Slapped Cheek Syndrome**
- Mild illness, fever in 30%, bright red rash on cheeks for 2 – 3 days
- A few days later, a **maculo-papular**, then lace-like rash may appear on arms, then trunk, buttocks and thighs. May recur over following weeks after hot baths
- Incubation 4 – 14 days
- Infectious period is before the rash appears
- Complications: Adolescents and adults may also have polyarthralgia/arthritis, aplastic crisis if chronically anaemic (eg immunocompromised)

**Orbital and Pre-Orbital Cellulitis**

• Orbital cellulitis:
  - Eg spread from anterior ethmoid sinus
  - **Proptosis** (eye pushed forward) and/or **ophthalmoplegia** (limitation of movement) and/or ↓visual acuity therefore must test eye movements and visual acuity
  - **Surgical emergency:** discuss with ENT, ophthalmologists, radiologist re imaging (CT not MRI)
  - Bugs: S Aureus, also S pneumoniae, S pyogenes, HIB
  - Cefotaxime and flucloxacillin
  - Complications: **intracerebral extension** (lumbar puncture contra-indicated until this is ruled out)

• Periorbital cellulitis:
  - In superficial fascia around the eye but not into the orbit. Fever and local tenderness
  - Investigations: FBC, blood cultures
  - **S pyogenes and S aureus** especially if contiguous skin lesion, S pneumonia, HIB if not fully immunised (can check urine for antigens). If HIB then ?HIB meningitis and Rifampicin prophylaxis for patient and family
  - Treatment:
    - If < 5 and not fully immunised: **cefoxime** or Cefotaxime (50 mg/kg/6hr, max 2 g)
    - If > 5 or <5 and fully immunised: **flucloxacillin** (50 mg/kg/6 hr, max 2 g)
    - If no response after 24 – 48 hours, treat as for orbital cellulitis or underlying sinus disease
  - **Local allergic reaction:** eg just erythema without tenderness or fever
Common Skin Infections

Streptococcal Skin Infections

- *Streptococcus pyogenes*:
  - Causes effects on skin due to toxins e.g. erythrotoxin in scarlet fever
  - Causes direct invasion of the skin e.g. impetigo

- **Skin infections** caused by *S pyogenes*:
  - Impetigo (superficial) – see dermatology section
  - Cellulitis (deep) – see dermatology section
  - Erysipelas (deep) – see dermatology section
  - Necrotising fasciitis (deep) – see infectious disease section
  - Scarlet fever – see infectious disease section

Staphylococcal Skin Infections

- *Staphylococcus aureus*:
  - The yellow pus-forming organism
  - Common cause of infections – some carry *S aureus* on skin without infection
  - Can also cause disease due to toxins

- **Skin infections** caused by *S aureus*:
  - Neonatal impetigo (superficial) – see infectious disease section
  - Hydradenitis (superficial) – see infectious disease section
  - Folliculitis (superficial) – see dermatology section
  - Furuncle/carbuncle – see dermatology section
  - Lymphadenitis (deep) – see dermatology section
  - Scalded skin syndrome (SSS) – see dermatology section
  - Toxic shock syndrome (TSS) – see dermatology section

Viral Skin Infections

- *Molluscum contagiosum* – see skin infection section

Paediatric Dermatology

- **Urticaria** – see dermatology section
- **Papular urticaria** – see dermatology section
- **Seborrhic dermatitis (and Leiner’s disease)** – see dermatology section
- **Naevi** – see dermatology section

- Café-au-lait spots:
  - Light brown macule – 1-10cm
  - Appear in childhood
  - Solitary lesions are not uncommon; if multiple, consider a genodermatosis (inherited genetic skin condition)
  - Associations with neurofibromatosis, tuberous sclerosis etc

- **Scabies** – see dermatology section
- **Head lice** – see dermatology section
- **Henoch-Schonlein purpura** – see vasculitis section
- **Kawasaki disease** – see vasculitis section

Paediatric Neurology

Neurological Exam in Children

*General (ALWAYS do these)*

- Are they well or unwell (esp toxic)?
- Growth:
  - Weight, height, and head circumference
  - Head exam:
    - Anterior and posterior *fontanelles* (while upright). Anterior closes ~18 months, posterior ~4 months
    - Sutures, shape of head
Check for shunts (subcutaneous tubes behind the ears)
Auscultation over closed eyes and temporal arteries for bruit

Dysmorphic features
Neurocutaneous stigmata:
- **Port-wine stains** (naevus flammeus; see right) – sturge-weber syndrome
- **Cafe-au-lait spots** – association with neurofibromatosis I
- Hypo/depigmented macules – *tuberous sclerosis*
- Use Woods lamp (UV light – some skin conditions will fluoresce) to look for depigmented lesions if fair skinned

Higher Cortical Function
- Ask questions appropriate to child’s age
- **Attention**: serial sevens, repeat numbers
- **Memory**:
  - Dependent on attention, processing and storing, ability to access and ability to communicate
  - Immediate (repeat numbers), recent (3 items at 5 minutes but not visual things), remote (old teachers name)
  - Object permanence
  - Visual: geometric reconstruction
- **Reading** and spelling
- **Speech**: dysphasia and dysarthria
- Draw a man
- Following instructions
- Behaviour
- Right left discrimination (crossed)
- Name objects – visual agnosia
- Construction of complex geometric figure
- Cortical sensation
- Abstract thought
- Looking for:
  - **Frontal lobe disturbances**: personality changes, irritability, lethargy, splinctor incontinence, primitive reflexes such as rooting (stroke on cheek – baby turns face towards the stimulus and make sucking motions), grasp re-emerge
  - **Temporal lobe disturbances**: altered ability to read, write and understand speech, memory dysfunction
  - **Parietal lobe dysfunction**: sensory perception abnormalities, 2 point discrimination, graphesthesia, stereognosis, apraxia

Cranial Nerves
- **I: Olfactory**: don’t often test unless abnormalities in the same area. Rarely impaired. Check each nostril separately. Use chocolate, mint or vanilla essence.
- **II: Optic**:
  - Visual Acuity:
    - Babies: *fix and follow*, optokinetic nystagmus, blink reflex (automatic closure of eyelid when object approaching, 50% at 5 months, 100% by 1 year)
    - Toddlers: offer toys of different sizes. Look in books for smaller and smaller things
  - Visual Fields:
    - Screen first: objects in the periphery – make sure they can’t follow your arm to your hand
    - If suspicious: test with wiggly finger (‘look at my nose and grab the finger that wiggles’)
  - Optic disc:
    - Very important
    - Use low light and small aperture
    - Get mum or dad to make funny faces behind you
    - Stay still and wait for optic disc to come into view
    - Look for venous pulsations – take pulse to get rhythm. If still can’t see them, push lightly on orbit – if veins collapse then OK. If no pulsations then ↑ICP.
  - Pupil: light + accommodation
- **III, IV and VI: Oculomotor, Trochlear and Abducens**:
  - Ptosis: nerve III and sympathetic. One eye doesn’t open as much as the other
  - III: down and out
IV: up and out
Variation: paralysis of upward gaze = pressure on quadregeminal plate
Get them to follow an object past the limit of head turning – don’t hold head
Hold them to your stomach and spin around with their head out. Nystagmus is normal
Doll’s eye test (open eyelids, turn head side to side: normal = eyes fixate like a moved doll, don’t follow head; BS lesion = eyes follow head)

V: Trigeminal:
Motor: temporalis – bulk, power, clenching, chewing. Get them to bite on a wooden spatula while you pull it away
Sensation: test from out of sight with feather
Reflexes: jaw and cornea (only if unconscious or other signs point to a problem)

VII: Facial:
Taste: anterior 2/3: very hard in children
Lacrimation and salivary glands
Motor:
- Tickle nose with tissue (try and get them to wrinkle face up)
- Close eyes/mouth open: look for asymmetry of facial creases
- Watch when crying – emotional movements less affected than voluntary ones (helps localised to UMN/LMN)

VIII: Vestibulochoclear:
Ask parents
Testing: whisper words (ice-cream, Wiggles) – rub fingers next to other ear (→ white noise)
Spinning
IX and X: Glossopharyngeal + Vagus:
Symmetry of uvula and palatal movements – say “ahh”
Voice: nasal ‘b’, ‘d’ and ‘k’, hoarse
Swallowing
Gag: only if really necessary
Taste on posterior tongue: too hard

XI: Accessory: shrug shoulders, turn head with resistance
XII: Hypoglossus: – “stick out your tongue at me” – bulk, fasciculation, power. Poke tongue through cheek and feel it

Motor
Observe:
- Abnormal movements: ticks, seizures, chorea, etc
- Bulk
- Scars
- Contractures
Symmetry (eg small thumb nail on one side – contralateral parietal lesion)
Posture: eg frog leg posture in hypotonia, fisting (thumb tightly enclosed by other fingers)

Tone:
- Must be relaxed. Lie on back and shake arms and legs to a song
- Range of movements: passive (no help from pt) and active (no help from dr)

Power:
Functional: Observe, including:
- Gait: walking forward and backward, running, hopping, tandem gait (eg heel-to-toe), on tiptoes, on heals, on insides and outsides of feet (Fog test). Look for dystonic posturing of hands while they do this.
- Proximal weakness: up steps, Gower’s sign, wheelbarrows, play ball, push-ups. Gower’s: lie on back – tell them to get up as quick as they can when you say ‘go’. Muscular dystrophy will roll onto front then climb up legs.
- Handedness (around 12/12 for girls, 15/12 for boys according to TVS)
Formal strength testing (grade 5 down to 0): Pull a toy, push me away, crazy glue (pretend to stick their finger to their nose and then try and pull it away), resistance, squeeze fingers
Pronator sign (tendency to pronate the hands when extending arms above head – feature of sydenham’s chorea – seen in rheumatic fever)
Remember:
Proximal weakness: myopathy
Distal weakness: neuropathy (except myotonic dystrophy)

**Reflexes**
- Must be relaxed, be patient
- Hit your hand, not the child
- Test ankle jerk on the sole
- Swing with gravity, don’t bash
- Use distraction (look over there...) and reinforcement: clenched teeth (chewing sticky lolly)
- Check for clonus
- **Primitive reflexes** (go at various ages):
  - Moro (baby held then head allowed to fall back, see symmetric opening of arms before they close again – up to 3/12)
  - ATNR (atonic neck reflex – archer’s, ~ 2/12 – 6/12) – turn head suddenly → extend arm on that side
  - Palmar grasp (birth to 3/12)
  - Sucking (from birth to 4/12)
  - Rooting (stroke on cheek – baby turns face towards the stimulus and makes sucking motions – birth to 4/12)
  - Babinski (birth to 1-2yrs)

**Sensation**
- Difficult
- Test from out of range
- Test with a broken spatula: show them sharp and dull and then always use sharp
- Touch, pain, vibration, proprioception

**Cerebellar**
- Gait: Walk along a line on the floor – should be able to do it well by 6
- Romberg
- Finger-nose: reach for toys (make sure they stretch)
- Foot tapping
- Rapid alternating movement
- Hands outstretched with eyes closed, look for drift

**Head Size**

**Microcephaly**
- Head circumference below the 3rd centile with abnormally slow head growth
- Incidence: 1/1000, recurrence in siblings 1/50
- Causes:
  - Familial: not associated with developmental delay
  - Autosomal recessive condition, associated with severe learning delay
  - **Congenital infection**: Rubella, CMV, Toxoplasmosis, Varicella Zoster, Listeria, Syphilis
  - Brain insult: eg perinatal hypoxia, neonatal meningitis. Likely to be accompanied by cerebral palsy, seizures, visual impairment, etc
  - Fetal Alcohol Syndrome

**Large Head**
- Megalencephaly = oversized brain
- **Hydrocephalus**: dilated cerebrum:
  - ↑CSF volume associated with ventricular dilatation and ↑intraventricular pressure
  - Due to:
    - Aqueduct obstruction: injury, infection or genes
    - **Arnold-Chiari malformation** (downward displacement and elongation of hindbrain, with herniation into the cervical canal)
    - Acquired causes: meningeal adhesions, mass lesions, etc
- Chronic subdural haematomas
- Hydraencephaly: no cerebrum
- Benign familial anatomic megalencephaly or macrocephaly
- Metabolic megalencephaly: late manifestation of many cerebral degenerative disorders (eg lysosomal storage diseases)
- Neurofibromatosis
- Cerebral tumour

**Headaches**

**History:**
- Pain characteristics: how bad, do they vary from one to the next, throbbing (migraine)/tight (tension)
- **Auras:** visual, unilateral slowly spreading tingling/numbness/weakness
- Photo & phonophobic
- Look pale/unwell → ?migraine
- Late afternoon → ?hypoglycaemic
- Suspect ↑ICP if vomit in the morning (without much nausea), ↑ severity, or wake in the morning or at night with a headache
- Stress: relationship to headaches to school and holidays
- Relieving factors: sleep, medication
- Associated with migraines:
  - Motion sickness – patient and family
  - ‘Ice-cream’ headaches – like shooting pain into head when biting an ice-block
  - Benign Paroxysmal Vertigo of Infancy (not the same as adult BPPV): 2–3 minute episodes of unsteadiness, queasiness, nystagmus
  - Cyclical vomiting
  - Abdominal migraine
- **PMHx:** head injury. To assess severity ask: did he lose consciousness, did he go to hospital and stay overnight, have any stitches or need imaging
- Family history:
  - What kinds of headaches do the rest of the family get (don’t talk about migraine – different meanings to different people)? There is a family history in 80% of migraine sufferers
  - Serious neurological disorders, strokes

**Exam:**
- General: Well/unwell, growth (if big head then measure parents), dysmorphic features, skin (stigmata)
- **BLOOD PRESSURE**
- ↑ICP: ↓venous pulsations in retinal veins, papilloedema, ↓visual acuity, 3rd and 4th nerve palsy
- Focal neurological signs: especially cerebellar (common site of lesion in kids 2–10)
- Cranial bruit to check for AVM: common finding. Interested in asymmetry, or if it can be eliminated by compressing the ipsilateral carotid artery
- Check sinuses, teeth, TMJ

**Differential:**
- Is it acute or chronic, recurrent or progressive, etc
- **Migraine:** normally throbbing. ↑when stressed. Most common cause in children
- **Tension headache:** Rare before adolescence. Presentation: constant daily bilateral headaches without well defined onset and ending, less impairment of function. Stress (ie doesn’t differentiate from migraine. But children usually somatise rather than tense up). More common in older girls
- ↑ICP
- Drugs: eg daily use of analgesics

**Management:**
- Reassure: most parents seek help to check its not serious
- Education: Migraines are familial, due to ischaemia and vasodilation (which stretches pain fibres in blood vessels)
- Symptom diary: check for food association (fairly rare)
- Avoid triggers
- ?Psychologist referral:
  - ↓Stress, get to the bottom of stress problems, relaxation, coping
  - It will be life long – learning skills to cope better than life long medication
- Medication:
  - Paracetamol: need a big dose and right at the start to make a difference (otherwise ↓gastric motility and fail to stop spread)
* Propranolol: tested in RCT, but not if asthmatic
  * Ergotamine: contraindicated if complex migraine (focal neurological signs)

**Migraine Definition:**
- Recurrent paroxysmal headaches with pain free intervals with normal health, plus two of:
  - Unilateral pain, nausea, visual or other aura, family history in parents or siblings

**Seizures**

- See also
- Epilepsy, page 200

**Classification:**
- Either focal or generalised
- And one of:
  - 1. **Acute symptomatic**: any person in that situation would seize eg hypoglycaemia, heatstroke, meningitis, hyponatraemia. Seizure will stop when cause goes away (unless scarring)
  - 2. Single
  - 3. Benign febrile convulsion
  - 4. **Epilepsy**: Repeated (x2 or more) unprovoked seizures

**Seizures:**
- Cortical neuronal discharge associated with a clinical sign
- A symptom – not a diagnosis or a disease
- Clinical sign depends on where the discharge is

**Diagnostic process:**
- Is it a **seizure or not**? Get parent/witness to show you what happened
- What type of seizure – is it **generalised or localised** (i.e. one arm/leg vs both arms/legs), etc
- Is it a **single seizure**, **acute symptomatic**, **febrile** or **epilepsy**?
- If epilepsy, what **syndrome** is it (this step is critical to treatment and prognosis, but often ignored in practice)?
- Brain **tumours** cause 1 – 2 % of all seizures in children, and 4 – 6% of partial seizures
- If it is a seizure, ask about whether they’ve experienced any other type of seizure e.g.:
  - **Absence** seizures (ever stop in middle of what you’re/they’re doing, go blank...)
  - **Any myoclonic** jerks (jerks just as dropping off to sleep – ever have these during the day?)
  - **Stiff/jerking** etc

**Neuro-imaging:**
- Indicated for:
  - Neurological deficit/asymmetry
  - Neurocutaneous syndrome
  - Developmental regression
  - Partial seizures
  - Infantile spasms or myoclonic seizures in 1st year of life
  - Persisting unclassifiable seizures
- Not indicated for:
  - Idiopathic generalised epilepsy
  - Benign childhood epilepsy with centrotemporal spikes (Rolandi)
  - Simple febrile seizures
- **CT:**
  - Initial scanning technique for exclusion of tumour
  - Shows calcification
  - Available and easier to perform
Health Care of the Elderly

MRI:
- Preferred imaging technique
- Sensitive to migrational abnormalities or very small lesions

PET/SPECT scan: localise lesion on the basis of metabolism. Only if considering epilepsy surgery

Epilepsy in Childhood

- Incidence: 0.5 – 1%
- Lifetime prevalence of a seizure is 5%
- Aetiology:
  - Idiopathic: normal kids, no structural abnormality, often family history, EEG normal, generally benign and good prognosis. Cause is assumed to be genetic – usually a channelopathy
  - Symptomatic: An underlying cause is known, and there are usually other signs of a problem
  - Cryptogenic: There are other problems besides seizures, eg retardation, focal signs, etc, but can’t find a cause
  - Symptomatic and cryptogenic: abnormal children, abnormal background on EEG, prognosis not so good and often seizures difficult to control

Electroclinical (Epilepsy) syndromes (see epilepsy):

- Neonatal (Many different syndromes)
  - Infancy
    - West syndrome (infantile spasms):
      a. **Age**: Birth to 5 years (mostly infants: 77% 3 – 7/12)
      b. **Seizure type**: Spasms
      c. **Clinical features**: May have initial normal development but deterioration of development is usual at onset; often present with visual difficulties
      d. **Examination**: normal or abnormal
      e. **EEG**: severely abnormal with multifocal spikes and slowing; 60% Hypsarrythmia (abnormal background)
      f. Often misdiagnosed – therefore **be vigilant** and wary of the baby with spasms!!
      g. **Aetiology**: multiple
      h. **Prognosis**: Spasms self limiting; Long term epilepsy (50-60%); 70-80% mental retardation (50% severe); Death 20%
      i. **Management**: Education and support; Vigabatrin and Steroids
  - Many others

- Childhood
  - Benign epilepsy with centrotemporal spikes (BECTS)/benign rolandic seizures:
    a. **Commonest focal** seizures in children
    b. **Age**: 3-14 yrs
    c. **Seizure type**: focal hemifacial +/- spread and secondary GTCS; occur during sleep often
    d. **Clinical features**: normal development; family history of epilepsy 30%
    e. **Examination**: normal
    f. **EEG**: Centrotemporal spikes enhanced by sleep; normal background
    g. **Prognosis**: Excellent – all will recover by 18 at latest
    h. **Treatment**: education and support

- Childhood absence epilepsy:
  a. **Commonest generalised** epilepsy in children
  b. **Aetiology**: genetic i.e. channelopathy
  c. **Age**: onset 4 – 10 years – often confused with daydreaming
  d. **Seizure type**: absence seizures only; frequent daily; rapid onset, short seizure, rapid offset with no post-ictal confusion
  e. **Clinical features**: normal development; family history of epilepsy 40%
  f. **Examination**: normal
  g. **EEG**: generalised spike and wave enhanced with hyperventilation; normal background
  h. **Prognosis**: 90% outgrow the absence seizures, but 30% will have GTCS in adolescence, no cognitive/behavioural difficulties at long-term f/u
  i. **Treatment**: ethosuximide or sodium valproate

- Many others

- Adolescence - adult
  - Juvenile myoclonic epilepsy (JME):
    a. **Age**: 8-26 years
    b. **Seizure type**: myoclonic seizures 100%; GTCS 80%; Absence seizures 10% 
    c. **Clinical features**: normal development; symptoms precipitated by sleep deprivation and alcohol 
    d. **Examination**: normal
EEG
- Normal background; Generalised fast spike/polyspike and wave; affected by photic stimulation (flashing lights) 40 – 90%; < 10% normal EEG (0% if sleep deprived)
- 10% of all epilepsies – most frequent adult IGE
- Aetiology: genetic
- Prognosis: 90+ % relapse rate - life long disorder; Seizures easily treated; Refractory 15%
- Management: Education and support; Sodium Valproate; Avoid Carbamazepine
  - Many others

- Less specific age relationship

  - Mesio-temporal lobe epilepsy with MTS:
    - Age: 1 - 35 yrs
    - Seizure type: mesial temporal lobe seizures
    - Clinical features: neuropsych – memory dysfunction in post-ictal period – indicates temp lobe as site; aura often seen – feeling yuck/emotional, aware seizure coming
    - Examination: normal
    - EEG: no spikes or Anterior – mid temporal spikes; normal or slowing in the temporal area
    - MRI: mesial temporal sclerosis
    - Aetiology: cell loss in hippocampus often due to meningitis/encephalitis
    - Prognosis: life-long epilepsy; majority intractable
    - Management: education and support; initial carbamazepine and then multiple AED’s; often require surgery

- Epileptic encephalopathy:
  - The epileptic activity itself may contribute to severe cognitive and behavioral impairments above and beyond what might be expected from the underlying pathology alone and can worsen over time – an example of this is West syndrome

EEG
- What is it?:
  - Electrical difference between two points over time
  - Standard electrode application – 21+ channels
- Not helpful in making a dx of epilepsy but is helpful to ascertain prognosis and direct therapy in those with epilepsy:
  - Sensitivity = 61%, specificity = 71%; helps to confirm a clinical dx but does not rule out epilepsy
  - Non-epileptic events can rarely have epileptiform abnormalities
  - Useful for making dx of epilepsy syndromes (as defined by EEG background and epileptiform findings)
- Need to do when sleep deprived and not on medication (i.e. before AEDs started as AEDs eliminate or change discharges)
- 2 – 4 % of normal children have an abnormal EEG
- 55% of epileptic children have an abnormal EEG
- Looking at frequency, morphology, location, reactivity, symmetry, dysrhythmia, etc
- EEG activity:
  - Background:
    - Normal activity
    - Amplitude, frequency, morphology, location, reactivity, symmetry
    - Change with state and age
    - Abnormal = dysrhythmia (focal or generalized)
  - Paroxysmal events:
    - Noises
    - Benign variants: associated with age and state
    - Epileptiform: inter-ictal and ictal

Psychosocial Aspects of Epilepsy
- More important than drugs. Peoples’ attitudes will do far more damage than a few seizures
- Normal life: emphasis on what child can do, not what they cannot; stress that they are a normal child (no different from the child across the road who has asthma or wears glasses – we all have ‘something’!
- Therapy: info on why we treat + how this applies to their syndrome
- Medications: give first-line therapy + info re efficacy + SE
- Lifestyle advice: info re potential triggers eg illness, sleep deprivation, stress, hyperventilation
- Support: epilepsy association + field officers
- SUDEP: sudden unexplained death in epilepsy pts – 1/900 incidence in children with epilepsy. Most of these were those with difficult to treat seizures or other underlying brain dysfunction, children with normal development + exam with seizures at no increased risk of death
• Education. Should be given verbally + written info. Should cover:
  ➢ **Seizure**: information about what seizures are and the specific type the child has. Important everyone caring for pt uses the same terminology
  ➢ **Epilepsy**: i.e. 2 or more unprovoked seizures + that epilepsy is common
  ➢ **Cause of epilepsy**: genetic, inherited (combination of mother + father’s genes = inherited mutation) mutations leading to channelopathies (dysfunction in ion channels [gates] leading to abnormal electrical activity – hyper-excitation)
  ➢ **Epilepsy syndrome**: should be told what syndrome their child has + the aetiology, incidence, + prognosis
  ➢ **Effect of individual seizures**: so long as these are not prolonged – there will be no damage to the brain
  ➢ **First aid**: stay calm, time seizure, ensure child’s safety, if >5min, call ambulance, recovery position post
  ➢ **Precautions**: should be adhered to until seizure free for at least 1yr:
    ➢ Should have **showers** not baths
    ➢ Wear **helmet** whilst cycling; avoid cycling on road until 6/12 free of seizures
    ➢ Learn to **swim** + never swim alone

**Pharmacology and Other Therapies**

• Rationale:
  ➢ 1. **Safety** issues
  ➢ 2. **Social stigma**
  ➢ 3. Frequent or long seizures can have an effect on the **developing brain**

• Principles:
  ➢ Seizure free with no side effects
  ➢ Start low and go slow
  ➢ Never stop abruptly
  ➢ Routine lab monitoring is costly + **ineffective** except for phenytoin
  ➢ When first medication fails, a 2nd should be introduced at full dose; if good effect, wean off first medication
  ➢ Those with difficult to control epilepsy have good periods and bad period often unrelated to meds – should aim for best seizure control over a prolonged period of time
  ➢ Start after 2 or more seizures
  ➢ Stop after 2 years seizure free

• AEDs used in various epileptic syndromes:

<table>
<thead>
<tr>
<th>Epilepsy Syndrome</th>
<th>First line therapy</th>
<th>Second line therapy or add in</th>
<th>To avoid</th>
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<tr>
<td>Benign childhood epilepsy with centro-</td>
<td>Usually no need for AEDs</td>
<td>Carbamazepine</td>
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<td>temporal spikes (BECTS)</td>
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<td>Valproate</td>
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<td>Childhood absence epilepsy</td>
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<td>Infantile spasms</td>
<td><strong>Steroids</strong></td>
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<td><strong>Vigabatrin</strong> (tuberous sclerosis)</td>
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<td>Benzodiazepines</td>
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<td>Focal epilepsy</td>
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<td>Genetic generalised epilepsy</td>
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Mesial temporal lobe epilepsy

- **Drugs** (main SE in brackets):
  - Common themes = sedation, nausea, weight gain + beware of child-bearing age females
  - **Carbamazepine**: Na+\(\rightarrow\) blocker (dizziness, gastric upset, sedation, behavioural difficulties)
  - **Sodium valproate**: ↑GABA (liver toxicity, nausea, vomiting, ↑ appetite, weight gain, personality change, hyperactivity, ↓ concentration)
  - **Clobazam**: ↑GABA (sedation, behaviour difficulties, weight gain)
  - **Ethosuximide**: Ca2+\(\rightarrow\) blocker (nausea, vomiting, stomach upset, sleep disturbance)

- **Other therapies**:
  - Surgery:
    - Next step in therapy in children with focal epilepsy who have failed 2 appropriate AEDs (especially mesial temp lobe epilepsy)
    - Referral to paediatric neurologist to assess potential for surgery
  - Ketogenic diet:
    - High fat, low carbohydrate diet that can result in some children with intractable epilepsy becoming seizure free
    - Must be maintained meticulously (even accounting for CH in antibiotics for example)

**Status Epilepticus**

- Continuous or intermittent fitting (without complete recovery) > **30 mins**
- Most seizures in childhood stop within 5min, therefore **treatment should start if >5min**
- Convulsive SE is life-threatening + can have serious neurological sequelae
- **ABCD + (DEFG)**:
  - Support **airway**, recovery position
  - Administer 100% O2, assess breathing
  - **Circulation** – check pulses + BP, ECG
  - Check **BG** urgently, give dextrose if low
  - Establish IV access
- Give effective anticonvulsant (starship guidelines):
  - At 5 min: **buccal midazolam** (or PR diazepam)
  - At 10 min (if still seizing): IV/PO/PR **diazepam**
  - At 15 min (if still seizing): IV phenytoin
  - At 35 min (if still seizing): IV phenobarbitone (ensure airway support)
  - At 45 min (if still seizing): IV midaz infusion + referral (PICU + neurology)

**Benign Febrile Convulsion**

- Types of seizure occurring with fever:
  - Benign febrile convolution
  - Epilepsy: eg first epileptic seizure unmasked by fever
  - Acute symptomatic seizure: meningitis etc
- **Benign Febrile Convulsions**:
  - Frequency: 2 – 5% of all children
  - Age: 6 months – 6 years
  - Temperature: usually > 38.5 C
  - Boys: Girls = 1.4:1
  - **Family history** common (polygenic inheritance)
  - Unrelated to prenatal and perinatal brain damage
  - Have seizures with fever only
  - NB. Fever is not the cause of the seizure, rather the trigger – is genetically inherited potential for fever to trigger seizure
  - Types:
    - Simple (75%): generalised, brief (< 15 minutes), does not recur in 24 hours
    - Complex (25%): focal and/or prolonged (>15min) and/or recurrence within 24 hours
  - **Treatment**:
    - Ensure surrounding safety + place in recovery position after seizing has stopped
    - Stop seizure if >5min: buccal midazolam (this is more effective than rectal diazepam) at home or in ambulance
- Measure blood glucose immediately
- Find the cause of the fever (e.g. urinalysis etc): seizure won’t hurt them but meningitis might!
- DON’T use anticonvulsants – ↓ recurrence but potentially significant side effects to treat something that is benign
- Consider LP in < 6/12 children and those with signs of meningitis

- **Prevention**: Avoid over-heating. Paracetamol/ibuprofen or tepid sponging don’t ↓ risk of seizure
- **Prognosis**: 30% will have a recurrence, 70% of these within the next year
- **Risk of subsequent epilepsy**:
  - Increased risk if
    - Neurologically abnormal prior
    - Family history of epilepsy or
    - First seizure is complex (but still small)
  - Otherwise very slight increase in risk only

- **Neurological sequelae**:
  - No impact on behaviour, growth, IQ
  - Prolonged febrile seizures associated with hippocampal sclerosis (temporal lobe). Controversial. (eg which direction is causation)

- **Parental education**:
  - Seizure does not cause brain damage (if less than 30 – 45 minutes)
  - 30% chance of another seizure
  - Next time: stay clam, clear airway, recovery position when stopped (low tone), time the seizure
  - Call ambulance at 5 minutes:
    - Most seizures stop by 5 minutes – so those that haven’t are more likely to go on for longer
    - Want to be at hospital and have it stopped by 45 minutes

**Anoxic Seizures**

- **Reflex anoxic seizures** (white breath-holding attacks):
  - Vasovagal events due to stimulus: eg pain, fear, vomiting, etc. [Big sympathetic drive → parasympathetic overcompensation?]
  - Occur in children from 0 – 10
  - Reflex bradycardia or brief asystole or peripheral vasodilation
  - Symptoms: pallor, ocular revulsion, don’t breath, lose consciousness, extensor posture, a few symmetrical clonic movements, spontaneous resolution and then fine

- **Blue breath-holding attacks** (prolonged expiratory apnoea):
  - 1 – 5 years.
  - Follow a stimulus, usually emotional eg anger or frustration, crying with prolonged expiration
  - Child cannot control these
  - Get worked up, don’t breath in, run out of breath and don’t breath in (actually stop breathing)
  - Cyanosis with retained heart rate
  - May lose consciousness and have some clonic movements (follows same course as reflex anoxic seizures)
  - Blow on face to start breathing

- Both white and blue breath holders are often iron deficient → do dietary history and Hb test
- Don’t treat them. Ensure parent isn’t being manipulated by breath-holding by child

**Tics**

- Brief, sudden, involuntary, stereotyped, purposeless movement involving the muscles of the face, trunk and extremities
- Worsen with anxiety
- Go away with sleep
- **Acute transient tic disorder of children**:
  - Onset <12 yrs
  - Boys > girls
  - Lasts 2/52-52/52
  - One or two tics (blink most common, may be vocal)
  - Common (12%)
Health Care of the Elderly

- Also called Gilles de la Tourette Syndrome
- Onset 2-15yrs
- Boys>girls
- Tendency for life
- Multiple motor and vocal tics
- Tics vary, wax + wane

**Cerebral Palsy**
- A persistent disorder of posture or movement caused by a non-progressive, non-hereditary pathological process of the immature brain, **acquired either in utero or later at a time of rapid development of the CNS (up to several years after birth)**
- May be accompanied by other impairments, eg retardation, vision defects or epilepsy
- Though lesion is static, the clinical features may develop for several years as brain function matures (may give appearance of being progressive – clinical signs have to wait until that part of the brain ‘kicks in’)
- Incidence:
  - Stable at about 2/1000.
  - 80/1000 for very preterm babies
- Stages of brain development:
  - Up to 20 weeks → major brain malformations:
    - Lissencephaly (flat brain without cortex)
    - Pachygyria and microgyria: brain layers completely abnormal
    - Migration defects: islands of grey matter in the middle of white matter
  - 26 – 32 weeks: neurons climb glial fibrils: intense growth – prone to ischaemia. If born then, prone to germinal matrix bleeds. But *ischaemia more important → periventricular leukomalacia* (PVL)
  - Myelination starts at about 30 weeks, but most is after birth. Damage only becomes obvious as myelination complete (conscious control of arm at 4 – 5 months, leg at 9 months)
- Causes:
  - *Anything that damages neurons*: ischaemia, hypoglycaemia, infection, head trauma, toxins
  - Only 10-30% attributed to “perinatal asphyxia” – but these are usually the worst cases
  - For many it’s due to an unknown earlier (i.e. in utero) adverse event
  - Significant proportion preterm (43%)
  - Intrauterine growth restriction →↑risk by 5 times
- Exam findings:
  - Hyperactive reflexes
  - Abnormal movements:
    - Chorea (brief, quasi-purposeful, irregular contractions that are not repetitive or rhythmic, but appear to flow from one muscle to the next)
    - Athetosis (*involuntary convoluted, withing movements* of the fingers, arms, legs, and neck)
    - Dystonia (muscle contractions causing twisting and repetitive movements or abnormal movements)
  - Abnormal absence or persistence of infantile reflexes
  - Other common features = epilepsy, high-tone deafness
- Differential:
  - Metabolic disorder
  - CNS degenerative diseases
  - Cerebellar dysgenesis or spinocerebellar degeneration

**Classification**
- Spastic hemiplegia:
  - 0.79/1000
  - Congenital:
    - Spastic paralysis of arm and leg on same side.
    - Full-term: arm usually weaker than the leg. Distal parts worse than proximal. Growth of affected parts reduced
    - Preterm: usually periventricular rather than cortical and leg weaker than arm
    - NB. “spastic” = velocity related change in tone (slow movement → move further; fast movement → catch)
    - Face not involved
    - Epilepsy common – correlates with degree of mental retardation (but IQ often normal)
    - Mechanism: vascular (*ie stroke in utero*).
Acquired:
- Following infection, trauma, CVA, status epilepticus, etc
- Most in first 3 years of life
- Flaccid with facial involvement, spastic later

Spastic diplegia:
- 0.9/1000

Spastic:
- Problem in preterm 28 – 32 weeks
- Follow bilateral periventricular injury, especially with hydrocephalus complicating, or injury to basal ganglia or parasagittal cortex
- Stiff lower limbs (may be floppy as neonates): flexion of hips and knees, scissoring (internal rotation and adduction), weak trunk and eventual contractures. May dislocate hips
- Upper limbs variably affected (if worse then more likely ↓IQ)
- Hyperreflexia and spasticity with variable wasting
- Epilepsy uncommon, intellect may be retained (69%). Head growth mirrors intellect

Quadriplegia:
- Global cerebral insult: massive haemorrhage, shock, obstructed umbilical cord
- Upper limbs often worse than lower, generalised spasticity and wasting
- Severe mental retardation, microcephaly, cranial nerve palsies, aspiration, etc

Athetoid:
- Extrapyramidal injury, especially perinatal insults (including kernicterus – unconjugated hyperbilirubinaemia)
- Appears after 5 months: involuntary movements and posturing, poor trunk control, hypotonia or normal, normal reflexes
- Impaired speech, drooling, facial grimacing, often deaf (especially high tone)
- IQ often normal but difficulties communicating. Epilepsy in 25%

Ataxic:
- Cerebellar symptoms predominate
- Cerebellum may be abnormal on imaging
- Presents at 1 – 2 years, but floppy and docile from the start
- Ataxia (incoordination with voluntary movements), intention tremor, late walking, high tone deafness, normal IQ in 50%
- Can be familial disease

Management:
- Team approach: physio, OT, orthopaedic surgeon, etc
- Prevent contractures and encourage normal developmental stages
- Treat epilepsy
- Rule out deafness, check special senses
- Encourage communication
- Prevent malnutrition
- Encourage mobility and upright posture (frees up hands for ‘learning’ activities)
- Support for child and family
- Manage constipation, incontinence

Muscular Dystrophy
- Not common. Most common is Duchenne: 1 in 3,500
- X linked recessive, females usually asymptomatic. 1/3 new mutations
- Caused by failure to make dystrophin (in muscle cell membrane)
- Present with muscle weakness that is slowly progressive. Gower’s sign: proximal weakness → climb up legs with hands to stand up
- Often mild intellectual handicap (IQ 85)
- Wheel chair bound by 12. ↓Respiratory function and ↑scoliosis → terminal bronchopneumonia
- Diagnosis: genetic tests, CK markedly elevated, myogenic pattern on EMG
- Treatment: supportive only

Acute Weakness in Childhood
- Consider:
  - Guillain-Barre:
    - Acute inflammatory demyelinating polyneuropathy, mostly motor but can be sensory/autonomic
- LP shows elevated protein but normal cells, post-infectious (eg mycoplasma), often sensory involvement, treat with Ig

- **Transverse myelitis:**
  - Acute inflammation of gray and white matter in one or more adjacent spinal cord segments, usually thoracic
  - Causes include MS, infections, autoimmune or postinfectious inflammation, vasculitis, and certain drugs
  - Symptoms include bilateral motor, sensory, and sphincter deficits below the level of the lesion
  - Responds to steroids

**Neural Tube Defects**

- = *failure of closure of the neural tube* (4 weeks gestation – often already happened by the time a woman knows she’s pregnant)
- At lower end, leads to spina bifida (failure of closure of dorsal processes of spine) and at upper end anencephaly or encephalocele
- Rate varies on population. High in Irish, Welsh, Scottish (3%) and those from poor backgrounds (poor nutrition, ↓ folate, etc)
- Multifactorial causes:
  - Genetic
  - Environmental (folate)
  - Drug associations (eg antiepileptics)
- Any **midline lesion of the skin overlying the CNS from the nose to the sacrum** may indicate an underlying NTD (same embryological origin) – eg hair, pigmentation, haemangioma, pit/sinus etc

**Types**

- **Myelomeningocele:**
  - Most common: 90% of spina bifida, failure of caudal closure of neural tube → failure of closure of skin and absence/leaking of the dura/meninges.
  - Lumbosacral (25%), lumbar or thoracolumbar (50%) or thoracic/cervical (11%).
  - Spinal cord opened out flat. Variable neuro deficit (often a mix of UMN + LMN) below lesion. Possible tethering
  - Leads to:
    - Paraplegia: paralysis of knee and hip extensors with retained flexion. Talipes – equinovarus is commonest (club foot)
    - Variable loss of sensation
o Autonomic problems: faecal incontinence, dribbling urinary incontinence on lifting baby or spastic urethral sphincter → urinary retention, spastic bladder → reflux, hydronephrosis
o Open lesion → risk of ascending infection
o Hydrocephalus: very common (80%; Arnold-Chiari II malformation). Dislocation of cerebellar tonsils and medulla into cervical canal, aqueduct stenosis (primary lesion or tethering).

**NB.** Signs of hydrocephalus and ↑ICP:
- Bulging fontanelles, rapid head growth, separation of sutures, ‘sun-setting eyes’ (looking down),
- Poor feeding
- Drowsiness, venous congestion of skull (prominent superficial vessels)
- If acute: vomiting, bradycardia, hypertension (Cushing’s triad; rarely seen in infant as fontanelles take the pressure)

- Management:
  - Multidisciplinary team (neuro, ortho, paeds, uro, physio, OT, incont etc)
  - Close back to prevent infection
  - Drain hydrocephalus (ventriculoperitoneal shunt)
  - Bladder and bowel management
  - Review motor and sensory function, prevent contractures and aid mobility

- Spina bifida occulta: Range from failure of formation of dorsal spine (cord intact) to abnormal cord contents
- Diastematomyelia:
  - Not actually a NTD. Bone or cartilage spur into the cord → progressive loss of spinothalamic function (pain and temperature; these decuss medially) with growth (slices as spine elongates).
  - Not common. Leads to regression of acquired skills as spine elongates.
- Lipoma: fatty mass → pressure effects on the cord
- Tethered cord:
  - Complication of many types of NTD
  - Cord fixed lower down and gets stretched as spinal column grows → progressive loss of power, sensation and autonomic function (ie sphincter function, weakness in toes + forefoot, saddle anaesthesia, may be loss of ankle jerk)
- Dorsal dermal sinus:
  - Looks like small pit/sinus
  - Epithelium lined tube from skin (lumbar/sacral) to dura or into spinal canal. May be associated dermoid (teeth, hair)
  - Risk of meningitis (coliform) and tethered cord therefore needs surgery
  - MRI to confirm
- Meningocele:
  - Rarer. Swollen lesion on back, full of CSF, brilliant translumination
  - Little neurological deficit, risk of tethering
  - Cranial meningocele: occurs on skull and contains CSF
- Encephalocele:
  - = cranial meningocele containing brain; occurs on skull – usually occipital or frontal
  - Prognosis more guarded
  - Can sometimes see midline skin lesion on head indicating underlying encephalocele
- Anencephaly: Failure of cephalic closure of neural tube → absence of cranium. Frequent polyhydramnios. Most live births die within 24 hours. Also occurs in other syndromes (⇒ always do karyotype)

### Prevention
- Folic acid levels in pregnant women only half the recommended – NEED TO SUPPLEMENT
- Recurrence after one affected child is 3 – 5% (?inborn error of folate metabolism)
- Low dose folate prophylaxis highly effective – but 50% pregnancies unplanned
- Adequate dietary intake hard (5 portions of broccoli a day!)
- Can detect NTD with antenatal ultrasound or ↑maternal or amniotic fluid alpha-fetoprotein

### Eye Disorders in Children
- See also The Red Eye, page 215
- Routine eye checks for infants:
  - Fixing and following: ophthalmology referral if not doing this by 4 months
  - Pupillary red reflexes: view from about 50 cm. Leukocornea (white pupil) ⇒ ?retinoblastoma. Other irregularities ⇒ ?congenital cataract

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Ocular alignment: symmetrical corneal light reflex (don’t have to be exactly central). Strabismus (misalignment of visual axis) → amblyopia. May be intermittent. Test with cover test. Accommodative Esotropia = convergent strabismus related to accommodation

Eye movements: if not following then test vestibulo-ocular reflexes using dolls eye

Adnexa Oculi: Eyelids. Check for Congenital Naso-Lacrimal Duct Obstruction (tears, pus or mucus discharged by pushing on lacrimal duct) due to incomplete canalisation. Most resolve by age 1 (⇒ usually managed conservatively by twice daily lacrimal sac massage)

Globes and cornea: of equal size

Serious disorders in the neonate (⇒ urgent referral):

- Congenital Glaucoma: photophobia, corneal haze/opacity, corneal enlargement or asymmetry
- Ophthalmia Neonatorum: conjunctivitis with infection and inflammation of the conjunctiva in first month of life. Urgent microbiology and iv antibiotics for chlamydia and/or N Gonorrhoeae

Red Eye in Children

- Conjunctivitis:
  - Common in newborns – may be serious
  - Bacterial: rapid onset, usually spills from one eye to the other. Pus.
    - Neonatal often Neisseria gonorrhoea (prevented with silver nitrate drops in new born if high risk). Can lead to perforation of orbit. If systemic spread then septic arthritis. Treatment: B Penicillin 25 mg/kg/12hr iv + 3 hourly 0.5% chloramphenicol drops for 7 days
    - 3 – 5 days post delivery: Chlamydia. Can progress to rhinitis and pneumonia. Diagnosis requires special chlamydia swab. Treatment: Erythromycin 10mg/kg/6hr po for 21 days to eliminate lung organisms + 1% tetracycline drops
  - Acute causes often Staph aureus, S pneumoniae, H influenzae or S pyogenes. Treatment: drops up to hourly (eg chloramphenicol)
  - Chronic: usually toxins or immune (eg Kawasaki, Erythema Multiforme, Reiter’s Syndrome)
    - Viral: acute onset, often bilateral, minimal pain, thin watery discharge, photophobia. Adenovirus, Herpes Simplex, measesles, etc. Generally clears spontaneously. If Herpes suspected (eg eyelid vesicles), start 4 hourly acyclovir and immediate referral
    - Allergic: history of atopy and itchy eyes. If mild then use astringent, topical anti-histamine or cromoglycate

Subconjunctival haemorrhage: common after blunt trauma (eg birth), coughing (eg whooping cough) and vomiting.

Corneal abrasions: trauma or infection (esp HSV)

Iritis/Uveitis: uncommon in children. May have no pain but strabismus or visual loss. Cornea red near iris (unlike conjunctivitis). Look for white cells in anterior chamber.

Renal Disease in Children

- See also Renal and Genitourinary, page 301

Proteinuria

- Definition: > 150 mg protein/day (same cut off as adults)
- Normally protein is lost from tubular cells (i.e. not through filtration across GBM). Pathological if:
  - Filtered protein from glomerulus (i.e. across GBM)
  - ↑Loss from tubular cells
- Categories:
  - Gross proteinuria: > 1 g/day (essentially nephrotic syndrome)
  - Acute low grade (<3/12, <1g/d)
  - Chronic low grade (>3/12, <1g/d)
- Diagnosis:
  - Dipstick: screening test - measures concentration of protein, so if urine is concentrated → ↑protein concentration
  - 24 hour urine: diagnostic test - if not continent this is not possible to measure
- Nephrotic syndrome:
  - = Proteinuria + oedema + hypoalbuminaemia
  - Oedema is due to ↓colloid osmotic pressure → ↑aldosterone → ↑Na → ↑H2O retention → this leaks out as well
  - Caused by leaky glomeruli
Causes

- **Minimal change disease:**
  - See also Minimal Change Disease, page 320
  - = No change under light microscope
  - Passing up to 8 – 10 g per day \( \rightarrow \) gross oedema
  - 3 rare complications:
    - Hypoperfusion: classically the gut \( \rightarrow \) abdominal pain
    - Lose Ig as well \( \rightarrow \) ↑risk of bacterial infection (eg pneumococcal)
    - Thrombosis (eg renal vein)
  - Usually grow out of it (eg over 6 months, although may persist until an adult). Unpleasant but not usually life-threatening
  - Treatment: **steroids** but side-effects
  - 10 – 20% have other causes which may \( \rightarrow \) chronic renal failure

- **Acute low-grade proteinuria:**
  - No long term significance
  - Can be:
    - Exercise induced in some teenagers/adults
    - Urinary tract infection
    - Postural proteinuria (\( \uparrow \) when standing up)
  - Have to f/u to demonstrate that it’s gone (ie that it's not chronic)

- **Persistent/chronic low grade proteinuria:**
  - Always have some proteinuria
  - Exclude exercise and postural (benign)
  - Significant finding: \( \uparrow \) risk of renal disease, eg in adult

Haematuria

- **Definition:** \( > 5 \text{ RBC} \) in high powered microscope field

- **Categories:**
  - Gross/Macroscopic:
    - UTI (most common cause by far)
    - Trauma: visceral damage easier in kids
    - Post-streptococcal glomerulonephritis
    - Stones (uncommon in kids)
    - Wilm’s tumour
    - Bleeding disorder (eg haemophilia)
    - Red food colourings (eg beetroot)
    - IgA nephropathy: IgA deposits on glomeruli
  - Acute microscopic:
    - Infection
    - Plus above list (which are more likely to be microscopic than macroscopic, and may be intermittent/chronic)

Acute Renal Failure

- = Acute renal ‘success’. If kidney didn’t shut down after ATN \( \rightarrow \) would continue filtering at 100ml/min with no reabsorption \( \rightarrow \) very rapid dehydration i.e. in ischaemia causing ATN (meaning that the tubular cells are unable to reabsorb) offers the potential for peeing out circulating volume very quickly therefore the JGA shuts down the afferent arteriole so GFR almost 0 to preserve circulating volume

- **Causes:**
  - Ischaemia \( \rightarrow \) ATN
  - Obstruction (eg congenital malformation – urethral stricture)
  - Sepsis: toxins killing tubular cells + hypoperfusion
  - Drugs: at glomeruli or tubular cells (eg. gentamycin, ibuprofen)
  - Haemolytic-uraemic syndrome (e.coli 0157 – shiga toxin causes thrombosis in small vessels)
  - Post-infective (eg PSGN)

- **Complications:**
  - Fluid overload: fluid restrict to insensible losses (breath, stools, skin = 400 ml/m² of body surface) plus urine and vomit
  - Hyperkalaemia:
    - No symptoms, so have to monitor
Treatment:
- Salbutamol or insulin + glucose → shifts K+ into ICF
- Calcium resonium: chelates K
- Encourage anabolism with ↑ calories → ↑ cell creation
- Frusemide if any urine output
- CaCl or Ca gluconate: prevents arrhythmia
- Dialysis

- Uraemia: vomiting, encephalopathy → dialysis
- Hypertension: due either to ↑ aldosterone release or fluid overload

Chronic Renal Failure

- Incidence: 1 – 2 kids per million per year
- Disaster for families → very demanding treatment
- Causes:
  - Obstruction/congenital
  - Dysplasia (never developed normally)
  - Severe reflux
  - Glomerulonephritis
- Problems:
  - Nutrition (need ↑↑ calories → ?NG tube)
  - ↓ Linear growth: due to ↓ nutrition, ↑ PO4 → secondary hyperparathyroidism, ↓ active vitamin D
  - Anaemia: due to ↓ erythropoietin
  - Na/H2O/K balance (may lose or retain too much)
  - Hypertension: angiotensin, overload, drugs
  - Ca balance
  - Development (always tired)

- Treatment: peritoneal dialysis

Duplex Kidney

- Common = ~ 2%, mostly asymptomatic
- Kidney split in two (upper and lower) — two ureters
- Weingurt-Meyer law = upper pole obstruction (ureter enters low into bladder) and lower pole refluxes (ureter enters high/laterally)
- May be associated with a ureterocele
- Rx: US, MCU, Mag3
- Rx: depends on anatomy and function

Multicystic Dysplastic Kidney (MCDK)

- Is the most severe form of cystic renal dysplasia
- Different to genetic polycystic kidney disease
- Probably due to an in-utero ureteral obstruction
- Antenatal dx – bunch of grapes seen where kidney should be
- No function on Mag3 scan
- Most resolve by 2yrs – if not, -ectomy

Genito-Urinary

Urinary Incontinence

- See UTIs in Children, page 334

Daytime Incontinence/Diurnal Enuresis

- Females > males
- More commonly urge incontinence (detrusor overactivity)
- Primary: has never been dry
- Secondary: was dry for at least 6/12, now not
- If daytime enuresis overlaps with nocturnal – treat daytime first
- History:

Health Care of the Elderly
Health Care of the Elderly

- Previously continent?
- Frequency, volume, urgency, pain, colour, continuous dribble (are nappies never dry - nearly always pathological)?
- Infection history:
  - Associated symptoms
  - Past infections, kidney complications
- Constipation (→ urinary retention due to pressure → infection). Need to fix bowels first
- Family History
- Exam:
  - Palpable/distended bladder
  - Kidneys: palpable, tender?
  - Boy: examine penis carefully: balanitis (inflamed foreskin), constricted urethra
  - Girl: effusion of the perineum, can labia be parted
  - Signs of occult spina bifida (eg skin or vascular lesions over sacrum)
  - Are legs neurologically normal
  - Blood pressure: whenever risk of kidney disease
  - Screen for infection
  - Not PR
- Investigations:
  - Urine microscopy
  - US referral
  - Further tests (not required generally):
    - Bladder volume scanning
    - MCU
    - Cystoscopy
    - Urodynamics
- Treatment: if urge incontinence, use oxybutinin
- If repeat infection:
  - ?Genitourinary malformation: do US/NM or MCU to check for reflux
  - Infection leads to temporary scarring, which predisposes to infection. Break the cycle with prophylactic antibiotics

Bed Wetting/Enuresis
- Very common: 12% at age 6, 4% at age 14
- Boys > girls
- Natural history: Resolves spontaneously at a rate of approximately 15 percent per year. The longer the enuresis persists, the lower the probability that it will spontaneously resolve.
- Pathophysiology:
  - Immature signals to brain to indicate full bladder
  - Deep sleepers
  - ?those with impaired urine concentrating ability
  - Monosymptomatic nocturnal enuresis can be caused by the following factors either individually or in conjunction:
    - Maturational delay
    - Genetics
    - Functional small bladder capacity
    - Abnormal diurnal secretion of ADH
    - Nocturnal polyuria
    - Detrusor instability
    - Sleep disorders
    - Psychological issues
- The child learns to suppress and eventually control and co-ordinate detrusor and sphincter activity:
  - Day-time continence achieved around 3-4 years
  - Night-time continence achieved from 5-6 years (7 is likely abnormal)
- History:
  - Is it primary or secondary?
    - Primary: have never been dry, most common (~80%), usually no associated pathology. No daytime problems. Pass large volume without waking. Ask about proportion of dry nights, getting worse or better?
Secondary: were dry, now wets (regression) → pathology common. Detailed history of when it began, pattern since then (↑ or ↓), symptoms of infection (dysuria, frequency), diabetes (weight loss, thirst), physical abuse. Can be induced by stress (eg starting boarding school, family disruption), constipation, epilepsy

- Just at night time, or day as well (pathology more likely – must fix this first)?
- Urinary symptoms: polyuria (and polydipsia), dysuria, frequency
- ?Constipation or soiling → need to fix this first
- Family history (if one parent wet the bed, 40% of children will wet, if both parents then 80%). This is key information – normalises it for parents and child → ↓anxiety
- Parents’ management style: punitive (unhelpful but common) or supportive (ignore wet pants, praise for waking to pass urine, not common but more helpful)
- Previous treatment experiences
- Expectations of parents and child
- General developmental screen, including faecal continence, bladder training
- Social history: how much extra support will the child or parent need to manage the treatment

- Exam:
  - End of bed: note weight loss, hydration
  - Growth
  - Blood pressure
  - Lumbosacral area (midline defects → ?spina bifida), perianal sensation and neurological exam of legs
  - Abdominal palpation: kidneys, distended bladder, constipation
  - External genitalia - ?malformations

- Investigations:
  - If primary then tests usually reveal nothing, therefore no tests required
  - MSU: blood, protein, glucose, casts, bacteria, urinanalysis
  - Unlikely to need, but may test: blood sugar (diabetes) and electrolytes (renal failure)

- Treatment:
  - Don’t treat until age 6 or 7 – but do treat then otherwise psychological sequelae as they head into teens
  - Fluid restriction 1hr before bed, anything more than this is overkill – doesn’t fix the problem
  - Explanation and reassurance:
    - Not silly or on purpose.
    - Primary enuresis is NOT a psychological problem, a personality disorder or ADD, but one of delayed maturation (however, stress can make bedwetting worse)
    - Often genetic component
    - Parental intolerance will worsen it and ↓ self-esteem
    - Avoid covert rewards (eg getting into parent’s bed when their bed is wet)
  - No night nappy, leave lights on in toilet, normal fluids before bed
  - Convenient hygienic care of bed (eg waterproof underblanket)
  - Keep a diary (good for any symptom):
    - Day, time of bed, hourly check till parents go to bed, size of wet patch
    - Helps keep accurate record and has therapeutic value (gives feedback, is something to do, etc)
  - Four options:
    - Pad alarms (bed wetting alarm):
      - Bed wetting alarms can train the sleeping brain to control the bladder and wake the sleeper if wetting occurs
      - Most effective option. Not funded.
      - Explain and demonstrate to child. Hard work for parents as they must get up (take turns, may need extra support if solo parent). Must wake child properly (eg cold flannel on face).
      - Relapse → immediate resumption of pad and alarm. Relapse reduced by over-training (once consistently dry, push fluids at bedtime, will recommence wetting but overcome it quickly)
    - Systematic waking: wake half an hour before normal wetting time, and shift toileting time closer to bedtime/morning by half an hour a week
  - If no improvement after two lots of 4 weeks then ?anatomical problem
  - Medication:
    - Nasal ADH/vasopressin (specialist only) treats symptoms but doesn’t change behaviour.
    - Useful for short term protection (eg school camps, etc) (NB. Could also use night nappy for this)
    - Don’t drink ½ hr before or after taking due to increased risk of cerebral oedema
**Urinary Tract Dilatation/Obstruction**
- DMSA is secreted by tubules + used to show scarring (see cold spot)
- DTPA (t = transport) is entirely filtered + used to show obstruction (Mag3 very similar to DTPA)

**Posterior Urethral Valves**
- = urethral stricture
- Commonly diagnosed antenatally
- Leads to bilateral urinary tract dilation + thick walled bladder; only seen in boys
- Prognosis depends on severity:
  - Poor prognosis = oligohydramnios (is seen as ↓ foetal pee is the driver for amniotic fluid production)
  - Potter’s syndrome = pulmonary hypoplasia if severe obstruction in utero (as ↓ amniotic fluid for lungs to ‘breathe’ and develop)
- Requires postnatal US + MCU + catheterisation if ureters dilated; Mag3/DTPA (NM) scan to show obstruction
- Most dilatation resolves but need to correct surgically (ablation of stricture) if ↓ function

**Vesicoureteral Reflux (VUR)**
- ~2% prevalence
- Related to tunnel length – ureters take a straight instead of an oblique course through bladder wall
- **Diagnosis**: MCU/US post first UTI +/- DMSA scan to assess renal scarring (s = scarring)
- Graded I-V (MCU) +/- scarring (DMSA scan)
- **Treatment**: prophylactic ABs +/- f/u (VUR often gets better as bladder grows). Reimplantation surgery if severe (grade V).
- Renal scars predispose to hypertension

**Testes**
- See also Male Genitourinary, page 337

**Undescended Testis**
- = Cryptorchidism (different to retractile testes)
- Descent complete in 96% at birth, in 99% at 3 months
- Premature will have ↑rate of undescended testis (5% at 1 year)
- Two types:
  - Arrest of descent: at internal or external ring, or at scrotal neck
  - Ectopic/maldescent: outside of the line of descent
- May present with a hernia
- Surgical correction (orchidopexy) at about 12 months
- If one testis + hypospadias → needs referral
- Sequelae of non-descent:  
  - 20 times risk of malignancy
  - ↓ fertility (due to higher temperature impairs spermatogenesis)
  - If don’t bring them down they may end up over the pubic ramus → very uncomfortable sex!

**No Testis/Testes**
- If bilateral undescended testes and hypospadias → ambiguous genitalia → urgent referral
- Torsion in uterus → no testis
- No testis = anorchia. May be no kidney on that side ⇒ check

**Retractile Testis**
- Normally in scrotum but retracts upwards during examination (ask if both are down when in bath)
- Testis normal size
- Follow-up 2 yearly
- Surgery unnecessary, will drop into scrotum at puberty
- May be fertility problems

**Hydrocele**
- Fluid collection between the visceral + parietal tunica vaginalis secondary to trauma, infection or idiopathic
- Implies a patent process vaginalis

*Health Care of the Elderly*
• May be bigger in the evening than in the morning
• Transilluminate, is non-tender and non-reducible, fluctuant
• Herniotomy if not resolved by age 2. 50% disappear in first year. Remove tunica vaginalis → removes potential space
• Predisposes to hernia
• Painless; if painful, implies hernia → refer

**Acute Scrotum**

• Must examine the genitalia of every boy who presents with acute lower abdominal pain or vomiting (may not localise to testis)
• In descending order of frequency, causes of an acute scrotum are:
  - Torsion of the appendix testis
  - Testicular torsion
  - Idiopathic scrotal oedema. Symmetric swelling, no testicular tenderness. May include penis, inguinal and perineal regions.
  - Rarely, epididymo-orchitis
• IX: urinalysis
• Management of torsion:
  - High probability: short duration and negative urinalysis → surgery
  - Low probability: longer duration and positive urinalysis → ?Doppler US for ↓blood flow
• Manual detorsion:
  - In patients with testicular torsion, the affected testis generally is twisted inward (medially), therefore detort = open like a book
  - With torsion of the left testis, hold the testicle with the right thumb and forefinger and then rotate the testicle clockwise 180 degrees. This manipulation may need to be repeated 2-3 times
  - For torsion of the right testicle, the procedure is similar except that the testicle is held using the left thumb and forefinger and the testicle is rotated in a counterclockwise direction

**Torsion of Appendix Testis**

• Most commonly caused by Hydatid of Morgagni (Mullerian duct remnant) at top of testis
• Peak incidence at 10 – 12 years. Oestrogen stimulates enlargement of the remnants → predisposes to torsion
• Symptoms range from minimal inflammation to florid, swollen hemi-scrotum indistinguishable from testicular torsion
• Urgent surgical referral

**Testicular Torsion**

• May not have pain in testis, sometimes only referred T10 pain (umbilicus) + tender testis
• US unreliable in pre-pubertal boys → surgery
• Testes are covered by tunica vaginalis – has parietal and visceral surface (like lungs in pleura)
• Testis rotates on its cord within parietal tunica vaginalis
• ? Bell-clapper deformity – congenital anomaly where long axis of testis oriented transversely, predisposes to torsion (TV attaches high)
• Once torsion has occurred in one, more likely in another
• <6 hours will probably not cause infarct
• Two peaks for incidence:
  - Neonatal: testis usually dead by diagnosis. May not operate (will atrophy). May ‘pex’ contralateral side to prevent torsion
  - Age 13 – 15: history and presentation variable. Surgical emergency. If testis viable, untwist and fix. Fix contra-lateral side
• Need to remove a torted testis, otherwise he will develop autoantibodies for spermatozoa → infertility of other testes

**Epididymo-Orchitis**

• Very rare in children. Two peaks:
  - Newborn, with underlying urinary tract anomaly. Do US and MCU. MSU to rule out infection
  - In 13+ due to reflux up the vas → infection/inflammation
• Mumps orchitis does not occur in pre-pubertal boys
Penis

- See also, page 340

Circumcision

- NB. Can cause decreased glans sensitivity in later life, therefore discourage

Smegma

- Yellowish coloured secretion-desquamation which occurs normally and keeps the foreskin separate from the glans
- May appear like a dermoid cyst underneath the skin
- Is normal, and will eventually extrude spontaneously

Retraction of the Foreskin

- By age three most boys foreskins will be able to be retracted (not before this time), nearly all by age 10
- May have intermittent pain during separation of the adhesions and the foreskin may be red or swollen for a day or two

Phimosis

- Irretractable, scarred foreskin with very little opening at tip. May balloon on urination
- If mild, application of Betnovate ointment (topical steroid) to the tight portion of the foreskin (retract loose bit to access) is effective
- If ongoing problems → circumcision (beware of circumcision in those with hypospadias – foreskin used in repair)

Paraphimosis

- Foreskin stuck behind glans (looks like circumcised) → swollen
- Always put foreskin back after catheterisation!

Balanitis

- Superficial infection of the foreskin, may remain distal or involve whole penile shaft
- Can be secondary to phimosis
- Treat with topical bactrim or oral antibiotics, circumcision only if recurrent

Hypospadias

- Lack of tissue at ventral end of penis
- Varies in severity:
  - 1. Dorsal hooded foreskin (deficient ventrally – shouldn’t be able to see tip of glans in normal boy)
  - 2. Recession of urethral opening
  - 3. Cordee (ventral penile tilt – bent penis when erect)
- May co-exist with intersex – bifid scrotum + severe hypospadias +/- gonadal asymmetry (check for testis)
- Correct at 9 – 12 months, using foreskin (therefore do not circumcise!)
- ↑ UTIs
- ↑ Infertility as the opening moves closer to the base of the penis

Ambiguous Genitalia

- Relative complexity of male differentiation → vulnerable to wide variety of incomplete masculinisation
- History and exam:
  - Exposure to progesterone, testosterone, phenytoin, aminoglutethamide
  - Previous neonatal deaths
  - Phallic size, position of urethral orifice, fused labia, descended gonads
- Don’t rely on appearances whenever babies have:
  - Bilateral cryptorchidism, even if there is a phallus
  - Unilateral cryptorchidism with hypospadias
  - Peno-scrotal or perineoscrotal hypospadias
- Causes:
  - Androgen resistance (extreme form: testicular feminisation):
    - XY, x-linked recessive condition
Loss of androgen receptor function means that, despite normal levels of androgen synthesis, the typical postreceptor events that mediate the effects of hormones on tissues do not occur. This results in the phenotype of prenatal undervirilization of external genitalia, absence of pubic and axillary hair, lack of acne, and absence of voice changes at puberty.

Early in boys’ development, Sertoli cells release anti-mullerian peptide → stops formation of the fallopian tubes, uterus and the upper 1/3 of the vagina.

Testosterone and dihydrotestosterone from Leydig cells responsible for the rest of male genitalia. If a problem in this pathway → girl with short vagina.

Present in puberty with primary amenorrhoea.

Adrenogenital syndrome/CAH:
- Incidence: 1 in 14,000
- Congenital adrenal hyperplasia: masculinised females
- ↑Androgenic hormones because of ↓21-hydroxylase, 11-hydroxylase or 3-B-hydroxysteroid dehydrogenase
- Can’t produce cortisol + aldosterone → adrenal hyperplasia → overproduction of cortisol precursors → ↑androgens
- Presentation: vomiting, dehydration and ambiguous genitalia. Hyponatraemia (with paradoxically high urine Na) and hyperkalaemia is common → may present with circulatory collapse in early life or hyponatraemic seizures (misdiagnosed as febrile convulsions).
- Boys may present with precious puberty or have ambiguous genitalia (reduced androgens in 17-hydroxylase deficiency).

Gastro-Intestinal
- See Appendicitis, page 247

Abdominal Radiology
- Should always be gas in the:
  1. Stomach. If not, then ask why. ?Oesophageal atresia without fistula to the bronchus. ?Too sick to swallow
  2. Rectum
  3. RLQ (caecum)
- Gas bubbles. If gas only seen in stomach:
  - Pyloric stenosis. Do US to confirm (not barium meal)
  - Duodenal atresia – “double bubble trouble”. Associated with Down’s. Antenatally: polyhydramnios (can’t swallow)
  - Jejunal atresia
  - Lots of bubbles but no normal caecal gas: ileal atresia (Colonic atresia very rare)
- Other signs:
  - Gas on both sides of bowel wall → wall stands out as opaque line → Rigler’s sign
  - Malrotation: wandering small bowel below duodenum with barium meal. If corkscrew then ?malrotation with volvulus
  - Pneumatosis Intestinalis: gas bubbles in intestinal wall (‘string of pearls’): if also in portal venous system (eg bubbles in liver) then necrotising enterocolitis

The Surgical Abdomen
- Only three important factors in the quick assessment:
  1. Distension
  2. Mass (e.g. sausage shape in intussusception)
  3. Bulge in groin (indicating herniae)
- If sick child + any of the above, insert NGT and suck, then refer

Appendicitis
- Pain can be localised, generalised, constant, or colicky
- Often see distension, tachycardia, dysuria

Non-Specific Pain
- Localised away from the midline
- Night pain
- Nausea + vomiting bile
• Should do an early US
• Potential causes = ureteric colic, chronic appendicitis, faecolith, intermittent torsion, crohn’s

**Congenital Abnormalities**

**Tongue Tie**
- Short lingual frenulum
- Rarely interferes with eating or speech
- Generally requires no treatment

**Oesophageal Atresia**
- Happens early in embryonic life:
  - Lots else happening then too – look for associations as well
  - Cardia, Renal, Anus, Vertebral, Oesophagus, Trachea: CRAVET
- Symptoms: dribbles all the time, can also see polyhydramnios antenatally, cough, choke
- Usually associated **tracheo-oesophageal fistula (TOF)** → air in stomach
- Urgent neonatal repair

**Pyloric Stenosis**
- = Hypertrophic pyloric stenosis
- 4:1 boys to girls. Males 1/200 – 1/400
- FHx: in 15% of siblings or previous generation
- Pathophysiology: **circular muscle hypertrophy** → progressive narrowing of pylorus
- Presentation: 3 – 6 weeks, initial spilling → progressive dysfunction → several days of **non-bilious** high volume projectile vomiting with or between feeds. Dryish nappies (from dehydration), still hungry
- Exam: peristaltic waves of exaggerated gastric peristalsis + **palpable lump in RUQ** (= pyloric tumour) when hips flexed and relaxed
- Test feed: immediately after a feed, mass can be seen/felt
- Differential:
  - Gastro-oesophageal reflux – but baby well and growing
  - Exclude infection: UTI, meningitis, gastroenteritis, chest infection
- Investigations: usually clinical diagnosis. Check electrolytes and blood gases for **hypochloraemic hypokalaemic alkalosis**
- Treatment:
  - Rehydration: IV saline + KCl + glucose prior to surgery
  - Surgery: pyloromyotomy

**Duodenal Atresia**
- Present in first 24 hours with bilious vomiting after feed
- Xray shows **double-bubble sign**: gas in stomach
- Associations: 1/3rd have **Down syndrome**; 10% of Down’s pts have duodenal atresia

**Small Bowel Atresia**
- E.g. duodenal atresia
- Due to loss of blood supply to that part of the gut in utero (this is the case for any atresia). Infarcts and heals (as opposed to after birth when bacteria → gangrene)
- Bowel distal to the obstruction may be malformed

**Malrotation**
- In 80% of cases, diagnosed in first month of life. Usually presents after 2 – 3 days with bilious vomiting
- Exclude: strangulated hernias, bowel obstruction secondary to adhesions, intussusception and sepsis
- Investigations: AXR, **urgent barium meal** → duodeno-jejunal junction hasn’t **ascended** to level of pylorus and **is not to the left of the midline**
- Pathogenesis: Dates from time when the midgut is in the umbilical cord. Failure of fusion (sygosis) of the small bowel mesentery to the posterior abdominal wall → narrow “**universal mesentery**” with the superior mesenteric artery supplying the whole mid-gut → predisposes to **volvulus** → mid-gut ischaemia (narrow mesentery allows twisting + rotation of gut)
- **Surgical emergency** as can lead to resection of large amounts of gut + short-gut syndrome
Meckel’s Diverticulum

- Most frequent congenital abnormality of the gut (2% of autopsied adults). Due to persistence of omphalomesenteric (vitilline) duct
- Illness of 2’s: incidence 2%, 2 feet from ileocaecal valve, symptomatic from 2 years onwards
- Wide mouthed diverticulum (approx 5 cm), on antimesenteric border of the ileum, usually within 100 cm of ileocaecal valve. 30% of the time ectopic tissue is opposite the diverticulum
- 50% have normal ileal mucosa, rest have duodenal, pancreatic, colonic or gastric (not subject to feedback → ulcers) mucosa

Symptoms:
- 40% of GI bleeds
- Maroon not melaena
- Intermittent
- ↓Hb but no shock
- 30% present with intussusception or band, 20% with diverticulitis like appendicitis, 5% with umbilical mass
- Meckel’s diverticulitis: blocked, inflamed → enlarged → burst
- Rarely symptomatic after age 5, but may →
  - Haemorrhage, before age 10, due to peptic ulceration of surrounding ileal mucosa
  - Inflammation, may mimic acute appendicitis
  - Obstruction in kids/teenagers: intussusception into lumen of bowel, or twist on fibrous remnant of the vitilline duct extending from bowel to abdominal wall (remnant of the yoke sac)

Diagnosis and treatment:
- Pertechnetate scan: looking for hot spot
- Diagnostic laparoscopy
- Treatment with laparotomy and end to end anastamosis

Meconium Ileus

- Tenacious meconium won’t shift, gets colonised and ↑gas
- See small bowel obstruction with ground glass appearance in bowel on AXR (meconium + gas)
- Use gastrografin to treat – contains a detergent that breaks up the thick meconium
- Often implies cystic fibrosis. See page 948

Hirschsprung’s Disease (Aganglionic Megacolon)

- Incidence: 1 in 3/5,000 live births. Boys four times girls. Familial tendency
- Aetiology: arrest in migration of ganglion cells from neural crest down GI tract
- Pathology:
  - Absent GI ganglion cells (co-ordinate motility of bowel – Meissner’s and Auerbach’s plexuses). Always includes internal anal sphincter and spreads proximally a variable length (50% to recto-sigmoid junction)
  - Affected colon can’t relax → greatly dilated proximal segment
  - Macroscopic: affected segment may look normal, proximal segment damaged mucosa, possible perforation, thickened wall
  - Microscopic: absence of normal ganglion cells (visible with acetyl cholinesterase stain) and hypertrophy of nerve fibres (non-specific – can occur with other conditions)

Clinical presentation:
- Age of presentation unrelated to length of affected segment. Eg someone with total colon affected can present after yrs
- See thin, ribbony poos
- 3 groups of kids:
  - Neonate: acute lower GI obstruction, abdominal distension, bilious vomiting, maybe fulminant diarrhoea, maybe perforation. Clue: no gas in rectum on x-ray
  - Infancy: constipation, abdominal distension possibly precipitated by change in bacterial flora on introducing other foods after exclusive breast-feeding (may → massive diarrhoea), faecal mass
  - Older: severe constipation, chronic abdominal distension, scybala (hard mass of faecal matter), failure to thrive, never soil pants

Diagnosis:
- Barium enema: narrow rectum, enlarged proximally. Usually rectum lumen twice the diameter of the colon. Don’t do an enema if risk of perforation (barium in the peritoneum → serious peritonitis)
- **Rectal manometry**: inflate balloon in rectum, distal rectum and internal anal sphincter should normally relax, this won’t
- **Rectal biopsy**: But finding ganglion cells is hard even in a normal specimen. Histochemistry – stain for ↑ACh (preganglionic nerve cells looking for ganglion cells)

**Imperforate Anus**
- In girls, often attaches into the posterior wall of the vagina – can have fistulae between rectovaginal fistula (girls) or rectovesical fistula (in boys)
- Adequacy of the levator sling depends on how high the lesion is. If low, only a superficial problem. If high (growth arrested above levator sling), then reconstruction is more difficult
- Look for other developmental abnormality: eg GU, vertebral, etc

**Gastrochisis/Omphalocoele**
- **Gastrochisis**: paraumbilical defect with evisceration (extrusion of viscera) of abdominal contents. Incidence 1.6/10,000. No covering. Usually only bowel hanging out. Usually no other defect. Corrective surgery has good outcome. Delivery in tertiary centre
- **Omphalocoele/exomphalos**: Herniation of abdominal contents (may include liver) into the base of the umbilical cord. Covered with peritoneum. Incidence 4.3/10,000. Other abnormalities often present

**Acquired Causes of Obstruction**
- In addition to congenital causes above (malrotation → volvulus, atresia, etc):
  - Hernias
  - **Adhesions** (always ask about previous surgery)
  - Intussusception
  - Volvulus

**Intussusception**
- Most common cause of BO in this age
- Peak incidence 3/6 months – 2 years
- Usually ileocolic
- Causes:
  - 95% idiopathic (although often due to lymphoid tissue inflammation secondary to a viral infection; can occur shortly after introduction to solids as mother’s milk contains Ig and this ↓ after solid intro, therefore more active lymphoid tissue)
  - 5% mechanical: intestinal polyp, Meckel’s diverticulum, lymphosarcoma (> 6 years old)
- Symptoms:
  - Often URTI 10 days before (→ adenovirus in Peyer’s patch)
  - Initial: severe abdominal colic every 15 – 30 minutes, very well in between
  - Later: red-currant jelly stools, prostration, pallor (shock)
- Exam: sausage-shaped mass → clinical diagnosis
- Treatment:
  - Hydrostatic reduction: air enema at 50% diastolic pressure. Not if small bowel obstruction or peritonitis
  - Surgery

**GI Bleeding**
- Causes:
  - Serious, life threatening bleeding rare: varices, stress ulcer, etc
  - **Serious disease** more common (the bleeding itself is not life-threatening):
    - Necrotising Enterocolitis (NEC)
    - Intussusception
    - Volvulus
    - Inflammatory bowel disease
    - Familial polyposis
  - Other differentials:
    - Meckel’s diverticulum
    - AV malformation
• Anal fissure

- History:
  - Is it really blood? Is baby vomiting mum’s blood (swallowed in delivery or cracked nipple), is it a UTI or PV blood not rectal?
  - Do they have a clotting problem? (Did they get vitamin K?)
  - How much, how fast?
- NB. blood is an irritant therefore passes through GIT very quickly

**Hernias**

**Inguinal Hernia**

- 4:1 male to female. 1% of boys
- Virtually all **indirect**. A widely **patent proximal processus vaginalis** allows bowel (and ovary in girls) to enter the inguinal canal
- 50% right, 25% left, 25% bilateral
- Do not resolve spontaneously
- If <1 more likely to present with strangulation

- **Can coexist with hydrocele** in boys; hydroceles are painless, therefore if boy with ‘painful hydrocele’ presents, suspect inguinal hernia

- **Presentation**: *intermittent swelling* overlying the external inguinal ring that has been noticed by a parent
- **Examine**: get baby to cry while feeling hernia orifices (to ↑ abdo P)
- **Incarcerated** (bowel loop stuck through):
  - Peak incidence in first year – main cause of obstruction. High index of suspicion in any child with abdominal distress
  - If neglected will strangulate – testes will die first due to ↓ venous return
- **Management**: Should be repaired ASAP.
  - 98% of acute or strangulated hernias can be reduced by taxis: manipulating it back in. Then fix electively (ie within a week)
  - If signs of ischaemic gut or peritonitis → surgery
- **Complications**:
  - Girls: fallopian tube + ovaries may be within the hernia. May tort. Care with surgery. Can completely close the internal ring
  - Boys: damage to vas or testicular atrophy if surgery while acute

**Umbilical Hernia**

- Rarely cause problems, even if large
- Repair at age 3 if haven’t resolved by then

**Congenital Diaphragmatic Hernia**

- 1:5,000 live births. 1:2,000 total births (⇒ lots of still births)
- Diaphragm should close just before midgut comes back from umbilicus but in DH the pleuroperitoneal fold fails to close. In this case, returning gut enters chest. Compromises ipsilateral lung development (more common on left) → **mediastinal shift and lung hypoplasia**

- Symptoms/signs:
  - Early respiratory distress/cyanosis
  - **Scaphoid** abdomen
  - Bowel sounds in chest
  - **Apparent dextrocardia** (diaphragmatic hernia most common cause)
- **Treatment**: *don’t bag the child* (or any with dextrocardia) → bagging blows up stomach and guts → compromises lung expansion further. Therefore, **ventilate and operate**. Can insert chest drain to inflate pleural space to stop mediastinum from moving quickly as hernia repaired.
- **Complications**: pulmonary hypertension in severe cases
- Overall survival of 40 – 60%

**Common Childhood Presenting Chronic Symptoms**

*My Child Won’t Eat*

- Often toddlers, in 2nd year of life (rate of growth drops off in 2nd year)
• Key issue: do they have normal growth (plot on growth chart):
  ➢ Normal growth (see Average Growth Parameters):
    o 1st year: go from 3.5 → 9 or 10 Kg
    o 2nd year: from 9 or 10 kg to 12.5 or 13 kg. i.e. Growth slows markedly
  ➢ Normal intake for first year:
    o 100 cal/kg/day
    o 150 mls fluid/kg/day
    o Breast milk has 67 cal/100 mls → 100 mls breast milk at 150 mls/kg gives 100 cal/kg
  ➢ If normal growth:
    o What are parent’s perceptions of amount the child does and should eat?
    o If perceptions not right then → stress, unhelpful dynamics around food (especially for strong-willed child) → parents give them lots of milk so they at least get something → iron deficient
  ➢ If not normal growth consider:
    o Are they constitutionally normally or abnormally small?
    o Disease/congenital syndromes/are they being offered enough (eg maternal depression/anorexia)?
    o See Average Growth Parameters, page 921

Reflux

• Symptoms: poor growth, vomiting/spilling, cry (especially after food), cough
• But:
  ➢ All babies have some reflux
  ➢ All babies cry – parents may not realise how much is normal! Reflux is a rare cause of crying
  ➢ Average baby peaks at 4 hours per day at 6 weeks, then declines. (is an association between crying + maternal depression)
• Diagnosis: can measure pH via NG tube over 24 hours, or scope them (only in Auckland). But most babies with presentation of reflux don’t have oesophagitis and therefore diagnostic tests not normally done
• If neuromuscular problems (eg Cerebral Palsy) then more likely to have problems with severe reflux oesophagitis
• Treatment:
  ➢ Gaviscon mixed with BM prior to feeds (thickens stomach contents)
  ➢ Antacids, ranitidine, omeprazole
  ➢ Crying decreases from 6 weeks – is this a treatment effect or normal development
  ➢ Ensure good support: wider family, Plunket, etc
• See The Crying Baby, page 921 for Colic

Abdominal Pain

• ‘Functional’ pain (no organic cause) is ‘benign’ (?children identify normal physiological processes as discomfort):
  ➢ Parents didn’t know until child said
  ➢ Distractible from it
  ➢ Central pain (point to umbilicus)
  ➢ No sleep or eating disturbance
  ➢ No associated symptoms
  ➢ Intermittent
• Organic causes mimicking functional pain:
  ➢ Constipation (parents may not be aware that child has problem with constipation)
  ➢ Abdominal migraine:
    o Migraine in 3 – 8 year old (but can be older than this) often presents as abdominal pain.
    o As they get older may develop into normal migraine. Check family history
    o The pain is moderate to severe and is felt in the midline of the abdomen, usually around the umbilicus, or poorly localised. The attacks of pain are usually accompanied by anorexia and nausea and about half of the patients will vomit with at least some attacks.
    o Intermittent, goes pale, last an hour or two, not distractible.
    o The pain is severe enough to interfere with normal daily activities and many children describe their mood during the attack as one of intense misery. The attacks are self limiting and resolve spontaneously and patients are completely well and symptom free between attacks.
  ➢ Always examine genitailia in a boy with acute abdominal pain
• Other causes: appendicitis, intussusception, UTI, testicular torsion, volvulus secondary to malrotation, Meckel’s diverticulitis, renal colic, pylonephritis, acute glomerulonephritis, drug ingestion, reflux oesophagitis
Other causes are rare without associated symptoms (eg coeliac, Crohn’s)

**Diarrhoea**

- Is growth normal?
  - Yes ⇒ no significant malabsorption:
    - Low grade infection, eg Giardia, Cryptosporidium
    - Diet, eg too much juice → overload sucrose absorption → osmotic diarrhoea
    - ‘Toddlers diarrhoea’: 18 – 24 months, sloppy poos 3 – 4 times a day. ?Variation of normal. Gets less messy/tiresome when toilet trained. Is a chronic non-specific diarrhoea seen in small children, between about one and four years. This condition accounts for a large proportion of children with chronic diarrhoea, but should be regarded as a **diagnosis of exclusion**
  - No:
    - Chronic infection: giardia, Cryptosporidium, parasites/worms
    - Immunosuppressed: any infection (eg Rotavirus, campylobacter etc) may become chronic
    - Coeliac: bloating, miserable, diarrhoea, signs of malabsorption
    - IBD: uncommon < 10 years. Abdominal pain, diarrhoea, blood in stool
    - Constipation → ?overflow diarrhoea

**Encopresis/Constipation**

- See also Constipation, page 263
- Definitions vary:
  - Mainly long term constipation/soiling pants, but may include inappropriate toileting behaviour (eg going on lounge floor!)
  - DSM definition = faecal soiling for >3/12 in a child >4 years with no underlying medical abnormality
- Epidemiology = 1-3% in 4-7 age group; boys > girls
- **Constipation is a feature in 95% of cases**; behavioural issues responsible for the rest
- Aetiology usually a combination of slow bowel, difficult toilet training, diet, toilet aversion, lack of activity
- The main issue is the **hardness of the stool**, not the frequency
- Pathogenesis:
  - Vicious cycle: constipation (sometimes starts with anal fissure or painful passage of poo leading to toilet aversion + worse constipation) → chronic dilation of rectum, sigmoid and descending colon → ↓sensation of fullness → go less often → faeces dry out more → hard → don’t completely evacuate → ↑distension → soiling/overflow diarrhoea (with no awareness)
  - Constipation is common post-gastroenteritis or after surgery
  - Can more rarely be due to food allergy
- History:
  - Need information from both parent and child. Perhaps ask child while you’re doing the exam – that way parents are off to one side. “I’m going to ask you some really silly questions about your poos…”
  - Soiling (HPC): when did it start?, frequency, severity, ever been continent
  - Normal bowel habits; associated constipation, withholding, absence of warning (likely), pain (eg fissure), associated wetting
  - Delayed meconium (?Hirschsprung’s)
  - Toileting behaviour: avoidance, motions in toilet rare
  - Diet history
  - Associated behaviours: hiding soiled underpants (common), scared of toilets at school, more serious conduct disorder (rare)
  - Parent’s management style: what’s been tried, punitive (unhelpful but common), supportive (ignore soiled pants, praise for toileting, not common but more helpful)
  - General developmental milestones
- Exam:
  - Inspection of perineum: situation of anus, dilated anus
  - Inspection of lumbar sacral area (spina bifida)
  - Neurological exam of the legs: (spina bifida), test ankle jerk (S1-2, anal reflex is S2-5)
  - Abdominal palpation: for palpable faeces
  - PR usually not necessary
- DDx:
  - NB. Need to rule out organic cause before diagnosing encopresis
  - Fissure: usually secondary to constipation → vicious cycle
  - Drugs: morphine, codeine, leukaemia drugs
**Hypothyroidism** (NB: associated with Down)
- Rare causes: Neuro probes eg *spina bifida*, *Hirschsprung’s* (ask about delayed passage of meconium), anorectal anomalies eg anal stenosis (often anal opening is more anterior)

**Management:**
- **Reassure** – common problem
- Explain *normal anatomy and function* of the rectum: as rectum fills with poo, signals to brain that need to poo, ball in your court from there
- **Explain process**: withholding stool → dilated rectum → loss of normal sensation → no warning its coming → he’s not being naughty and will take a while to come right (ie stick with treatment)
- Test transit time by eating a pile of whole kernel corn (Pringle test) and seeing how long it takes to come out the other end. The ideal is < 24 hours (if > than this, increase fibre)
- **Structured toileting programme**: diary and reward system for sitting at toilet (take a book if they’re bored) not for clean pants. *Toilet for 10 minutes after each meal*. Use timer
- Fibre and adequate fluids to keep stools soft
- **Laxatives** such as lactulose or movicol (special authority) (osmotic laxatives: are sugars, work by drawing more fluid into bowels) – often need a higher dose initially to clear out bowels and allow rectum size and therefore sensation to return to normal, then maintenance dose
- **Exercise**
- Treatment of severe constipation:
  - Use enemas to completely empty bowel – get visiting paediatric nurse to do it – easier on Mum and Dad
  - Laxatives every day to empty bowel (eg lactulose, magnesium sulphate) + regular toileting. Coloxyl drops (a stimulant) may → colic in kids. Lubricants (eg paraffin oil) are good but not very palatable
  - Continue for weeks/months until rectum normal size again
- Frequent visits for support of parents and encouragement of child

**Gastroenteritis**

**Differential of Acute Vomiting/Diarrhoea**

**Surgical conditions:**
- Appendicitis, intussusception, bowel obstruction, *Hirschspung’s* enterocolitis, pyloric stenosis, incarcerated inguinal hernia, testicular torsion
- Need to check for herniae
- Ask re bilious vomiting
- Is child sick? (see “when is my child really sick?”)
- If well but bilious vomiting, ?malrotation → needs urgent upper GI study

**Enteric infection:**
- **Virus**: *rotavirus* (45% of acute gastro), also enteric adenovirus, caliciviruses, astroviruses
- **Bacteria**: *Campylobacter*, *Salmonella* (more common spring/summer), also *Yersinia*, enterohaemorrhagic *E coli*, *shigella*
- **Protozoa**: giardia, cryptosporidia, also microsporidia, amoeba
- **Food poisoning**: (had anything different to eat from the rest of the family?) *Staphylococcus enterotoxin*, *bacillus cereus*, *Campylobacter*, *salmonella*, *E coli*, Norwalk virus
- **Systemic infection**: if sicker than history suggests then UTI, pneumonia, otitis media, meningitis, sepsis (including meningococcaemia)
- **Metabolic/other disorders:**
  - Diabetic ketoacidosis
  - Antibiotic associated diarrhoea
  - Haemolytic uraemic syndrome (renal failure, haemolytic anaemia and thrombocytopenia, eg due to *E Coli* verocytotoxin, also drugs, SLE, etc)
  - Poisoning

**Warning Signs**
- Seek urgent advice if any of:
  - Vomiting bile or blood
  - Severe abdominal pain
  - Toxic appearance (ie more than just gastro): lethargy, poor perfusion, hypo/hyper ventilation, cyanosis
  - Abdominal signs: distension, tenderness, guarding, mass, hepatomegaly
  - Failure to thrive
  - Neonate
Diagnostic Clues

- Sudden onset of fever, vomiting and watery diarrhoea: **viral gastroenteritis**
- Cramping abdominal pain and frequent bloody, mucousy stools: **bacterial gastroenteritis**. If an infant and severe pain or pallor, consider **intussusception**
- Colicky pain, RIF pain, bile stained vomiting and distension → **surgical case**
- Season: Rotavirus during winter epidemics, giardia and cryptosporidia during the spring and campylobacter in the summer

History

- **Vomiting**: bile, blood, coffee grounds, volume, frequency, total duration
- **Diarrhoea**: nature, colour, consistency, blood, mucus, frequency, volume, total duration
- Amount and type of recent **food and fluid intake**
- Urinary output (wet nappies)
- Other symptoms:
  - Fever
  - Abdominal, groin or scrotal pain
  - Urinary symptoms
  - Respiratory symptoms
  - Recent illness
- Other:
  - Antibiotics and other drugs
  - Infectious contacts
  - Possible contaminated food ingestion, including shellfish
  - Overseas travel in the last 2 months
  - Immunisation
  - Other medical conditions, GI, diabetes, heart or renal

Management

- Principles:
  - Dehydration is the most important complication. In infants it can appear in several hours
  - See Assessing Fluid Loss, page 990 for assessment of dehydration and rehydration
- Investigations:
  - Stool microbiology: Only if:
    - Blood in the stool
    - Recent overseas travel
    - Suspected epidemic or food poisoning
    - Child in an institution
    - Chronic diarrhoea (> 3 weeks)
  - Biochemistry: Na, K, Cr +/- glucose +/- ABG if severe, < 3 months, or on IV therapy
  - Other: urines, blood, and CSF culture, CXR, AXR, LFT etc if indicated
- Management:
  - Ambulatory if diagnosis not in doubt, family able to cope, have transport, no dehydration and good fluid intake
  - Admission if: diagnosis in doubt, < 3 months, high risk, dehydration, failure to improve, pre-existing condition (get sicker quicker: eg ileostomy, short gut, cyanotic heart disease, renal failure, diabetes, etc)
  - IV rehydration if: shocked, severely dehydrated, failed trial of oral therapy
- Treatment principles:
  - For a non-dehydrated child:
    - Small, frequent sips of Gastrolyte (doesn’t fix diarrhoea) – not for bloody dysentery (dehydration not the biggest concern). 5 – 7 ml/kg/hr
    - ½ strength formula feeds
    - Fruit juice diluted 1:4
  - Maintain nutrition: **Get back to solids within 6 – 12 hours if possible**: banana, apple, rice, potato, noodles, toast and vegemite
  - Breast-feeding is continued
  - Do not use anti-emetics nor anti-diarrhoeal agents
  - For a dehydrated child, see page 991
Lactose Intolerance

- Small bowel injury e.g. post infection → temporary lactose intolerance
- Most common in bottle feed babies <6 months. Uncommon in breast-fed babies.
- Clues are consistent fluid stools, or their restarting with reintroduction of milk feeds, excess flatus, perianal excoriation
- Testing: collect 5 drops of stool from a plastic lined nappy, mix with 10 drops of water and add a Clinitest tablet. Colour reaction of > ¾% indicates sugar is present
- Change to a lactose free formula for 3 – 4 weeks, then introduce the old feed over 2 – 3 days

Nutritional Deficiencies in Childhood

Iron Deficiency

- See Iron Deficiency Anaemia, page 460
- Commonest deficiency in NZ and worldwide
- Marker of poor diet generally
- Associated with:
  1. Inadequate iron intake:
     - Homogenised cows milk
     - Late introduction of iron-rich foods
     - Prolonged sole breast feeding (> 6 months)
  2. Intrauterine growth retardation and placental insufficiency (especially rapid catch up growth)
  3. Excess losses: chronic gut losses (eg infestation, food intolerance) and skin loss in severe ectopic eczema
- Sources of iron:
  - Poor sources:
    - Spinach: poorly absorbed
    - Cows milk: poor source and may lead to gut bleeding
    - Breast milk: only sufficient to 4 – 6 months, but ↑ absorption once food is introduced
  - Good sources:
    - Meat: haem iron well absorbed. Especially dark red meat (eg liver)
    - Pulses: lentils, peas, baked beans and soya beans (not green beans), but ↑ gas
    - Dark fish, shell fish and spices
  - Breast milk and vitamin C ↑ absorption
  - Cow's milk and tea ↓ absorption (NB some Polynesians call tea milo – so ask what sort of tea)

Anaemia:

- At birth, Hb = 170, several weeks later = 105
- Clinical effects: tired, lethargic, irritability, slow cell mediated immunity, pica (eat anything) which may → lead poisoning (small RBCs and anaemia)
- Diagnosis:
  - Look for pale earlobes
  - Blood tests, iron studies etc. MCV < 71 in child over 3 months
  - Ferritin low (but high if infection – test CRP as well and ignore ferritin if raised)
  - Serum iron – altered in presence of infection. Zinc Protoporphyrin is a new, sensitive test (Zn substituted for Fe in haem)
  - Reticulocyte count useful test of response to treatment. Should respond within a week
- Treatment:
  - Find and fix cause: if diet then → dietician.
  - Ferrous gluconate elixir: 50 mg/kg/day (= 6 mg/kg/day elemental iron) in 2 – 3 doses with fruit juice until MCV normal

Rickets

- See Parathyroid, page 145
- Usually a lack of Vitamin D. With fear of sunburn, it is likely to increase
- At risk:
  - Dark skin
  - Low dietary vitamin D intake
  - Low sunlight exposure
  - Breastfed children with other risk factors (breast milk is not a rich source)
  - Preterm infants with low Vitamin D intake
- Fat malabsorption
- Other rarer causes: anticonvulsant therapy, chronic renal disease, Ca or phosphate deficiency

**Diagnosis:**
- Clinical: broad wrists, tender joints, avoidance of weight bearing, bowed legs if weight bearing, bent pelvis (→ obstructed labour later in life), Rickety Rosary (swelling of costochondral junctions)
- Lab: ↑ALP, ↓PO4, Ca usually normal
- Xray: *widened metaphysis* and splaying of softened bones, generalised osteopenia

**Treatment:**
- 1-α cholecalciferol: 0.05 – 0.1 mcg/kg/day until ALP normal
- Surgery to bones not usually necessary, even when very bent

**Other Deficiencies**
- Breast Milk is short of:
  - Vitamin K (fat soluble). Deficiency → haemorrhagic disease of the new born in first few weeks/months
  - Vitamin B12: if mother is vegan → CNS symptoms (fits, abnormal movements, mental retardation) + macrocytic anaemia
- Chronic malabsorption or prolonged TPN → Zn deficiency → Acrodermatitis Enteropathica (rash, especially around buttocks) and immunodeficiency
- Vitamin A deficiency: from fat malabsorption or ↓intake → night blindness and ↑risk of complications from eg measles
- Folic Acid: Deficiency during pregnancy → ↑risk of neural tube defects

**Food Allergy**
- See also Allergy and Hypersensitivity Disorders, page 496
- Commonest in first years of life (gut less good at keeping allergens out)
- 5 – 6% of children cf 1 – 2 % of adults
- Commonest allergens: milk, eggs, peanuts, nuts
- Milk allergy **tends to go** by 2-3yrs, egg by 3-4yrs, and some peanut allergic pts may lose allergy (unlikely if >6yrs)
- Mechanisms include:
  - IgE mediated – rapid onset, due to mast cell activation and histamine release
  - May be delayed hypersensitivity
  - May involve gut-associated lymphatic tissue (GALT)
- Presentations:
  - Urticaria/angioedema:
    - “hives/swelling”
    - Rapid onset after contact with oral mucosa
    - Chronic urticaria rarely due to foods (except ?food colourings)
    - Confirmed by skin testing
      - IgE mediated
      - Small risk of future anaphylaxis (systemic reaction distant from contact point).
      - Risk factors for fatal outcome: Asthma, peanut/nut allergy
    - Treatment: **Adrenaline 0.01 ml/kg of 1:1000 im** (10 mcg/kg) [relatively safe im, compared with iv, where risks are tachycardia and arrhythmia so would only want to do in cardiogenic shock]
  - Atopic dermatitis/eczema:
    - Takes days to weeks following food exposure. Strong association between severe asthma and food allergy (60%)
    - Prick or patch testing may be of some help
  - GI symptoms:
    - May be at any point in the gut: oesophagus (reflux), stomach (vomiting), small bowel (colic, diarrhoea, malabsorption) to large bowel (diarrhoea, gas, bloody stools, mucus, constipation)
  - Anaphylaxis:
    - Systemic reaction at a site distant from contact point
    - Risk factors for fatal outcome = asthma, peanut/nut allergy, older child, delay in treatment
    - **Adrenaline 0.01ml/kg of 1:1000 im** (10mcg/kg)
  - Respiratory symptoms: much less common with foods. Asthma rarely due to foods
  - Oral allergy syndrome: pollen allergic individuals may get oral tingling/swelling after eating some fruits/vegetables
- GI symptoms after food may not be allergic at all:
Wind, pain, pallor, frothy stools seen after milk: lactose intolerance
Wind, pain, loose stools after fruit/ juice: fructose intolerance
Wind, pain, loose stools after artificial sweetener: sorbitol intolerance

Neck Lumps

Cervical Lumps
- 99% of general neck lumps are lymph nodes:
  - Large nodes can take up to 5 weeks for swelling to resolve, therefore watch and wait
  - Three types:
    - 1. Reactive hyperplasia: due to infection, not painful
    - 2. Acute lymphadenitis:
      - a. Acutely tender, erythematous mass with accompanying fever, usually settle with rest/analgesia
      - b. Results from URTI, cellulitis or other skin infections
      - c. Cervical lymphadenitis: S aureus or S pyogenes
      - d. Management: antibiotics (with flucloxac for staph cover) and/or drainage
  - Rare/persistent causes of lymph node enlargement (consider if subacute, minimal tenderness, fixed or overlying skin changes):
    - 1. Chronic reactive nodes
    - 2. Cat-scratch disease
    - 3. Toxoplasmosis
    - 4. Atypical Tb:
      - a. Submandibular, preauricular region
      - b. Collar stud abscess [multiple separated abscesses, connected]
      - c. Bruised looking [red-blue], no systemic symptoms, non-tender
      - d. 6 mths to 5 years
      - e. Specialised excision not drainage, Mantoux and chest x-ray
    - 5. Real TB
    - 6. Cancer: leukaemia; Hodgkin’s lymphoma: Child > 5, rapid enlargement, rubbery spherical lymph non-tender nodes, night sweats, fever, weight loss, lymphadenopathy elsewhere, splenomegaly

Surgical Lumps
- Lymphangiomas, haemangiomas
- Blocked branchial sinus/fistula
- Branchial cysts
- Ranula (sublingual gland cysts)

Malignant Nodes
- < 5 = leukaemia or neuroblastoma
- > 5 = lymphoma or leukaemia

Lateral Neck Lumps
- Branchial cysts and branchial sinuses (small sinus/pit at the anterior border of the sternocleidomastoid, can drain saliva, excise promptly whether discharging or not, no Ix needed)
- Preauricular sinus = small pit in front of ear; surgery if discharging; look for branchial abnormalities (eg sinus)
- Cystic hygroma = congenital lymphatic lesion classically found in left posterior neck triangle (transilluminates)

Midline Neck Swellings
- Thyroglossal cysts:
  - 80% of midline cervical lumps
  - Peaks in pre-school child and young adulthood
  - Swelling near the hyoid that moves with swallowing or when pokes tongue out
  - May transilluminate
  - Early referral: get it out before it becomes infected
  - Treatment: surgery and excision of the tract
- Submental nodes: Usually superficial and anterior. Check mouth for primary infection (eg ulcer)
- Dermoid cysts: Common at the corner of the eyebrow (external angular dermoid). In the cervical region they are subcutaneous and mobile, and appear yellowish. Require excision

Health Care of the Elderly 987
• **Ectopic thyroid**: Rare. May be only thyroid tissue. Tend to become hypothyroid

**Salivary Gland Swellings**

**Parotid Gland**
- Mumps
- **Sialectasis** (*duct inflammation* – periodic swelling)
- Infection
- Atypical TB
- Lymphangioma, haemangioma, rhabdomyosarcoma

**Submandibular Gland**
- Mumps
- Lymphatic tissue
- Atypical TB
- Dental abscess
- Duct calculus

**Sternocleidomastoid Tumour**
- = torticollis
- Hard lump in SCM of a baby
- Is an *inflammatory condition*, seen more commonly after forceps delivery
- 98% resolve on their own by 6/12
- Can see muscle shortening leading to restriction of shoulder movement + head tilt, important age for these changes = 12-18/12

**Tilted Head Differential Diagnosis**
- Shortened SCM as in SCM tumour
- Spinal abnormality
- Posterior fossa tumour (in conjunction with squint, nystagmus etc)

**Retropharyngeal Abscess**
- Sore throat
- Neck extended
- Drooling
- Swelling/abscess posterior triangle
- **DDx**: tonsillar abscess, epiglottitis, caustic ingestion, FB, perforation

**Diabetes in Children**
- See Diabetes Mellitus section

**Childhood Cancer**
- Cancer: **10% of childhood deaths**, most common cause of death after accidents ⇒ have high index of suspicion
- Incidence = ~ 15/10,000; around 150 cases in NZ/yr; is *increasing*
- Mortality rates are decreasing
- Distribution:

<table>
<thead>
<tr>
<th>Type</th>
<th>% of cancers</th>
</tr>
</thead>
<tbody>
<tr>
<td>ALL</td>
<td>23</td>
</tr>
<tr>
<td>CNS</td>
<td>21</td>
</tr>
<tr>
<td>Neuroblastoma (→chemo)</td>
<td>7</td>
</tr>
<tr>
<td>Non-Hodgkin’s Lymphoma</td>
<td>6</td>
</tr>
<tr>
<td>Wilm’s (Kidney)</td>
<td>6</td>
</tr>
<tr>
<td>Hodgkin’s Lymphoma</td>
<td>5</td>
</tr>
<tr>
<td>AML</td>
<td>4</td>
</tr>
<tr>
<td>Melanoma</td>
<td>2</td>
</tr>
</tbody>
</table>

• Signs and Symptoms:
- Often non-specific (eg fever, lymphadenopathy, bruising, anorexia, tiredness, localised pain, incidental abnormal FBC)
- Adult symptoms rare, eg epistaxis, dysphagia, non healing lesion, rectal bleeding, change in bowel habit
- Para-neoplastic syndromes are rare

**Headaches** warranting investigation. Headaches are common, but watch out for:
- Recurrent *morning* headaches
- One that wakes the child
- Intense and incapacitating
- Headaches that change in quality, frequency and pattern (eg getting more frequent)
- Focal signs or ataxia
- MRI more sensitive than CT

**Lymphadenopathy:**
- Common finding in cervical, axillary and inguinal chains. Usually < 1 cm
- Most enlarged nodes are due to infection
- Suspicious if found in mediastinum, posterior auricular, epitrochlear and supraclavicular

**Bone and joint pain:**
- Early symptoms rarely include pain – except in bone (bone cancer and malignancy)
- Usually no pathognomic signs on Xray → need biopsy

**Pancytopenia:**
- Common finding in ALL and AML
- Need neutrophil count specifically. ↑Lymphocytes may mask ↓neutrophils.
- From 6 months to puberty, anaemia is 110 g/L. 50% of leukaemia presents with Hb < 75 g/L
- Involvement of two or more lines → bone marrow evaluation

**Leukocytosis:** *Common in AML and ALL*. But count may get up to 50,000 with septicaemia and some viruses, also in Down syndrome and post-natal

**Presenting signs of cancer:**
- Recurrent bone pain, paleness, weight loss: leukaemia
- Morning headache with vomiting: brain tumour (usually a migraine)
- Lump in neck not responsive to antibiotics: Lymphoma
- White dot in new born eye: Retinoblastoma
- Proptosis (bulging eye): Leukaemia, neuroblastoma
- Swollen face and neck: lymphoma, leukaemia (compression of veins)
- Abdominal mass: Wilms, neuroblastoma, liver & spleen enlargement in leukaemia
- Cough, stridor, haemoptasis, Horner’s: Mediastinal tumour

**Neuroblastoma** = most common extracranial solid tumor in infancy. Embryonal malignancy of the sympathetic nervous system. Seen in sympathetic ganglia, adrenal medulla, and other sites

**Risk factors:**
- Ionising radiation → ALL, osteosarcoma
- Race → various types
- Genetics → eg Down syndrome → 20 x ↑ risk of ALL
- Infections → eg EBV → Burkitt lymphoma
- Cryptorchidism → malignant germ cell tumours
- Immunodeiciency → acquired, congenital, or therapeutic → NHL

**Diagnosis:**
- FBC/coags/blood film, tumour markers (only in neuroblastoma: catecholamine), imaging, bone scan, biopsy (NB lymph node FNA cannot rule out malignancy – need bx)
- Early dx = better prognosis

**Treatment:**
- Chemotherapy:
  - In combination to overcome drug resistance, to ↓ toxicity effects, for the synergistic/additive effects
  - In blocks/cycles in max tolerated dose; gives normal cells a chance to recover
- Surgery
- Radiation therapy
- Stem cell transplant – chemo wipes out all cells (is the cure) then SCT (is the rescue)
Emergency Management

Assessing Vital Signs

- Rate is always subservient to quality:
  - Thready pulse: eg palpable at neck and groin only
  - Respiration: more important than rate are grunting, flaring, subcostal retraction, use of accessory muscles (in neonate → bobbing of head)
- Blood volume:
  - Neonate: 90 ml/kg
  - Child: 80 ml/kg
  - Adult: 70 ml/kg
- In a trauma situation, guess the weight: (age + 4) * 2
- Urine output:
  - In nappies: 2 ml/kg/hr
  - Toilet trained: 1 ml/kg/hr
- Nutrition: to maintain weight need 75 calories/kg/day
- Heat loss:
  - 70 kg person: surface to mass ratio is 0.02
  - 2 kg person: surface to mass ratio is 0.08
  - Rate of heat loss is proportional to (body temp – room temp) to the power of 4. Best way to maintain body heat is therefore to heat the room.

Assessing Fluid State

- Only reliable indicator is pulse
- BP doesn't drop till severe dehydration (compared with adult where BP declines proportionately with losses)
- No physical signs until > 3% loss
- Most signs of dehydration are those of shock
- Change in body weight is the most accurate estimate of fluid loss – but is rarely available
- Dehydration in obese children is often under-estimated

<table>
<thead>
<tr>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td>Loss: total body weight</td>
<td>3 – 5%</td>
<td>6 – 9%</td>
</tr>
<tr>
<td>Mental state</td>
<td>Thirsty, alert</td>
<td>Thirsty, lethargic</td>
</tr>
<tr>
<td>Skin turgor</td>
<td>↓</td>
<td>↓↓</td>
</tr>
<tr>
<td>Mucus membranes</td>
<td>Dry</td>
<td>Very dry</td>
</tr>
<tr>
<td>Skin colour</td>
<td>Pale</td>
<td>Grey</td>
</tr>
<tr>
<td>Urine</td>
<td>Oliguria</td>
<td>Oliguria</td>
</tr>
<tr>
<td>Blood pressure</td>
<td>Normal</td>
<td>+/- Normal</td>
</tr>
<tr>
<td>Peripheral temperature</td>
<td>Cool</td>
<td>Cool</td>
</tr>
<tr>
<td>Pulse</td>
<td>+/- ↑</td>
<td>↑</td>
</tr>
<tr>
<td>Capillary refill</td>
<td>- / ↑</td>
<td>↑</td>
</tr>
</tbody>
</table>

Assessing turgor: pinched edge of skin goes down slowly. Do centrally on abdomen, chest, thighs

- Also when severe: rapid, sighing respirations (Kussmaul breathing)
- Poor predictors of dehydration: sunken eyes or anterior fontanelle, dry mucous membranes, absence of sweat or tears
- Principles of fluid replacement:
  - Replacement of deficit fluids + electrolytes
  - Provision of maintenance daily fluid + electrolytes
  - Replacement of ongoing losses
  - Resuscitation boluses

Fluid Replacement

- Use enteral route if possible (body can absorb what it wants from solution)
- Replacement fluids:
  - Orally, or by NG tube if necessary
  - Replace calculated losses over 6 hours (don’t worry about maintenance requirements). Hourly observations and reassess and reweigh after 6 hours
A child’s water deficit in mls can be calculated following an estimation of the degree of dehydration expressed as % of body weight.

- Deficit in ml = wt (kg) x % dehydrated x 10
- e.g. 1 = a 10kg child who is 5% dehydrated has a water deficit of 500mls i.e. 50ml/kg deficit
- e.g. 2 = 10kg child, 7.5% loss = 75ml/kg = 75 (i.e. 75ml/kg deficit) x 10 = 750ml; give over 6 hrs therefore 125ml/hr
- If cannot give oral/NGT fluids, then use the same calculation as above but give IV over 24 hrs (add to maintenance fluids)
- NB. WHO rehydration fluid = 1tsp salt, 1Tsp sugar, 1L water

Maintenance fluid requirements in absence of sweating (4–2–1 rule):

<table>
<thead>
<tr>
<th>Per hour</th>
<th>Per Day</th>
</tr>
</thead>
<tbody>
<tr>
<td>First 10 kg</td>
<td>4 ml/kg/hr</td>
</tr>
<tr>
<td>2nd 10 kg</td>
<td>2 ml/kg/hr</td>
</tr>
<tr>
<td>Each 10kg thereafter</td>
<td>1 ml/kg/hr</td>
</tr>
</tbody>
</table>

- Use ½ NS with 5% dextrose + 20mmol/L KCl
- Can give orally but use either breast milk, ½ strength formula or fruit juice:water (1:4)
- Need less fluid (i.e. 2/3 maintenance dose):
  - SIADH = brain: meningitis/HI; chest: bronchiolitis, pneumonia; sick children
  - CHF
  - Renal failure
  - Mechanical ventilation
- Need more fluid: ↑ losses (eg diabetes insipidus, d + v, fever, burns, drains etc)

Resuscitation fluids: **Initial bolus: 20 ml/kg normal saline** (or ringer’s lactate) stat, reassess and repeat if necessary

**Management of a Non-Dehydrated Child**
- If no or infrequent vomiting that is not interfering with fluid intake then 5 – 7 ml/kg/hour of:
  - Breast milk
  - ½ strength formula
  - Fruit juice 1 part in 4 with water
- After 6 – 12 hours introduce: bananas, rice, potato, parsnips, pumpkin, dry biscuits/toast with vegemite

**Management of Mild-Moderate Dehydration**
- Admit or observe in a short stay facility for several hours
- Don’t use home-made solutions – use Gastrolyte/Pediolyte
- Give replacement fluids (as above):
  - Orally, or by NG tube if necessary
  - Replace calculated losses over 6 hours (don’t worry about maintenance requirements). Hourly observations and reassess and reweigh after 6 hours
  - Deficit in ml = wt (kg) x % dehydrated x 10
- Give the remainder of the daily fluid maintenance over the next 18 hours
- Resume breast feeding as soon as rehydration is complete or sooner if this takes longer than 6-hours
- If after 4 – 6 hours the child remains dehydrated, then IV

**Management of Severe Dehydration**
- WEIGH THE CHILD to assess progress
- ABC (including IV/IO line) DEFG
- 3 stages:
  - 1. Resuscitation: initial bolus. **20 ml/kg normal saline** (or ringer’s lactate) stat, reassess and repeat if necessary
  - 2. Replacement + maintenance
  - 3. Maintenance only
- NB. take bloods for electrolytes + Cr prior to this

**Themes and Variations**
- Rehydration of isotonic dehydration:
  - Replacement: normal saline using rule as described above
  - Maintenance: using 4-2-1 rule, 1/2 normal saline + 5% Dextrose + 20 mmol/L KCl [Barts]
If initially shocked, do not add KCl until urine is passed. If they have ATN following shock (→ renal failure) don’t want to overload K
Also need to replace losses ml for ml eg NGT on suction
Timing:
- Infuse replacement fluid over 24 hours with the first 24 hours of maintenance using ongoing replacement: ½ normal saline + 2.5% dextrose + 10 mmol KCl (in 500 ml)
- Monitor electrolytes before, and during, up to 6 hourly
- Once they are able to tolerate oral fluids, treat as for mild/moderate dehydration

Rehydration of hypotraemic dehydration (serum Na < 130):
- Resulting from gut or renal losses, or excessive hypotonic fluid administration
- Appear more dehydrated than they are as fluid shifts into the ICF. Can → cerebral oedema, seizures, etc
- Never give 1/5th normal saline (except to keep vein open). Do serial Na measurements
- If asymptomatic: As for rehydration of isotonic dehydration, over 24 hours. Fluid restrict to 50% of maintenance
- If symptomatic (seizures, coma) or if severe (Na < 120) then give 5 – 10 ml/kg of 3% hypertonic saline IV over 60 – 120 minutes in addition to the calculated fluid requirements

Rehydration of hypernatraemic dehydration (eg serum Na > 150):
- Hypernatraemia → water shift from ICF → ECF
- Brain doesn’t like to lose fluids therefore brain cells ↑ their osmolarity by releasing osmoles, this protects against ICF → ECF shift
- This can become a problem when too rapid correction of dehydration leads to fluid shift from ECF → ICF → cerebral oedema
- Often the result of administering hyper-osmolar fluids (eg sports drinks) with vomiting and diarrhoea → greater water loss due to water sucked into GI from circulation then vomited/passed
- Will be more dehydrated than they appear due to fluid shifts from ICF → ECF
- If shocked give 10 ml/kg boluses of normal saline until circulation restored
- Calculate deficit
- Calculate ongoing requirements over 48 hours
- Give both over 48 hours – serum sodium should not fall faster than 0.5 mmol/hr
- If oral rehydration, replacement is over 24 hours

Diarrhoea:
- Lost Na, HCO3, Cl and K from GI mucosal cells – replace slowly
- Resuscitation with bolus of crystalloid, eg Ringer’s lactate, normal saline
- Maintenance with: ½ normal saline + 2.5% dextrose + 20 mmol/L KCL
- If persistent acidosis due to HCO3 loss or lactic acidosis (dehydration → poor peripheral perfusion → anaerobic metabolism → lactic acid) then add in HCO3

Diabetic ketoacidosis:
- If give insulin too fast, serum glucose will drop quickly → rapid change in ECF osmolality → cerebral oedema
- If giving hypotonic solution then ↑cerebral oedema – go slow

Notes:
- Be careful about measuring volume: never hang a bag straight into a child
- If lung or brain disease (eg meningitis), SIADH is common ⇒ may need to fluid restrict (eg to 50% maintenance fluids). Check serum Na regularly
- In a term baby, born water logged (ECF > ICF). Can pass 500 ml urine per day (7 ml/kg/hour). Handles water well but not used to passing a NaCl load
- Enemas for constipation can → dehydration
- If K+ high, monitor ECG
- Dehydration can lead to pre-renal renal failure therefore can see a Cr rise
- Na+ rises when more H2O than Na+ is lost (e.g. secretory diarrhoea)

Paediatric Coma
- Assessment: Coma scales – main function is to assess progress
  - AVPU scales (alert, voice, pain, unresponsive)
  - Glasgow scale (but designed for adults)
  - Child Coma scale
- General observation:
  - Alert states:
    - Fully alert (what this mean depends on age of child)
Confused
Delirium: agitated and confused

- Reduced alertness:
  - Lethargic: fails to maintain wakefulness without stimulation
  - Obtunded: drifts into sleep unless constantly woken
  - Stuporose: unconscious but withdraws to painful stimuli
  - Comatose: fails to respond. May be decorticate or decerebrate. At risk of airway failing

**Differential in children:**
- Hypoxic: respiratory or circulatory failure
- Epileptic seizures
- Trauma: intracranial haemorrhage, brain swelling
- Infections: meningitis, encephalitis
- Poisons
- Metabolic: Renal, hepatic failure, Reye’s syndrome, hypoglycaemia, diabetes, hypothermia, hypercapnea
- Vascular lesions: bleeding, AV malformations, arterial or venous thrombosis
- Hypertension

**Diagnosis:**
- Must be bilateral cortex or brainstem involvement
- Is it focal, multifocal or diffuse
- Is it getting better or worse
- Metabolic disturbances (including hypoxia and seizures) account for 90% of unconscious children
- Supratentorial mass lesions compressing the brain stem: 3rd nerve palsy and dilated pupil on same side – NOT 6th nerve palsy
- Subtentorial lesions affecting the brain stem directly: slow pulse, high BP, irregular breathing

**Management:**
- Stabilise vital functions: ABC then DEFG
- Complete history: esp trauma, poisoning, previous diseases – diabetes, epilepsy
- Exam: vital signs and progression, trauma, neck stiffness, CNS function, and:
  - Verbal responsiveness
  - Ocular responses: eye opening, papillary responses and spontaneous eye movement, ocular reflexes (eg Dolls eye)
  - Respiratory patterns: Cheyne Stokes (rate slows down, stops, restarts), irregular, apnoeas, stridor
  - Motor system: Motor responses, reflexes, tone, posture
- Investigations:
  - Blood: gases, electrolytes, glucose, FBC, LFT, ammonia, calcium, lactate, clotting factors
  - Urine: poisons, sugar, organic acids, ketones
  - Chest Xray, consider skeletal survey
  - ECG
  - CT Scan
  - LP only when safe: risk factors – prolonged fits, focal neuro signs, purpuric rash, CGS < 13, dilated pupils, reduced Dolls Eye, abnormal posture, signs of herniation, coagulation disorder, papilloedema, hypertension

**Paediatric Trauma**
- Most common cause of death < 14 years (way out in front)
- Under 1 year: cause of death – congenital abnormalities > infection > trauma
- Trauma = poisoning > suffocation > MVA
- What makes kids different:
  - Large, poorly supported head. Always land head first
  - Thin skin →↑evaporative skin losses and burn at a lower temperature
  - ↑Surface area: mass ratio →↑rate of heat loss
  - Relatively large, poorly attached spleen
  - Renal function, conserves water, secretes sodium
  - Greenstick fractures
  - Child abuse: differential diagnosis in all cases of trauma (do history and physical findings correlate)
- Dealing with children:
  - Never lie – say if it’s going to hurt
  - Kid that is injured will almost always have been injured doing something they were told not to do – child will consider you part of the punishment
Parents will get mad at you because they feel guilty. Wear it – this is not the time to deal with it
Child will regress
See When is a Child Really Sick?, page 891

Resuscitation

A and cervical spine
B
C including haemorrhage control: exsanguinating haemorrhage (if it’s not bleeding, ignore it)
D
E
Get help early

Airway and cervical spine immobilisation: Look/listen/feel

Assessment of both airway and breathing:
- NB. Upper airway obstruction – often see neck extended; lower airway obstruction – leaning forward
- NB. If child can talk sensibly – airway + breathing + circulation is generally OK
- Effort:
  - Airway noises eg grunting (air against a partially closed glottis to ↑ PEEP), stridor, wheeze, absent, sigh
  - WOB: recession, accessory muscle use
- Efficacy:
  - Pulse oximetry: cyanosis is seen between 80–90% O2 sats therefore oximetry helpful to know when to give O2
  - Need reasonable peripheral perfusion and a regular waveform
  - Give O2 when sats < 94%
  - Below 85% = dangerous
  - Effects of inadequate breathing:
  - HR = tachycardia to try and ↑ CO + therefore deliver more O2 to tissue; if severely hypoxic, can see bradycardia
  - Skin colour: peripheral vasoconstriction leads to cyanosis
  - Mental state: agitated → drowsy → coma

Management:
- Airway opening: jaw thrust
- Suction of foreign material under direct vision
- Airway devices:
  - Oropharyngeal/nasopharyngeal airways, ET tube, surgical airways.
  - Oropharyngeal: Right size: should reach from midline of lips to angle of the jaw. Use tongue depressor to help insert oropharyngeal (cf adult)
- Give O2 if sats <94%

Breathing:

Assessment: see above

Monitor:
- Work of breathing: rate, noises, recession, accessory use, grunting
- Effectiveness of breathing: breath sounds, chest expansion, SpO2
- If inadequate commence assisted ventilation

Indications for intubation:
- Inadequate O2 via bag mask
- Inability to protect airway (eg do they have gag reflex, muscle tone in jaw, etc)
- Prolonged ventilation required, or control required (eg in transport)
- Flail chest
- Inhalational burn injury

Intubating:
- If using sedating drugs, must be confident you can completely manage ventilation, do surgical airway if necessary, etc
- Pre-oxygenate if possible with high flow O2
- Need: working, correctly sized laryngoscope, suction, bag valve mask, syringe
- Take collar off to intubate
- Tube size = (age/4) + 4 (or size of kids little finger)
- Must secure tube or it will slide out
- Auscultate the chest to check air entry and check end-tidal CO2
Identify and treat life-threatening problems:
- Tension pneumothorax: ↓ sounds on affected side, trachea shifts to good side → needle decompression in 2nd intercostal space, midclavicular line, then chest drain. Little harm if they don’t have a pneumothorax.
- Open pneumothorax: 3 sided sealed dressing then chest drain
- Massive haemothorax: chest drain and cardiothoracic consult
- Flail chest: intubate and ventilate. Rare in kids as ribs too spongy – but can get very severe injury without breaking ribs
- Cardiac tamponade: Urgent cardiothoracic consult

Circulation:
- Circulatory failure caused by shock:
  - Hypovolemic
  - Obstructive
  - Cardiogenic
  - Distributive – blood diverted to other areas eg anaphylaxis
  - Dissociative – eg Hb not binding O2 due to poisoning (eg CO)

Assessment of cardiovascular signs:
- Heart rate:
  - Increased to ↑ CO, or with fever
  - Decreased in severe illness/myocardial hypoxia
  - Irregular – arrhythmia
- Pulse volume:
  - Compare central with peripheral
  - Bounding peripheral pulses seen in early sepsis + heart conditions
- BP:
  - Hypotension is a late sign therefore not hugely important
  - SBP = 80 + (age in years x 2); neonates SBP = 50-60mmHg
  - Central capillary refill, skin temperature:
  - Press 5s over sternal area; CRT should be <2s in a warm, well perfused child

Effects of circulatory problems on other organs:
- RR: ↑ in acidosis (shock → poor perfusion → anaerobic metabolism → metabolic (lactic) acidosis → ↑ RR); sighing respiration etc
- Skin colour/temp
- Mental state changes: agitated → drowsy → coma
- ↓ UO (NB. UO in infants = 1ml/kg/hr; 0.5ml/kg/hr in children)

Identify and treat life threatening problems:
- Shock
- Stop uncontrolled haemorrhage
- Stabilise pelvis

Initial management of shock:
- O2
- Large IV line placement. If can’t then intraosseous needle. 1 cm medial and distal to tibial tuberosity. Have to squeeze in fluid
- Crystallloid 20 mls/kg bolus. Reassess and repeat if needed. After that, warmed blood. After transfusion of > ½ blood volume then FPP.
- If still unstable consider blood and urgent surgical opinion
- Keep them warm

Disability – neurological (ie simplified coma scale):
- Neurological signs:
  - Altered conscious level:
  - AVPU (alert, responds to voice, to pain, unresponsive): P or U equates to GCS <8 + likely need for intubation
  - Modified GCS level (AVPU easier)
  - Posture:
    - D ecerebrate = arms + legs extended; implies BS level
    - Decorticate = arms flexed, legs extended; implies higher than BS
    - Opisthotonus = arched back, sign of meningism
    - Pupils + bulging fontanelles
    - Other: papilloedema, reflexes etc – do these after initial assessment
Effect of neurological failure on other organs:
  - RR:
    - Central hyperventilation
    - Cheyne-stokes ventilation
    - Apnoea
  - BP + pulse:
    - Cushing’s triad: cerebral oedema – pressure on the medulla leading to hypertension (to perfuse brain) and bradycardia

- Exposure:
  - Assessment:
    - Temperature
    - Rash: urticarial + angioedema (eg anaphylaxis); purpura/petichiae/bruising
  - Uncover to inspect for injuries
  - Keep warm and minimise embarrassment
- GLUCOSE: all severely injured children at risk of hypoglycaemia: check during primary survey
- Assessment:
  - Monitors: Pulse/BP/RR/SpO2/Temperature + EtCO2 if intubated
  - History taking: parents/ambulance crew/child, past medical history, medications, allergies, last meal
  - Blood tests: baseline FBC and U&Es, cross matching, glucose
  - X-rays: Trauma series – AP chest, AP pelvis, lateral C-spine. NB Soft bones are less likely to break despite strong force ⇒↑chance of internal organ damage in absence of breaks than in an adult (eg ribs)
  - Urinary catheterisation/nasogastric tube placement
  - Analgesia: morphine, 0.1 – 0.2 mg/kg IV (not IM)
  - NG tube to empty stomach: kids graze all day so stomach never empty. Also, swallow lots of gas when in pain →tube lets air out →↓risk of aspiration due to pressure in stomach and less pressure on thorax
- Then secondary survey: head to toe inspection

Traumatic Injury
- Head injury almost never causes shock
- Frequency of visceral injury: spleen > liver > kidney
- Splenectomy. The younger the child the greater the risk of fatal post-splenectomy sepsis (adults have greater previous antigenic exposure so less susceptible). Leave it in if vital signs stable
- Kidney trauma: most common injury is contusion ⇒mild haematuria
- Bladder: easily ruptured
- Closed head injury:
  - Full neuro exam
  - Level of consciousness: Awake, responds to Voice, to Pain, or is Unresponsive
  - Localising signs: can be very subtle, watch for changes
  - Pupils
  - Can rupture middle-meningeal artery without fracturing skull
- Pain management: early – consider regional blocks (eg femoral nerve block in fractured femur)

Car crash
- Without seat belt, risk of death is ↑10 times. All children being held in the front seat die
- Assessment of severity:
  - Speed of crash
  - Was seatbelt on
  - Was child thrown from car
  - Was any other child killed

Burns
- > 50 % of burn admissions are children
- Full thickness burns don’t hurt (nerves are dead)
- Partial thickness burns blister and heal
- Rule of 9’s doesn’t work – needs age adjustment
- Fluid resuscitation: Ringer’s 4ml/kg/% of burn (half in 1st 8 hours) + maintenance (ie pour it in till they urinate)
Paediatric Anaesthetics

*Pre-operative assessment of child with a URTI*

- Peri-operative risk variably increased
- Postpone high risk:
  - Neonates and infants
  - Existing upper airway/respiratory pathology (eg CF) - ↓ reserve – easy to tip over the edge
  - Systemic symptoms
  - Lower respiratory tract involvement
  - Surgical impact on respiratory function (eg upper abdo surgery)
- Complications usually manageable

*Pre-operative assessment of child with a murmur*

- Innocent murmurs often detected by anaesthetists
- Murmurs in up to 95%, but pathology in only 0.5%. May need referral for investigation
- 3 Common innocent murmurs:
  - Early systolic from ventricular outflow tracts (either pulmonary or aortic)
  - Continuous murmur from SVC
  - Grade 1 – 2
- Bad murmurs mimicking benign ones:
  - Severe hypertrophic obstructive cardiomyopathy
  - Critical aortic stenosis
  - These develop after birth – so may not have been picked up in post natal checks
- Postpone and refer if suspicious, esp if < 1 year
- ECG recommended if echo unavailable (can fax to a paediatric cardiologist for interpretation)
- SBE prophylaxis may be indicated

*Risk Factors for Aspiration*

- High risk for aspiration: Treat as full stomach
  - Full stomach
  - Regurgitation
  - Impaired protective reflexes
  - Airway obstruction (big negative pressure in thorax in order to suck air in past obstruction – but this also sucks contents out of stomach)
- Hazards of fasting:
  - Discomfort
  - Hypovolaemia. Guidelines are:
    - Clear fluids till 2 hours before
    - Breast milk till 4 hours before
    - Food till 6 hours before (no chewing gum)
  - Hypoglycaemia: only an issue for neonates

*Assessment for Sedation*

- Need to risk assess any child before any sort of sedation – its all too easy for something to go wrong (or more usually, for lots of little things to mount up)
- Always need to be confident you could ventilate, intubate and get IV access quickly if necessary

*Pain Management in Children*

- Myths:
  - Neonates don’t experience pain
  - Neonates have no memory of pain (they retract from a needle the 2nd time)
  - Pain is not harmful (it leads to stress response → ↓ healing, etc. ? Impact on the development of pain pathways)
  - It is dangerous to treat pain
- Management principles:
  - Mild to moderate pain relief is achieved through oral or rectal doses
  - Children hate needles, especially repeated IM injections
  - Using loading doses and regular maintenance doses to achieve therapeutic effect
  - Don’t overdose with paracetamol (may → hepatotoxicity). Limit duration
Child-friendly environment and parental involvement important

Available drugs:
- Paracetamol (oral better than rectal). Only use aspirin where specially indicated (eg Rheumatic fever)
- NSAIDs: Diclofenac, Ibuprofen, Naproxen
- Codeine Phosphate (metabolised to morphine): constipation, plus dose related opioid side-effects – sedation, respiratory depression, nausea and vomiting
- Morphine for serious pain (eg burns and fractures)
- Pethidine less used in kids – ↑toxicity (including seizures)
- Tramadol – not often used but less respiratory depression
- Nitrous Oxide (always administered with O2). OK for brief analgesia (eg fracture immobilisation). Ensure resuscitation equipment available. Mouth pieces preferred to masks

Child Abuse

Central Elements in Maltreatment
- Parent’s strong negative and irrational engagement with the child, featuring a distorted perception of the child
- Parent’s lack of ability to engage positively with the child
- Child is continually left in a state of worry or anxiety

Doctor’s Role
- Be suspicious!
- Recognise potential abuse
- Treat injury and medical follow-up
- Pregnancy prevention/STI treatment
- Referral to CYF/police
- Attention to behavioural consequences
- Take a thorough history and careful forensic examination
- Keep detailed records

General History
- History of injuries – how, who, when, where
- Note details of different caregivers, change over times, etc
- Clarify custody arrangements well
- Developmental history and growth
- PMH, especially previous injuries (do you need notes from hospital, other GPs etc)
- Social history: social situation, supports, domestic violence, other stresses, previous CYFS referral
- What are parent’s expectations of toddler behaviour, etc

Physical Abuse
- Non-accidental injury to a child or young person
- Includes: bruises, cuts, fractures, head injuries, injuries to internal organs, suffocation, poisoning, burns
- Risk factors:
  - Hard to parent child: eg disability or behaviourally difficult
  - Poor parenting skills/experience
  - Unrealistic expectations of the child
  - Poor mental health of the parents
  - Reduced social support
  - Alcohol or substance abuse
  - Domestic violence
  - History of child abuse in the abuser
  - Triggering event precipitating loss of control by the perpetrator
- Be suspicious when:
  - No history is given for the injury
  - The history changes
  - History is partial
  - Unbelievable explanation
  - Unreasonable delay in seeking help
  - Previous similar episodes
• Parents affect or behaviour is abnormal

• Questions to include in history taking:
  • When, where and how did the injury occur
  • What was the child doing at the time
  • Who saw it
  • What is the child’s developmental level
  • Is a scene examination necessary?

• Patterns of injury suggesting non-accidental injury:
  • Fractures: multiple sites or different ages, rib fractures, any fracture in a child < 2: consult radiologist. Look for missing teeth
  • Head injuries: any child < 1, unexplained coma, retinal haemorrhages (from shaking). Usually closed head injury rather than a fracture
  • Bruises: on face or back, non-mobile baby, fingertip pattern bruises, other pattern bruises (strap, belt), yellowing ⇒ older than 18 hours. If suspicious, referral immediately to a paediatrician (who can arrange for evidential photos to be taken). Tell mum you need to refer so they can be checked for other injuries
  • Burns: child will withdraw hand or foot before a burn is full thickness, pattern burns (eg held in hot bath, cigarette burns), burns on back

• Examination:
  • Observe attachment behaviours
  • Normal general assessment: growth, consciousness, play and behaviour, language
  • Careful full survey (get them naked!): looking for bruises, tenderness, acute abdomen (eg splenic rupture), genital bleeding (leave full genital exam for an expert)
  • Developmental assessment
  • Systems review – any other possible cause for the injuries
  • Document everything carefully, use a body chart and measure lesions, ask for explanation of each injury

• Investigations:
  • FBC and coagulation
  • Referral for specific investigations: X-ray (NB skeletal survey requires paediatrician approval prior to undertaking), ophthalmologist, ENT surgeon, CT
  • Consider urine toxicology

• Differential to physical abuse:
  • Bruising: mongolian spots, coagulopathies, coin rubbing
  • Cigarette burns: bites or vesicles
  • Hot fluid burns may be non-intentional
  • Fractures: osteogenesis imperfecta, spiral fractures of the tibia in toddlers

Sexual Abuse
  • NB. Consent + a support person are required for medical examination
  • Any act resulting in sexual exploitation of a child – whether consensual or not, including:
    • Non-contact abuse: exhibitionism, suggestive behaviours, exposure to pornography
    • Contact abuse: fondling, masturbation, oral sex, object or penis penetration

• Risk factors:
  • Family dysfunction
  • Female sex
  • Pre-adolescence
  • Previous victimisation: don’t think they’re worth it – won’t say no
  • Non-biological parent
  • Developmental delay: don’t understand, scared to say no

• Alleged perpetrators are all ages. If < 10 years, are they acting out abuse to them. 60% are family members

• History taking:
  • Evidential interview is the job of the police and CYPFS – usually videoed
  • If child discloses to a doctor, record questions and answers carefully. Don’t ask leading questions. Qualify notes with “the above history was taken in order to direct the exam and does not necessarily constitute a full or detailed history”. If not acute, leave questions for police

• Presentation:
  • Behavioural indicators: non-specific so don’t over interpret. They’re the same for anything that’s upset them, eg parents separating: sleep disturbance, change in appetite, regression, running away, fear (specific or generalise), anger, ↓concentration, sexualised behaviour
- Adolescence: self-harm, suicidal ideation, alcohol/drug abuse, eating disorders, unprotected consensual sex, promiscuity, school failure, loss of peer group

- Vaginal discharge in a pre-pubertal child is common:
  - Non-specific eg irritant/allergic
  - Infection: Gp A strep, shigella, Candida (uncommon once out of nappies)
  - Foreign bodies
  - Polyps
  - Systemic illness eg measles, chickenpox
  - Vulvar skin disease
  - Vaginal bleeding: accidental straddle injury, vaginitis, foreign body, precocious puberty

- Normal sexual development:
  - 0 – 2: genital exploration, masturbation (boys > girls), learning names
  - 3: talk about sexual differences, genital interest increases, masturbation common
  - 4: play doctors and nurses, mothers and fathers, games involving undressing, exhibitionist activities, demand privacy for themselves, interested in others bodies
  - 5 – 6 years: familiar with and has less interest in sexual differences, likely to be more modest
  - Sexualised behaviour:
    - Masturbation is normal, but inappropriate if older and still public
    - Sexual play: if > 5 shouldn’t be touching other genitals

- Physical findings in abuse:
  - > 50 % of disclosures will have no physical findings
  - Urgent forensic exam only if incident < 72 hours ago
  - Perpetrator usually doesn’t want to hurt the victim, otherwise won’t have continued access ⇒ physical injuries less common

- Investigations:
  - Pre-pubertal: don’t screen for STD’s unless symptomatic. HIV testing in time if high risk
  - Adolescents: screen for STDs and ?pregnancy test

- Prognosis: 25% have no adverse psychological sequelae. The more invasive the abuse, the more severe the effects long term

**Neglect**

- = Act or omission that results in impaired physical functioning or development, or injury.
- Includes physical neglect, neglectful supervision, medical neglect, abandonment, refusal to assume parental responsibility
- Risk factors:
  - Poor attachment
  - Parental psychiatric illness
  - Maternal depression
  - Isolated unsupported parent
  - Poverty
- Presentation:
  - Often associated with physical and emotional abuse
  - In an infant: failure to thrive, frequent attendance at A&E, severe nappy rash, unexplained bruising, cold injury, developmental delay, attachment disorder
  - Pre-schoolers: short stature, unkempt and dirty, delayed language, very disorganised play (eg aggressive and impulsive, indiscriminate friendliness)
  - School children: short stature, poor hygiene (including teeth), unkempt, learning difficulties, ↓self esteem, disordered/few relationships, unusual patterns of defecation or urination

**Emotional Abuse**

- = Act or omission that impairs the psychological, social, intellectual or emotional development of a child or young person.
- Includes: Rejection, isolation, oppression, deprivation of affection, inappropriate criticism, threats or humiliation, exposure to violence, involvement in illegal or anti-social activities, negative impact of substance abuse or mental/emotional condition of parent or caregiver
- Risk factors:
  - Poor attachment
  - Parental psychiatric illness
  - Maternal depression
Isolated unsupported parent
Parental alcohol and/or drug addiction
Domestic violence

Presentation:
- Socio-emotional indicators: cannot enjoy themselves, refuses to defend self, cheats, steals, bizarre or extreme behaviours, failure to accept responsibility for behaviour, low self-esteem, withdrawal, defiance, compulsivity, seeks love and acceptance outside the home, apathy
- Cognitive indicators: learning problems, short attention span, hypervigilance, hyperactivity, developmental delay, lack of curiosity
- Physical indicators: Failure to thrive, accident prone, self-destructive behaviour, eating disorders, GI and bowel problems, poor posture, sleep disorders, ↓energy

Differential: Munchausen’s by proxy

Management of Abuse
- Paramount principle: the interests, safety and well being of the child should be the paramount concern (Section 6, Children, Young Persons and Their Families Act)
- Doctor’s role is medical management, not the assessment of child abuse
- If child abuse is suspected:
  - Trust your instincts
  - Look for signs of abuse
  - Document the facts
  - Recognise and treat medical sequelae
  - Prevent pregnancy
  - Provide ongoing support, and watch for and help behavioural sequelae
  - Contact CYFS immediately and discuss your concerns (if you have good reason to suspect abuse/findings on examination). You cannot be guaranteed anonymity, but when reporting to CYFS or the police you are protected from court action if acting in good faith
  - Mother/other person can also contact CYFS [good approach if you consider this is really a custody issue or if you don’t actually find anything on examination. Alternatively advise the mother to get a lawyer]
  - There is no legal requirement to contact CYFS or to give a CYFS social worker information if they contact you. There is likely to be an ethical obligation, and referral guidelines will exist and should be followed.
- Investigation and management is multi-disciplinary: should involve paediatrician, social worker, police, psychologist
- If a child discloses abuse:
  - Listen to the child but do not interview them
  - Wellbeing of the child comes before the interests of any other person
  - Write down what the child says
  - Reassure them they’ve done the right thing
  - Tell them that they will get help – but don’t make promises. Say it’s got to stop but that you’ll need to tell someone else who will help
  - Tell your manager/supervisor as soon as possible
  - Look after yourself: discuss the matter with someone you trust
  - If nothing seems to be happening, contact CYFS again
  - Complete an ACC M45 form and forward to the Sensitive Claims Unit at ACC
- Care for mother: may be domestic violence, depression, addiction, etc
- Care for perpetrator: talk with intake social worker about help for them (eg violence prevention programmes)

Mental Health

Attention Deficit/Hyperactivity Disorder (ADHD)
- Background:
  - Estimates range from 2 – 5%
  - Boys > girls
  - 60% take some symptoms into adulthood (eg restless, disorganised, poor attention, impulse control)
  - Is strongly genetic and is biological (frontal lobe pathology, not well understood)
  - 3 key components:
    - Inattention
    - Impulsivity
    - Overactivity
Don’t necessarily have all of these components

**Diagnosis:**

- **Behaviour:**
  - **Inattention:** easily distracted, doesn’t finish tasks, works best with supervision, poor short-term memory. “How does he get on with daily tasks like dressing/eating breakfast/doing homework” “Do you ever have to stand over him to make sure he finishes”
  - **Impulsiveness:** acts without thinking, short fuse, aggressive, little self-control. “How often does he get into trouble for not thinking before he does something”
  - **Overactivity:** restless, fidgets. “How easy is it for him to sit still”
  - **Insatiability:** rarely satisfied, interrogates, over-intrudes in others space
  - Also poor co-ordination, disorganisation, fluctuation, and specific learning disabilities
  - Older child: low self esteem, mood swings, aggression, underachievement

- **Other information:**
  - Pervasive across at least 2 settings (eg home and school – important to speak with teacher)
  - Onset < 7 years
  - Impairs social and academic functioning
  - Hard to diagnose pre-school – tantrums and ↓ attention common. Issue is whether they mature on transition to school. Gap widens as they get older. A 6 year old should be able to complete tasks, concentrate, etc
  - Usually normal to high IQ
  - Diagnostic boundary is disputed – this falls on a continuum (like everything else!)

- **DDx:**
  - Specific learning disability (e.g. dyslexia) → not coping at school, frustrated → acting out
  - Gifted child who is bored
  - ASD
  - Organic problem: hyperthyroidism, sleep/hearing problem, absence seizures, **fetal alcohol syndrome**
  - Psychosocial stress: disruption at home, abuse
  - ODD: oppositional defiance disorder (oppositional + defiant!; stubborn + negative; RF for depression)
  - Conduct disorder (juvenile delinquency; see predatory aggression, fire starting, stealing; precursor for antisocial personality disorder)
  - Anxiety disorder (recent change in social situation, unrealistic/excessive worry, restless, difficulty concentrating etc etc)
  - Problems with parenting – no boundaries or inconsistent boundaries

- **Associated factors:**
  - Lower socio-economic status: poverty, poor housing, unemployment, illness, family breakdown
  - Childhood depression/anxiety → ↓ concentration
  - Auditory/visual perceptual difficulties → inattention, lose interest
  - Reading problems: visual sequencing, letter-word orientation → appears inattentive

- **Assessment:**
  - When was the onset of behaviours?
  - Situation specific or pervasive? i.e. home and school?
  - Other learning difficulties
  - Context: parents **management style**, life events, teacher, etc
  - What are child’s strengths? – basis of self esteem
  - Get information from teacher: general behaviour, problems in specific situations (transitions between lessons, unstructured time eg playground, changes to routines eg outings, academic problems
  - Thorough developmental history (HABE WIMP MAFS), especially:
    - Head injury
    - Perinatal problems
    - Attachment problems in first 2 years (eg PND, stresses, violence, drugs)
  - Exam:
    - Dymsorphic features
    - Tics (more common in ADHD and also side-effect of ADHD medication)
    - Observation during interview
    - Hearing and vision

- **Classifications:**
  - Primary: early onset, feeding/sleeping problems from early on, overactive/unmanageable toddler, parents exhausted
  - Secondary:
Psychosocial causes: family disruption, demands of school, etc
Specific learning disability (→ ↑stress once school starts)

- Mixed: an adolescent presenting with all of the above, plus ↓self-esteem

- Management:
  - See Behaviour Management, page 895
  - Multidisciplinary assessment
  - Behaviour strategies:
    - Use RAIDER:
      - Remove (time out)
      - Anticipate/avoid situations where conflict is likely
      - Ignore minor things, particularly tantrums
      - Distract
      - Example (set a good one!)
      - Reward acceptable/wanted behaviour
    - Clear, firm, consistent guidelines
    - Check understanding of instructions
    - Anticipate problems and have planned responses ready → ↓parental stress and ↑consistency
    - Avoid triggers (eg crowds)
    - Predictable routines (eg at bedtime)
    - Managed use of time out, withdrawal of privileges
    - At school:
      - Structured approach – plan day
      - Sit near teacher, between quieter kids
      - Brief, clear instructions
      - Supervision during transition times (coming in from breaks, etc)
    - At home:
      - Force leads to confrontation, resentment, broken relationships
      - Behavioural techniques work poorly – it’s a biological problem
      - Ignore all but the important misbehaviours. Have a few clear rules, with clear consequences, if broken act without argument. Don’t debate or escalate
    - Esteem: Encourage. Find something they are good at. Swimming, bike riding, cooking, judo and computers may be better than team sports. Encourage friendships – take a friend on outings
    - Diet: < 10% sensitive to synthetic food colouring
    - Many dodgy therapies: avoid unless proven

- Stimulant medication (this is the most effective option):
  - Ritalin stimulates CNS activity by blocking the reuptake of and therefore ↑conc of NA + DA
  - 75%-90% have a marked positive response
  - → Concentrate for longer (stimulates inhibition) → complete tasks → less disruptive and ↑self-esteem
  - First: education for child and parents:
    - “Have you heard about medication for ADHD – what?”
    - Address common myths:
      - They’re addictive
      - They sedate the child
      - Child at ↑ risk of substance abuse later in life
  - Side effects:
    - Sleep disturbance
    - Appetite suppression (small effect, if marked → growth suppression)
    - Moodiness
    - Rebound (when dose has worn off)
    - Tics
  - First line options are Methylphenidate (Ritalin) or Dexamphetamine.
  - Both require specialist endorsement. Introduce slowly.
  - Short T½ ⇒ need to fine tune dose times. Eg give before school → Ok at school but difficult by the time they get home.
  - There are standard (4hr), slow release (6hr), and long acting (10-12hr) forms
  - Not in evening otherwise ↓sleep
  - Review with parents/school – should have noticeable improvement, if not re-evaluate and consider ↑dose or changing to dexamphetamine

- Referral if:
Diagnosis/differential in doubt
Assistance with management of challenging behaviour
Assessment of role of family relationships in perpetuating the problems

**Anxiety Disorders**
- See also Anxiety Disorders, page 700
- Fears are normal during childhood and adolescence:
  - Age 1 – 2: fear of separation from parents
  - Young child: scared of the dark, animals, storms, monsters
  - Age 7 – 8: begin to worry about their performance
  - Adolescents: concern about being disliked, rejected, or criticised by their peers
  - Fears generally reflect developmental stage
- Anxiety disorder:
  - Fears become intense or pervasive and substantially impair functioning
  - Can follow chronic, fluctuating course
  - Not easy to recognise as young people often know that their fears are groundless and feel ashamed of what they think is a flaw in their character
- Anxiety disorders: Separation anxiety disorder, social phobia, generalised anxiety disorder, obsessive compulsive disorder, post-traumatic stress disorder

**Separation Anxiety Disorder**
- Child very anxious away from home or from their parents
- May present with:
  - Refusal to attend school – but school’s not the problem, the separation is
  - Feeling physically ill in the morning. Monday’s the worst day
  - Reluctance to sleep at friends places, school camps, etc
  - Worried that harm will befall their parents while they’re away
  - Difficulty coping with parents going out
  - Difficulty going off to sleep, or needing company of a parent while they do
- History should include:
  - School: problems, bullying, fears, etc
  - Home: stressors, conflicts
  - Maternal depression, anxiety, adjustment disorder, etc
  - Parents may have some insight – but usually underestimate the severity of the maternal-child dependence and are very defensive
- Diagnosis: irrational fear of harm to parents or that they will be abandoned by them
- Differential for school non-attendance:
  - Truancy, conduct disorder: doesn’t go to school – but doesn’t stay at home either
  - Anxiety-based refusal
  - Major depression: lacks motivation
  - Other reasons: at home to help with work, etc
- Epidemiology: F > M. Peaks in early adolescence
- Course:
  - May be triggered by a worrying or traumatic incident. May be family history of anxiety problems
  - Eventually become isolated from friends and get behind at school. Feel embarrassed and different. ↓Self esteem. All makes returning to school more difficult
  - Prognosis depends on the young person, family strengths and severity
  - Increased risk of agoraphobia in adulthood
- Management:
  - Support for parents and child
  - Quick return to school before problem becomes entrenched, even if only for a small portion of the day
  - Education for child and parent. Facing the fear is initially distressing but reduces the anxiety, avoidance increases it
  - Parents need to be consistent in their commitment to return the child to school
  - Involve school teachers (eg meet at gate, etc). Problem is actual separation – once settled into the day problem is likely to reduce
  - Severe or chronic → referral. Support for parents if they’re having difficulties. SES Behaviour Support Teams or Resource Teachers for Learning and Behaviour (RTLBs) for child.
  - No place for medication unless underlying conditions
Bullying

- An act of aggression/harassment by a child/youth
- Starts mid-primary, peaks 3rd form, nearly gone by 7th form
- Typical bullying behaviour: boys hit, girls tease and exclude
- Teachers generally under-estimate bullying
- Characteristics of someone who is bullied:
  - Something different: high achiever, less physically attractive, etc
  - Vulnerable: more anxious, cry easily, don’t fight back
- Problem compounded for the bullied in that no one wants to be friends with a person who is bullied → ↑ isolation. Standing up to a bully is pretty sophisticated behaviour in early teens – not developmentally consistent with wanting to identify with the peer group
- Long term outcomes worse for the bully than for the bullied

Depression

- See also Mood Disorders, page 709
- Mood disorders are prevalent and serious disorders in children and adolescents. Leads to difficulties at school and in social relationships
- 1 year prevalence estimated as high as 10%
- Same diagnostic criteria as for adult – but diagnosis harder. More likely to present with separation anxiety, phobias, somatic complaints and behaviour issues. More likely to talk of profound boredom and feeling unloved and lonely than appetite and sleep change
- Diagnostic criteria = depressed mood, diminished pleasure, weight change, insomnia, fatigue, worthlessness, decreased concentration, suicidal thoughts
- Most do recover, but recurrence is more common than in adults
- Clinical approach:
  - See the teen on their own
  - Observe: ↓ energy, anxiety, anger, shame, variability in affect
  - Listen: the teen is more likely to talk if they feel they are being heard
  - Consider differentials:
    - Depression
    - Drug abuse
    - Eating disorder
    - Psychosis (actual or prodrome)
    - Medical eg hypothyroid etc
  - Suicide assessment
- Aetiological factors to consider:
  - Do HEEADSSSSS assessment
  - Family context
  - Cultural context: are they comfortable about who they are in a cultural sense
  - Peer group: Have they friends, how do they support him/her?
  - School: bullying, what’s hard at school, current stressors
  - Life events: losses, abuse
  - Psychological: negative ways of thinking, learned helplessness
- Advantages of diagnosing depression = validates concerns, informs people that this is common, gives clues as to prognosis, lets them know that is an actual illness, can get the right help
- Disadvantages of diagnosis = stigma, carries a sense of inevitability – believing things cannot be changed etc, stereotyping
- Treatment involves the child, parents and school. Aim is to shorten the episode. Should be individualised. Treatment can include:
  - Education
  - Counselling: for milder depression, no remediable family factors, recent life events, if they want it
  - CBT
  - Family therapy
  - A range of individual therapy types – usually through referral
  - Medication:
    - Less evidence of effectiveness in adolescents but still an excellent option – probably, in combo with CBT, the best treatment
    - Use SSRIs – black box warning = ↑ discussions about suicide but no actual ↑ in carrying this out
Health Care of the Elderly

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- Need to follow up closely and ask about suicidal ideation
- Takes at least 2/52 to see effect and 6/52 for maximal effect
- Consider discussion with a psychiatrist

- Referral when:
  - Significant suicide risk
  - Possible psychosis
  - Abuse
  - Severe family discord
  - Failure to improve

Youth Suicide

- See also Suicide Assessment and Management, page 693
- Epidemiology:
  - Second only to MVA as cause of death – but still uncommon.
  - 3 fold rise in last 30 years.
  - Females attempt, males succeed
  - Second highest rate for 15-24, Finland higher
- Postulated factors contributing to increase:
  - ↑Depression and substance abuse
  - Unemployment
  - ↑Isolation and alienation
- Key issue: identifying those at risk
- Risk factors:
  - Male gender
  - Psychiatric illness: depression (most common association), alcohol or substance abuse, personality disorder, psychosis
  - Previous suicide attempts
  - Available means: firearms, toxic medications
  - Social adversity: recent interpersonal loss, homelessness, school failure or drop-out, family or relationship problems, unemployment
  - Recent exposure to suicide
- Most common presentations are over-dose, self-poisoning and lacerations
- Management:
  - Treat underlying psychiatric disorder (not TCAs – too lethal in overdose. Use SSRIs)
  - Reduce ongoing stress: counselling to reduce interpersonal conflict
  - Promote social supports
  - Liaise with specialist health services

Other Mental Health Issues

- Eating disorders: See Eating Disorders, page 754
- Substance Abuse:
  - Drug and alcohol use prevalent
  - Often comorbidity
- Sexual maturation: sexual behaviours, orientation, attitudes to sex and relationships, awareness of socially defined roles. Knowledge about pregnancy and STIs doesn’t automatically translate into behaviours
- Risk taking behaviour:
  - Adolescence is a time of experimentation, pushing boundaries
  - Contributing factors: ignorance, impulsiveness, cognitive immaturity (sense of omnipotence and poor comprehension of long term consequences), peer groups, drugs and alcohol

Adolescent Health

Definition of Adolescence

- Developmental period between childhood and adulthood
- WHO definitions:
  - Adolescents: 10 – 19
  - Youth: 15 – 24
  - 10 – 24: Young people
Demographics
- Young people are the only age group whose health status has not improved in the last 40 years
- Current issues:
  - Accidents and injuries
  - Mental health issues
  - Health risk behaviours: smoking, alcohol, drugs, sex
  - Chronic illness: eg obesity, asthma, diabetes, etc
- Access to health services for adolescents fragmented – fall between child and adult services

Adolescent Development
- Also see Cognitive Development, page 903
- Summary:
  - An age of transition
  - Experimentation and change: inherent risk taking
  - Behaviours reflect maturational tasks
  - May use maladaptive behaviours to achieve developmental goals (eg smoking to gain peer acceptance).
- Physiological:
  - Puberty: highly variable – generally from 9 – 14 years. Can take 2 – 5 years to complete
  - Gain 25 cm in height, 50% of ideal adult body weight
- Stages of adolescence:
  - Early: coming to terms with body/biological changes
  - Middle: establishing self among peers as a worthwhile individual
  - Late: vocational/education direction and one-to-one intimate relationships
- Developmental issues:
  - Lack of forward planning/abstract reasoning - inability to conceptualise consequences
  - Preoccupied with their own thinking
  - Peer group membership and conformity important
  - Consolidation of self-image and identity
- Psychosocial:
  - Who am I and where do I fit in
  - Identity: self, culture, ethnicity, sexuality
  - Autonomy vs relatedness/connectedness
  - Goals and future direction
- Developmental tasks of adolescence:

<table>
<thead>
<tr>
<th>Tasks</th>
<th>Early: 10 – 13 years</th>
<th>Mid: 14 – 16 years</th>
<th>Late: 17 – 21 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Psychological tasks</td>
<td>Separates from parents: questions, tests</td>
<td>Separation creates anxieties, ambivalence as retreats to family</td>
<td>Comfortable away from home, able to return for counsel without shame</td>
</tr>
<tr>
<td></td>
<td>Adjust to dramatic changes in body</td>
<td>Try on images to find real self (incl. Sexual identity), attempts to improve image</td>
<td>Satisfied with realistic body image</td>
</tr>
<tr>
<td></td>
<td>Constant comparisons</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sexual drives</td>
<td>Marked sexual curiosity, masturbation</td>
<td>Sexual experimentation, narcissistic sexual relationships</td>
<td>Beginnings of intimacy and caring</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Social Tasks</td>
<td>Boys ‘gangs’, girls ‘best friends’. Crushes on adults</td>
<td>Other sex friendships, dating, try on other philosophies and beliefs</td>
<td>Individual relationships more important than group, ↑ intensity of relationships</td>
</tr>
<tr>
<td>Relationships</td>
<td>Vague, unrealistic</td>
<td>↑Efforts but influenced by ‘escape’ from home, glamorousness of career</td>
<td>Hard decisions →occupational identity. Delayed by higher education</td>
</tr>
<tr>
<td>Career plans</td>
<td>Concrete, literal, limited abstraction</td>
<td>Formal operations; use abstractions (what if...), introspection, less literal</td>
<td>Mature abstractions, problem-solving &amp; self-reflection</td>
</tr>
<tr>
<td>Cognition</td>
<td>Need to follow rules of peer group or family</td>
<td>Narcissistic: feels good or is what I want →right →impulsiveness</td>
<td>Idealism, rigid standards of right and wrong, intolerance</td>
</tr>
<tr>
<td>Moral Growth/Values</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Health Care of the Elderly
Talking with Adolescents

- Keys to effective intervention:
  - A positive relationship
  - Thorough assessment
  - Inclusive of family and young person
  - Plans made with the young person and family

- Building a trusting relationship: introductions
  - Friendly, confident welcome but still professional
  - Introduce yourself directly to the teen, ‘And is this your mum?’
  - Clear introductions: yourself, your role, what you’ll be doing and why
  - Clear boundaries: explain that you see young people alone and with family
    - ‘You’re on your way to being an adult. Want to support that process. But your parents also still have a role’
    - ‘I want to talk about confidentiality. Do you know what that means? Want to keep your information private’
    - ‘There are 3 things I can’t keep a secret: if someone’s harming you, if you’re harming yourself or if you’re harming someone else. I need to do something about it – but will tell you what I’m doing’
    - ‘OR: “what we talk about today is just between you and me and these four walls – I won’t tell anyone else unless…”’
  - Outline confidentiality:
    - ‘Consider what you put in notes (they get around). Use standardised abbreviations.’

- If adolescent doesn’t want you to tell parents (and you think it’s in adolescents best interests for them to know):
  - ‘Why doesn’t teen want parents to know (‘You seem worried about your parents knowing this. Can you tell me about that?’)
  - ‘Attempt to persuade the teen to tell her parents
  - ‘Offer to tell them yourself’

- Keys to building the relationship:
  - Be keen to get to know this young person now
  - Accepting atmosphere
  - Respect
  - Non-threatening explanations
  - Give adolescent some control – encourage normal independence
  - Reveal hidden agendas
  - Give them time to talk – hold off asking questions
  - Make plans with the young person and family
  - ‘If they don’t want to talk, probably anxious/frightened. “It seems you’re pretty angry about being here. Did someone make you come?”’

- Communication:
  - Use language that is understood (no medical or adult jargon). Check understanding
  - Listen
  - Move from less sensitive to more sensitive topics
  - Move from third person approach to the personal

- Set clear boundaries: It is appropriate to identify what is and is not acceptable behaviour (eg creating risk of harm to themselves or others). Middle adolescents still require the security of clear boundaries. However, try not to be judgemental

- Telling an adolescent not to do something often doesn’t work
  - ‘They often interpret this as, “they think I will do this”
  - ‘Like being “told off for something I’m not doing so may as well do it anyway”
  - ‘Talk to adolescents as if you believe in them and have high expectations of them

- Beware:
  - Transference: person projects their feelings about someone else (eg parents) onto you
  - Counter-transference: You transfer feelings appropriate to someone else (eg your own kids) onto the adolescent (eg act as though you were their parent)
  - ‘Objectivity: understand the most likely reason they won’t talk is that they’re frightened’
SHEEADSSSS Risk Assessment

- Gives an overview of this individuals risk and resiliency
- Use this tool to emphasise positive and protective factors instead of just focusing on the negative risk factors
- A lot of risk factors are hard/impossible to change (eg age, gender, personality traits, SES, even smoking etc)
- **Resiliency** is the key character trait to thrive in the face of adversity and **connectedness** (especially to a caring adult) is a key indicator of resiliency
  - Risk factors are hard to change
  - Connectedness is easier to change
  - Focus less on the negative and more on the positives/strengths/protective factors
- If you don’t ask they won’t tell you; do ask, even if you think you know the answer
- Motivational interviewing techniques:
  - What are the good things? Not so good?
  - Use of rating scales e.g. on a scale of 1-10, what would you...?
  - Reframing
  - Looking forward (or back)....?
- SHEEADSSSS:
  - **Strengths**: what are some of the things you really enjoy/are good at? What positive things would your friends say about you?
  - Home:
    - How are things going at home for you?
    - Where do you live and who do you live with?
    - Who do you get on with, who would you talk to if you had a problem?
  - **Education/Employment**:
    - What year are you in again?
    - What do you enjoy most about school? What subjects do you like?
    - How are you getting on at school? Are you an average/above/below average student?
    - Have you ever had any problems?
    - How do you get on with your teachers/friends?
  - **Eating**:
    - Do you worry about how much you weigh?
    - What do you like about/not like about your body/weight?
    - Do you ever diet?
    - Do you ever make yourself sick after a meal?
  - **Activities**:
    - What things do you like to do with your spare time?
    - What do you do after school/in the weekends?
    - What do your mates do? (Get an idea of peer relationships)
    - What did you do last weekend that you enjoyed?
  - **Drugs/alcohol/smoking**:
    - ‘I check with all young people – not picking on you. Remember it’s confidential.’
    - Lots of people your age smoke/take drugs/drink. Is it like that at your school?
    - What do you think about that?
    - What have your friends tried? What about you?
    - Do you smoke? Have you tried?
    - The smoking youth: “have you ever tried to quit? If so, how far did you get? “OK, that’s great, those first few days are the hardest, so we know you can do it; if you want to stop, we can help you to do that”
    - If no, make it positive “that’s fantastic - how come you don’t and lots of others do?”
  - **Sex and sexuality**:
    - Have you got a boyfriend/girlfriend? Interested in boys/girls/both?
    - Most young people have become interested in sex at your age. Have you had sex education at school? What was it about – body changes, infection, preventing pregnancy, relationships?
    - Have you had a sexual relationship with anyone? What was good about it? What was not so good? Who was the partner? Age? Ever felt forced into having sex?
Want to help you stay healthy... ask about safe sex

If not active – encourage them. But also check they can get condoms, etc: ‘if you ever were to, where would you go for information or contraceptives (tie them down to specifics)

Suicide risk and depression:

‘Everyone has good days and bad days. Do you ever have really good days? Really bad days?’

‘Often adolescents see me because they’ve been feeling down. How have you been?’

‘Have you been happy with the way things are going? How would you rate yourself over the last couple of weeks if 1 was foul and 10 was brilliant?’

‘Do you ever feel like you want to end it all?’

‘Do you have a plan to hurt/kill yourself?’

‘How do you plan to?’

Safety: Do you feel unsafe at all?

Spirituality

Determining the degree of risk:

Well adjusted

Vulnerable

Experimenter

Troubled

Out of control

See Youth Suicide, page 1006

Physical Exam

Use chaperones

Be thorough but assure privacy and modesty (work around clothing)

Talk and explain (especially about growing bodies)

Pubertal ratings: Get them to self report genital development off an Adelaide chart – don’t examine yourself unless specific problem

Puberty

Physiology:

Pre-puberty: inhibition of GnRH pulse generator by higher centres

Puberty: ↑ frequency and amplitude of pulsatile GnRH secretion (gonad independent), initially at night, with FSH (→ follicles or Sertoli cells; predominates in early puberty) and LH (→ Leydig cells in boys → hormone production = testosterone, converted to oestrogen in ovary) secretion in response

Also involvement of adrenal glands → androgens → secondary sex characteristics (eg pubic hair but not ↑ testicular size)

Adult hypothalamic-pituitary-gonadal responses established in late puberty

Terminology:

Gonadarche: onset of gonadal function, at the beginning of puberty

Thelarche: onset of breast development, first sign in females

Adrenarche/Pubarche: Onset of development of sexual (pubic/axillary) hair

Menarche: Onset of menstruation, late puberty

Spermarche: Onset of production spermatozoa, late puberty

Clinical signs:

Measured in Tanner stages (1 = no development, 5 = adult)

Girls: breast development 1st (ovaries enlarge 1st but can’t see them)

Boys: testicular enlargement 1st (use orchidometer), NB. 1 testis can enlarge before the other therefore DDx (hydro/varicocoele, torsion, tumour, hernia)

Pubic hair development initially related to adrenal androgens and may be discordant with other changes

What’s normal:

Girls: traditionally < 8 years or > 13 years abnormal. But ↑ number of girls have breast development at 7. Menarche relatively unchanged at 12 (ie earlier onset, but endpoint relatively unchanged). Getting earlier by 3-4 months per decade (but psycho-social development unchanged)

Boys: < 9 or > 14 abnormal. No strong evidence of it getting younger
Normal Variants

- **Mini-puberty in neonatal period:**
  - Usually neonate – but generally resolves by 4 months
  - Due to hormones in utero and underdeveloped CNS inhibitory mechanisms
  - Breast development +/- milk ("Witches milk" - completely normal)
  - Withdrawal uterine bleeding (following endometrial development in utero)
  - Estrogenic effects on genitalia

- **Premature thelarche:**
  - Isolated early breast development due to subtle overactivity H-P-ovarian axis
  - Tanner 2 or 3 maximum
  - No advancement in bone age
  - Follow-up to ensure it is isolated not progressive (ie that it’s a normal variant)

- **Premature adrenarche:**
  - Isolated early pubic hair development +/- acne +/- body odour
  - Caused by adrenal androgens
  - No advancement in bone age or virilisation and normal menarche/spermarche
  - Need follow-up (eg to exclude adrenal tumour)
  - ?Association with future hyperandrogenism (eg polycystic ovary syndrome)

- **Gynaecomastia:**
  - Breast development up to stage 3 during male puberty (up to 75% of males)
  - Usually in early puberty – resolves in about 2 years
  - Reassurance, occasionally surgery
  - Pathological:
    - In rare instances: Klinefelter’s syndrome, gonadal failure
    - Outside of puberty (eg oestrogen producing tumour or liver disease)

- **Key sign indicating normal:** normal bone age/no growth spurt

Precocious Puberty

- **Definition arbitrary (i.e. <8 in girls, <9 in boys)**
- **Consequences:**
  - Short stature
  - Psychosocial (out of sync with peers)
- **Clinical signs: Old bone age and growth spurt** (in addition to eg breast development)
- **Gonadotrophin dependent:**
  - = Central/complete. Hypothalamic or pituitary cause and → balanced development
  - Girls:
    - Normal progression through puberty (ie variant of normal?)
    - Rapid progression suggests pathology
  - Boys:
    - Normal progression of puberty
    - Less common than girls, more likely to be pathology
  - Causes:
    - Idiopathic (95% in girls)
    - Hypothalamic hamartoma: developmental anomaly (benign growth of normal tissue in wrong place)
    - Tumours (eg of hypothalamus or pituitary)
    - Other CNS conditions (eg hydrocephalus, spina bifida)

- **Gonadotrophin independent:**
  - = Peripheral/Incomplete. Peripheral cause and not all characteristics of normal puberty
  - Girls: rapid progression or virilisation
  - Boys: testes remain small (as no FSH/LH, only testosterone), rapid progression
  - Causes:
    - Hormone ingestion (e.g. OCP)
    - Congenital adrenal hyperplasia (ie adrenal androgens)
    - Tumours: adrenal, gonadal or hCG secreting
    - Autonomous hormone production (rare)

- **Investigations:**
  - Bone age (hand x-ray)
  - Measure hormones
- **GnRH stimulation test** (measure FSH/LH levels + test/oes response to determine central vs peripheral cause)
- Imaging

**Treatment:**
- Treat underlying cause
- GnRH agonist for central precocious puberty via depot. If GnRH is not pulsatile it switches off FSH and LH via saturating the receptors
- Girls: progesterone (e.g. mirena) delays menarche

### Delayed Puberty

- Definition arbitrary: >14 in boys, >13 in girls
- **Hypogonadotropic:** i.e. ↓GnRH: suggests *central* – hypothalamic/pituitary causes:
  - Constitutional delay (check for bone age)
  - Exercise/nutrition (e.g. anorexia)
  - Generalised pituitary failure (e.g. post surgery/radiotherapy for CNS tumour)
  - Rare isolated deficiencies
- **Hypergonadotropic:** i.e. ↑GnRH: suggests *peripheral* – gonadal failure:
  - Chromosomal: e.g. XO, XXY
  - Infections (e.g. mumps, especially during puberty)
  - Autoimmune
  - Surgery, radiotherapy, chemotherapy
  - Galactosaemia
- Other:
  - Structural (e.g. normal puberty but no menarche)
  - Intersex disorders: chromosomal sex <> phenotypic sex
  - Pubertal arrest: always pathological (e.g. pituitary tumour)
- Investigation and treatment:
  - Gonadotrophins +/− GnRH stimulation test
  - Hormone replacement
  - Fertility issues (e.g. with gonadal failure)

### Chronic Illness and Disability in Adolescents

- See also: Effect of Chronic Disease on Development, page 907
- Between 1-20% of young people have a chronic or disabling condition
- US prevalence:
  - Asthma: 50/1,000
  - Mental retardation: 25/1,000
  - Epilepsy: 4.1/1,000
  - Diabetes mellitus: 4.1/1,000
  - Down syndrome: 1.1/1,000
  - Cystic fibrosis: 0.2/1,000
- Survival rates are improving
- Developmental impacts:
  - Primary: effects of the disease
  - Secondary: effects of delayed development
  - Tertiary: effects of treatment
- Similar risk taking behaviours to healthy adolescents
- Impacts on development:
  - Most don’t have major problems, and consider their illness less severe than doctors do
  - Process of separation from parents may be slowed if dependent on parents for care or limited opportunities to socialise with peers
  - Learning disorders → embarrassment, failure, frustration, ↓self worth, performance anxiety, learned helplessness
  - Slowed sexual development or physical deformity → problems with sexual identity
  - Normal developmental issues such as struggle for independence, concrete thinking, narcissism (what feels good is right) and sense of omnipotence (future is a long way off) → non-compliance with treatment
- Mental health in those with chronic illness:
  - Highly variable
  - Vulnerable periods: early years, transitions, severe illness
- Important variables: onset, disruption to early attachments, premorbid function, family stress, mental health of parents, experience of failure or victimisation, repeat hospitalisation, life expectancy

- Resilience:
  - Focus on the young person not just the disability/illness
  - Focus on building strengths, achieving successes
  - Competence in self-care/management of illness/disability
  - Access to age appropriate coping strategies
  - Opportunities for responsibility/required helpfulness
  - Family relationships
  - Peer relationships
  - School attendance
Health Care of the Elderly

- References: Medicine in the Older Adult, Dr Mark Weatherall, Wellington School of Medicine

History

- History should include:
  - **Function** of the person *before* their illness
  - Current function of the person
  - Their aims and aspirations:
    - Where do they anticipate living on discharge from hospital
    - What functional level must they achieve for this to happen
    - Has the availability, ability and opinions of *carers and family* been taken into account
    - Are there special social or cultural considerations
    - Are the goals of the person and the family reasonable within a realistic timeframe
    - Has there been sufficient consultation
  - What is the **physical layout of the home**, access to and within it
  - Screen for disorders

Assessment of Functional State

- Include the following in the **social history**
- Basic activities of daily living:
  - **Mobility**: can they move in bed, get in and out of bed, in and out of a chair, on and off a toilet, ability to get around the house, to get outside, to get to the shops or visit friends. Can steps and stairs be managed
  - **Urinary & Faecal Continence**: is there a problem, how is it managed
  - **Bathing, shaving, teeth, dressing**: how much assistance is needed, can they reach all body parts
  - **Feeding**: how much assistance is needed (eg cutting up food)
- Advanced activities:
  - Handling of finances
  - Shopping
  - Use of public transport
  - Preparation of a hot drink

Screen for Disorders

- **Cognitive impairment**: delirium, dementia, focal cognitive impairments (dysphasia, non-dominant hemisphere problems). May need to use an assessment instrument (eg mini-mental state) and/or interview others
- **Visual and hearing** impairment
- Postural hypotension
- Malnutrition
- Faecal impaction
- Pressure areas
- Iatrogenic disease, including adverse drug reactions
- Weakness secondary to immobility
- Untreated or under-treated pain

Residential Care History

- Reasons for living in a residential care facility, how long have they lived there
- Past health problems and current concerns
- Current medical treatment
- Current functional state
- **Social network** (family and other visitors), and interests and activities
- General physical examination
- Screen for common impairments
- Formulate a problem list, and management strategies (including preventative) that may be appropriate

Ageing

- = Net effect of age related changes → ↑likelihood of dying
• Age related changes affect all body systems: cardiac, respiratory, CNS, musculoskeletal, vision, hearing, skin, immune and renal
• Demographics:
  ➢ ↑ In absolute number of 60, and > 60s as a proportion of total population

<table>
<thead>
<tr>
<th>Year</th>
<th>Number &gt; 65</th>
<th>% of total population</th>
</tr>
</thead>
<tbody>
<tr>
<td>1976</td>
<td>275,000</td>
<td>8.9%</td>
</tr>
<tr>
<td>1996</td>
<td>423,000</td>
<td>11.7%</td>
</tr>
<tr>
<td>2016</td>
<td>659,000</td>
<td>15.5%</td>
</tr>
</tbody>
</table>

➢ Life expectancy at birth for NZ females is 79.5 years and for males 74.3 years (3rd to lowest in OECD)

Concepts
• Cohort Effect: Each current age group (eg adults now aged 80 – 90) have experienced a distinctive history, leading to the following cohort effects:
  ➢ Disease and disability with roots in environmental exposure varies from cohort to cohort (eg tobacco, diet, peak bone mass)
  ➢ Cross sectional studies should consider cohort effect (eg medical care available to 80 year olds when they were 30, compared with 30 year olds now). A difference may not be due solely to ageing
  ➢ Cultural and social differences between cohorts: eg response to health professionals, access to services, gender and spiritual issues
• Diversity of physiology and function increases with age: stereotypes are unhelpful, need individual assessment
• Multiple pathology: Not a single disease process presenting acutely, but a person presenting with disease(s) and/or disabilities. Need a model of care and assessment that considers individual disease processes, individual experience, the social context, and interactions between and within these dimensions
• Failure to present (professionals need to initiate strategies to overcome):
  ➢ Self stereotyping: I’m just old, there’s nothing they can do, etc
  ➢ Cognitive impairment and depression
  ➢ Disability: eg ↓mobility
  ➢ Atypical presentation: Strange or unusual presentations are more common compared with younger people, due to multiple diseases, reduced homeostatic capability, etc. Can be non-specific (not coping, immobile, etc)
• Threshold effect: change in functional status can occur in the absence of a clear precipitant due to build up of subclinical dysfunction and loss of physiologic reserve
• Disordered homeostasis and the cascade effect: Age related effects →↓ability to maintain homeostasis in the presence of a threat (eg medication). Disordered homeostasis in one system can trigger dysfunction in another
• Caring for carers is important in maintaining people in the environment of their choice

Disability
• Disability is understood by (WHO definition):
  ➢ Pathology: abnormal structure or function of an organ or system. Eg osteoarthritis
  ➢ Impairment: loss or abnormality of psychological, anatomical or physiological function. In ↓order of prevalence in the elderly these are (in a CHCH study):
    o Visual impairment
    o Hypertension
    o Symptomatic spinal osteoporosis
    o Hearing impairment
    o Stroke/TIA
    o Osteoarthritis of the hip or knee
    o Urinary incontinence
    o Dementia
    o Postural hypotension
  ➢ Disability: Any restriction or lack of ability to perform a task or activity. Eg: housekeeping, shopping, bathing, mobility
  ➢ Handicap: disadvantage for a particular individual resulting from impairment or disability that limits fulfilment of a role normal for someone of that age, culture, gender, etc. Eg reading a newspaper, shopping, etc
  ➢ However, some things don’t fit well into this model (eg psychiatric illness). WHO currently revising. Will also include impact of environment (eg not being able to drive is not always a disability – eg if you live in the 3rd world)
• Interventions should address all levels, and acknowledge the interaction between each level
• Reported disability has a clear age associated increase

**Age Related Problems**

• For Osteoporosis and Osteoarthritis, see Metabolic Bone Disease, page 407
• For Postural Hypotension see Measuring Blood Pressure, page 28
• For Congestive Heart Failure see Heart Failure, page 67
• For Hypertension see Hypertension, page 47
• For Alcohol Withdrawal see Alcohol Withdrawal, page 753
• For Delirium and Dementia, see Dementia, page 731
• For Urinary Incontinence, see Urinary Incontinence, page 336
• For Constipation see Constipation, page 263
• For Pressure Ulcers see Pressure Ulcers, page 524
• For Pharmacology and Age see Age, page 849
• For Stroke see Stroke, page 190
• For Hearing Impairment see Presbycusis, page 226
• For Insomnia, see Sleep, page 859

**Iatrogenic Disease**

• **Hospitalisation is dangerous** to older people, especially leading to: drug toxicity, injury and mental deterioration
• There is often a decline in functional status following discharge, unrelated to disease process
• Elderly have ↑susceptibility to variety of stressors
• **Bed rest** (eg in hospital, especially if on drips, monitors etc) **generally leads to ↓outcomes**, due to:
  ➢ ↓Muscle strength and aerobic activity
  ➢ Volume depletion therapy (also results from bed rest) + age related vasomotor instability →postural hypotension
  ➢ Supine position worsens V/Q mismatch
  ➢ Bone demineralisation
  ➢ ↑Urinary incontinence due to high beds or distance from toilet
  ➢ Pressure sores
  ➢ Sensory deprivation (eg boring rooms, not wearing glasses or hearing aids)
  ➢ ↓Nutrition (altered dietary habits, unappetising food, ↓social component to eating)
  ➢ All lead to a cascade of interaction
• Most deterioration happens in first two days in hospital. Examples of prevention include:
  ➢ Low bed without rails
  ➢ Carpeting
  ➢ Minimisation of tethers
  ➢ Encouragement and assistance
  ➢ Orientate with clocks, calendars, dressing, undressing, communal dining
  ➢ Sensory stimulation: proper lighting, decoration, glasses, hearing aids, available recreation

**Nutrition**

• Can be measured through body weight (eg BMI), body composition, or direct measurement of micro-nutrients
• Under-nutrition in the elderly can be due to:
  ➢ Age related ↓in gastro-intestinal function predisposes to poor nutrition (eg ↓teeth, ↓pancreatic secretion, etc)
  ➢ Life-style factors: inability to shop, prepare and cook food, living alone, alcohol abuse, poverty
  ➢ **Diseases:** eg stroke, arthritis, dementia make eating harder
  ➢ Anorexic effect of illness and drugs
• Management:
  ➢ Multidisciplinary: dietician to advise on what and how much to eat. Occupational therapist to advise on food preparation. Meals on wheels. Social worker in involve family and ensure adequate finance
  ➢ Medication review
  ➢ Nutritional supplements: eg add milk powder to food, eat high-density foods, take supplements

**Falls**

• In elderly, refers to a fall during an activity that is usually safe
• 25 – 35% of those over 65 fall each year. Occurrence ↑ with age
• <5% of falls cause a fracture (40% of these to proximal femur). Soft tissue injury in 40%
• Staying upright (a homeostatic function) requires:
  ➢ Safe environment
  ➢ Information on body position: visual, vestibular, mechanoreceptors, proprioception, central processing
  ➢ Motor systems: cortex, brainstem, cerebellar, spinal cord, muscles
  ➢ Stable base: joints, limbs, feet
  ➢ Intact judgement

Causes
• ‘Threshold model’ in which a number of factors combine to ↑risk
• Sedative use, cognitive impairment, abnormalities of balance and gait, polypharmacy, history of stroke, hypotension
• Fall over things that are safe to others ⇒ changing the person more important than changing the environment. But check for rugs, clutter, cords. In hospital, care with ability to transfer, agitation and frequent toileting
• Associated diseases:
  ➢ Nervous system: stroke, Parkinson’s, dementia, seizure, peripheral neuropathy, ↓visual acuity
  ➢ Musculoskeletal: proximal muscle weakness, arthritis of lower extremity
  ➢ Cardiac: aortic stenosis, arrhythmia, postural hypotension
  ➢ Iatrogenic: sedatives, psychotropic medication, alcohol

Assessment
• Previous history of falls
• When, where, what was experienced, associated environmental factors
• History of vertigo, dizziness, imbalance, blackouts, medication
• Examination: postural changes in BP, vision and hearing
• Observation: stand up without using hands, observe gait, stop smoothly, turn around, stand on one leg, reach up, bend over, heel toe walking, can they speed up, nudge them, sit down without hands

Management
• Active management of injuries: watch for occult pelvic fractures, hypothermia. Care with soft tissue wounds – can go on to ulcers
• Acute precipitating illness that requires treating: eg stroke, MI
• Identification of risk factors
• Rehabilitation: active mobilisation after a fall
• Interventions targeted at identified risk factors, including medical review of medication, physiotherapy for transfer skills and exercise program
• Avoid giving psychotropic medication to people at risk; it WILL make them fall over
• Consider home alarm

Visual Impairment
• Major causes of ↓visual acuity in adults are (See also Loss of Vision, page 213):
  ➢ Cataract: due to ↑bulk of the lens and discolouration. Age, diabetes, and UV light are the main risk factors. Treatment by extraction and implantation improves visual acuity in about 90% but a smaller proportion benefit in terms of activities of daily living
  ➢ Age related macular degeneration: Variety of causes. More serious ones include choroidal neovascularisation ⇒ detachment and scarring
  ➢ Glaucoma
  ➢ Diabetic neuropathy
• Senile arcus: ring of lipid and calcium salts in a ring at the junction of the cornea and sclera. Very common in elderly. Not a sign of hyperlipidaemia (as it is in the young)
• Ectropion: low lid falls away and tears don’t drain into lacrimal sac
• Lens becomes thicker and less flexible (Presbyopia) ⇒ can’t accommodate, need reading glasses

Elder Abuse
• = When a person aged over 65 experiences harmful physical, psychological, sexual, material or social effects caused by the behaviour of another person with whom they have a relationship implying trust (Age Concern definition)
Types

- Elder abuse can be:
  - **Physical**: physical pain, injury, force, under/over medication
  - **Psychological**: causing emotional anguish or fear, including intimidation, humiliation, harassment, threats, removal of decision making powers
  - **Sexual**
  - **Financial**: improper use of funds or other resources

- Can be:
  - **Active neglect**: conscious deprivation by a carer of basic necessities
  - **Passive neglect**: refusal/failure of a carer to provide the basis necessities due to inadequate knowledge, infirmity, or dispute over the value of services

Epidemiology

- Prevalence: *Significant under-reporting* due to cognitive impairment, fear, life long pattern of abuse, access to someone to complain to, stigma associated with domestic violence. About 5% of elderly people subject to abuse, usually by a spouse, child or relative

Risk Factors for Abuse

- **Dependence** by the older person for all or part of their care
- **Cognitive impairment**, especially disruptive or aggressive behaviour
- Substance abuse or mental illness of the abuser
- Shared living arrangements
- External stress
- Social isolation
- History of violence

Screening for Elder Abuse

- Will not be volunteered: *need to ask* the right questions
- Watch for injuries or health or emotional problems with vague or inconsistent explanations
- Observe interactions, especially in own environment
- Question older person away from carer:
  - Do you feel safe at home?
  - Are you afraid of anyone at home?
  - Have you ever been hit or pushed?
- Question carer in empathetic not confrontational way: Caring for X must be difficult... How do you cope.... Have you ever lost control?
- Careful physical examination and documentation of findings

Management

- Age Concern have people trained in the assessment of abuse, plus case workers and advisory groups
- Use ATR social workers
- If person accepts intervention, then initiate a safety plan
- If person declines intervention (but has the capacity to do so) then educate and review
- If person declines but doesn’t have the capacity to make this judgement, then family court can decide on welfare guardianship through the *Protection of Personal and Property Rights Act* (PPPR Act)

Driving

- 50% of 76 – 80 year olds still have a licence, 27% of those over 80. Half still drive regularly
- Driving depends on cognitive function, motor function and sensori-perceptual function
- Elderly are only 14% of those killed in crashes, but have a higher death to injury ratio
- Older drivers more likely to be at fault in accidents involving intersections, merging and manoeuvring
- In elderly people with Alzheimer’s, crash rates approach those of 15 – 25 year old males
- Age associated changes affecting driving include: vision, psychomotor function, strength and dexterity, cognitive function (especially attention to multiple stimuli and finding ones way, ↓in dementia)
- **Medical assessment a legal requirement at 75, then 80 and every two years thereafter** (including vision check). Cognitive screening should be included due to the profound effect on driving, the insidious nature of cognitive impairment, good social facades by patients, and frequent lack of insight. Psychoactive drugs (especially BDZs) →↓psychomotor function
Services for the Elderly

Rehabilitation

- Can classify approaches to rehabilitation by patterns of disability:
  - Localised injury or isolated disability: involvement of one discipline may be appropriate
  - Expectation of return to premorbid function: but more than one discipline necessary (eg fractures)
  - Where optimal recovery depends on well integrated team approach (eg amputation, stroke)
  - Progressive deteriorating conditions where the aim is to maintain optimum ability, with regular review of goals, and emphasis on emotional, social and environmental factors rather than specific rehabilitation techniques (eg Parkinson’s)
- Can classify rehabilitation by types of people:
  - Impaired physical function, but not obviously ill → disability management
  - Chronic illness without manifest disability → education and anticipatory care
  - Those with a combination of illness and disability
- Can classify rehabilitation by approaches:
  - Medical: Specific control of disease and impairment
  - Prevention: Of secondary disability (eg pressure areas, constipation)
  - Restoration: Using physiotherapy, occupational therapy and nursing interventions to ↑ function
  - Adaptation: Equipment, modification of living environment, and family adjustment
- Also need to assess the strengths and abilities of the individual and carers
- Goal Setting:
  - Central task in management of disability
  - Needs accurate assessment of pre-morbid and current function (eg using formal assessment tools). Is often unrealistic to aim for future function better than pre-morbid function
  - Goals must be meaningful and appropriate to the problems and circumstances
  - Goals should be agreed by negotiation with older person, the carer and the rehab team
  - Goals should include: who will do what, under what circumstances, and to what degree of success
- Barriers to Rehabilitation:
  1. Unidentified medical problems: don’t want to over or under-medicate. Check for malnutrition, anaemia, fluid and electrolyte abnormalities
  2. Cognitive impairment: If they can’t concentrate or remember, their involvement is compromised. Always screen for impairment
  3. Depression: Unwell and disabled people have a high prevalence of usually treatable depression. Diagnosis can be complicated due to overlapping symptoms (eg fatigue, apathy, psychomotor retardation and sleep disturbance)
  4. Communication problems: Screen for poor eyesight and hearing
  5. Low expectations and ageism: decline is not always as inevitable or severe as thought. Patients, carers and professionals can all have misconceptions and unrealistically low expectations
  6. Right to dependency: some old people may not participate because they feel they should be looked after

Common rehabilitation interventions: physiotherapy (especially musculo-skeletal problems and mobility), occupational therapy (therapy to ↑ function in tasks, ↓ impairment), doctors (diagnosis, prescribing, prognosis, co-ordination), nursing (implementing therapies, assessing disease, function and well being), speech language therapy (including swallowing), dieticians, appliances, adaptations, daily living aids, advice, education, counselling, encouragement, listening

Whether inpatient or outpatient setting is assessed on the basis of: level of dependency (especially night care), degree of complexity of disability, speed of response needed, housing and domestic circumstances, availability of in or outpatient services

Rest Home and Hospital Care

- 6% of the population over 65 live in institutions (about 25,000), 24.5% of those over 85
- Rest homes are licensed by the Ministry of Health and payments are made by the Ministry of Health
- Access to funding by an individual is dependent on a needs assessment and an asset test done under contract from the Ministry of Health by WINZ
- Maximum weekly fee paid is $636: average rest home fees are around $550 per week and hospital fees around $1100
- If receiving the subsidy, you lose super and get and allowance of $27 per week

Health Care of the Elderly
Needs assessment assigns a Support Need Level (SNL) from 1, little help needed, to 5, 2 person help needed – levels 1 and 2 general aren’t funded to be in rest homes

Comorbidity common in rest homes, plus evidence of mental illness (in addition to stroke and dementia)

Other health issues include vitamin D supplementation, immunisation (including of staff), and loss of continuity of care on shifting into a rest home

Also broader issues are maintenance of privacy, whether sexual needs can be met, encouragement of health promotion activities such as exercise, appropriate recreation, monitoring dietary intake, provision of alcohol and attitudes to smoking
Introduction

- **WHO Definition of Health**: A state of complete physical, mental and social well being, not just the absence of disease or infirmity
- **Public Health**:
  - = The art and science of preventing disease, prolonging life and promoting health through the organised efforts of society
  - = Population health
- **Roles of Public Health**:
  - Traditional role: communicable disease control, environmental and occupational health
  - Information: disease and health surveillance
  - Policy: policy, legislation, goals, priority setting
  - Health services: planning, evaluation, needs assessment
  - Health promotion/disease prevention: promotion, screening, immunisation
- **Steps in public health**:
  - Public health intelligence (monitoring/analysis)
  - Developing policy
  - Delivering services
- **Equity and access**:
  - Need = capacity to benefit (but from whose perspective?)
  - Vertical verses horizontal equity (but equity of what – outcomes, access, opportunity)
  - Dimensions of affordability, accessibility, availability, acceptability, accommodation

Health Care Delivery

*Issues in Service Delivery*

- **Key international trends**:
  - Changing demographics: esp ↑ elderly
  - Communicable → non-communicable diseases
  - Concern with economy given rising costs
  - Who should pay: public vs private
- **Issues in service delivery**:
  - Institutional arrangements:
    - Output funding
    - Priority setting
    - Funder/provider splits
    - Managed care
  - ‘Cultural’ issues:
    - Competition vs cooperation
    - Control vs community voice
    - Management vs technology
- **Influences on NZ history**:
  - 19th century legacy:
    - Parochialism (isolation → self-government)
    - Adhocracy (new problem → new organisation)
    - Egalitarian myth: services by right

*System in NZ*

- References: Introduction to the New Zealand Health System, Peter Crampton and Anne Viccars, Departments of Public Health and General Practice, Wellington School of Medicine
- **Factors facing health systems in developed countries**:
  - Ageing populations
  - Medical technology
  - Rising expectations
  - Treaty of Waitangi
- **Health Care expenditure in New Zealand**: 
1998 total: around $8 billion. Vote health was $5.6 billion in 97/98.
7.6% of GDP (compared with Australia 8.3% and UK 6.7%)
Public 77%, private 23%
18% of total government expenditure
Proportion of people covered by health insurance has declined since 1994/95

- Health Legislation:
  - Health and Disability Services Act 1993 (now repealed)
  - Health Act 1956: main piece of public health legislation

- Health Policy Agencies:
  - Ministry of Health
  - Other central agencies: Te Puni Kokiri, Treasury, State Services Commission
  - Other advisory bodies:
    - National Advisory Committee on Health and Disability (National Health Committee)
    - Mental Health Commission: established in 1986 following Mason Inquiry
    - Health and Disability Commission: established in 1994 – responsible for the Code of Health and Disability Consumers’ Rights
    - Health Sponsorship Council: Established under smoke-free environments Act 1990 to sponsor activities previously sponsored by tobacco companies

- Purchasers: Used to be the HFA, including Pharmac and Health Benefits Limited

- Purchaser-Provider Split:
  - Potential benefits were:
    - Efficiency: due to competition
    - Equity: reflect need not historical provision
    - Accountability clearer
    - Cost containment due to capped budgets
    - Consumer sovereignty
    - Better information
    - Improvements in primary care: IPAs and Maori services
  - Problems:
    - Short term market lead decision making
    - CHE debt/missed business plans
    - Transaction costs -> bad contracting relationships -> 3rd party intervention
    - Asset specificity: providers locked in -> little real competition
    - Fragmentation of services
    - Loss of co-operation

- Primary Care:
  - Numbers:
    - 2,800 GPs (about 2,500 FTEs)
    - 1,600 practice nurses
    - 1800 – 2000 practising midwives
  - Funding:
    - GP income derived from: Subsidies (depending on patient age and CSC/HUHC), patient fees, ACC
    - Primary Care Expenditure: 59% pharmaceuticals, GMS 15%, labs 13%, maternity benefit 8%
  - Themes: managed care, budget holding, integrated care

- Latest reforms:
  - Ministry of Health and HFA merged
  - 21 District Health Boards created (roughly around old Hospital and Health services): have a purchasing and a provision function
  - Maternity providers funded by MoH
  - DHBs fund NGOs, GPs, Private providers, public health providers
  - ACC continues direct purchasing from primary and secondary providers
  - Key changes:
    - No purchaser-provider split
    - Community control
    - Budget tension between primary and secondary services forced down from central agencies to DHBs
    - 21 Boards too many: diseconomies of scale
Measures of Health Status

- No single or ideal way of measuring a person's or a population's health status → wide range of tools
- Purposes of measuring health status:
  - Diagnostic: to discriminate between people with different health states
  - Prognostic: to predict future events
  - Evaluative: before and after a health intervention
- Measuring health status of individuals and populations:

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<th>Dimension of Health</th>
<th>Measures in Individuals</th>
<th>Measures in Populations</th>
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<tr>
<td>Mortality</td>
<td>Age at death</td>
<td>Life expectancy</td>
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<tr>
<td>Disability</td>
<td>Existence of a disability</td>
<td>Prevalence of a disability</td>
</tr>
<tr>
<td>Self-rated Health</td>
<td>Self-rated health</td>
<td>Average self-rating</td>
</tr>
</tbody>
</table>

**Mortality**
- Definitions:
  - Crude Mortality Rate: number of deaths per year for an entire population
  - Specific Mortality Rate: Number of deaths occurring within a subgroup of the population. Eg age, sex, or cause specific
  - Age adjusted mortality rate: adjusts with reference to a standard population to allow comparisons between populations with different age distributions
  - Premature mortality: death occurring before the average life expectancy within a given population
- Advantages:
  - Death is easy to diagnose
  - Is recorded, and doctors are legally bound to state the cause
- Disadvantages:
  - Cause not always accurately described
  - Reduces health status to being alive or not. Ignores the continuum of suffering and unhappiness

**Life Expectancy**
- = The expectation for life at birth for a population born in a specific year
- Calculation:
  - Period life expectancies: average life-time of a hypothetical group born in a specific year, assumes age and sex specific death rates won’t change
  - Cohort life expectancy: follow through a real cohort until all are dead
- Making comparisons, eg between Australia and NZ:
  - Migration between the two countries
  - Ethnic groups (Maori, Pacific Islanders, Aborigines)
  - Socio-economic differences
- Potential years of life lost (PYLLs): potential years of life lost for a specific cause. Difference between age of death + LE at that age
- Changes over time have largely been due to social and economic changes (particularly public and personal hygiene). Contribution from health services is much less important

**Morbidity**
- = Incidence or prevalence of a condition or disease in a population over a set period of time
- Measurement:
  - ‘Objective’ measures:
    - Biochemical markers (eg blood glucose)
    - Physiological markers (eg blood pressure)
    - Pathological markers (eg tumour size)
  - Functional measures:
    - See also Disability, page 1015
    - Impairment: reduction in physical or mental capacity – usually due to an organ/system. May be able to be corrected (eg reading glasses)
    - Disability: restriction in a person’s ability to perform a certain task (eg walking)
    - Handicap: If disability limits ability to perform a normal role – depends on social context
    - Many measures assess degree to which people can undertake activities of daily living
- Sources of morbidity data: cancer registers, notifications (infectious diseases, workplace accidents), hospital discharges, GP registers
- Advantages: examines range of diseases beyond those that cause death
Disadvantages:
- Diagnosis can be ambiguous
- Variation in recognition or reporting of disease

**Self-reported or Self-rated Health Status**
- More subjective
- Overlaps with health-related QOL, encompassing physical health, psychological well-being, emotional well-being and social functioning
- For assessing Maori health need to incorporate relations with extended family and spirituality (obviously non-Maori are not spiritual and don’t care about family!!)

**Composite Measures of Health Status**
- Independent Life Expectancy: average number of years living without disability. Equals life expectancy + prevalence of dependency. Ignores reversibility of some disabilities and transition from good to poor health
- Measures of the burden of disease:
  - Takes into account fatal and non-fatal outcomes
  - **Disability Adjusted Life Years**:
    - Estimate of years of healthy life lost
    - Similar to QALYs but standardised for use between populations and they also use age weights (lower weights in childhood and elderly)
    - Used to assess the burden associated with certain diseases or with particular risk factors (e.g., smoking)
    - In NZ, CV disease accounts for 24% of DALYS lost, followed by cancers and mental disorders
- Criticisms:
  - Limited use to policy makers because they focus on health loss rather than potential gains
  - Don’t take into account disability associated simply with old age
  - Requires extensive epidemiological data

**Determinants of Health**
- **Social environment**: education, friends, income
- Genetic endowment
- **Physical environment**: housing, working conditions, security
- **Health services**: access and orientation
- **Health behaviours**: lifestyle, risk behaviours (e.g., smoking and substance abuse)

**Key Measurements/Indicators of Health**
- Mental health status
- Life expectancy, number of years one can expect to live with current mortality levels staying as they are
- Infant mortality
- Mortality rates by causes of death
- Health expectancy, is the number of years from birth a child growing to become an adult can expect to live independently, that is, free of functional impairment

**Biostatistics**
- Choosing study subjects:

<table>
<thead>
<tr>
<th>Group</th>
<th>Specified by</th>
<th>Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Target population</td>
<td>Clinical and demographic characteristics</td>
<td>Well suited to the research question</td>
</tr>
<tr>
<td>Accessible population</td>
<td>Temporal and geographic characteristics</td>
<td>Representative of the target population and easy to study</td>
</tr>
<tr>
<td>Intended sample</td>
<td>Sampling procedure</td>
<td>Representative of the accessible population and easy to do</td>
</tr>
<tr>
<td>Actual sample</td>
<td>Availability, and obtaining informed consent and required information</td>
<td>May or may not be still representative of accessible population</td>
</tr>
</tbody>
</table>

- Populations may be people, institutions, records or events
- Sampling frame is a complete list of individuals in the accessible population
- A sampling procedure is used to select a representative intended sample from the sample frame
- Avoiding systematic errors:
  - Trying to use sample mean to estimate the population mean
Statistic = parameter + bias + confounding bias + chance

Statistic: summary measure in a sample
Parameter: underlying value in the target population
Bias or Confounding → ↓ internal validity
External validity is whether the study can be applied to the population I’m interested in – is it similar enough to the study population?

**Bias**
- **Bias** = systematic deviation between the statistic and the parameter, due to defect in the design, conduct or interpretation
- Occurs predominantly in design and data collection
- **Selection bias**: systematic error due to those who were selected and those who were not → sample not representative of the defined population
- **Information bias**: a flaw in measurement of exposures or outcomes that results in results systematically different from the truth
  - **Misclassification bias**: Subjects erroneously categorised. If a random bias then ↓ association in results and odds ratio moves towards 1
  - **Interviewer bias**: systematic difference in soliciting, recording and interpreting of responses (↓ by training the interviewers – always check this has been done)
  - **Recall bias**: should be < 2 weeks for health events. Diet recall ~ 24 hours. If not random (eg case-control studies) then biased (eg if cases taken from records then there is variability in what was asked and recorded, verses uniform questionnaire for controls)
- **Response bias**: systematic error due to differences between those who volunteer and those who do not (eg bias from drop-outs and non-responders and loss-to-follow-up)
- See EBM Glossary, page 1045, for further examples of bias

**Confounding**
- A measure of the effect of an exposure on the risk of an outcome is inaccurate as the exposure is independently associated with other factors that influence the outcome
- Standard ones: age, gender, ethnicity, socio-economic status, obesity, smoking, alcohol (ASSES)
- As long as you collect data about the confounding factor, you can do something about it
- Can control for confounding using matching, logistic regression or stratifying data

**Chance Effect**
- Standard error:
  \[
  \text{standard error} = \frac{\text{standard deviation}}{\sqrt{\text{sample size}}}
  \]
  - Quantifies the precision with which the sample mean estimates the population mean
  - Says NOTHING about variability in the data
- **Confidence interval:**
  - Turns standard error into something we can interpret: sample mean +/- 1.96 * standard error
  - 95% sure the true value lies in the range
  - Width is dependent on:
    - Variation in observed data
    - The sample size (larger sample → narrower confidence interval → more precise estimate)
    - Degree of confidence we want
  - Accuracy depends on presence or absence of bias
- Tests of significance:
  - Tests of significance are a tool for statistical inference
  - Test compatibility of a set of data with the null-hypothesis: assume there is no difference between the means – what is the probability we would observe a difference as big by chance
  - **P value**: measure of the evidence we have against chance; probability of results being due to chance. Threshold usually 0.05
  - Most common test statistics are chi-squared and t-statistic (compares two means). Both depend on degrees of freedom
- **Power**: = probability that the study will find a statistically significant difference if a true difference of a given size exists
Data

- Qualitative: not numeric (eg hair colour)
- Quantitative: can be continuous or discrete
- Measurement scales can be nominal (categorical and unordered), ordinal (categorical and ordered) or interval (continuous)
- Data description:
  - Categorical and discrete data: bar graphs, frequency distributions
  - Continuous data: histograms, frequency polygons
  - Central tendency: Mean or median (best measure of central tendency if skewed distribution)
  - Spread/variability: Standard deviation, percentiles or inter-quartile range
  - Correlation co-efficiency – degree of clustering around a straight line
  - If two variables are categorical and unordered then use relative risks and odds ratios

Epidemiology *

- For Definitions of Risk and Odds Ratios, see Risks and Odds, page 1045
- Includes 2nd and 3rd year PDS notes
- * = Study of distribution and determinants of health and disease in populations
- **Bradford Hill Criteria for causation:**
  1. Time sequence: did the factor come before the disease – only necessary factor
  2. Strength: large relative risks are seldom artefacts
  3. Consistency: has an association been found elsewhere, using different methods?
  4. Specificity
  5. Dose-response relationship: does the risk ↑ with the level of exposure to the factor
  6. Biological plausibility: is a causal risk consistent with current knowledge
  7. Experiment: can an intervention study validate the result

- Summary of study types: (↑ power as you go down)
  - **Descriptive** (ecological) studies
  - **Analytical** (observational) studies:
    - Cross-sectional studies
    - Case-control studies
    - Cohort studies
  - **Intervention** (experimental) studies

Descriptive Studies

- Personal characteristics (age, sex, occupation, social class, etc), place and time
- Measures of occurrence (⇒ descriptive):
  - **Prevalence**: Number with disease/ Relevant population at a designated time
  - **Incidence**: Rate of development of a disease in a group over a period of time = number of new cases during a specific period/total at risk population
  - Need to compare for specific groups, or standardise for compositional differences in populations
  - Long duration illness →↑ prevalence, short duration →↓ prevalence
  - Incidence and prevalence are similar for short illnesses (eg diarrhoea) but not for long illnesses (eg TB)

- Useful for:
  - Understanding occurrence
  - Suggesting hypothesis – but correlation doesn’t prove cause
  - Often called ecological studies
- Don’t have unaffected people in the series so no information about relative risks

Ecological Studies

- Captures data about exposure and outcome and compare between either different population or over specific time periods
- Can compare trends, patterns
- Quick, cheap, uses existing data sources, usual first step
- No causality, can’t control for confounding
- Ecological fallacy, not able to link exposure disease to individuals
**Cross-sectional Studies**

- Examine relationship between disease and other variables (e.g., risk factors) in a defined population at one time (snapshot in time)
- If prevalence not high enough, use sentinel populations (i.e., those with greater risk)
- Normally **considering prevalence**, not incidence ⇒ also called Prevalence Studies
- Limitation: time sequence of cause and effect cannot be determined

**Case-control Studies**

- Tries to compare factors amongst patients with a disease compared with a control group without the disease
- Looking backwards to the exposure (i.e., the outcome has already happened) ⇒ also called retrospective studies
- **Advantages:**
  - Can be done quickly (compared with cohort study)
  - Are therefore cost effective
  - Can do it with **diseases with low prevalence** (cohort study better for more prevalent diseases)
  - Defined endpoint
- **Disadvantages:**
  - Retrospective, so can introduce bias
  - Selection criteria create difficulty
  - **Biases:** non-volunteer bias, recall bias, etc
  - **Causation not proven** – just an association
  - Can only get information on one outcome
- **Selection of cases:**
  - Representative of those presenting over a defined period
  - **Select according to diagnostic criteria.** If these cast the net widely, then will include people with unrelated disease → odds ratio moves towards 1 (if random effect)
- **Selection of controls:**
  - Representative of the population from which cases drawn but without the outcome
  - Aim is to establish expected exposure in case group
  - Want to compare exposures between the cases and the population at large. If, for example, you match on age, you won’t be able to conclude anything about age as a risk factor, so choose controls so you get an unbiased example of risk factors in the population. Matching does reduce the effect of confounding – but there are other ways to deal with that when doing the number crunching
- **Identical methods must be used to collect information from both**
- **Can’t** estimate relative risk in a case-control study:

<table>
<thead>
<tr>
<th>Exposure</th>
<th>Outcome (eg Disease)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Yes (Cases)</td>
</tr>
<tr>
<td>Yes</td>
<td>A</td>
</tr>
<tr>
<td>No</td>
<td>C</td>
</tr>
</tbody>
</table>


- Odds Ratio = \( \frac{A}{C} \div \frac{B}{D} \) = odds of disease in the exposed cf those not exposed
- Relative Risk:
  - \( = \frac{A}{A+B} \div \frac{C}{C+D} \)
  - = Risk of disease among exposed/risk of disease if not exposed
  - In a case-control study, the ratio between the cases and the controls is fixed by the study design, not the prevalence in the population. The relative risk is therefore meaningless. That is, you can’t estimate the risk of the disease in the population in those not exposed to the risk factor
- But if the condition is rare and there is no bias in controls, then the odds ratio approximates the relative risk ratio well
- See also Risks and Odds, page 1045

**Cohort Studies**

- Groups observed over time: forward looking from exposure, waiting for outcome ⇒ also called Prospective or Follow-up Studies
- Either compare within the cohort, or select a comparison cohort
- **Advantages:**
  - ↓Bias over a case-control study
  - Can examine more than one outcome
  - People who don’t take part don’t bias the outcome, just its generalisability
- **Disadvantages:**
Public Health

- Large numbers are required ⇒ information collected has to be simpler ⇒ ↑ risk of confounding
- Need to follow people over time ⇒ expensive and takes a long time
- Not good for rare diseases

Strengths: People who don’t take part don’t bias the result – just affect its representativeness (ie external validity) ⇒ less susceptible to bias

**Intervention or Experimental Studies**

- Test whether removing suspected aetiological factors reduces frequency of disease
- Evaluate preventative measures and treatments (→ clinical and community trials)
- Best test of cause and effect
- Often not ethical nor logistical to do a RCT
- Blind assessment → ↓ information bias

**Miscellaneous Stuff**

- **Risk reduction:** lower risk to health without eliminating the risk eg avoid sun
- **Harm reduction:** tolerance of risk behaviour, aim to *minimise adverse outcomes related to it* eg needle exchange
- **Standardisation:**
  - Adjustment (to a standard population) of the crude rate of health outcomes to allow comparisons
  - ↓ likelihood of confounding by common confounders eg age
  - Can adjust for age, ethnicity, sex, prevents drawing misleading conclusions by comparing crude rates between dissimilar populations

**Communicable Disease Control**

- See Vaccination, page 838
- Reasons for notification:
  - High morbidity and mortality (in epidemiology terms, ie deaths per 100,000 of well population)
  - Intervention available
  - Other:
    - High public interest. Eg CJD – is both rare and untreatable
    - Historical. Eg decompression sickness
- **Notifiable Diseases:**
  - Under Health Act 1956
    - Section A: infectious diseases notifiable to a medical officer of Health and Local Authority [involve water or food transmission]: acute gastro-enteritis (where common source or person in high risk occupation), cholera, giardiasis, legionellosis, primary amoebic meningitis/encephalitis, shigellosis, yersiniosis, campylobacteriosis, cryptosporidiosis, Hepatitis A, Listeriosis, salmonellosis, typhoid and paratyphoid fever
    - Section B: infectious diseases notifiable to Medical Officer of Health: HIV, CJD, HIB, Hepatitis C, Hydatid disease, Leptospirosis, measles, Neisseria meningitidis, plague, rabies, rickettsial diseases, tetanus, yellow fever, anthrax, brucellosis, diphtheria, Hepatitis B, Leprosy, malaria, mumps, pertussis, poliomyelitis, rheumatic fever, rubella
    - Notifiable non-infectious diseases: cysticercosis, taeniasis, trichinosis, decompression sickness, lead poisoning, poisoning from contamination of the environment
  - All forms of TB (under TB Act 1948)
  - Venereal Diseases Act (1986?): covers gonorrhoea and syphilis, and contract tracing

**Classification of Notifiable Diseases**

- Vaccine preventable diseases
- Blood borne and sexually transmitted diseases
- Food and water borne diseases
- Vector borne eg Malaria
- Zoonoses (ie animal stage) eg Brucellosis, Hydatids, Rabies
- Other Infectious diseases: eg CJD, Hepatitis, Leprosy, TB
- Non-infectious diseases: Decompression illness, Lead poisoning, environmental contamination
- Process of notification:
  - Is a legal requirement, although compliance is poor with common things like campylobacter. Only a small proportion contact doctor, only a few of these tested, only a few of these reported, etc
When to notify:
- If serious on suspicion (e.g., meningitis)
- If not serious (e.g., gastroenteritis) then on confirmation

Possible Interventions
- Food borne – isolate source and close it down
- If HIV and spread by blood products → screen blood
- If HIV and confined to a locality → education campaign

Surveillance
- Report to medical officer of health
- Clinical labs also report to medical officer of health (if a special case then refer sample to the CDC Reference Lab – ESR)
- These all report to the CDC Epidemiology Group (also at Porirua), produce the Public Health Report
- In turn report to the Ministry of Health and MAF, so they can form surveillance and disease control policy (e.g., vaccination and screening policy, promotion, etc)
- Other surveillance systems: coroner, Births, Deaths and Marriage, OSH, Cancer Registry

Epidemics
- An outbreak or epidemic is relative, is ‘more cases than you would expect’
- An outbreak investigation involves analysis of the time over which illnesses have occurred, the places and the characteristics of the people affected
- Patterns of epidemic:
  - Point source out-break (e.g., food poisoning) – short duration
  - Multiple source out-break: eg measles, index case spreads to multiple cases – long duration with fluctuating incidence
- Want to find:
  - Agent
  - Vector
  - Source
  - Can affect rate without known the agent. Eg cholera was controlled through clean water in London before the bug was discovered

Environmental Health

Classification
- = Effect of environment on health at a population level (want to stop people being sick…)
- Classify by route of exposure to agent of harm: Classify water, air and soil by physical, chemical and microbial (prion, virus, bacteria, protozoa, etc):
  - Water:
    - Physical
      - Drought
      - Drowning: in NZ have the hazard and lots of exposure (outdoor pursuits, fishing, swimming pools)
    - Microbial:
      - Virus: HAV, rotavirus
      - Bacterial: shigella, campylobacter
      - Protozoa: amoeba, Cryptosporidium, Giardia
    - Chemical: arsenic poisoning in Bangladesh
  - Air:
    - Physical:
      - Suffocation: plastic bags, volcanic gases, faulty gas appliances
      - High winds
      - Noise
    - Microbial: Tb, legionaries
    - Chemical: pesticides, asbestos, work place
  - Soil/Food:
    - Physical: landslide, earthquake, desertification
    - Microbial: tetanus
Chemical: heavy metals, selenium deficiency

Other: Sun (UVB → cancer), radiation

- Occupational health and psycho-social health often separated off from environmental health
- Need multi-disciplinary teams to solve problems (eg housing: doctors, engineers, sociologists, economists)

Inter-relationship of Host and Environment

Malaria

- Background:
  - Lifecycle: plasmodia in human blood → mosquito sucks blood → migrate into mosquito saliva glands → passed on in next bite
  - Host factors:
    - Sickle cell anaemia → ↓ contagious
    - Immunocompromised: kids, malnourished, concurrent infection, maybe AIDS
  - Pathogen factors: which strain
  - Vector attributes: right species of mosquito
- Interventions:
  - Vector – Host relationship: Interrupt exposure eg nets, repellent, clothing
  - Host: general health, nutrition
  - Host – Pathogen relationship: chemoprophylaxis
  - Pathogen: Air-conditioning → ↓ temp → ↓ plasmodium
  - Pathogen – Vector relationship: Remove infected hosts (ie cure them)
  - Vector: source reduction (spray, ↓ water traps)
- Effect of the environment:
  - Vector: if warm and wet breed faster
  - Host: if hot take clothes off and open windows
  - Pathogen: plasmodium replicated faster if warmer

Yellow Fever*

- Swotted for Public Health Test Question. Source: Harrison’s and CDC Website
- Haemorrhagic fever with prominent hepatic necrosis
- Incidence declining since the turn of the century. Outbreaks mainly now only in West Africa. South America also at risk
- Urban Yellow Fever:
  - Spread by Aedes Aegypti mosquito
  - Human – mosquito – human cycle. Mosquitoes pass it to their offspring via ovary infection
  - Deposit eggs in any container with water in or around homes (so can still get it if low rainfall or dry season) ⇒ women and children more at risk if they’re around home a lot
- Sylvatic Yellow Fever:
  - Mosquitoes infected from viraemic monkeys (monkey’s don’t get ill so are a continuing reservoir)
  - Infects humans in or living around forests ⇒ men who do the hunting more at risk
- Prevention (in addition to Malaria factors above):
  - Put bed nets over infected people – stops onward transmission of infected people. They are viraemic for 3 – 6 days, following a 3 – 6 day incubation period.
  - Treatment is supportive only. There is no chemoprophylaxis
  - Vaccination:
    - Safe, lasts for 10 years
    - Only vaccinate child < 12 months and pregnant women if high risk
  - Epidemics occur if poor maintenance of vaccination and lack of plans for detection and response to epidemics

Consequences of Global Environmental Changes

- ↑ Population:
  - Main driver of global changes
  - Carrying capacity of the world around 10 – 15 billion, currently 6 billion
  - Compounded by unequal distribution of resources: 20% have 80% of the resources
  - Technological change will only affect the 20% with resources ⇒ little impact on carrying capacity
- Demographic transition: As countries shift from ‘3rd world’ to ‘1st world’ their pattern of disease shifts from infectious diseases with high infant mortality to degenerative diseases → the 80% will have ↑↑ resource requirements following this transition

- **Global warming** (due to ozone depletion, ↑CO2, etc)
  - ↑ Vector born disease
  - Thermal expansion of oceans *(melting ice caps comes later)* + *more frequent storms* → flood low lying areas

- Resource depletion:
  - Wood, fossil fuels, food
  - Sources → resources used by people → sinks. If transfer is too fast, sources and sinks can’t keep up

- **Deforestation/desertification** as a result of resource use and climate change

- War:
  - Due to competition for resources
  - Leads to all extremes of environmental health (death in combat, poor health, refugees, socio-economic effects)

- Trans-boundary population shifts (eg refugees)

### Screening

#### Definitions

- **Screening**:
  - The presumptive identification of *unrecognised/preclinical disease* or defects by the application of tests, examinations or other processes that can be applied rapidly (and cheaply)
  - Sorts people into high and low risk groups for further diagnosis of high risk
  - Is NOT diagnostic on its own

- **Mass/population screening**: *systematic* screening of populations

- **Opportunistic screening**: *non-systematic*, when the opportunity arises

- **Selective Screening**: systematic screening of high risk groups

- **Screening test**: a test performed without a clinical indication

#### Objectives of screening:

- ↓Mortality/morbidity from disease on the individual
- Limit the impact of disease on a community
- Identify compensatable disability (eg poor eyesight in kids)

#### Criteria for Screening Programmes

- Is the disease an *important health problem* (incidence, impact, preventability)?
- Is a suitable screening test available:
  - Acceptable, simple,
  - *High sensitivity*, as specific as possible
  - PPV: probability that a person with a positive test does have the disease, depends on *sensitivity*, *specificity* AND *prevalence*
  - NPV: probability that a person with a negative test does not have the disease
  - Yield (proportion of cases of the disease accurately identified by a screening test),
  - Repeatability (depends on variation in method, subject variation, observer variation)

- Is the *natural history* of the disease well understood:
  - A recognisable latent or early symptomatic stage
  - The length of the asymptomatic stage determines screening frequency. Is this long enough to make the screening interval reasonable?

- Does screening lead to *interventions* that improve quality of life:
  - Does early intervention offer benefits over later intervention
  - *Accepted treatment, proven effectiveness*. Ideally want an RCT that demonstrate screening verses no screening improves mortality/morbidity

- Is there an appropriate *infrastructure* available to provide screening and follow-up services:
  - Are there pilot studies demonstrating how it should work?
  - Is there local and national support?
  - Are the services accessible (in terms of geographic, cultural barriers, cost), does the system have sufficient capacity, and is there appropriate quality control processes in place

- Is the screening programme *cost effective*?
• Is there **RCT evidence** supporting the use of the screening programme?

**Screening Test**

• Eg PSA for prostate cancer, intra-ocular pressure for glaucoma, etc
• For a screening test, you want a test that maximises sensitivity: maximise true positives (minimises false negatives), so that you identify all diseased cases
• The **downside is an ↑ rate of false positives** who have unnecessary further investigation
• A highly specific test would maximise true negatives (ie minimise positives, so would not further test anyone unnecessarily), but at the cost of ↑ false negatives – who are the people you actually want to detect
• See also Evaluation of Diagnostic Tests, page 1047

**Biases**

• **Lead-time bias**: *interval from detection to point where diagnosis would have been made without screening.*
  - Depends on length of pre-clinical phase, frequency of testing, and the test sensitivity
  - Lead time is the period between early detection of disease and the time of its usual clinical presentation
  - When evaluating the effectiveness of the early detection and treatment of a condition, the lead time must be subtracted from the overall survival time of screened patients to avoid lead time bias. Otherwise early detection merely increases the duration of the patients' awareness of their disease without reducing their mortality or morbidity
• **Length** bias: cases with a disease with a longer natural history are more likely to be detected by a screening programme. But these cases also have a better prognosis. Thus screening leads to a better prognosis, regardless of whether screening itself confers any benefits
• **Selection** bias: selection, referral or volunteer bias results in a selected subset of the population being screened

**Screening Programmes in NZ**

• National screening programmes:
  - Neonates: inborn errors of metabolism – Guthrie Card (See Genetic Testing, page 777)
  - Cervical Cancer (See Cervical Cancer, page 598)
  - Vision/hearing testing at school entry (erratic)
  - Mammography (see Breast Screening, page 673)
• Controversial and not currently recommended population screening programmes:
  - Prostate (PSA)
  - Colorectal cancer
  - Otitis media with effusion
• Current screening pilots: Hepatitis B
• Opportunistic screening
  - Antenatal screening
  - Blood pressure
  - Cholesterol
  - Blood glucose
  - HIV
  - Osteoporosis
  - Glaucoma, etc
• Deciding to implement a screening programme:
  - The decision to implement a population based screening programme is complex, must be justified on the basis of standard WHO criteria and supported by research evidence
  - The rules to do with population health are NOT those of an individual clinician (ie just because you would screen an asymptomatic man for prostate cancer is not a reason to implement a national programme)
  - Potential to do harm at a population level is considerable (‘first do no harm’)
  - We are ‘imposing’ something – need sound evidence

**Ethical Considerations**

• Costs and benefits:
  - Costs should include adequate support, counselling, etc. Benefits should include quality of life (but subjective)
  - Many harms are personal – false alarm, false reassurance. Difficult to account for
• Justice:
  - Distribution: benefits accrue to a few and are large; harms fall on many and are minor. Is this fair?
Inconvenience borne by many to benefit the few – but this also benefits the group (social welfare function)
Collective gains depend on high levels of individual participation

- **Autonomy:**
  - Motivation: altruism only effective if participants well informed/educated
  - Imposition: opt-out strategies – trade-off between recruitment level and maximal choice
  - Results: safeguards on third party disclosure

- **Opportunistic screening:**
  - Cost and benefit usually borne by the same individual
  - Offered responsively rather than proactively
  - Appropriate treatment or other follow-up available

- For Prostate Screening, see Prostate Cancer Screening, page 339. Prepared for Public Health test.

### Health Promotion

- The **“process of enabling people to increase control over, and to improve, their health”** (Ottawa Charter)

**Ottawa Charter** had 5 strategies (DRSHC):
- **Develop personal skills** (increase knowledge and skills, encourage positive life style changes; behaviour change)
- **Reorient health services** (change ambulance at the bottom of the cliff mentality → build a fence at the top instead)
- **Strengthen community action** (authority must be transferred to the community leaders to implement the plan)
- **Healthy public policy** (legislation, resource distribution, addressing other determinants of health like housing)
- **Create supportive environments** (making the healthy choice the easiest one)

- The **Treaty Understanding of Hauora in Aotearoa NZ (TUHANZ)** is a framework adapting this to NZ (issued by the NZ Health Promotion Forum):
  - Goal for Article 1 (**Kawanatanga/Governance**): achieve meaningful **Maori involvement** in **all** aspects of **health promotion**
  - Goal for Article 2 (**Tino rangatiratanga/Maori control and self-determination**): actively support the advancement of Maori health aspirations
  - Goal for Article 3 (**Oritenga/Equity**): prioritise health promotion action that improves Maori health outcomes

- Progress has been made on: Heart disease, SIDS, Road traffic accidents, cervical cancer
- Issues of concern: Maori to non-Maori gap, melanoma, youth suicide, obesity, ↑STDs
- Compared to other OECD countries, NZ has high mortality from ischaemic heart disease, respiratory diseases, breast and bowel cancers, MVA, suicide

- **Role of health care sector:**
  - See patients as part of a community, not just as individuals
  - Integrate with programmes delivered by others
  - **Move to a focus on the determinants of health** (including socio-economic status – income and housing – culture, health care system, in addition to genetics, etc)

- **Strategies in the health care sector:**
  - Care and support
  - **Screening:** eg alcohol in pregnancy, cervical, six week check, opportunistic screening for diabetes, breast screening
  - **Immunisation:** childhood and influenza
  - **Health education:** eg antenatal education including sun protection, diabetes, HIV, nutrition, exercise, smoking
  - Helping to build healthy public policy
  - Creating healthy institutions (eg Healthy Hospitals – integrating health promotion into their work)

- **Barriers:**
  - Insufficient time with patients
  - Perceived or real cost disincentives
  - Uncertainty among providers about the evidence
Social Inequalities in Health

- ↓SES strongly associated with poor health
- There is a social gradient in health – it exists in all countries but the slope varies
- Targets for intervention:
  - Socio-economic status: issues around distribution
  - Intermediary factors: housing, targeted support
  - Health issues: access. Most countries target their intervention here
  - Link from Health to SES: disability support
- Poor health → deprivation through stigma and ↓earning potential
- Deprivation → poor health through the following:

Effect of Deprivation on Health

- Poor access to health care:
  - Culturally foreign
  - Financial barriers: GP services, transport, class and language differences between doctor and patient
- Income:
  - Key SES lever. Can have a rapid effect on:
    - Effects of a drop in absolute income
    - Rise in income inequality → divisive effect on society → alienation of ‘work poor households’:
      - Measured by the Gini Co-efficient for household equivalent disposable income
      - Has ↑ for NZ since 1988 from 0.26 to 0.33 (biggest change in the OECD)
      - Is followed with a small lag by indicators such as youth suicide, youth unemployment, etc
    - Formation of social capital. People in ‘survival’ mode don’t have energy to contribute to community
  - Policy levers: monitoring income inequality, change tax rates and social wage, alter WINZ rules about supplements
  - Single parent families, women, Maori and Pacific Islanders are over-represented in the poor
- Education: Increases human capital. Students from poor households are more likely to underachieve, have lower participation rates in tertiary education.
- Occupation and labour force participation:
  - Translates human capital into income. Also indicator of social class
  - Higher injury rates in low SES jobs (forestry, construction)
  - Unemployment: ↑stress, social isolation, lack of purpose →↓self esteem
- Housing:
  - Impacts of rent, neighbourhood, number of bedrooms, quality of construction and maintenance (eg insulation, ventilation).
  - Issue for the poor, and also for former institutionalised psychiatric patients
  - Damp housing → respiratory illness, overcrowding → infectious diseases, ↑mental distress
- Feelings of hopelessness and being devalued → less cohesive society → violence, exploitation, drug use
- Ethnicity:
  - Interacts with SES
  - Sensitive policy area
- NZDep (NZ Deprivation Index) is a composite measure of deprivation
- Individual health risks:
  - Adequate food in sufficient quantities (‘food security’)
  - Physical exercise: affected by range or sports facilities, clubs, etc
  - Alcohol/tobacco consumption: affected by taxes, restrictions on distribution
  - Early pregnancy
  - Also indicators such as obesity, high blood pressure, high cholesterol, diet, exercise
- Health behaviours/At-risk behaviour (eg lifestyle factors)
  - Health damaging behaviours more common in low SES
  - Knowledge alone insufficient to change behaviour (eg smoking may be a coping strategy)
- Relate these factors to health status using measures of mortality, morbidity (including measurement of self-rated health status, suffer from specific diseases or measure role limitation), health risks, health service utilisation
- NZ approach:
  - Monitor social and economic determinants of health
  - No systematic cross country comparisons
  - Slow policy development and implementation
- Lacks cross party and public support
- Emphasis on health providers not determinants

**Conclusions:**
- Socio-economic determinants of health are multi-causal
- Issues around policy making under conditions of uncertainty
- Policies should be monitored against goals

**Maori Health**
- Includes 2\textsuperscript{nd} and 3\textsuperscript{rd} year PDS notes on Maori Health

**Who is Maori**
- 3 concepts:
  - **Biological**: amount of blood
  - **Descent**: descended from a Maori but not worried about %age of blood
  - **Cultural identification**: group to which individual feels most closely aligned

**Ethnic Classification in the Census:**
- Prior to 1974: based on > 50% Maori blood
- Till 1986: Based on descent
- 1986 census: What is your ethnic origin (ie self-identification)
- 1991 census: What ethnic group do you belong to
- All leads to differences in the way trend data are presented (ie adjustments made to the denominator)

**World-view:**
- Io (supreme being)
- Te korekore (the nothingness at the beginning)
- 3 realms which interpenetrate each other:
  - Realm of ultimate reality: Io, Rangi (sky father), Papa-tua-nuke (earth mother), Tipuna (Gods, spirits, ancestors), mana and tapu
  - Realm of the human
  - Realm of the dead

**Mana:**
- Enduring, indestructible power of the Gods
- Mana atua: sacred power of the Gods
- Mana tupuna: power or authority handed down through chiefly lineage
- Mana whenua: power associated with possession of lands
- Mana tangata: power acquired through developing skills

**Tapu:**
- Sacred, set apart, forbidden, restricted
- Everything created by gods has tapu (people, land, river, forests)
- People become tapu by their desire to stay under the influence and protective powers of the gods
- There is good tapu and bad tapu (the devil has tapu too!)
- Compares with noa (free from tapu, common)

**Epidemiology**
- *Life expectancy has improved* compared to Pakeha since 1950, *has levelled off*, and is now about 10 years less than Pakeha
- Maori have worse health statistics but *fewer hospitalisations* (ie use services less)
- Wide disparities across all indicators of education, health, income, housing, employment and criminal justices
- Maori concentrated in lowest 3 deciles of deprivation index – 25\% in lowest: a **distribution gap**
  - “Sole” Maori more likely to be distributed among more deprived-deciles than mixed Maori (census definition)
  - Deprivation distribution of mixed M remains worse than NM
- Health outcomes of Maori are different from non-Maori after controlling for deprivation: this is an **outcome gap**
  - Eg LE for NM residing in decile 10 (worst) is higher than M in the same decile
  - Maori utilisation of health services is less despite poorer health
- A **gradient gap** also exists: the relationship between ethnicity and increasing deprivation. The effect of ↑ deprivation compounds the risk for Maori as cf NM
When controlling for deprivation, Maori life expectancy is still worse, and gets even worse in the lowest decile
⇒ Maori are not just sick because they’re poor. Possible explanations:
- Not Maori behaviour – common to ethnic minorities around the world
- Not genetic – why would Maori and black Americans have the same predispositions given the degree of genetic separation

To many Maori, these disparities are clear evidence of a breach of the TOW

While the Crown regularly report on health, M health outcomes are frames as different from ordinary NZers, M are portrayed as abnormal or as the “other”

Social and economic determinants of health:
- Michael Marmot: epidemiology of British civil service – position in hierarchy better predictor of life expectancy than smoking, hypertension, etc
- Postulate: Don’t have more problems but have fewer choices ⇒ chronic stress from poor control over life (can only worry, can’t do anything else) ⇒ elevated hormone response (eg Corticosteroids) ⇒ lipids, obesity, insulin resistance, CHD, etc. Effectively aging quicker.
- Stress levels impact on the degree of impact of lifestyle factors on your health

Urban shift:
- In 1945, 25% of Maori lived in urban areas. In 1980, 80% lived in urban areas
- Due to development of manufacturing industries and centralisation of agricultural production (eg freezing works) ⇒ fewer jobs in traditional tribal areas

Common Myths

Interventions based on ethnicity are racist: what about poor NM?
- Deprivation data highlights that ethnic disparities in health outcomes exist along the entire social gradient
- The existence of these ethnic disparities is racist, not the analysis or intervention to deal with them

By focusing on disparities we promote NM levels of health as the M goal: we want to be like NM
- M seek to remove ethnic disparities, not to become NM – it is a necessary part of M health development

Disparities analyses promote negative stats – it’s all bad news – it’s paralysis by analysis
- Disparities focus vs development focus
- Is a tension between the need to recognise and honour the scale, scope and effects of disparities and need to implement interventions – not a matter of either/or, they are complementary strategies
- Purpose of monitoring disparities is to intervene appropriately and eliminate inequity

Before NM arrived in Aotearoa, M life was haphazard and accidental – they were uncivilised and desperately needed rescuing
- M had sound PH principles, clean water supply, sanitation + waste disposal etc before NM arrived
- This perhaps made it easier to justify the dispossession of land and resources that is integral to colonisation

Colonisation

Colonisation transforms a nation, from its demographic, political, economic, and social order, to the shape of the society
- Is a process whereby power + resources are obtained from the indigenous inhabitants then redistributed to the newcomers
- At worst colonisers have openly denied the humanity of indigenous groups + at best they have deprived indigenous peoples of their rights through paternalism + neglect
- The ability to dehumanise is derived from a sense of group superiority
- The net result has been the alienation of rights + resources from M to colonial beneficiaries
- The effect of colonisation of markedly ↑ mortality led to depopulation of up to 75% of M (first interpreted as “survival of the fittest”)
- All this lead to the rejection of Aotearoa as a country and the construction of NZ and the imposition of a new order that was fundamentally ethnocentric and therefore racist
- The taking of land not only makes people poor – it also makes them more susceptible to diseases that flourish under conditions of poverty, overcrowding and malnutrition; it destroys or disrupts social networks that provide practical emotional support in times of need
- As well as immediate effects of land loss, dispossession of land propels a group into future socioeconomic deprivation as these territories can no longer be used as economic + social equity
- Central to colonisation is creating a ‘new history’. In this ‘new history’ indigenous knowledge and beliefs are relabelled as myths, legends and superstition. The land gets ‘discovered’ by colonisers and the landscape is renamed. Unless we recognise colonisation as a deliberate and continuous process it is easy to assume that colonising events are accidental, inevitable and over. We must never assume that colonisation is something
confined to our past. The confiscation of Māori rights to the foreshore and seabed confirms colonisation as our constant contemporary.

- These new systems are built on new values: they promote new ideas about who is normal (and therefore who is not); who is knowing and who is ignorant; who is civilised and who is barbaric; who is deserving and who is undeserving; and who is good and who is bad. Through this process Māori move from being normal to being ‘different’ from Pākehā, non-Māori, non-indigenous norms.

Racism

- **Institutionalised** racism is defined as “differential access to the goods, services, and opportunities of society by race”. It is illustrated by the different distributions of Māori and non-Māori across deprivation deciles, income brackets and occupational classes. These differences will mean that these two population groups have different capacities to participate in various activities, make a full range of choices, to be represented and to be heard.

- **Interpersonal** racism is defined as “prejudice and discrimination, where prejudice means differential assumptions about the abilities, motives and intentions of others according to their race and discrimination means differential actions towards others according to their race”. We have seen recent examples in the differential treatment of Māori seeking employment or rental housing. Jones notes that this personal aspect of racism is what most people think of when they hear the word ‘racism’.

- **Internalised** racism is defined as “acceptance by members of the stigmatised races of negative messages about their own abilities and intrinsic worth”. It is manifest when Māori are anti-Māori.

To accept that environmental factors such as racism can influence our physical health we have to visualise a pathway that enables this. Krieger and colleagues argue that our social environment affects our bodies just as our physical environment does. It shapes what we know, how we understand the world and relate to it, the level of access we have to societal resources and opportunities, as well as our ability to navigate our way through social systems. A critical measure in this model is power and control. That anyone should experience racial discrimination is an unacceptable breach of human rights.

Ethnic Inequalities in Health

- 1. Differential access to the determinants of health or exposures leading to differences in disease incidence. New Zealand evidence includes the very different profile of Māori to non-Māori with respect to the determinants of health such as education, employment, income, housing, income support, dealings with the criminal justice system, health literacy, deprivation, etc. These factors also pattern exposures to other risks like tobacco use, poor nutrition, overcrowded and substandard housing, unsafe workplaces, problem gambling, and ‘binge’ patterns of alcohol use.

- 2. Differential access to health care. Examples include: Māori experiencing longer and slower pathways through health care; hospitalisation rates that are disproportionately low in disease categories where Māori have high death rates and a health service configuration where people without access to transport or resources have more difficulty attending health services for both treatment and prevention.

- 3. Differences in the quality of care received. Evidence of Māori being less likely to receive appropriate levels of care is seen in screening for and treatment of ischaemic heart disease, pain relief during labour and childbirth, the diagnosis and treatment of depression, diabetes screening and management, and higher levels of adverse events in hospital.

Reasons for smoking

- Part of history: tobacco given as gifts at Waitangi, Goldie images of smokers, etc.

- Advertising: eg Howard Morrison (role model) advertising lighters

- It has become culturalised: carved pipes, woven pouches for lighters →reinforce link between smoking and Māori

- Responses:
  - Smoke free hui
  - Aim at young (‘Why start’) – counter image that its cool to smoke
  - Smoke free areas
  - Enforce bans on underage sales
  - Needs whanau, local, national integration

Cardiac Intervention as an Example

- Based on 2001 NZMJ article

- ↑ in HF with higher deprivation was evident

- Hospitalisation rates for HF for M were more than double the NM rates.
Rates for cardiac intervention were much lower (1/3 – 1/2) for M as cf NM (but how is cardiac intervention – CABG/PTCA related to HF??)

Poorer Health Status When Deprivation Adjusted For
- Lower levels of hospital service access, present late with more significant illness
- Structural racism in the health sector:
  - Hospitalisation rates for heart failure and for cardiac interventions. Study found that there were higher hospitalisation for Maori for heart failure when cf non-Maori (especially amongst males) but the rates for cardiac intervention were much lower, this finding was independent of deprivation status, but also in addition to deprivation
  - Davis et al (2006) found higher rates of ADR in Maori when age standardised, ?quality of care not as high
  - Maori have higher rates of unmet needs for GP services – too expensive, too busy, don’t want to make a fuss, difficulty getting an appointment, unexplained cultural barriers

Consequences of first nation status, second class, separation from land, separation from language and separation from culture, eg. Mauri Ora smoking program was a success because it developed old knowledge about the sacredness of the life breath, compared this with the poison of smoking
- Tipu ora, using kuia as parenting mentors, experienced and non-smoking, pragmatic approach → by Maori, for Maori
- Poorer levels of education

The Treaty of Waitangi (Te Tiriti O Waitangi)
- Maori view of the TOW: was and is an insurance policy to protect M from the detrimental effects of colonisation while ensuring M access to the benefits of the new society
- Pre-treaty history:
  - ↑ availability of guns and overcrowding in the north → ↑ inter-tribal wars
  - Introduced diseases → high mortality
  - 1831: Chiefs wrote to the king to ask for protection. Busby sent as NZ resident in 1832
  - 1835: Northern tribes declaration of independence
  - 1839: Hobson sent by colonial office to do a new deal

At the time of the treaty:
- Maori significantly outnumbered non-Maori
- Settlers wanted land
- Maori needed British government to control sailors, whalers and convicts who came here
- Maori needed national identity to trade inter-nationally (eg ships needed a flag)
- Maori and non-Maori had a mutual need for each other

The Treaty:
- 1. Kawanatanga (Governance) vs Sovereignty in English – no Maori would have given this up
- 2. Tino Rangatiratanga (Chieftainship, Control, Autonomy) vs Possession in English
  - 2a: Queen promised protection, and exercise of their chieftainship over lands, villages and treasures
  - 2b: Queen had exclusive right to buy land (and sell it on at a profit to finance the colony)
- 3. Oritenga: Equity: speaks of equal citizenship, equal health outcomes

Application of Treaty to health:
- Implicit in treaty were concepts of equity, partnership, economic and cultural security
- Concepts of health firmly based in Maori culture, which under the treaty are recognised and protected
- Kawanatanga (Governance): Government has responsibilities to govern and should take reasonable steps to improve health. Crown has obligations as well as power. Applies to all citizens
- Tino Rangatiratanga (Chieftainship, Control, Autonomy). Applies to Maori. Right to establish and provide services (but its not just a right, it is also effective)
- Oritenga: Equity. Maori have poorer health and poorer access, so neither equality of opportunity nor outcome

Post Treaty:
- Treaty was basically sound – but the Crown didn’t stick to it:
  - Others brought land directly
  - Crown brought land unfairly or confiscated it
  - Maori discriminated against in social policy, entitlement to vote, treatment of returned servicemen, etc
- 1841: unused land deemed Crown land
1844: law enabling Maori to be educated in English. Speaking Maori in school punishable offence till relatively recently
1852: right to vote given to individual land owners – Maori excluded as land held collectively
1863: law allowing confiscation of the land of rebels
1867: ↑Maori individual ownership of land → threat of majority in some electorates → set up 4 Maori sets so Maori remain a minority
Rapid loss of land (from 26.8 m hectares to 3 m hectares by 1900), ↑Pakeha, concern among Maori about loss of clout → Kingitanga movement
Land wars in Taranaki and Waikato: complex and changing politics, many tribes at one point or another were allied with the British against Maori enemy tribes

**Impact on Health**
- Socio-economic: low incomes, poorer housing, higher unemployment, less education
- Lifestyle: diet smoking, alcohol, drug use
- Cultural factors: alienation, loss of wairua and cultural identity, urban drift → fragmentation of whanau
- Due to:
  - Failure to give same rights and privileges
  - Failure to protect treasures
- See also Maori Mental Health, page 682

**Is NZ Safe For Maori?**
- The evidence would suggest not: NM will live longer, be more privileged by the education system, be more likely employed and earn more, be more likely to own a home, more likely to obtain a full benefit, less likely to be arrested, more likely to get diversion, more likely to be able to listen to TV + radio in their own language, learn about their own culture etc etc etc
- All this with a treaty guaranteeing equity

**Maori Right to Monitor the Crown**
- From our indigenous rights embodied in the United Nations Declaration on the Rights of Indigenous Peoples (United Nations 2007) and reinforced by the Treaty of Waitangi
- The primary right of indigenous peoples is to self-determination, which includes to name ourselves as tangata whenua and be recognised as such. As tangata whenua, our duty includes ensuring the wellbeing of all people in our territories
- This necessitates Māori monitoring health, including any disparities in health outcomes
- Secondly, our right to monitor the Crown is derived from the consistent, comprehensive and compelling disparities in health outcomes, exposure to the determinants of ill-health, the lack of health system responsiveness and the underrepresentation of Māori in the health workforce
- These human rights charters acknowledge that inequities are unjust and assert that where systematic inequalities exist governments have a duty to provide interventions such as affirmative action programmes and legislative protection (Bill of Rights Act 1990, NZ; Human Rights Act 1993, NZ; United Nations 1965, 1980, 2001)
- Despite this legal obligation to intervene, efforts to reduce and prevent ongoing inequalities in health between Māori and non-Māori continue to be met with powerful resistance by non-Māori, who benefit from them and by those Māori recruited to support this resistance

**Cornerstones of Maori Health**
**Cornerstones**
- Attempt to get away from purely bio-medical model of health
- Taha hinengaro: mind and emotions
  - Includes cultural identity: Te whanau (family), te whena (land) and te reo (language)
  - Mana important to maintenance of mental health
  - Whakama: encompasses shyness, embarrassment, shame. Confused with depression, guilt, subordination
- Taha wairua: spiritual health
  - Life force: reflects where you come from, guides your future
- Taha tinana: physical health
  - Tapu: complex: places/objects (eg tiki)/body parts (head & genitals)
  - Don’t mix food and heads, 2 ends of GI tract should never meet
- Taha whanau: family.
Belonging, identity, security
Whakapapa: whanau → hapu → iwi
Fragmented by urbanisation
Check family and social history (eg family effected by mental illness, family health impacts on personal health eg abuse, etc)

Eg – application to type 2 diabetes:
- Taha hinengaro: Need understanding to manage disease and prevent disability, needs coping strategies
- Taha wairua: colonisation and cultural dislocation → cultural identity and recovery: need a passion to live, to know their place in the world → more likely to beat the illness
- Taha tinana: Medical response, treatment of complications
- Taha whanau: Family breakdown contributes to poor lifestyle and support. Need support of family in making lifestyle changes

Other factors *
- Tino rangatiratanga: control of own destiny
- Economic security
- Self esteem, pride and confidence
- Measures of Maori health: value of resources in Maori ownership, drop in crime rate, use of te reo
- Tohunga: traditional Maori healer (common in Maori communities)
- Mate Maori: illness due to wrong doing → refer to kaumatua

Death and Dying *
- For family and friends, seeing the patient while alive is important, bring koha, say karakia
- Following death:
  - Everything is tapu – those at the bedside are responsible for ensuring customs carried out
  - Avoid post-mortem: sanctity involved, impedes release of spirit (spirit lingers 3 – 8 days)
  - Dead person never left unattended
- Tangi:
  - 2 – 5 days after death
  - Farewell speeches and lamenting
  - Conflict over where to bury the deceased: te tupapaku may be taken to a number of marae as a compromise
  - Encourage wairua to depart
  - After burial: hakari – sacred feast – turning point

Maori services
- Health services in NZ were founded on racist ideological assumptions and the prioritisation of the needs of the NM majority. In the 1800s this prioritisation was often achieved by the explicit exclusion of M from health services
- Disparities in health outcomes were explained away by blaming M physical, cultural + socioeconomic characteristics
- Interventions were ad hoc + underfunded ‘clip-ons’ to universal services
- Kaupapa Maori: by Maori for Maori; have gained ↑ acceptance + link between Aotearoa and NZ
- Tipu Ora: in Rotorua, building on traditional role of ‘Kuia’ (“nanny”) – Maori, non-smoking, young grandmothers. Pragmatic focus (ie get them to smoke outside rather than insisting on smoking cessation). Has reduced SIDS

Maori Cultural Differences
- Contributing factors to cultural dislocation:
  - Perceived value of self
  - Social position
  - Cultural dislocation → shattered spirituality → ↓ Taha wairua
  - Ignore cultural values and they’ll ignore you
- Responses:
  - Don’t blame – beating up on beaten up people doesn’t change anything
  - Give them resources: e.g. to population group (cf. AIDS control)
  - Use cornerstones on consultation check list
  - Are we contributing to peoples stress or reducing it?
Drug and alcohol policy

- See also Regulation of Medicines and Drugs, page 859
- See also Approximate addictivity (highest to lowest): nicotine → opiates → stimulants → alcohol
- Cannabis/Marijuana, page 747
- Drug epidemiology:
  - Deaths attributed to drug use:
    - 79% Tobacco
    - 19% Alcohol
    - 1% Other drugs
  - Male deaths twice female deaths
  - Social costs (including lost production, mortality, health costs, benefits from consumption etc) reveal alcohol is more ‘expensive’ than tobacco (Tangible and intangible costs of alcohol = 6% of GDP, tobacco = 4.9%). Alcohol takes people from production and has greater secondary costs (on family, accidents, etc, and effects production from earlier in life)
- Prevention Paradox: To get greatest gain from prevention need to target the mean, not the tail (although they drink the most), as most people, and therefore the biggest cost, relates to people around the mean. (Eg cholesterol, alcohol, etc)
- Historical influences:
  - Colonial society: more men than women (miners, whalers, etc)
  - Brewing industry and pubs a large employer of labour
  - Brewing industry characterised by wealthy and influential families
  - Other communities had other drugs (Chinese – opium, Italians – wine, which were subject to different regulations)
  - Women settlers in later 19th century saw alcohol as a problem → strong temperance movement → push for ↑ regulation in early 20th century
- Interests/stakeholders in drug policy today:
  - Politicians: libertarian vs conservative
  - Legal drug companies: tobacco/alcohol (invest $ into ‘education’ to control the climate of what is ‘cool’)
  - Illicit drug dealers: large gang involvement
  - School sector: teachers/principals
  - Medical profession (also issues around medicinal use, eg of cannabis)
  - Lobby groups: ASH, DARE, Drug foundation, Life Education Trust
  - Police: $30 mill per year for cannabis control, 12,000 arrests for cannabis offences, 6000 prosecutions, only 500 get diversion
  - Mao: 2 views: it’s dangerous so should be illegal vs it is criminalizing young Maori
- Cannabis: have had a debate without good information

Health Economics

- Study of how individuals and societies, experiencing virtually limitless wants, choose to allocate scarce resources to best satisfy their wants
- Scarcity:
  - Resources (main factors of production – natural resources, capital, labour) are scarce
  - Goods and services produced from them are scarce
  - Can’t have as much as we would want if they are free
  - Will always be medical interventions that cannot be funded
- Choice: Because of scarcity, we must make choices
- Opportunity cost:
  - The loss of the next best opportunity we could have chosen (ie if we use time/money on one thing, it’s not available for something else)
  - When doing an evaluation: deduct GST (it’s a transfer), use real price (eg not subsidised cost of a drug), include indirect costs (eg patient travel)
  - Can be calculated from different perspectives: eg provider, funder, society
- Marginal analysis:
  - = Incremental benefit (ie marginal benefit) from incremental cost (ie marginal cost)
  - Decisions are usually about whether to expand or contract – not stop or start
  - Marginal cost is NOT the same as average cost
- Efficiency:
= Maximising benefits from certain cost of inputs
Not the same as cost-cutting: if you cut costs and output falls then haven’t improved efficiency
Effectiveness: are patients better off (eg have better health) with intervention than without
Technical efficiency: providing effective services at least cost – doing things right
Allocative efficiency: concentrating resources on effective services that offer the biggest payoff in terms of health – doing the right things
Inefficiency is unethical (if budget is constrained)

• Equity:
  ➢ = Fairness: usually of distribution or payment
  ➢ Equal access for equal need (what is need – ill health or capacity to benefit)
  ➢ Equal resources for equal need (same amount of money for equal needs – basis of the DHB funding formula)
  ➢ Equal outcomes: allocate resources to achieve same health status of different populations

• Markets:
  ➢ Means of allocating scarce resources
  ➢ Result from the interaction of demand and supply, mediated by price
  ➢ Consumers can signal demands, maximise their ‘well-being’ or utility, producers can shift resources accordingly
  ➢ If there is perfect competition, theoretically you get allocative efficiency
  ➢ For this to work, requires:
    o Perfect information (eg about quality, costs, etc)
    o No externalities (someone else bears a cost or benefit)
    o Goods and services must be rival in consumption (ie if I buy it no one else can have it) and excludable (you can’t have it if you can’t pay)
    o Freedom of entry and exit
    o Perfect competition – no monopolies
    o No supplier-induced demand
    o Equity is not an issue (ie no merit goods – goods that society believes should be more widely available than would occur through markets alone)
  ➢ Market failure in health care:
    o Externalities eg immunisation
    o Monopolies eg secondary services, labour markets
    o Asymmetric information eg health professionals
    o Supplier induced demand (especially if fee-for-service)
    o Highly inelastic demand

• Health Insurance Markets
  ➢ Uncertainty about future health needs + high costs → demand for insurance
  ➢ Moral Hazard: will now consume more health care than they otherwise would as someone else is paying (can control with co-payments)
  ➢ Adverse selection: patients who know they will need it are more likely to purchase it. Insurers won’t know so premiums won’t reflect risk

• Want to getting advantages of market efficiency and overcoming market failure → ?government failure, purchaser provider splits, quasi markets (health care plans)

• International Comparisons: Health Expenditure per capita and GDP. NZ is on the line

• Economic Evaluations:
  ➢ = Comparative analysis of alternative courses of action in terms of their costs and consequences
  ➢ Informs choices about the allocation of scarce resources
  ➢ Needed to determine efficacy (in lab conditions), effectiveness (more good than harm in practice)
  ➢ Can be prospective or retrospective
  ➢ Types of evaluation:
    o Cost minimisation: compare inputs, assume outputs are equal
    o Cost benefit: compares different outcomes (eg flu jabs and hypertension screening). Convert to common unit ($) to compare – but can human life be valued?
    o Cost effectiveness: relates cost to a clinical measure (eg ↓blood pressure, morbidity, life years gained). Has superseded cost-benefit analysis due to problems allocating monetary values to all outputs
    o Cost utility: cost per QALY gained. Can compare across a whole range of interventions – but methodological problems. Example: Impact on QALYs of dialysis versus kidney transplant

• Common approaches to valuing human life:
Human capital: future earnings (but elderly have none)
Implied valuations: value implicit in past policies
Insurance values: but this is paid to survivors
Willingness to pay to reduce low probability of death: survey or observe (e.g., how much do people spend on safety)

Theory X and Y: Summarising different approaches to health care in health economics

<table>
<thead>
<tr>
<th></th>
<th>Theory X</th>
<th>Theory Y</th>
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</thead>
<tbody>
<tr>
<td>View of Health</td>
<td>Health and disease occur randomly</td>
<td>Health determined by lifestyle choices</td>
</tr>
<tr>
<td>Medical Care</td>
<td>Special. Market Failure</td>
<td>Same as other goods and services</td>
</tr>
<tr>
<td>Practice of Medicine</td>
<td>A Science</td>
<td>An art</td>
</tr>
<tr>
<td>Economics</td>
<td>Financial rewards reduce the quality of caring</td>
<td>Financial rewards generate high quality care</td>
</tr>
<tr>
<td>Policy</td>
<td>Regulation needed to mitigate economic forces. Tax the health, subsidise the sick. Discourage new medical technologies</td>
<td>Reduce regulation, encourage market forces. Tax the sick, not the healthy. Encourage new technologies</td>
</tr>
</tbody>
</table>
Evidence Based Medicine

- Reference: 4th Year Evidence Based Medicine Notes
- See also Epidemiology *, page 1026

Introduction

What is Evidence Based Medicine

- = 'The conscientious, explicit and judicious use of current best evidence in making decisions about the care of individual patients. This practice means integrating individual clinical experience with the best available external clinical evidence from systematic research'
- Why is it necessary:
  - Wide variation in clinical practice
  - To minimise clinical error
  - High use of treatments not proven to do more good than harm
- Can be extended from medicine to health care
- Need to understand new types of evidence: randomised controlled trials (started in 1948), meta-analysis and systematic reviews
- EBM approach is better than traditional continuing medical education (which is largely ineffective). Clinical knowledge and performance deteriorates over time
- Application of evidence:
  - Generalisability: do trials apply to a whole population
  - Applying probabilities from a population to an individual
  - Multiple treatments: trials only test one at a time
  - Acceptability
  - Also need to consider economic impact given limited resources

Developing a CAT (Critically Appraised Topic)

- Title: Answer to the clinical question that initiated the search
- Clinical Scenario: brief summary of the context in which the question arose
- The clinical bottom line: a description of the clinical action to be taken as a result of the critical appraisal
- Well Built Question: good for defining pre-test probability and narrowing search strategy (PICOT)
  - The patient of population or problem being addressed in what setting (e.g. In otherwise healthy, non-smoking adults presenting to a GP with a common cold...)
  - The intervention being considered (...does a 5 day course of XX ....)
  - The comparison intervention (where relevant) (...compared with a placebo...)
  - The clinical outcome of interest (...improve symptomatic control and/or reduce the duration of an existing common cold)
  - The time frame involved
- Search the evidence: list search terms
- Description of study methodology
- Table summarising key results
- Quantitative take home messages
- Notes on validity issues: bias, levels of evidence, research design and methodology, harmful effects of intervention, etc
- References to the articles used in the critical appraisal

Cochrane Collaboration

- Aims:
  - Evidence based
  - Easily accessed
  - Clinically useful
  - Quality controlled
  - Periodic updates
- Prepares, maintains and disseminates systematic reviews
- Systematic reviews are a structured process:
  - Well formed question
  - Comprehensive data search (including non-English, unpublished)
Evidence Based Medicine

- Unbiased selection and abstraction process
- Critical appraisal of data
- Synthesis of data
- Width of diamond on Cochrane logo = confidence interval of meta-analysis

Levels of Evidence
- 1 – RCT or reviews of them
- 2 – Cohort studies or reviews of them
- 3 – Case control studies
- 4 – Case series or poor quality cohort or case-control studies
- 5 – Expert Opinion

EBM Glossary
- Bias: systematic deviation of study results from true results due to the study design.
  - Interviewer bias: systematic error due to interviewer’s gathering of selective data.
  - Lead time bias: if patients not enrolled at similar point in their illness, differences in outcome may only reflect differences in duration in illness.
  - Recall bias: systematic error due to differences in accuracy or completeness of recall. Referral filter bias – process of referral from primary to secondary ↑ proportion of severe cases → ↑ unfavourable outcomes.
  - Selection bias: a bias in study design rather than chance when study and control groups differ in ways that may affect the outcome
  - Publication Bias: results from studies with positive results are more likely to be published
- Study types:
  - Case-Control Study: retrospective comparison of exposures of persons with disease and without disease
  - Prospective Study: cohorts who have not yet had the outcome event are monitored for the occurrence of the event
  - Systematic Review: study in which trials on a topic have been systematically identified, appraised and summarised according to predetermined criteria. May or may not include a meta-analysis combining the results of the trials
- Clinical Practice Guideline: systematically developed statement to assist decision-making in specific clinical circumstances
- Study Design:
  - Decision Analysis: application of explicit, quantitative methods to analyse decisions under conditions of uncertainty
  - Intention to treat analysis: analyses individuals according to the group to which they were randomised, even if they didn’t receive the treatment, rather than confining to those who completed treatment (treatment may have intolerable side-effects). Better measure of effectiveness; ↓ potential bias
  - N-of-1 trials: blinded patient and doctor undergoes pairs of treatment periods with experimental and placebo treatment with outcomes monitored
- Study Analysis:
  - Confounding: a variable associated with the factor under investigation. Unless it is possible to adjust for the confounding variables, their effects cannot be distinguished from those of the factors being studied
  - Efficacy: benefit of an intervention under ideal conditions
  - Efficiency: benefit of intervention, including efficacy and acceptance (e.g. compliance, side effects – does it do more harm than good)
  - Precision: the range in which the best estimates of a true value approximate the true value
  - Statistical power: statistical chance of a study being able to detect a difference if one actually exists
  - Strength of inference: likelihood that an observed difference represents a real difference, rather than due to chance. Is weakened by bias and small sample sizes
  - Validity: results are unbiased and give trust estimate of the measured effect. Extent to which a variable or intervention measures or accomplishes what it is supposed to. Does it measure what it claims to measure – described by specificity and sensitivity, etc

Risks and Odds

<table>
<thead>
<tr>
<th>Exposure</th>
<th>Outcome</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td></td>
<td>A</td>
<td>B</td>
</tr>
<tr>
<td>No</td>
<td></td>
<td>C</td>
<td>D</td>
</tr>
</tbody>
</table>
• Event Rate: proportion of patients in a group in whom an event is observed. Applied to Controls and Experimental/exposed groups → CER and EER
• Relative Risk = (A/(A+B))/(C/(C+D)) = EER/CER (rate in exposed cf rate in those not exposed)
• Absolute Risk Reduction (ARR) = C/(C+D) – A/(A+B) = CER - EER
• Relative Risk Reduction: percent reduction in events in the treat group event rate compared to the control group = ((CER – EER)/CER * 100 = (C/(C+D) – A/(A+B))/(C/(C+D))
• Risk Ratio = EER/CER Odds: ratio of events to non-events
• Odds ratio: odds of an experimental patient suffering an adverse event relative to a control patient = (A/(C+B))
• **NUMBER NEEDED TO TREAT** (NNT): number of patients needing treatment to achieve one favourable outcome = 1 /ARR – always rounded up to the nearest whole number and accompanied by the 95% CI
• Number needed to harm (NNH): number of patients who need to be treated to achieve one adverse outcome = 1/Absolute Risk Increase (ARI = EER - CER)
• RRR and OR do not say anything about absolute risk. An RR of 30% can mean a risk reduction from 60% to 20%, or from 3% to 1%. The ARR and NNT varies dramatically
• Time frame: all measures (RR, RRR, ARR, OR) must be qualified by giving them a time frame (e.g. the length of the period of the study)

**Evaluation of History Taking and Clinical Examination**

*Using an article about history taking or clinical examination*

• See Using an Article About a Diagnostic Test, page 1048

**Kappa Statistics**

• A measure of agreement after chance is removed from consideration
• = Actual agreement beyond chance / potential agreement beyond chance:
• E.g. If observed agreement = 78% of cases, and agreement on the basis of chance is 51%, then Kappa = (78 – 51)/(100 – 51) = 0.55

<table>
<thead>
<tr>
<th>Kappa Statistic</th>
<th>Degree of Agreement</th>
</tr>
</thead>
<tbody>
<tr>
<td>-1</td>
<td>Perfect disagreement</td>
</tr>
<tr>
<td>0</td>
<td>Chance agreement</td>
</tr>
<tr>
<td>0 – 0.4</td>
<td>Poor agreement</td>
</tr>
<tr>
<td>0.4 – 0.6</td>
<td>Moderate</td>
</tr>
<tr>
<td>0.6 – 0.8</td>
<td>Substantial</td>
</tr>
<tr>
<td>0.8 – 1.0</td>
<td>Almost perfect</td>
</tr>
</tbody>
</table>

• Hard to compare between studies – a different case-mix would yield a different k
• A weighted k can be used to measure agreement in ordinal data
• For larger samples (> 100) sampling distribution is normal, so it is possible to calculate a standard error, confidence intervals and P values
• Other non-parametric tests (e.g. chi-squared, correlation coefficient) are measures of association not agreement

**General Evaluation of Studies**

*Are the Results Valid?*

• Were the patients **randomised**?
• Were the clinicians **blinded** to treatment/intervention?
• Were outcome assessors blinded to group allocation?
• Were the **groups similar** in their make up?
• Was the follow up complete and long enough?
• Were the groups treated equally except for the intervention?
• Were all patients **analysed**? (ie no loss to follow-up)
• Were the right exposure and outcome measures used?
• **Internal validity** → depends on bias and confounding
• **External validity** → can results be **applied to population** I am interested in?
What are the Results?

- Impact of treatment?
- Power of the study? Subject numbers? Correctly rejecting a null hypothesis when it is false
- Confidence intervals, the result is significant because the Cl does not include 1, the null effect value, therefore we can be 95% certain that the risk value is not due to chance, but in fact represents the true value for the population. However, there is a potential of 5% that the value is due to chance and does not represent the true value for the population. Width is dependent on sample size, variation of the data collected

Are the Results Relevant to My Patient? (External Validity)

- Are the results clinically significant?
- Can I apply the results to my patient population?
- Are the likely treatment benefits worth the potential harms and costs?

Evaluation of Diagnostic Tests

Sensitivity and Specificity

- **Sensitivity**: proportion of people with disease who have a positive test (i.e. true positive). How good is the test at picking up people who have the condition? SnNout = when a test has a high sensitivity, a negative result rules out the diagnosis
- **Specificity**: the proportion of people free of a disease who have a negative test (i.e. false positive). How good is this test at correctly excluding people without the condition? SpPin = When a test is highly specific, a positive test rules in the diagnosis
- Necessary Sensitivity and Specificity depend on setting. E.g. if screening for a disease occurring 1 in 10,000 in a population of 100,000 then a test with sensitivity of 99% and specificity of 99% will find 9.9 true positives and 999.9 false positives. But if the disease occurs 1 in 100 then you’ll find 9990 true positives and 998 false positives – far better strike rate

Pre-test Probability

- \( P(D+) \) = probability of target disorder before a diagnostic test result is known. Depends on patient (history and risk factors), setting (e.g. GP, A&E, etc) and signs/symptoms
- Is useful for:
  - Deciding whether to test at all (testing threshold)
  - Selecting diagnostic tests
  - Interpreting tests
  - Choosing whether to start treatment without further tests (treatment threshold) or while awaiting further tests
- Based on epidemiology (e.g. prevalence) or clinical experience

Likelihood Ratio

- **Positive LR** = the likelihood that a positive test result would be expected in a patient with the target disorder compared to the likelihood that the same result would be expected in a patient without the target disorder
- **Negative LR** = same but for negative result
- Less likely than sensitivity and specificity to change with the prevalence of a disorder
- Can be calculated for several levels of the symptom or test
- Can be used to calculate post-test odds if pre-test odds and LR known
- Impact of LR:
  - \(< 0.1 \text{ or } > 10\): large changes in disease likelihood (i.e. large change to pre-test probability)
  - 0.2 – 0.5 or 2 – 5: small changes in disease likelihood
  - 1: no change at all

Post-test Probability

- \( = \) Proportion of patients with a positive test result who have the target disorder
- Positive Predictive Value (PPV): proportion of people with a positive test who have disease. If the person tests positive, what is the probability that s/he has the disease? **Determined by sensitivity and specificity, AND by the prevalence of the condition**
- Predictive value of test depends on sensitivity and specificity AND on prevalence. E.g., for a test with 99% sensitivity:

<table>
<thead>
<tr>
<th>Prevalence</th>
<th>Positive Predictive Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
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</tbody>
</table>

Evidence Based Medicine
Evidence Based Medicine

Formulae

<table>
<thead>
<tr>
<th>Test</th>
<th>Diseased</th>
<th>Normal</th>
</tr>
</thead>
<tbody>
<tr>
<td>+ive</td>
<td>a</td>
<td>b</td>
</tr>
<tr>
<td>-ive</td>
<td>c</td>
<td>d</td>
</tr>
</tbody>
</table>

- Sensitivity = a/(a+c)
- Specificity = d/(b+d)
- LR + = sensitivity / (1 - specificity)
- LR - = (1 - sensitivity)/specificity
- PPV = a/(a+b)
- NPV = d/(c+d)
- Prevalence = (a+c)/(a+b+c+d)
- Pre-test odds = prevalence / (1 - prevalence)
- Post-test odds = pre-test odds * LR
- Post-test probability = post-test odds / (post-test odds + 1)
- Accuracy = (a+d)/(a+b+c+d) = what proportion of results have given the correct result

Study Design for Researching a Test

- Spectrum composition: what population was it tested on. Sensitivity and specificity may vary between populations with significant disease and the general population
- Are pertinent subgroups assessed separately? Condition for test use must be narrowly defined to avoid heterogeneity
- Avoidance of work-up bias: if there is bias in who is referred for the gold standard. All subjects given a test should receive either the gold standard test or be verified by follow-up
- Avoidance of Review Bias: is there objectivity in interpretation of results (e.g. blinding)
- Precision: are confidence intervals quoted?
- Should report all positive, negative and indeterminate results and say whether indeterminate ones where included in accuracy calculations
- Test reproducibility: is this tested in tests requiring interpretation

Using an Article About a Diagnostic Test

- Is the evidence about the accuracy of a diagnostic test valid?
  - Was there an independent, blind comparison with a reference standard?
  - Did the patient sample include an appropriate spectrum of patients to whom the diagnostic test will be applied in clinical practice
  - Did the results of the test being evaluated influence the decision to perform the reference standard?
  - Were the methods for performing the test described in sufficient detail to permit replication?
- Does the evidence show the test can accurately distinguish between those who do and don’t have the disorder? Are the likelihood ratios for the test results presented or data necessary for their calculation provided?
- Can I apply this test to a specific patient?
  - Will the reproducibility of the test and its interpretation be available, affordable, accurate and precise in my setting? Is interpretation of the test tested on people with my skill level?
  - Can I generate a sensible estimate of the patient’s pre-test probability?
  - Are the results applicable to my patient? (e.g. do they have the same disease severity)
  - Will the results change my management?
  - Will the patients be better off as a result of the test? An accurate test is very valuable if the target disorder is dangerous if undiagnosed, has acceptable risks and effective treatment exists

Bayesian Theory

- Combining information from history, exam and investigations to determine overall likelihood (ie as cf looking at a single test result with no context)
Evidence Based Medicine

Evaluation of Therapy

Assessment of an Article about Therapy

- Are the results of the study **valid**?
  - Was the assignment of patients to treatments **randomised**?
  - Was **follow-up complete**? (Non-follow-ups may have died, etc → bias)
  - Were patients analysed in the groups to which they were randomised?
  - Were patients and researchers ‘blind’ to the treatment?
  - Were the groups similar at the start of the trial (i.e. **confounders evenly spread**)?
  - Other than the intervention, were the **groups treated equally**?

- What were the **results**?
  - How large was the treatment effect? RR, RRR, ARR
  - How precise was the estimate of the treatment effect? Point estimate & Confidence intervals. What is the P value?

- Will the results **help me in caring** for my patients?
  - Can the results be applied to my patient care?
  - Were all clinically important outcomes considered: were the outcomes relevant for the patient? Or was only a benefit to intermediate outcomes considered?
  - Do treatment benefits out-weight harms and costs? ARR and NNT/NNH

Evaluation of Prognosis

**Glossary**

- **Prognosis**: the possible outcomes of a disease or condition and the likelihood that each one will occur. How to estimate your patient’s likely clinical course over time, or anticipate likely complications of the disorder
- **Prognostic factor**: characteristics associated strongly enough with a condition’s outcome to predict accurately the development of these outcomes. E.g. demographic (e.g. age), disease specific (e.g. tumour stage), or co-morbidity (e.g. other conditions present)
- **Prognostic results** are the number of events occurring over time, expressed in absolute terms (e.g. 5 year survival rate), relative terms, or survival curves
- **Risk factor**: patient characteristics associated with an increased probability of developing a disease in the first place. Neither prognostic or risk factors imply a cause and effect relationship

**Using an Article About Prognosis**

- Are the results of the study valid?
  - Was there a **representative and well-defined sample of patients** at a **similar point in the course of the disease**? (ideally at its onset). Is the disease clearly defined (what are the inclusion/exclusion criteria)? Is the sample representative of the whole spectrum of disease? Sources of bias: e.g. **selection bias** (referrer bias) or lead-time bias
  - Was **follow-up sufficiently long and complete** (what were the potential characteristics of those lost to follow-up?)
  - Were objective and unbiased outcome criteria used? Were the investigators blind?
  - Was there adjustment for important prognostic factors? Were subgroups with different prognoses stratified?

- What are the results?
  - How large is the likelihood of the outcome event(s) in a specified period of time?
  - How precise are the estimates of likelihood? Precision best expressed in confidence intervals

- Will the results help me in caring for my patients?
➢ Were study patients similar to my own?
➢ Will the results lead directly to selecting or avoiding therapy?
➢ Are the results useful for reassuring or counselling patients?
Professional Boundaries

- Defines proper/improper behaviour in a professional relationship
- Types of boundaries:
  - Physical
  - Emotional: strengthened by right to say yes/no, respect, weakened by ridicule, belittling, judgementalism
  - Sexual: serve to protect most sensitive part of us
- Differences from personal boundaries: Paid for, time limited, power more imbalanced, greater responsibility for maintaining relationship, requires knowledge and training
- Sources of power:
  - Personal power: size, gender, age, strength, skills, intellect, charisma, money, weapons
  - Position power: role, job, money, legal status

Recognising and Respecting Differences

- Sometimes differences obvious, sometimes subtle
- Can lead to misunderstanding, poor compliance
- Avoiding recognition of differences is a way of preventing challenge to our world view

Working in Teams

- 7 components of teams that need to be functioning for the team to work:
  - Raison d'être: clear idea of what the team is therefore
  - Rules: each person needs to know them
  - Roles: same person often adopts the same role in different teams
  - Relationships
  - Rituals: joining and farewell rituals, birthdays, etc
  - Rewards
  - Results: do you achieve your raison d'être

- Developmental cycle:
  - Forming:
    - Becoming acquainted: polite, impersonal, hierarchical
    - Trial and error: pairing, turf guarding, role conflict, ambiguity (still working as individuals)
  - Storming:
    - Collective indecision: covert anger, decision by default, poor morale, no accountability/leadership
    - Crisis: open anger, recognition of conflict, leadership assumed
    - Maintenance: commitment to team work
    - Performing: management of conflict, sharing information, tolerance or ambiguity/difference, flexibility, breaking down of inter-professional rivalries

- Power in groups:
  - Always ask 'who holds the power'
  - Positional (assigned from outside the group), assigned, knowledge, personal, factional

- Group processes:
  - Problem solving
  - Decision making: who, when, how, what
  - Conflict management:
    - Competing: It’s win/lose and I’m going to win
    - Accommodating: I don’t mind losing
    - Avoiding
    - Compromising
    - Collaborating

Physical Hazards of Medicine

- Hospital hazards:
  - Biological (infection control):
    - Blood and body fluid exposure (e.g. risk of seroconversion following needle stick HBV 30%, HCV 3%, HIV 0.3%)
- Tb (high prevalence → high index of suspicion, wear face mask in high risk situations, ensure contact tracing)
- Meningitis (spread via respiratory secretions, need close contact, wear mask)
- MRSA (spread via direct contact, could be almost totally managed by hand-washing). Manage via vaccination, possible prophylaxis
- First aid after exposure (needle stick, splash, spill, bite): rinse affected area under running warm water for at least 3 minutes, squeeze a puncture wound gently, paint with povidone-iodine or isopropyl alcohol
  - Chemical (drugs, latex, hand washing → hand dermatitis: usually irritant dermatitis not allergic dermatitis → dose dependent)
  - Ergonomics (patient handling, keyboards)
  - Physical (lasers, radiation, heat, noise)
  - Stressors (shift work, overload – usually insidious)
- Behaviour:
  - Knowledge doesn’t change behaviour
  - Consider own and patient safety
  - Hazard vs. risk vs. perceived risk

Medical Crises
- Need to:
  - Understand and manage our reactions to critical medical incidents
  - Learn methods of debriefing
  - Maintain confidentiality when managing reactions to unusual events
- A crisis can be:
  - Death of a patient: especially if similar age or if relationship has developed
  - Patient complaints, medico-legal action
  - Blaming yourself for bad outcomes
- Responses can be depression, anger, physical illness, ↑use of alcohol or self medicated drugs, isolation, suicide
- Coping strategies:
  - Accept that it is normal to be stressed by stressful events
  - Develop an active interest in details of the crisis (eg read up)
  - Be open about your feelings, don’t say you’re fine
  - Actively pursue social support, leisure pursuits
  - If medico-legal action, keep close contact with your lawyer and as much contact with the patient as the patient desires
  - Watch out for avoidance behaviours (dropping out, sick days) or intrusive re-experiencing (eg nightmares) – usually indicates need for help
  - Talk to counsellor, GP, colleagues, mentor – not to family or non-medical friends

The Doctor’s Health
- Stress = marked discrepancy between perceived demands and perceived ability to respond
- Burnout = set of symptoms leading to a debilitating psychological condition usually associated with:
  - Chronic stress
  - Emotional exhaustion
  - Depersonalisation
  - Reduced personal accomplishment
  - Development of negative and callous attitudes about the people one works with
  - Negative self worth
  - Result of a prolonged period of trying to cope with demanding stressors
- Medical Practitioners Act: Must notify the Medical Council if you consider a colleague’s health is affecting his or her competence
- Doctor is unfit to practice if: unable to make safe judgements, demonstrate reasonable skill, behaves inappropriately, risks infecting patients, etc
- Medicine has many stresses: business demands, patient expectations, difficult patients, mistakes, rosters → tiredness, litigation, ↓time for family
- On population estimates, there should be 200 – 300 medical practitioners who are alcoholic – only about 50 are being treated
There are many barriers to seeking help: admitting to illness, financial consequences, not wanting to be seen as inadequate, isolation.

Prevention is key: good health habits (especially in hard times), avoid self-treatment – *have your own GP, formal and informal peer support, develop interests outside medicine*, seek help early.

Resources to help:
- Doctor’s Health Advisory Service (DHAS): partly funded by the medical council
- In Sickness and In Health: a handbook for medical practitioners

**Code of Health and Disability Services Consumer’s Rights**

- Right 1: Right to be *treated with respect* (incl. privacy respected and right to services that respect their needs/culture/religion)
- Right 2: Right to *freedom from discrimination*, coercion, harassment and exploitation
- Right 3: Right to *dignity* and independence
- Right 4: Right to *services of an appropriate standard* (incl. co-operation among providers)
- Right 5: Right to *effective communication* (incl. right environment and interpreter if necessary)
- Right 6: Right to be *fully informed*
- Right 7: Right to make an informed choice and *give informed consent*
- Right 8: Right to *support* (ie to have support people present if at all possible)
- Right 9: Rights in *respect of teaching or research* – all other rights extend to when patient is participating in research or teaching
- Right 10: Right to *complain*

- Pt does not need be harmed (mental/physical harm) for the code to be breached

**Provider compliance:**
- A provider is not in breach of this code if they have taken reasonable actions in the circumstances to comply with duties in the code
- The onus is on the provider to prove that it took reasonable actions
- Relevant circumstances includes consumer’s clinical situation and the provider’s resource constraints

**Medical Error and Misadventure**

- Medical mishap = *treatment was properly given but suffered a rare side-effect* (<1% occurrence) and was *severe* (ACC definition is in hospital for at least 14 days, incapacitated for 28 or died)
- Medical error = person treating you *did not provide treatment of a reasonable standard*
- Medical misadventure = mishap + error

**Negligence:**
- Do you owe a duty of care
- Did you fail in that duty (according to standard of a reasonable practitioner)
- In failing, did the person suffer as a consequence
- Court decides whether error is negligence

**Types of censure:**
- From Health and Disability Commissioner (mediate, refer to professional body, referral to their director of proceedings)
- From Medical Council (censure, practice restrictions, struck off, fines)
- Criminal charges – eg Manslaughter – only if ‘major departure’ from accepted practice (1997 Crimes Act amendment)

**Medical Council**

- Protects public by determining competence of and registering doctors
- To be registered must have: acceptable degree, competent in English, no convictions with a possible prison term > 3 months, be mentally and physically fit and not subject to disciplinary proceedings
- Types of registration include: probationary, general, vocational
- Council can review or monitor competence or ‘fitness to practice’
- Also has disciplinary process
- Council consists of 4 doctors elected by doctors, 4 people appointed by the Minister, 1 Ministry of Health and 1 Med School Dean.

**Forensic Pathology**

- Definition of death:
  - Somatic death = no respiration, no pulse, unreactive pupils
Brain death = fixed, dilated pupils, no brainstem reflexes

Cell death = depending on cells, can take minutes to days (fibroblasts last for days)

Need to determine:

- **Cause** of death – e.g. stab wound to chest (determined by pathologist)
- **Mode** of death – e.g. exanguination (determined by pathologist)
- **Manner** of death – e.g. suicide or homicide (determined by coroner)

**Signs of death:**

- No circulation: no carotid pulse or heart sounds over 1 – 3 minutes
- **Absent respiration:** no movement or fogging of a mirror
- Unreactive pupils
- ‘Railroading’ of retinal blood vessels – rows of RBCs settling out
- Absence of pattern on EEG or ECG

**Signs of brain death** (ie on respirator):

- Fixed dilated pupils
- No corneal reflex
- No tracheal reflex (ie tug on ET tube)
- No eye movements on putting cold water in ear
- No CN response to pain (eg supra-orbital pressure)
- No respiratory response to hypercapnea

**Changes following death:**

- **Algor mortis** – cooling (indicator of time elapsed since death. Depends on temperature at death, BMI, clothing, etc). Rule of thumb = **plateau of 1-3hrs → ↓1°C per hr** → slows down when approaching 24hrs
- **Rigidity** – ‘rigor mortis’. Linking of actin and myosin fibres following ATP depletion. **Starts at 3 hrs, max stiffness after 12hrs + dissipates until 72hrs after death.** Is a chemical reaction therefore can be accelerated by ↑temp + ↓ by ↓ temp
- **Hypostasis/lividity** – bloods seeps downwards – **red congestion on downside of body. 20min → 3hrs after death; fixed in 4-5hrs**

**Decomposition:**

- **Autolysis** – body itself
- **Putrefaction** – bacterial infestation
- **Infestation** – flies/bugs infestation
- **Predation** – large animals
- **Weathering** – by wind/elements etc
- Is often very uneven (ie L to R or arms to legs), depending on position of body

See wet or dry or mixed decomposition

**Wet decomposition:**

- **Autolysis**
- **Putrefaction**

**Dry decomposition:**

- **Parchmentation** (superficially dried out)
- **Mummification** (entirely dried out)

**Rough guide to time of death:**

<table>
<thead>
<tr>
<th>Warm</th>
<th>Flaccid</th>
<th>&lt; 3 hours</th>
</tr>
</thead>
<tbody>
<tr>
<td>Warm</td>
<td>Stiff</td>
<td>3 – 8 hours</td>
</tr>
<tr>
<td>Cold</td>
<td>Stiff</td>
<td>8 – 36 hours</td>
</tr>
<tr>
<td>Cold</td>
<td>Flaccid</td>
<td>&gt; 36-72 hours</td>
</tr>
</tbody>
</table>

Glaister equation: estimates hrs since death = (37°C – rectal temperature) x 1.2

**Certification of Death**

- Confirm identity of patient
- Problems when deeply unconscious: near drowning, hypothermia, epilepsy, drugs (eg barbiturate poisoning)
- Suspicious injuries on a dead person: bruise, abrasion, laceration, incised wounds (suicide look for tentative cuts, assault look for defence injuries), stab wounds (go deeper than the length of the blade, always check), pattern wounds
- Person certifying death should have no conflict of interest

**Death Certificate:**

- If you’ve attended a patient → must issue a certificate or report to the coroner, if you are ‘available’
- Are now able to sign for eg GP partner if you’ve reviewed notes and seen body
Different form for infants over 20 weeks gestation or > 400 gm and < 28 days old. Can be filled in by midwife

Other forms:
- Need an additional form before cremation, which is then cleared by the Medical Referee
- **Certificate of Life Extinct; police form** to say the person is dead – eg if being referred to the Coroner. Does not include cause of death. Always take your own careful notes

Homicide:
- = Killing another, either directly or indirectly, or by accelerating death
- Murder = intent to kill or cause serious injury or to facilitate another crime
- Infanticide = death of child under 10 by a mother who has given birth or lactating
- Can be hard to distinguish murder from suicide or accident in MVA, fire, drowning, or cot death

**The Autopsy**

- Process:
  - **Story** → follows same process as a normal hx (eg PC, HPC etc etc)
  - **Scene visit** may be necessary → allows consolidation of the story
  - **External examination**:
    - Bodily configuration
    - PM changes eg wet decomposition
    - **Marks of identification** eg tattoos, scars
    - Marks of recent trauma
    - Marks of past trauma
    - Marks of medical intervention
  - **Dissection**:
    - General observations eg hydration, decomposition
    - Systems based approach eg CV, respiratory
  - **Further investigations** eg toxicology, histology etc
  - Conclusions
  - Report
  - Court

**Types of Injuries**

- Blunt force:
  - **Bruise**:
    - RBC escape into tissue
    - As cf **contusion** → more of an **internal bruise**
    - Ecchymoses, petechiae, imprint, senile, tramline, finger pad, alcoholic (eg shins)
    - Ageing: blue → red → yellow → green → brown
    - **Yellow** = >18hrs, no other colours are correlated with age
  - **Abrasion**:
    - Patterns: crush, superficial loss, graze, scratch, patterned
    - May dry out and scab
  - **Laceration**:
    - Tearing/splitting/stretching as cf a sharp force injury eg incised wound eg glass/knife
    - Ragged, not sharp edged (see tissue bridging across the wound)

- Sharp force:
  - Knife/glass:
    - **Penetrating**: eg stab; wound is deeper than is long
    - **Incised**: eg slashed; if longer than deep
  - Defence injuries: see on backs of arms or palms (grab knife)

- Firearm, electrical, fire, water, drugs of abuse, medicinal drugs, non-medicinal drugs etc

- Head injuries:
  - Scalp: bruise, abrasion, laceration
  - Skull #: transverse (eg MVA), linear (eg through occiput post falling backwards)
  - Intracranial haemorrhage
  - Extradural haemorrhage (MMA); subdural haemorrhage (bridging veins); SAH (traumatic/non-traumatic)
  - Cerebral coup + contracoup contusions
  - Intracerebral petechiae:
    - **Gliding** contusion – **rotational deceleration**
- **Diffuse axonal injury** – deceleration due to *direct force*
  - Secondary effects: cerebral oedema → cerebellar herniation/coning → vertebrobasilar circulation squashed → pontine haemorrhage

- **Firearm** injuries:
  - Handgun vs rifle vs submachine gun vs shotgun
  - If bullet passes right through the body then *less kinetic energy is dissipated in the body* = less damage
  - If bullet does not exit the body then the body absorbs all the bullet’s kinetic energy = more damage
  - Close range = round hole; distance = ragged
  - Lacerations with cavity formation are seen
  - If > speed of sound then shock wave damage also contributes

- **Entry wound**:
  - Smaller than exit
  - If close-range → round entry, ragged exit; if long-distance → entry + exit are ragged
  - See abrasion rim (red-brown), microlacerations at edges, bullet wipe (lubrication + debris), powder burns (soot, propellant) surrounding the wound (powder tattooing) + hair singeing + skin burning
  - Can see muzzle injuries (imprint bruise/abrasion) resembling barrel of the gun
  - Can see bevelling outwards (away from the bullet direction) of bone (esp skull)

- **Shotgun injuries**:
  - Depend on bore (pellet size) + choke
  - Also depends on pellet ballistics + wadding ballistics (further distance → wider spread)
  - Unusual to get exit wounds (therefore all kinetic energy is absorbed by the body)

- **Drowning**:
  - Diffusion of H2O from airspace → *vasculature* → *change in osmotic pressure* → RBC haemolysis → hyperkalemia → arrhythmia → death (do not suffocate as widely thought)
  - Fresh water drowning = faster death than salt water
  - See foam at the mouth, emphysema aquosum (distended alveoli + lungs have fine crepitant texture); fresh fluid in stomach

- **Fire**:
  - Need to determine *ante- vs post-mortem* (accidental vs deliberate)
  - Smoke inhalation is the key killer (as cf burns)
  - Soot in the airways (past the vocal cords) + oesophagus indicates the deceased was alive + breathing during the fire
  - CO poisoning contributes
  - Fire artefacts = skin splitting (can appear as a lac/incised wound); skin + organ shrinkage; ICH consequent to heat; heat #
  - Burn types = moist (scald) or dry (flame); scald; flame; electrical; chemical

**Coroner**
- Has the status of a *district court judge*
- To initiate a coroner’s case, report the death to the police (who act as the coroner’s investigating agents)
- **Must refer** a death to the coroner if:
  - No known cause, suicide, unnatural or violent
  - No certificate issued
  - Died undergoing medical, surgical or dental procedure
  - Detained under A&D Act, committed or in prison
  - Child in CYPS or foster care
- Coroner can order an autopsy and/or hold an inquest

**The Doctor in Court**
- Need to be honest, truthful, trustworthy
- Dignity is key → must respect the truth and own up to mistakes if necessary
- Preparation is key
- **Ordinary** witness = anyone
- **Professional** witness = eg GP: took BP + found these results
- **Expert** witness = eg cardiologist: the BP means this...
- **Expert witness can give an opinion**, ordinary witness can only recount facts
- Don’t take sides, be fair, stick to what you know, use notes taken on the occasion (with the permission of the judge)
Ethics Exam Approach

- **Define concepts** referred to in an answer eg autonomy or competence and use the terms consistently
- **Use flow charts** for different scenarios eg “I would do x or y depending on z”
- **If unsure of legal obligations in a question,** write that you’d consult with hospital legal council or colleagues
- **Ethics exam:**
  - Clinical ethics scenario
  - Information given in vignette is important, USE IT!
  - Rewarded for completeness, awareness of all key issues, don’t focus on 1 element of the question
  - Bullet points OK if run out of time
  - Be specific, define terms
  - Make reasoning explicit (“because”)
  - Reach a conclusion (“in summary...”)
  - Generally not black and white, can choose a stance and justify it
  - Don’t just use 4 ethical issues, think about duty of care, best interests, competence, futile/medically indicated treatment, trust, confidentiality etc
  - Use references to Code of Rights, PPPR etc if appropriate

Ethics Decision Framework

- **Define the Problem:** clearly state the concern(s) or issues(s)
  - Identify the relevant parties and their interests (including pt, dr, family, public)
  - How do these interests conflict?
  - Who has responsibility for addressing this problem? What are the limits of your role?
- **Gather the Facts:** Consider clinical, patient, family, staff involved, cultural, social and public health issues.
  - What is known?
  - What is uncertain?
  - What further information do you need and how would you get it?
- **What are the Options:**
  - Be creative
  - Consider doing nothing
  - Consider legal and professional obligations
  - Do you have the time to take incremental steps? Do something small, consider outcome, and revaluate.
- **Consider potential Restraints that rule out some options:**
  - Limited resources (financial or staff time)
  - Laws
  - Code of Health and Disability Services Consumers’ Rights
  - Codes of Professional and Ethical Practice (Cole’s Medical Practice in NZ)
- **Pick Preferred option:**
  - Usually based on a cost-benefit analysis: if you have time, you may do an explicit cost-benefit analysis of all options, but often we do this intuitively. **Weight up benefits and harms of preferred option**
  - Be wary of a ‘perfect’ solution that seems to satisfy all parties – it probably means you have missed something.
- **Evaluate and defend preferred option:**
  - What impact would this course of action have on relationships (within and between – patient, family, healthcare team(s))?
  - What are the potential objections to your preferred option?
  - What is the worst case scenario for this course of action? Are you prepared to defend this outcome?
  - Whose interests are denied? How would you justify your decision to this person/group?

Ethical Principles

- **Beneficence:** acting in a way that benefits the patient
- **Paternalism:** substituting the doctor’s judgement for that of the patient. The patient’s autonomy is over-ridden. If the patient is not autonomous there is no paternalism. Can be justified or unjustified
- **Non-maleficence:** minimising harm. Harms should be outweighed by benefits
- **Justice:** fairness – all members of society share in its benefits and burdens
• **Autonomy**: respect for the individual and their ability to make decisions with regard to their own health and future. Exercising autonomy requires intellectual and emotional competence and the opportunity for action.
• **Dignity**: preserving self respect, treating as a means not an end.
• **Truthfulness**: central or absolute?
• **Futility**: endeavours that are doomed to fail. Depends on what the goal is.
• **Duty of care** (especially to vulnerable patients)
• Best interests
• Competence
• Treatment that is ‘medically indicated’
• Treatment that is ‘futile’
• Trust
• Confidentiality
• Privacy
• Professional boundaries

**Morality and Standpoints**

• Standpoints: law, religious belief, social conventions, morality – all give standpoints from which can define right and wrong – and they may disagree.
• The scope of morality:
  - Self-imposed from within (cf. law – imposed form without)
  - Prescriptive: guides my action
  - Has universal character (moral principles don’t always apply to everyone – but demand consistency in judgements)
  - But these things don’t demarcate morality from other standpoints
• Bernard Gert: morality is a public system applying to all rational persons governing behaviour which affects others and which has the minimisation of evil as its end. I.e. it is an ‘invention’ for improving the human condition.
• 4 competing concepts of ethics:
  - General principles impinging on human well-being
  - Principles providing a practical antidote to certain types of behaviour (e.g. those which exhibit limited sympathies) which impact on human well-being
  - Principles guiding the behaviour of a particular professional group (which makes a distinctive contribution to he human good)
  - Principles focusing on a particular dimension of human well being

**Two Classes of Moral Theory**

• Deontological: *right/wrong due an essential feature of the behaviour* – intrinsic
  - Excludes relevance of consequences
  - How do you work out what duties are – have to explain it in terms of intrinsic qualities
  - Kant is a prominent theorist: the principle (e.g. value of human life) embodied in an action makes an action a duty. End never justifies the means
• Teleological: right/wrong depending on whether it’s a means to a good or a bad end – instrumental
  - Largest group is consequentialists of which utilitarianism is the most popular flavour
  - **Utilitarianism**: judge consequences by the greatest good for the greatest number
  - Must know consequences before you can judge it right or wrong
  - Is it limited to human happiness (what about animals)
• Both theories say liberty is important – but for different reasons

**Confidentiality**

• Hippocratic Oath: “Whatsoever things I see or hear concerning the life of men, in my attendance on the sick or even apart there from, which ought not to be noticed abroad, I will keep silence thereon, counting such things to be as sacred secrets”
• NZMA code of ethics:
  - Protects patients secrets even after death
  - Maintain confidence unless patient consents or required by law
• Benefits:
  - Access to information for the patient’s benefit
  - **Autonomy**: patient has control over information about them, respect for patient’s choice
  - Dignity
Consequences: positive reinforcement of trust

Legal requirements:
- Health Information Privacy Code:
  - Rule 10 (1): information obtained for one purpose cannot use that information for any other purpose
  - Rule 11(1): an agency must not disclose information unless...
- **Code of Health and Disability Service Consumer’s Rights**: every consumer has the right to have his or her privacy respected

Legal exceptions:
- With patient’s consent
- Within the team of doctors caring for the patient. Not disclosed to students unless anonymised
- Statutory e.g. Notifiable diseases, Land Transport Safety Authority (Driver’s licence)
- **Disclosure in the public interest**: Health Information Privacy Code allows disclose to prevent a ‘serious and imminent threat’
- Common Law: e.g. Tarasoff v Regents of the University of California case, Duncan v Medical Practitioners’ Disciplinary Committee

Special cases:
- Children: does the child have the understanding and maturity to form a relationship of confidence
- Incompetent adults: duty of confidentiality remains. The HIPC allows a representative of the patient to authorise disclosure
- The dead: Patient’s representative must authorise disclosure of information

Collection of health information discusses (Privacy code?):
- Purpose e.g. necessary for a lawful purpose
- Source: usually individual concerned
- Collection: reasonable steps to ensure individuals aware of purposes, recipients and rights of access & correction
- Manner: e.g. overly intrusive
- Storage and security
- Rights of access
- Right for correction
- Reasonable steps to ensure accuracy
- Retention: not kept longer than required
- Use limited to purpose for which it was collected
- Limits on disclosure – breaching confidentiality:
  - Necessary to prevent/lessen serious and imminent threat to life/safety
  - Disclosure will lessen or prevent risk
  - Minimal information released compatible with preventing harm
  - Patient must be identified to reduce this risk
  - There is no better alternative
  - Recipient of the information can do something about it

Consent
- See Paediatric Ethics
- Function: to uphold and enhance the patient’s autonomy – the right to think and act without coercion
- **Code of HDS right 7**: to make an informed choice and give informed consent except where any enactment of common law provides otherwise... (The code treats adults and children the same)
- NB. We can take blood from someone without their consent if for purposes of evidential blood alcohol level
- Consent is a process of communication, openly gives information, honestly answers questions, in a setting and manner that the patient can understand

Autonomy:
- Requires the ability to form beliefs, make decisions, form preferences, form practical intent
- Problems when these are completely or incompletely lacking, fluctuating, manifestly irrational
- = A set of practical skills through which we make and act on decisions which accord with our own values
- We should respect autonomy as this gives superior outcomes and because of underlying assumption that individual is best judge of his/her own good

Requirements for consent (DCVC):
- Disclosure of information
- Competence:
  - Presumption of competence: Right & (2)
  - Is task relative: how serious is the decision? Blood test vs life saving treatment
  - Competence of a minor to consent to treatment depends on capacity, not age
Requires (based on PPPR Act and NZMA consent for minors):
- The ability to communicate
- Understanding of the relevant information
- Understanding of the consequences
- Ability to manipulate the information

Voluntariness: Patient has control over the decision – ie lack of negative consequences, accustomed to obeying authority figures, feeling threatening by someone

Comprehension: information is understood

- Individual must be able to understand that:
  - They have a choice (no coercion)
  - Why they are being offered treatment
  - What is involved
  - Probable benefits, risks, side effects, failure rates
  - Alternatives

- When you can’t get consent:
  - Children lack legal capability to consent until 16. If patient under 16 doesn’t want parents to know can’t tell them.
  - If they are mentally or physically incapacitated
  - Can NOT use implied consent if the patient is incompetent – need consent of guardian, etc. But must treat in an emergency

Presumption of competence: assumed competent until demonstrated otherwise (including children)
- Varies with complexity of condition and treatment
- Ask the patient! Do they understand why treatment is needed, what is involved, benefits, risks and alternatives

Children
- Issue is not whether to get consent – but how
- Inconsistency about when they are autonomous:
  - Guardianship Act: 16
  - Common Law (Gillick case 1985) and H&D code: Capacity to make decision

- Exceptions to age limits and parental consent
  - Emergencies
  - Blood transfusion when life saving (if under 20 years)
  - Compulsory treatment (eg Mental health Act, Tb)
  - Blood alcohol
  - Abortion and contraception (CSA Act 1977): at any age, and no requirement to inform parents
  - Child Abuse examination (CYFS Act 1989)
  - When Guardianship invested in the Court or DG of Social Welfare
  - Good practice to involve the parents wherever possible

- Consent and the UN Convention on the Rights of the Child
  - The best interests of the child are paramount (article 3)
  - Have the right to express their views and have them taken into account (article 12)
  - Privacy and Confidentiality (article 16)
  - Accessibility of information (article 17)

Conflict over Consent
- Maori issues: greater expression of autonomy collectively, and collective responsibility for Tamariki. Involve whanau
- If a child says no – it’s usually because they are frightened. Take a child’s views seriously. Reduce fear by ensuring understanding. But best interests may be in conflict with their wishes
- If parents say no, consider reasonable alternatives and legal (last option). CYPS Act, sections 14 & 67 – child in need of protection. Guardianship Act 1968 may place child under guardianship of the court
- Allow time to work it through, plan ahead
- Avoid rushing important decisions
- Give information, check it is understood, opportunity to ask questions
- Enlist supports, Maori/IP staff, translator, etc

Consent in Research
- Dates from Nuremberg trials → Declaration of Helsinki
- Underlying principle: Concern for patient must be greater than the concern for science
Patient has same right to informed consent as with treatment

**Incompetence**
- Consider the incompetent patient's **best interests**, according to:
  - Previous statements from patient when competent
  - Family/friends
  - Medical/our judgement

**Compulsion**
- Reasons for over-riding autonomy:
  - *Autonomy is lacking*: individual is no longer the best judge of his/her own good
  - *Public well-being takes priority*: autonomy present but over-ridden – well-being of others takes priority
  - *Paternalism*: autonomy present (perhaps diminished) – prioritising the doctor's view of the patient’s good over that of the patient

**Current legislation:**
- TB Act 1948: compulsory treatment
- Health Act 1956: compulsory treatment of some infectious diseases
- Alcohol and Drug Act 1966
- Guardianship Act 1968: Dr can apply to make a child a ward of the court
- CYPF Act 1989: some services parents can’t refuse for their kids
- *Mental Health Act* (Compulsory Assessment & Treatment Act) 1992  (See Electroconvulsive Therapy)

**History:** insulin shock therapy → chemically induced seizures. Early ECT done in asylums when few meds available

- Relieves symptoms in 80% of all severe depression (not just those resistant to medication)
- **MOA:** NT levels all ↑ in CSF after seizure, results in downregulation of β-adrenergic receptors. **After seizure, blood flow and metabolism is ↓ especially in the frontal lobes** → research shows this is correlated with response

**Indications:**
- **Major depression** with or without psychotic features
- BAD – manic or depressed phase. Bipolar mania: indications for first line treatment include recent MI with acute mania or pregnancy with acute mania
- Acute or catatonic schizophrenia
- Some studies have shown efficacy in treating OCD, delirium, NMS, chronic pain syndromes, and intractable seizure disorders

**Pre-ECT workup:**
- Physical exam
- CXR
- FBC, U & E
- ECG
- ?CT head

**No** absolute contraindications but relatively contraindicated with recent MI, berry aneurysm, brain mass or ↑ICP

- Number of treatments: 2-3/week; **5-12 sessions** although up to 20 is possible
- Adverse effects: death (very low rates), sore muscles, headache, short term confusion/delirium, memory impairment
- Response is proportional to length and quality of seizure. Usual course is about 6 cycles. If no response after 12 cycles then stop
- Also need to establish on an antidepressant that they haven’t failed on
  - Compulsory Treatment, page 768)

**Refusal of Treatment**
- Refusing Consent:
  - Adults may refuse medical treatment even if it results in the person’s injury or death (Section 11, Bill of Rights)
  - A pregnant woman may refuse treatment even if that jeopardises the life of her unborn baby
  - Not clear whether a competent child (under 20) can refuse treatment
  - Parents may refuse on behalf of children, except where refusal endangers the life of the child. Parent’s right to practice religion etc does not extend to placing their child’s health at risk
Issues to consider:
- Competence: are they ‘autonomous’. Normal presumption is that they are, unless clear evidence to the contrary. Is the condition affecting their judgment? You can only have ‘justified paternalism’ where the person is autonomous. You are not being paternalistic where patient in incompetent
- The higher the level of risk, the greater need for evidence of competence (not just competence per se, but evidence of competence)
- Informed consent: requires a competent person to voluntarily make a decision, who understands all the relevant information, including the doctor’s recommendation
- Prognosis: if advanced terminal illness then this is different to where recovery is likely
- Is the patient absent from coercion?
- Irreversibility of a decision not to intervene vs. reversibility of decision to intervene. Given this asymmetry, strong bias to intervention
- Weighing families’ wishes against patient’s
- Loss of liberty and prolongation of misery if you intervene

When is paternalism justified:
- If intervention will probably prevent significant harm
- Where benefits outweigh risks
- Where the least autonomy restricting option that ensures the benefit is adopted

Refusal of treatment on grounds of religious belief:
- They still want treatment
- Danger in accepting refusal to accept treatment at face value
- Ensure understanding (‘Why do you think this? Do you realise you are going to die without it?’)
- Ensure authenticity of beliefs (do they say they’re JW to avoid blood products they think are contaminated)
- Identify acceptable treatment options

Consequences of treating without consent:
- Battery
- Breach of the patient’s rights under the Bill of Rights/Code
- Negligence
- Disciplinary action

End of Life Issues

Euthanasia
- Euthanasia: = Killing someone where, because of his or her distressing physical or mental state, it is thought to be in the person’s own best interests
  - Voluntary euthanasia: killing a competent person, when that person requests it
  - Non-voluntary euthanasia: assumed to be in the person’s best interests – but they are not competent (eg babies, unconscious, mental incapacity)
- Involuntary euthanasia: against the person’s will
- Passive euthanasia: withholding/withdrawing treatment leading to pt’s death
- Active euthanasia: doing something that will hasten death

Arguments for euthanasia:
- Autonomy and the right to die
- Gives the person the choice to avoid pain and distress, loss of dignity, etc

Arguments against:
- Hazards of voluntary euthanasia in practice: fluctuating views, pressure from family
- Life belongs to God
- Intrinsic value of life

Legal position is clear: doing anything to bring about death is murder, regardless of motive

Doctor-Assisted Suicide
- If doctor gives the patient the means (eg leaves pills by the bed) then they have committed the offence of aiding and abetting suicide, punishable by up to 14 years imprisonment under s 179 of the Crimes Act
- Different from euthanasia as:
  - Doctor may not approve, but may respect the patient’s choice
  - Clearer that the patient is making their own decision without coercion
- Reasons why doctors should be involved:
  - For:
They understand the medical condition (ie know the prognosis)
- They are not an interested party (unlike families)
- They know the best way of helping

Against:
- They have a duty to preserve life
- It might undermine confidence in the medical profession

**Doctrines Of Double Effect**
- It is wrong to perform a bad act even if there are good consequences
- It may be possible to do a good act, even if there may be bad consequences (eg giving pain relief knowing that it may hasten death)
- If the consequence is virtually certain, then it is considered ‘intended’ even if it wasn’t the primary reason

**Acts and Omissions**
- Legally there is a distinction between doctors not doing something (ie failing to provide treatment) and doing something (ie giving a lethal injection). However, if the person has a legal obligation to act (eg a doctor), failing to do so may be culpable
- Doctors have a duty to provide the necessities of life to those under their care. *Failing to do so is an offence* under s151 of the Crimes Act. Considering medical treatment is not indicated, or that it is not in the patient’s best interests, is a lawful excuse
- Ethically, omission is generally less bad than acts of commission

**Withdrawal of Life-Sustaining Treatment**
- Is the patient competent – if so, the decision is the patient’s. They have the right to refuse medical treatment under the bill of rights
- Incompetent patients:
  - Any advance directive?
  - Anyone authorised to make the decision on the patient’s behalf (a guardian under the PPPR act or a formally appointed attorney). Patient’s next of kin are not entitled to consent on a patient’s behalf
  - Decisions about whether treatment serves no therapeutic purpose are a medical decision (although see section 7(4) of code or rights re informed consent). There is no duty to continue with life-sustaining treatment where there is no prospect of recovery or any quality of life
  - Should discuss with family
  - Discuss with colleagues (safety in numbers)
- Cause of death will be the underlying cause, not the withdrawal of treatment
- Withdrawal will be treated as an omission, not an act. Courts have ruled there is no difference between turning the ventilator off and not turning it on to start with
- Rules of thumb:
  - Intention is always to act in the patient’s best interests
  - Err on the side of caution. Always get a second opinion. If in doubt, seek a court judgement

**Advance Directives**
- Every competent patient has the right to refuse treatment, even if this leads to his or her death. This includes the right to leave clear instructions in case they may be incompetent in the future ⇒ an advance directive. Recognised in the Bill of Rights
- A directive is valid if:
  - The patient was competent at the time is was made
  - They were free from undue influence
  - They were sufficiently informed
  - They intend their directive to apply to circumstances which subsequently arise
- These conditions should be tested at the point where a directive is applied

**Protection of Personal and Property Rights Act (1988)**
- = PPPR Act
- Designed originally with intellectual handicap in mind. In acute or geriatric care, used mainly in cases of dementia
- Two underlying principles:
  - A person is competent until proven otherwise. Act asserts right to autonomy, to refuse treatment and to manage their own affairs
Any order imposed shall be the least restrictive alternative. Encourages self-reliance, normalisation and community integration.

The judge has three decisions to make:
- Determine jurisdiction
- Determine whether an order needs to be made
- Determine the type of order:
  - **Enduring power of attorney** (normally Powers of Attorney expire if the person becomes incompetent)
  - **Welfare Guardian** order (wholly lost capacity)
  - Property Manager order (wholly or partially lost capacity)
  - Personal order (wholly or partially lost capacity)

5 questions to assessing competency:
- Does the person appreciate their situation
- Can they understand the options that address their situation
- Are they aware of the pros and cons of their choice
- Do they express their choice clearly
- Is their choice influenced by a distorted mind

6 stages in an application:
- Consider clinical strategies
- Assess competency
- Complete application forms and a medical report
- File application at family court
- Family court appoints counsel
- Pre-hearing conference, may lead to a full hearing

Ethical Issues in Dealing with Impaired or Incompetent Colleagues

Summary:
- Collective responsibility as important as individual
- Maintenance of public trust vital
- Better team work and error reporting will help
- Self regulation: use it or lose it

Issues:
- Trust of patients in doctors: patients in vulnerable position
- Beneficence
- Legal requirement to report impaired or incompetent doctor
- Collective responsibility: to patient population as a whole
- Uncertainty: may explain but not excuse failure to act
- Professional etiquette (often disguised as ‘clinical freedom’) — not wanting to interfere in other’s livelihoods
- Loyalty to the group: key to cooperation but should be overridden by maleficence
- Pattern of error not a single mistake is indicative of incompetence

Criteria for whistle-blowing:
- Evidence of severe harm
- Good chance of reducing harm
- All other avenues explored

Ethical institutions
- Encourage reporting of error (ie about safety not culpability)
- Mechanisms for self/peer assessment
- Internal complaints mechanisms (with protection)
- Guard against malicious complaints

Culture within a group:
- Less competent influencing each other
- Professional isolation (big risk factor for incompetence)

Hard to pin down doctors because:
- Lack of benchmarking (little medical practice has been validated)
- Clinical freedom
- ‘Half of all doctors are below average’
- The learning curve: period of necessary and acute incompetence

Informed consent: what is it reasonable for patients to know about their doctors (eg individual success rates) vs. doctors right to privacy
Professional Ethics

- Characteristics of a profession: an important service, monopoly, self regulating, extensive training with intellectual component, autonomy in work

- Professional ethics:
  - Ethics and values in roles and conduct of professionals
  - Aspirational and regulatory component

- Ethics should reflect common social values: freedom, protection, equality, privacy, etc

- Obligations to patients:
  - Previously paternalism
  - Then contractual model (but didn’t acknowledge power imbalance)
  - Fiduciary model: built on trust → doctor makes a recommendation, patient has informed consent

- Values:
  - Honesty – eg conflict of interest
  - Competence
  - Diligence – give sufficient time and effort to the patient
  - Loyalty and objectivity
  - Fairness
  - Discretion
  - Professionals as employees: issues around obligation to obey vs autonomy, whistle blowing, strikes

- Economic issues: fee splitting (eg taking a cut out of a referral), accepting gifts, limits on advertising

- Professional self-regulation: admitting, setting and applying norms

Resource Allocation

- Rule of rescue (the moral response to imminent death demands we rescue the doomed) vs:
- Cost effectiveness → but this can be bloody expensive
- Difficult as the population ages
- Intervention that has little chance of prognostic benefit may result in unnecessary suffering for patients in terms of side effects → may be preferable to redirect resources

Tissue Donation

Problems of Supply

- Fair distribution (resource allocation)
- Dead bodies:
  - When are they dead (brain death criteria, PVS, anencephalic infants)
  - Who gives consent, family distress vs need for a quick decision
  - Should there be a presumption of donation (with right of opt out) – small constraint on freedom outweighed by significant benefit?
- Live bodies:
  - Increased supply
  - Operative and consequent risks for donor
  - Consent (especially if donor is a child or non-competent adult)
  - Donor/recipient relationship as source of pressure
- Buying and selling:
  - Increase supply
  - Objections: Consent (free and informed?), exploitation, degradation, misinformation
- Fetal tissue:
  - Increases supply
  - Fewer rejection problems
  - Sourced from abortion
  - ‘Surplus’ embryos
- Animal Tissue

Regulation

- Health Act 1956 controls donation and prohibits profit making
- Human Tissue Act 1964 regulates organ removal after death – mixed opting in/opting out arrangement
- Living Donors: common law – unlawful to remove a body part if not therapeutic for the donor (Blood is covered by the Health Act)
Assisted Human Reproduction

- 3 types:
  - Couples using their own genetic material
  - Techniques using other people’s genetic material
  - Techniques using another woman’s womb (surrogacy)

- Current issues:
  - Surrogacy – non-commercial IVF
  - Posthumous use of sperm (creation of fatherless families)
  - Should women have access to IVF if they already have children (eg following tube reversal) – is there a fair innings?
  - Intergenerational gamete donation (assisted incest!)
  - Pre-implantation genetic diagnosis (PGD)
    - To what extent should families be free to make their own choices
    - The significance of life
    - Does PGD devalue affected individuals
    - What is the meaning of disability
    - Who will have access to these diagnostic techniques

- Ethical issues:
  - Human dignity, the value of life and what it is to be human
  - Autonomy:
    - Procreative liberty vs the role of the state (reflecting the welfare of society)
    - Informed consent – eg pressure on surrogate mums
  - Beneficence:
    - Who benefits
    - What are the best interests of the child not yet conceived. They should be an end in themselves, not a means to someone else’s end
  - Non-maleficence (do no harm):
    - Commodification of children
    - Incrementalism – the ‘slippery slope’
    - Unknown/possible harms – Intra-cytoplasmic sperm injection has become common without any long term trials looking for any effects on kids
  - Justice:
    - Fair access to AHR procedures
    - Prioritisation of need and benefit
    - Infertility vs social reasons (eg post vasectomy, freezing eggs till after you’ve had a career, etc)

Innovative Treatment

- Ethics committees must review research and innovative treatments

- The difference between research + innovation:
  - Research is for the benefit of society and future patients
  - Treatment is for the benefit of the patient
  - Innovative practice sits between these

- Defn: Innovative treatments are those procedures which are new to a particular provider setting in NZ, or which are being used for a new purpose (Has often been harmful, at a minimum it introduces greater or new risk of harm)

- 3 issues:
  - Proving they are safe and effective. Issues here vary – if it is an established technique overseas the issue is whether the NZ practitioners are and will remain competent. If it’s entirely new, is it safe? Etc. Proving safety is difficult in surgical procedures – the surgeon is gaining skill, case comparison is complicated, random allocation may be unethical. Safety should be established early on. Effectiveness should be assessed in a way that gives good statistical evidence
  - Gaining informed consent to non-standard treatment
  - Defining what constitutes an innovative procedure

Research Ethics

- Codes:
  - Nuremberg code:
    - Informed consent of subjects, and liberty to withdraw
    - Benefits to society (can’t be got by other means)
Avoid unnecessary suffering and injury

Degree of risk not greater than potential benefit of problem to be solved

Only conducted by scientifically qualified persons

- Declaration of Helsinki: 1964, revised 1975. Main difference: required to be supervised by medically qualified person

Experiments on people that won’t benefit current patients

- If study not sound then won’t answer questions ⇒ risk not worth it and waste of resources
- Informed consent by participants
- Ensure study remains ethical in progress ⇒ ‘stop’ criteria and monitoring of interim results
- ‘Therapeutic Research’ a misnomer (although used in Declaration of Helsinki). In research, if the patient happens to benefit that’s coincidental. Research subject gives up normal expectation of tailored treatment

Placebos:

- ‘Equipoise’: randomisation only ethical if there is justifiable uncertainty of merit between intervention and control – but reasonable possibility that the new treatment is better than placebo
- Must be significant knowledge to be gained from a placebo trial

Implications of randomisation:

- Severs normal connection between patient and individually tailored treatment
- Must be able to break the code if things don’t go as expected

Investigator requirements:

- Competence
- Moral Character? Hard to specify or enforce
- Conflicts of interest:
  - Intrinsic: interested in gaining knowledge verses care for the patient
  - Extrinsic: funding, reputation
  - Clinical equipoise

Balancing harms and benefits:

- Principle of non-maleficence
- Healthy problems: only very small risk acceptable. Problem of financial inducements (attract people to take too much risk?)
- Extrapolation from healthy volunteers not always possible

Equitable subject selection:

- Respect for people (informed consent)
- Principle of justice (equal sharing of benefits and burdens)
- Vulnerable groups: reduced capacity to protect their own interests: eg incompetent, dying, minority groups, 3rd world countries (but nothing in ethical codes to preclude their use – justification becomes harder as degree of risk and degree of vulnerability increases)

Therapeutic orphans:

- = Drugs not licensed for some groups, eg:
- Children: difficulties of doing research on children. So package says “not recommended” ⇒ informed consent issues for the doctor and patient
- Women: pregnancy and lactation, financial implications of teratogen testing

Problems with informed consent:

- People often don’t easily understand things like randomisation
- People often reticent to ask questions

Role of Ethics Committees:

- No statutory requirement for ethical review – but defacto requirement
- Composition: Lay chairperson, 50% lay membership (following Cartwright)
- Should journals publish research that hasn’t undergone ethical review:
  - For: if its sound, would deprive society of valuable information and would require the study to be repeated
  - Against: journal editors should be ethical gatekeepers

Problems with Prof Greens cervical cancer experiment:

- Poor study design but still approved
- Consent not gained from patients
- Study not monitored properly (should have been stopped due to evidence of harm)
- Concerns of other doctors not acted on properly

Questions it raises:

- To whom should the doctor be accountable: their own conscience, patients or colleagues
- Women were vulnerable, being examined by men ⇒ asymmetry of power exaggerated
**General Approach**

- Read instructions carefully
- **Stop and think:** despite the pressure of time this is important – don’t just launch in
- ALWAYS introduce yourself to the patient
- Appear warm and confident to the patient
- At the end:
  - Forget the station – especially if it went badly. Focus on the next station
  - Don’t rush between stations. There’s plenty of time. Take some time to breathe deeply!
  - Check the sample questions at the end of this book to give you a feel for what they’re after

**Communication Skills**

- Remember their name and use it
- The two things patients want most from their doctor is for the doctor to *listen* and to *explain* conditions, investigations and treatment plans clearly
- Good listening skills: good eye contact, use silence, don’t interrupt
- Acknowledge the emotions they show
- Care about their condition – don’t forget the empathy
- Offer praise: “you seem to be coping well”
- When discussing impressions or findings, identify their emotional response
- Don’t give false reassurance or information you’re unsure of
- If discussing a poor prognosis, discuss family and community supports
- Address the patient’s concerns!

**History Stations**

- **Form the DDx as soon as you know the PC** (if PC is given in the instructions don’t look up until you have the differential in your head)
- Always start with open ended questions
- Try and phrase closed questions as open ones
- **Only ever do a focused history** based on the presenting problem (only got 4 – 5 minutes):
  - HPC with relevant positives + negatives only
  - PMHx
  - Medications and allergies
  - FHx
  - SHx – especially smoking and alcohol
- Consider:
  - What organ system am I dealing with
  - What are the *likely causes*
  - What RISK FACTORS may have contributed (eg cardiac = HTN, DM, smoking, dyslipidaemia, FHx)
  - What are the possible complications
- If the patient (or you!) dries up:
  - Repeat their last statement
  - Don’t rush. Silence is OK
- At the end if you have time:
  - Summarise back to the patient (especially if you’ve run out of ideas – buys time!): “So the main problem is…. Anything we’ve missed that you think is important…. This has left you feeling ... You’d like me to ....”
  - Ask if they have any questions or anything else that they would like to tell you
- **Structure:**
  - PC: form your differential diagnosis now to guide your questions. This list should be brief (eg max 5-6 diseases) otherwise you won’t be able to keep it in the front of your mind. The differential list is made up of two "types" of disease:
    - The most *likely* diseases which could cause the symptoms
    - The most *serious* diseases which could cause the symptoms
  - HPC
    - Start with open-ended questions. Don’t interrupt till they dry up
    - Symptom assessment: explore the presenting symptom (*SOCRATES*)
ROS: ask questions for the systems which could be involved. Eg for chest pain you need to ask the CVS, respiratory and GI ROS questions.

Risk assessment: try to determine the level of risk a patient has for each differential diagnosis. Eg for chest pain ask about smoking, high cholesterol, diabetes (DM), hypertension and family history of MIs

"Is there anything you think is relevant that we’ve missed?", “any other symptoms or changes you’ve noticed”

- PMHx: any other illnesses, ever been in hospital, blood pressure
- Medications and Allergies, including OTC drugs, pain killers, contraceptives
- Family History
- Social History: consider the following as you have time
  - Smoking, alcohol, drugs
  - Lifestyle factors: diet, exercise, sexual history
  - Occupation: could be causative (eg asbestos exposure in a respiratory history) or illness will affect their ability to work
  - Problems/stressors
  - If appropriate, exposure to allergens – pets, occupational exposure, hobbies etc
  - Overseas travel
  - Who lives at home with you? What other supports do you have?
  - If elderly:
    - Activities of daily living: DEATH: dressing, eating, ambulatory (ie getting around), toileting, hygiene
    - Instrumental activities of daily living: SHAFT: Shopping, housework, accounting (ie money management), food preparation, transport

- Systems review:
  - A systems review in one minute, for systems not covered in the HPC. Only if you’re stuck. It will have a very low yield of both responses and marks! For each system keep the questions
  - General: Any changes in weight, appetite, sleep or energy. Fevers
  - Cardiovascular: any chest pain, unusual heart beats or ankle swelling
  - Respiratory: any trouble with your breathing or a cough
  - Neuro: any dizziness, blackouts, strange sensations or weakness
  - Psych: How have you been feeling in yourself lately
  - Endocrine, metabolic: covered in general and in renal
  - Renal: Any problems with your waterworks (including going more often)
  - GI: any vomiting, tummy pain, or change in your bowel motions
  - Gynae: Any change in your periods, any vaginal discharge
  - Musculo-skeletal: any problems with your joints or with weakness
  - Skin: anything different you’ve notice about your skin (eg rashes, itching, etc)

Summarise back:
- Key issues for patient,
- Their biggest worry, etc
- “Any questions you’d like to ask?”

Surgical Sieve

- VITAMIN C & D
  - V = vascular
  - I = inflammatory/infective
  - T = trauma
  - A = autoimmune
  - M = metabolic
  - I = idiopathic/iatrogenic
  - N = neoplastic/nutritional
  - C = congenital
  - D = drugs/ degenerative

- COTDIM
  - C = congenital
  - O = oncological
  - T = trauma
  - D = degenerative/drugs
  - I = infective/inflammatory
  - M = metabolic
Education Stations

- Could be:
  - Explain a drug
  - Explain a procedure
  - Explain a disease
  - Explain a result
  - Explain a lifestyle change

- Structure: wwwirbuq
  - What do you know already? What did you hope to gain from this appt? Do you know why you need this?
  - Have you got any questions?
  - What have you tried already?
  - Explain why it is needed/wanted
  - Explain what is involved
  - Explain the risks/benefits
  - Check understanding
  - Ask if any questions

- Chunk and check along the way – give small pieces of info
- Give a road map from the outset = going to start with a bit about the drug/condition then... then ... OK?
- The actor needs to feel as if they have been given sufficient information to reach a decision (will get 2 marks for this)
- Generally can use these for any drug SE = potential for reaction/rash/nausea
- Will not be any marks for any history questions, therefore be very scant on any you deem necessary
- Benefit/risk ratio = this procedure will allow us to have a better understanding of what’s going on for you and help us to work out the best way to treat you, we think the benefits outweigh the risks
- Risk factors for most procedures include infection and bleeding and failure
- Can lose marks if use jargon
- If do not know the answer – better to be honest and say you’ll just check that/discuss with colleague
- Preventative measures:
  - Alcohol/drug/smoking (Quitline number is 0800 778 778)
  - Counselling
  - Screening: breast, cervical, skin
  - Infectious diseases: STDs, Vaccination
  - Diet and exercise
  - Stress reduction
  - Environmental/occupational hazards
  - Injury prevention (especially kids)

- Examples:
  - Bob has just been diagnosed with hypertension and is started on metoprolol. Explain what this involves:
    - Ask what he knows about hypertension and metoprolol (“do you know why you’ve been prescribed this?”)
    - Explain why hypertension is bad = causes heart attacks, strokes etc
    - Explain how metoprolol works = slows down the heart and decreases BP etc
    - Check understanding
    - Explain how to take = every day etc
    - Explain the risks = with any drug = can work too well or not well enough
      - If it works too well, you can feel dizzy or may not tolerate exercise so well – if that happens, come back to see us and we either decrease the dose or change the medication
      - We will monitor your response to the drug (i.e. BP), if it doesn’t work well enough, we can either increase the dose or change the medication
    - Check understanding
    - Any questions?

  - Jane, a 19 y/o women wants to start the OCP. Discuss with her and evaluate her risk factors:
    - Ask why she wants to start on OCP
    - Ask what she understands about OCPs
    - Etc

  - A 50 y/o woman has been told she has an abnormal smear result. Discuss what this means:
    - Ask what she understands about her abnormal result
    - Explain that this is a screening test = doesn’t mean she has cancer – will need to have another test to confirm/deny; if cancer then explain that early detection = better outcomes
Do you understand?
Any questions?

40 y/o man about to have a gastroscopy due to 3/12 of dyspepsia. Explain the procedure to him:

- Ask what he understands of the procedure
- Explain the procedure
- Check understanding
- Explain risk factors and benefits = this procedure will allow us to have a better understanding of what’s going on for you and help us to work out the best way to treat you
- Check understanding
- Any questions?

**Starting a New Medication**

- **With any DRUG:**
  - Do you have any allergies?
  - Are you taking any other meds? OTCs? Do not take with certain other drugs, herbal meds, grapefruit etc
  - Try and take pills everyday at the right time – routine
  - Do not stop abruptly – follow the instructions
  - If notice a rash, diarrhoea or vomiting, see your doctor
  - See your doctor or go to hospital immediately if you develop any of the following:
    - Swollen face, lips or mouth
    - A severe rash or itching
    - Sudden wheeziness or problems breathing
  - If AB: finish the course
  - Some drugs = avoid alcohol, driving, heavy machinery
  - Offer written information
  - Arrange follow-up

- **Understanding the purpose of the medication is vital to informed consent and to adherence to treatment**

- **Drug history:** For each drug they’re on or have recently taken:
  - Name of drug and dose
  - Why did you start
  - Why did you stop
  - Did it help
  - Any side effects
  - What drugs have you had previously for the same condition

- **Using any Oral Contraceptives, OTCs, herbal remedies, supplements**

- **Medical history:**
  - Are you pregnant or breast-feeding
  - Do you have any medical illness, especially: liver disease, kidney disease, bleeding disease, GI disease (eg malabsorption, chronic diarrhoea)

- **Do they have any drug allergies**

- **Any family history of problems with medications**

- **Social history:** Do you smoke or drink

- **Starting a new drug:**
  - Used the drug before or know anyone else who has: any misapprehensions?
  - On any other medications: check interactions
  - Check contraindications: pregnant or breastfeeding?
  - Allergies?
  - Smoke or drink?
  - For the drug to be prescribed:
    - Why the medication is needed
    - Name of drug and how it works
    - Dose and how to take (when and with/without food)
    - What it is expected to achieve
    - How long until an effect should be noticed
    - When to stop/likely duration and any requirements when stopping (eg anti-depressants – taper off)
    - Restrictions eg no alcohol with metronidazole, no grapefruit juice with OCs
    - Possible side effects
    - Whether the medication is addictive
    - Importance of continuing with other non-drug treatment
    - Questions?
Compliance:
- Few people take their medication as prescribed. Non-compliance is multi-factorial:
  - Rapport with doctor
  - Not knowing how to take medication
  - Not understanding the importance of the drugs
  - Taking many drugs
  - Anticipation or experience of side-effects
  - Forgetfulness
  - Impaired physical function or other disability
  - Community and family support

Strategies for improving compliance:
- Education about disease and treatments (spoken instructions are quickly forgotten)
- Simplifying drug regimes (fewer drugs and fewer doses)
- Involving carers
- Education about common side effect which may subside
- Use of drug diaries, calendars, medication charts
- Use of ordinary bottle tops (not childproof) for elderly people
- Large print labels
- Dosage forms (eg small pill size, pleasant taste)
- Compliance aids such as pill trays and blister packs
- Return or destruction of old drugs

Fatigue Station
- How long? Sleeping?
- General: fever, weight loss, night sweats, rigors, anorexia
- Psych: mood, stresses/worries?
- Haematology: lumps or bumps, bruising, infections, anaemia
- CNS: fits, fainty or funny turns, any weakness
- CVS: heart failure, valve disease
- Resp: malignancy, infection (TB)
- GI: malignancy, malabsorption
- Renal: RF
- Endocrine: DM, hypothyroid, addison’s

Behaviour Change Stations
- Help patient clarify problem - where in the cycle of change are they?
- Do you want to change?
- Why do you think you need to change?
- Knowledge - what do they know about the problem
- Attitudes and fears - how do they feel about changing
- Practices - what have they already tried to change
- Barriers - what has stopped them succeeding
- Validate - their concerns and attempts
- Educate - problem is common, difficult to change on first attempt “this is hard”
- Suggest strategies for change - need to link the change in behaviour with something that is very important to them eg stopping smoking and living to see the grandchildren grow up, stopping drinking and been able to stay at work.
- Let patient choose the strategies most appropriate to them
- Set goals and prioritise
- Arrange follow-up and on-going support

Examination Stations
- Ask permission to do the exam
- Don’t wash hands – the purists can point out that they normally would but don’t have time!
- Check the light
- Check the patient’s position
- Tell the patient what you’re going to do
- Show consideration for pain
- Keep patient draped – ask permission before uncovering/removing clothing. Get the patient to do as much as possible
- Assist the patient off the table
- Invite them to get dressed
- Explain findings

**Management Options**
- Listen!!!
- Reassurance
- Education
- Lifestyle:
  - Smoking/drinking
  - Diet
  - Exercise
  - Stress reduction
- Supports/support groups
- Psychotherapy
- Medication (remember O2 if acute, and pain relief for everything)
- Surgery
- Referral/multidisciplinary involvement
- FOLLOW-UP
<table>
<thead>
<tr>
<th>Causes of Acute Sinusitis</th>
<th>Causes of Acute Infectious exacerbations of Chronic Bronchitis</th>
<th>Causes of Otitis Media</th>
</tr>
</thead>
<tbody>
<tr>
<td>Strep pneumoniae</td>
<td>Strep Pneumoniae</td>
<td>Strep Pneumoniae</td>
</tr>
<tr>
<td>H influenzae</td>
<td>H Influenzae</td>
<td>H Influenzae</td>
</tr>
<tr>
<td>[Also B catarrhalis and Strep pyogenes]</td>
<td>Branhamella Catarrhalis</td>
<td>Branhamella Catarrhalis</td>
</tr>
<tr>
<td><strong>Urinary Tract Infections</strong></td>
<td><strong>Causes of Acute Pharyngitis</strong></td>
<td><strong>Adenovirus</strong></td>
</tr>
<tr>
<td>Usually E. Coli.</td>
<td>• Viral (commonest): Rhinovirus, coronavirus, Influenza A &amp; B,</td>
<td>Sore throat (erythema + maybe exudate even though a virus), fever, headache, myalgia, conjunctivitis</td>
</tr>
<tr>
<td>Treatment:</td>
<td>Parainfluenza 1 – 3, Adenovirus, Herpes Simplex, EBV</td>
<td></td>
</tr>
<tr>
<td>• 1st line: Oral Trimethoprim (effective against community acquired E Coli, Klebsiella, Proteus, Strep faecalis)</td>
<td>• Bacterial: Strep Pyogenes (Gp A), Strep Group C, Mixed anaerobes (gingivitis – poor dental hygiene), Corynebacterium diphtheriae, Neisseria gonorrhoeae</td>
<td></td>
</tr>
<tr>
<td>• 2nd line: Oral Quinolones (eg Norfloxacin)</td>
<td>• G+ive anaerobic bacilli. Dominant gut microbe</td>
<td></td>
</tr>
<tr>
<td>• Single dose therapy less effective</td>
<td>• Causes: abdominal wound sepсидs, peritonitis, pelvic sepsis, septic abortion, purerperal sepсидs, any abscess incl. brain abscess from otitis media or haematogenous spread</td>
<td></td>
</tr>
<tr>
<td><strong>Aspergillus</strong></td>
<td><strong>Bacteroides Fragilis</strong></td>
<td></td>
</tr>
<tr>
<td>A saprophytic hyaline mould – lives on dead organic matter</td>
<td>G+ive anaerobic bacilli. Dominant gut microbe</td>
<td></td>
</tr>
<tr>
<td>Haemorrhagic pneumonia in immunocompromised (incl. acute leukaemia)</td>
<td>Causes: abdominal wound sepсидs, peritonitis, pelvic sepsis, septic abortion, purerperal sepсидs, any abscess incl. brain abscess from otitis media or haematogenous spread</td>
<td></td>
</tr>
<tr>
<td>Treatment: Amphotericin B. Itraconazole for prophylaxis</td>
<td>Treatment: Erythromycin (used to be ciprofloxacin [a quinolone] but it's been put in chicken feed → resistance)</td>
<td></td>
</tr>
<tr>
<td><strong>Candida Albicans</strong></td>
<td><strong>Campylobacter Jejuni</strong></td>
<td><strong>Bordetella Pertussis</strong></td>
</tr>
<tr>
<td>Yeast causing white plaques</td>
<td>G+ive rod</td>
<td>Causes whooping cough</td>
</tr>
<tr>
<td>↑ Infection in immunocompromised, steroid use or long term antibiotics</td>
<td>Treatment: Erythromycin (used to be ciprofloxacin [a quinolone] but it's been put in chicken feed → resistance)</td>
<td>Cough followed by inspiratory gasp (whoop), apnoea, vomiting</td>
</tr>
<tr>
<td>Treatment:</td>
<td>• Topical: Nystatin</td>
<td>• Can →encephalitis. 50% of &lt; 6 months get admitted</td>
</tr>
<tr>
<td>• Oral: Terbinafine for scalp or nails</td>
<td>• Oral: Terbinafine for scalp or nails</td>
<td>Incidence: up to 5000 cases a year</td>
</tr>
<tr>
<td>• STD: Clotrimazole pessary</td>
<td>• Topical: Nystatin</td>
<td>Treatment: Erythromycin</td>
</tr>
<tr>
<td>• Severe: Fluconazole 400mg CSF</td>
<td>• Oral: Terbinafine for scalp or nails</td>
<td></td>
</tr>
<tr>
<td><strong>Clostridium</strong></td>
<td><strong>Cytomegalovirus (CMV)</strong></td>
<td><strong>Chlamydia Trachomatis</strong></td>
</tr>
<tr>
<td>G+ive anaerobe, spore forming</td>
<td>Transmission: saliva, blood, organ donation</td>
<td>Obligate Intracellular bacteria</td>
</tr>
<tr>
<td>C Perfringens: Abdо wound sepсидs, peritonitis, pelvic sepсидs, puerperal sepсидs, gas gangrene (clostridial mononecrosis), food poisoning (Enterotoxic)</td>
<td>Immunocompetent:</td>
<td>Rarer cause of pneumonia (farm animals). Tx: erythromycin (has penicillinase)</td>
</tr>
<tr>
<td>C Tetani</td>
<td></td>
<td>• STD (types D – K):</td>
</tr>
<tr>
<td>C Botulinum</td>
<td></td>
<td>• Incubation 7 – 21 days. Need Endocervical sample</td>
</tr>
<tr>
<td><strong>Corynebacterium Diphtheriae</strong></td>
<td><strong>Cryptococcus Neoformans</strong></td>
<td><strong>Coliforms (= G+ive bacteria)</strong></td>
</tr>
<tr>
<td>G+ive bacilli</td>
<td>Yeast with mucinous capsule</td>
<td>Incl. E. Coli + Klebsiella + Proteus mirabilis</td>
</tr>
<tr>
<td>Causes diphtheria</td>
<td>Indian ink stain +ive</td>
<td>Cause UTIs, Pyleonephritis, abdo wound sepсидs, peritonitis, biliary tract infection</td>
</tr>
<tr>
<td>Rare now (1 NZ case in last 20 years)</td>
<td>Causes encephalitis in AIDS, Pneumonia &amp; aseptic (+lymphocytic) meningitis in immunocompromised</td>
<td>Tx:</td>
</tr>
<tr>
<td>Sore throat, fever, pain on swallowing, headache, vomiting, grey/green exudate on pharynx</td>
<td>Tx: Fluconazole or Amphotericin B</td>
<td>Meningitis &amp; brain abscess: 3rd gen Cephalosporin → good CSF penetration</td>
</tr>
<tr>
<td>Toxin →cardiac &amp; neuro toxicity</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>E Coli</strong></td>
<td><strong>Cryptosporidium</strong></td>
<td><strong>Cystosporidium</strong></td>
</tr>
<tr>
<td>G+ive rods. A coliform. Grows on Maconkey agar</td>
<td>Respiratory spread, usually young adults</td>
<td>Common protozoan parasite</td>
</tr>
<tr>
<td>Most are harmless bowel commensals but can →peritonitis (burst appendix), cistitis, neonatal meningitis</td>
<td>Sore throat (erythema/exudate in 50%), fatigue, malaise, fever, headache, posterior cervical lymphadenopathy, splenomegaly, hepatitis, atypical mononucleosis</td>
<td>Profuse watery diarrhoea</td>
</tr>
<tr>
<td>Tx:</td>
<td>Sore throat (erythema/exudate in 50%), fatigue, malaise, fever, headache, posterior cervical lymphadenopathy, splenomegaly, hepatitis, atypical mononucleosis</td>
<td>Diagnosis: stool microscopy (ZN stain for acid fast cysts)</td>
</tr>
<tr>
<td>48% resistant to amoxycillin, Augmentin resistance growing</td>
<td>Don’t eive penicillin →rash mistaken</td>
<td>No effective antibiotic treatment (can try Paromomycin – oral, nonabsorbable aminoglycoside)</td>
</tr>
<tr>
<td><strong>Epstein Barr Virus</strong></td>
<td><strong>Enterococcus Faecalis</strong></td>
<td><strong>Cystosporidium</strong></td>
</tr>
<tr>
<td>Respiratory spread, usually young adults</td>
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<td><strong>Enterococcus Faecalis</strong></td>
<td><strong>Cystosporidium</strong></td>
<td>No effective antibiotic treatment (can try Paromomycin – oral, nonabsorbable aminoglycoside)</td>
</tr>
<tr>
<td>Arobe</td>
<td>Arobe</td>
<td><strong>Cystosporidium</strong></td>
</tr>
<tr>
<td>Causes UTI, abdominal wound sepсидs</td>
<td>Arobe</td>
<td>Common protozoan parasite</td>
</tr>
<tr>
<td>Tx: Amoxycillin (not penicillin G)</td>
<td>Arobe</td>
<td>Profuse watery diarrhoea</td>
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</tbody>
</table>

**Epstein Barr Virus:**
- Respiratory spread, usually young adults
- Sore throat (erythema/exudate in 50%), fatigue, malaise, fever, headache, posterior cervical lymphadenopathy, splenomegaly, hepatitis, atypical mononucleosis
- Don’t give penicillin → rash mistaken

**Enterococcus Faecalis:**
- Aerobe
- Causes UTI, abdominal wound sepсидs
- Tx: Amoxycillin (not penicillin G)
<table>
<thead>
<tr>
<th>Otitis Media</th>
<th>Acute Infectious Exacerbations of Chronic Bronchitis</th>
<th>Acute Sinusitis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adenovirus</td>
<td>Acute Pharyngitis</td>
<td>Bladder Infections (UTIs)</td>
</tr>
<tr>
<td>Bordetella Pertussis</td>
<td>Bacteroides Fragilis</td>
<td>Aspergillus</td>
</tr>
<tr>
<td>Chlamydia Trachomatis</td>
<td>Campylobacter Jejuni</td>
<td>Candida Albicans</td>
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<tr>
<td>Coliforms</td>
<td>CMV</td>
<td>Clostridium</td>
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<td>Cryptosporidium</td>
<td>Cryptococcus Neoformans</td>
<td>Corynebacterium Diphtheriae</td>
</tr>
<tr>
<td>Enterococcus Faecalis</td>
<td>EBV</td>
<td>E Coli</td>
</tr>
<tr>
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<td>EBV</td>
<td>Corynebacterium Diphtheriae</td>
</tr>
<tr>
<td><strong>Gardnerella Vaginalis</strong></td>
<td><strong>Haemophilus Influenzae</strong></td>
<td><strong>Herpes Simplex 1 &amp; 2</strong></td>
</tr>
<tr>
<td>--------------------------</td>
<td>---------------------------</td>
<td>-------------------------</td>
</tr>
<tr>
<td>Causes Bacterial Vaginosis</td>
<td>G +ive bacilli</td>
<td>Incubation 2 – 25 days</td>
</tr>
<tr>
<td>Symptoms: greyish-white, smelly discharge</td>
<td>Type A: Causes acute otitis media, sinusitis, infections, exacerbation of chronic bronchitis, pneumonia in chronic lung disease, rarely meningitis (→ 3rd gen Cephalosporin → ↑ CSF pen)</td>
<td>Type 1: face, use zovirax cream. Also STI.</td>
</tr>
<tr>
<td>Clue cells on Gram stain</td>
<td>Tx: 6% resistant to penicillins, not sensitive to erythromycin → cefaclor</td>
<td>Type 2: STI. Prevalence 20%. Tx Acyclovir</td>
</tr>
<tr>
<td>Crowds out Lactobacilli</td>
<td></td>
<td>Encephalitis: confusion, convulsions. PCR test of CSF. Give acyclovir on suspicion</td>
</tr>
<tr>
<td>Tx: Anti-anaerobe: Metronidazole (oral and/or pessaries)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Helicobacter Pylori</strong></th>
<th><strong>Influenza A &amp; B</strong></th>
<th><strong>Listeria Monocytogenes</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>G –ive rod, curved/spiral shaped</td>
<td>Causes flu: common cold + fever, headache, generalised myalgia; most common cause of viral pneumonia</td>
<td>G +ive bacilli</td>
</tr>
<tr>
<td>Urease breath test: swallow C13 labelled Urease, expire C13 labelled CO2</td>
<td>400 deaths per annum</td>
<td>Tx: amoxycillin</td>
</tr>
<tr>
<td>Investigations: CLO test, biopsy, micro, serology</td>
<td>Vaccinate each year for new strains due to antigenic drift</td>
<td>Neonatal meningitis</td>
</tr>
<tr>
<td>Prevalence 30% but declining</td>
<td></td>
<td>Elderly/immunocompromised: Tx ciprofloxacin (a quinolone – not in kids)</td>
</tr>
<tr>
<td></td>
<td>Causes gastritis (usually asymptomatic)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Legionella</strong></th>
<th><strong>Mycoplasma</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Pneumonia: fibro-purulent exudate in 40 – 70 year old smoker. Slow onset, headache, delirium, 7more GI effects</td>
<td>Common cause of URTI</td>
</tr>
<tr>
<td>Tx: erythromycin (has penicillinase) + rifampicin if severe</td>
<td>Pneumonia: benign, self-limiting, age 5 – 15</td>
</tr>
<tr>
<td></td>
<td>Tx: Erythromycin</td>
</tr>
<tr>
<td></td>
<td>2nd line: Tetracyclines (eg doxycycline) except pregnant/kids</td>
</tr>
<tr>
<td></td>
<td>Resistant to Augmentin</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Moraxella Catarrhalis</strong> (= Branhamella Catarrhalis)</th>
<th><strong>Neisseria Gonorrhoea</strong></th>
<th><strong>Measles</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Causes: acute otitis media, acute sinusitis, acute infectious exacerbation of chronic bronchitis, pneumonia in chronic lung disease</td>
<td>G +ive diplococci, bean shaped, hard to culture (chocolate agar), survives intracellularly</td>
<td>Interstitial pneumonia in immunocompromised kids</td>
</tr>
<tr>
<td>Tx: 70% has penicillinase ⇒ augmentin, cefaclor, tetracycline, cefuroxime</td>
<td>STD incubation: 1 – 14 days</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Male: discharge and dysuria. Female: only 20% symptomatic ⇒ PID</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Tx:</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Stat: Amoxycillin + Probenecid</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Parainfluenza virus (1-3)</strong></th>
<th><strong>Pneumocystis Carinii Pneumonia</strong></th>
<th><strong>Neisseria Meningitidis</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Causes Group (laryngotracheobronchitis)</td>
<td>Extrapulmonary protozoan parasite</td>
<td>G +ive diplococci (bean shaped). Liberated endotoxin</td>
</tr>
<tr>
<td>Initial: sore throat, rhinorrhoea, mild cough</td>
<td>Exclusively infects the lung, mainly in AIDS (also transplant, leukaemia)</td>
<td>Kids &amp; adults meningitis, not otitis media</td>
</tr>
<tr>
<td>Leads to: sever cough (seals bark), hoarseness, inspiratory stridor (subglottic inflammation)</td>
<td>Tx: Cotrimoxazole (=trimethoprim + sulfamethoxazole)</td>
<td>Notifiable disease</td>
</tr>
<tr>
<td></td>
<td>Relapse common</td>
<td>Tx: Penicillin, Cefotaxime if allergic</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Respiratory Syncytial Virus</strong></th>
<th><strong>Rhino Virus and Coronavirus</strong></th>
<th><strong>Pseudomonas aeruginosa</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Major cause of URTI, esp winter/spring</td>
<td>Common cold</td>
<td>G +ive rod. Low virulence but antibiotic resistance. Grows in anything</td>
</tr>
<tr>
<td>Starts as URTI (cough, fever, sore throat) → LRTI (mainly bronchiolitis) with dyspnoea, tachypnoea</td>
<td>Fever uncommon except in kids</td>
<td>Common in burns, immunocompromised and CF</td>
</tr>
<tr>
<td>Tx: If severe then Ribavirin aerosol</td>
<td></td>
<td>Causes haemorrhagic pneumonia</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Tx:</td>
</tr>
<tr>
<td></td>
<td></td>
<td>↑ resistance. ALWAYS to sensitivities</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Meningitis: Ceftriaxone</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Staph Aureus</strong></th>
<th><strong>Strep Pneumoniae</strong></th>
<th><strong>Syphilis</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>G +ive, Coagulase +ive (fibrinogen → fibrin)</td>
<td>G+ive diplococci, haemolytic</td>
<td>Caused by Treponema pallidum</td>
</tr>
<tr>
<td>Causes: mastitis, diabetic foot infections, furuncles (if recurrent then ?nasal carriage → rifampicin), infected lines, hospital acquired pneumonia, abscess, endocarditis, food poisoning (esp in cream), osteomyelitis</td>
<td>Causes: acute otitis media, sinusitis, community acquired pneumonia, infectious exacerbation of chronic bronchitis, meningitis</td>
<td>→ ↓ lumen of small arteries due to ↑ intima</td>
</tr>
<tr>
<td></td>
<td>Oral: amoxycillin. IV: Penicillin G (1% adults resistant, 10% kids). Allergy: erythromycin (not for meninitis: poor)</td>
<td>Primary: chancre – painless hard macule at site of sexual contact. Secondary: 4 – 8 wks later, fever, malaise, lymphadenopathy, rash, alopecia</td>
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<td>--------------------------------</td>
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<td>--------------------------------</td>
</tr>
<tr>
<td>Herpes Simplex 1 &amp; 2</td>
<td>Haemophilus Influenzae</td>
<td>Gardnerella Vaginalis</td>
</tr>
<tr>
<td>Listeria Monocytogenes</td>
<td>Influenza A &amp; B</td>
<td>Helicobacter Pylori</td>
</tr>
<tr>
<td>Measles</td>
<td>Mycoplasma</td>
<td>Legionella</td>
</tr>
<tr>
<td>Neisseria Meningitida</td>
<td>Neisseria Gonorrhoea</td>
<td>Moraxella Catarrhalis</td>
</tr>
<tr>
<td>Pseudomonas aeruginosa</td>
<td>Pneumocystis Carinii Pneumonia</td>
<td>Parainfluenza Virus 1 - 3</td>
</tr>
<tr>
<td>Staph Epidermidis</td>
<td>Rhino Virus and Coronavirus</td>
<td>Respiratory Syncytial Virus</td>
</tr>
<tr>
<td>Syphilis</td>
<td>Strep Pneumoniae</td>
<td>Staph Aureus</td>
</tr>
<tr>
<td>Haemolytic Strep Group B</td>
<td>Strept Pyogenes</td>
<td>Viridians Strep</td>
</tr>
<tr>
<td>--------------------------</td>
<td>-----------------</td>
<td>-----------------</td>
</tr>
<tr>
<td>β Haemolytic: clear on blood agar. Eg Strep agalactiae (vaginal flora). [NB Strep pyogenes in β haemolytic Lancefield Group A]</td>
<td>βhaemolytic, Lancefield Group A. G +ive singly or in chains</td>
<td>= α haemolytic (green on blood agar). G +ive</td>
</tr>
<tr>
<td>Causes: meningitis, respiratory distress syndrome</td>
<td>Common cause of cellulitis, pharyngitis, impetigo</td>
<td>Eg Strep Sanguis</td>
</tr>
<tr>
<td>Tx: Penicillin</td>
<td>Can →Rheumatic fever &amp; glomerulonephritis</td>
<td>Causes: UTI, wound sepsis</td>
</tr>
<tr>
<td></td>
<td>Tx: Penicillin (little resistance)</td>
<td>Infective endocarditis: Tx: penicillin or amoxycillin +/- gentamycin (for G –ive cover)</td>
</tr>
<tr>
<td></td>
<td>Erythromycin if allergic</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>TB</th>
<th>Trichomonas</th>
<th>Varicella Zoster</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mycobacterium Tuberculosis</td>
<td>Causes Trichomoniasis</td>
<td>Chicken pox.</td>
</tr>
<tr>
<td>Waxy coat resists lysis after phagocytosis →granulomas. Infects anything (lung, lymph nodes, brain, gut)</td>
<td>Watery green/yellow fishy smelling vaginal discharge</td>
<td>Latent in dorsal root ganglia →shingles</td>
</tr>
<tr>
<td>Acid fast bacilli – use ZN stain</td>
<td>Protozoa</td>
<td>Culture possible if transported in viral medium</td>
</tr>
<tr>
<td>Tx: Rifampicin + isoniazid + pyrazinamide (also ethambutol)</td>
<td>Common 3rd world STD</td>
<td>Tx for shingles:</td>
</tr>
<tr>
<td></td>
<td>Tx: Doxyccycline, metronidazole</td>
<td>Acyclovir as early as possible</td>
</tr>
<tr>
<td>Toxoplasmosis</td>
<td>Malaria</td>
<td>Analgesic or low-dose amitriptyline for pain</td>
</tr>
<tr>
<td>Protozoa/parasite. In meat cysts (and kitten faeces)</td>
<td>Irregular fever, headache, malaise, vomiting (like typhoid). Lab: Blood film when febrile.</td>
<td>Plasmodium Falciparum</td>
</tr>
<tr>
<td>Causes: lymphadenopathy (eg unilateral), maybe fever, myalgia, acute pharyngitis, hepatosplenomegaly, atypical mononucleosis, takes while to settle. AIDS: CNS involvement, retinal lesions</td>
<td>Chemophyrexiasis</td>
<td>No reinfection, cerebral malaria, Africa</td>
</tr>
<tr>
<td></td>
<td>Megafoque weekly: good against chloroquine resistant Falciparum. Not if epilepsy, pregnant, babies</td>
<td>Quinine sulphate + Doxycycline 7 days</td>
</tr>
<tr>
<td></td>
<td>Doxycycline daily: Eso in SE Asia</td>
<td>Cerebral malaria: IV quinine</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Plasmodium Vivax</th>
<th>Giardiasis</th>
<th>Amoebiasis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asia/Oceania, exo-erythrocystic liver cycle</td>
<td>Explosive, watery diarrhoea</td>
<td>Malaria: prophylaxis if &gt; 7 days. Risk in resort areas low</td>
</tr>
<tr>
<td>3 days of Chloroquine</td>
<td>Stool exam, 3 samples, 48 hours apart →trophozoites</td>
<td>Hep A: Usually given</td>
</tr>
<tr>
<td>Radical cure (P Vivax or P Ovale): Primaquine 2 weeks (test for G6PD deficiency first)</td>
<td>Tx: Tinidazole stat or Metronidazole 7 days</td>
<td>Typhoid: injectable or oral vaccine</td>
</tr>
<tr>
<td>Relapse common →3 days chloroquine then higher dose of primaquine</td>
<td>Relapse not uncommon</td>
<td>Yellow fever: equatorial Africa &amp; South America</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Filariasis</th>
<th>Intestinal Worms</th>
<th>Travel Medicine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eg Wuchereria Bancroft</td>
<td>Hookworm, roundworm, pinworm: Medendazole (treat whole family)</td>
<td>Malaria: prophylaxis if &gt; 7 days. Risk in resort areas low</td>
</tr>
<tr>
<td>→Elephantitis. May need Surgery to relieve blocked lymphatics</td>
<td>Strongyloides Stercoralis: Thiabendazole</td>
<td>Hep A: Usually given</td>
</tr>
<tr>
<td>Tx: Ivermectin</td>
<td>Tapeworms: Niclosamide</td>
<td>Typhoid: injectable or oral vaccine</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Yellow fever: equatorial Africa &amp; South America</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Polio, tetanus and diphtheria</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Meningococcal (Types A, C, W, 13): Nonal</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Cephalosporins</th>
<th>Macrolides</th>
<th>Vancomycin</th>
</tr>
</thead>
<tbody>
<tr>
<td>1: Cefazolin: Better for G+ (not E faecalis) and anaerobes (not B Fragilis)</td>
<td>Good against streps, mycoplasma, chlamydia or legionella pneumoniae, Campylobacter</td>
<td>Only active against G+</td>
</tr>
<tr>
<td>2: Cefuroxime: Better against Coliforms. Active against H influenzae</td>
<td>Not H influenzae</td>
<td>Systemic MRSA/MRSE infection</td>
</tr>
<tr>
<td>3: Ceftriaxone, Cefotaxime: Good against most coliforms. Not Bacteroides or Enterococcus. Good CSE penetration</td>
<td>No CSF penetration</td>
<td>Staph or Strep Endocarditis with penicillin allergy</td>
</tr>
<tr>
<td></td>
<td>Chlamydia trachomatis in pregnancy</td>
<td>C Difficile colitis (oral) – use</td>
</tr>
<tr>
<td></td>
<td>Erythromycin, Roxithromycin (Rulide), Clarithromycin (for MAC), Azithromycin</td>
<td>Metronidazole first</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Otto and nephro toxic</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Cotrimoxazole</td>
</tr>
<tr>
<td></td>
<td></td>
<td>= Trimethoprim + sulphamethoxazole</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Broad spectrum</td>
</tr>
<tr>
<td></td>
<td></td>
<td>For acute infectious exacerbations of chronic bronchitis, PCP</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Trimethoprim only for community acquired UTI (so those with sulphur allergy can use)</td>
</tr>
</tbody>
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<table>
<thead>
<tr>
<th>Rifampicin</th>
<th>Aminoglycosides</th>
<th>Cotrimoxazole</th>
</tr>
</thead>
<tbody>
<tr>
<td>Always in combination (except meningitis and HIB prophylaxis)</td>
<td>Active against all coliforms, pseudomonas</td>
<td>= Trimethoprim + sulphamethoxazole</td>
</tr>
<tr>
<td>Tb, Severe staph or legionella infection</td>
<td>Inactive against strep, anaerobes</td>
<td>Broad spectrum</td>
</tr>
<tr>
<td></td>
<td>For G- sepsis, perforated appendix</td>
<td>For acute infectious exacerbations of chronic bronchitis, PCP</td>
</tr>
<tr>
<td></td>
<td>Otto and nephro toxic</td>
<td>Trimethoprim only for community acquired UTI (so those with sulphur allergy can use)</td>
</tr>
<tr>
<td>Viridians Strep</td>
<td>Strep Pyogenes</td>
<td>β Haemolytic Strep Group B</td>
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<td>Trichomonas</td>
<td>Tb</td>
</tr>
<tr>
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<td>Toxoplasmosis</td>
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<tr>
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<td>Travel Medicine</td>
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<td>Filariasis</td>
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<tr>
<td>Vancomycin</td>
<td>Macrolides</td>
<td>Cephalosporins</td>
</tr>
<tr>
<td>Cotrimoxazole</td>
<td>Aminoglycosides</td>
<td>Rifampicin</td>
</tr>
<tr>
<td><strong>Quinolones</strong></td>
<td><strong>Tetracyclines</strong></td>
<td><strong>Metronidazole</strong></td>
</tr>
<tr>
<td>----------------</td>
<td>------------------</td>
<td>------------------</td>
</tr>
<tr>
<td>• Broad spectrum (except anaerobes and streps)</td>
<td>• Eg Doxycycline</td>
<td>• Active against all anaerobes (eg B fragilis)</td>
</tr>
<tr>
<td>• Not in kids (damages growth cartilage)</td>
<td>• Active against staph, streps, coliforms, HIB</td>
<td>• Inactive against aerobes (except Gardnerella Vaginalis – drug of choice)</td>
</tr>
<tr>
<td>• Norfloxacin: resistant UTIs</td>
<td>• Used in STDs</td>
<td>• Active against protozoa: eg Giardia</td>
</tr>
<tr>
<td>• Ciprofloxacin: Pseudomonas</td>
<td>• Syphilis and Gonorrhoea if penicillin allergy</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Antifungals</strong></th>
<th><strong>Quinolones</strong></th>
<th><strong>Tetracyclines</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>• Nystatin (topical): vaginal/oral candida</td>
<td>• Broad spectrum (except anaerobes and streps)</td>
<td></td>
</tr>
<tr>
<td>• Miconazole (topical): Candida and dermatophytes (except scalp and nails)</td>
<td>• Not in kids (damages growth cartilage)</td>
<td></td>
</tr>
<tr>
<td>• Terbinafine (oral): dermatophytes of scalp and nails</td>
<td>• Norfloxacin: resistant UTIs</td>
<td></td>
</tr>
<tr>
<td>• Fluconazole (oral/iv): Yeasts (candida, cryptococcus). Good CSF penetration</td>
<td>• Ciprofloxacin: Pseudomonas</td>
<td></td>
</tr>
<tr>
<td>• Itraconazole (oral): Dermatophytes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Metronidazole</td>
<td>Tetracyclines</td>
<td>Quinolones</td>
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<td></td>
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<td>Antifungals</td>
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</tbody>
</table>
### Back Exam

- **Walk**: gait, walk on toes (S1), walk on heels (L5, ie neuro signs)

- **Look**:
  - Is belt line horizontal
  - Skin: Scars, pigmentation
  - Shape & Posture: if scoliosis then bend over

- **Palpate**:
  - Spinous processes (support forehead for neck) for tenderness or a step
  - Sacroiliac joint

- **Move**:
  - Neck: flexion, extension, rotation, lateral flexion
  - Back:
    - Flexion: Schober’s test
    - Extension
    - Lateral Flexion
    - Rotation (sitting on a chair)

- **Special tests**:
  - Check neurology in arms and legs if neck or lumbar pain (Sciatic pain – Lasègue’s test, power, tone, reflexes, sensation, co-ordination)
  - Do abdominal exam if lumbar pain (eg AAA)

### Hip Exam

- **Standing**:
  - Gait
  - On toes (S1), on heels (L5) (checking neurology)
  - Bend over – how can they reach (examine back)
  - Crouch down (test knees and extensor mechanism)
  - Observe: gluteus bulk, posterior scars
  - Trendelenburg test and sacroiliac joint

- **Look**:
  - Skin: scars, redness
  - Soft tissue: swelling
  - Muscle: wasting – quads, abductors, adductors
  - Bony deformity
  - Apparent and real leg length

- **Feel**:
  - Groin: hernias, lymph nodes
  - Greater trochanter tenderness → ilio-tibial band pain

- **Move (compare sides)**:
  - Thomas test: fixed flexion deformity
  - Flexion (comparing sides)
  - Adduction and abduction with pelvis fixed
  - Internal and external rotation (comparing sides)

- **Exam knee and lower back** (did this while standing)
  - Check pulses
  - Check leg neurology

### Knee Exam

- **While standing**:
  - Observe:
    - Varus/valgus or fixed flexion deformity
    - Scars, symmetry, swelling
    - Popliteal fossa: Baker’s cyst
  - Gait
  - Squat down and duck walk

- **Observe on the bed**:
  - Swelling, muscle wasting, scars, deformity
  - Actively push knee into bed (muscle bulk, fixed flexion deformity)
  - Straight leg raise: tests extensor mechanism

- **Palpate**:
  - Warmth each side
  - Effusion: stroke test, patellar tap
  - Joint line (meniscal tears), collateral ligaments, ischial tuberosity and patellar ligament. Baker’s cyst, popliteal pulse

- **Move**: Flex both knees

- **Ligaments**: (sit on foot, compare sides)
  - PCL: posterior sag and posterior draw test
  - ACL: anterior draw test, Lachman’s, Pivot-shift
  - Collaterals: Varus and valgus stress test
  - McMurray’s for meniscal tears

- **Patellar-femoral joint**: Solomon’s test. Feet over side: pointing straight ahead, raise leg (crepitus?), apprehension test

### Shoulder Exam

- **Look** (comparing both sides):
  - Skin: redness, scars
  - Shape (in front and behind): asymmetry, wasting, dislocation, swelling, sub-acromial sulcus

- **Feel**:
  - Temperature
  - Around bones from clavicle to scapular
  - Tendons under acromion
  - In axilla: tenderness, lymph nodes

- **Move**:
  - Abduction to 180° and adduction across chest
  - Flexion and extension
  - External rotation (forearms at 90°)
  - Internal rotation (scratch up back)

- **Rotator Cuff**:
  - Supraspinatus: abduction from 0 - 30° against resistance with thumbs to the ground
  - Infraspinatus: externally rotate against resistance
  - Subscapularis: Lift-off test (try and push it away)

- **Stability**:
  - Sulcus test: pull arm down and look for sulcus
  - Anterior draw test
  - Apprehension test
  - Push-ups against the wall

- **Examine neck and elbow**

- **Distal pulses and neurology**
Respiratory Exam (Chest Only)

- Introduce yourself, wash hands, light, position patient
- Observe:
  - General: Cyanosis, pallor, cachexia, distress, LOC
  - Chest:
    - Respiratory distress, dyspnoea, rhythm
    - Listen for cough, wheeze, hoarseness, stridor
    - Scars
    - Shape: scoliosis, kyphosis, pigeon
    - Movement: accessory muscles, indrawing, paradoxical breathing of abdomen, expansion
  - COUNT RESPIRATORY RATE
- Palpate:
  - Neck:
    - Nodes – especially supraclavicular
    - Trachea – central, inspiratory tug
  - Push sternum to spine (broken ribs)
  - Tactile fremitus: 99 (on front and back)
- Percussion: Stony dull, dull, or hyper-resonant
- Auscultate:
  - Breath Sounds (front and back):
    - Air entry each side
    - Vescicular or bronchial
    - Wheeze, crackles, rubs
  - Forced expiration
  - Vocal resonance
- Peak Flow

CVS Exam (Precordium Only)

- Introduce yourself, wash hands, light, patient at 45º
- Observe:
  - General: cyanosis, pallor, cachexia, distress, LOC, Marfan’s, Down’s etc, oedema
  - Chest: Scars, deformity, pacemakers, pulsations (look from side as well)
  - JVP
  - Palpation:
    - Apex beat (and count down ribs – 2nd IC space at sternal angle): sustained, hyperkinetic, etc
  - Parasternal heaves (RV activity), Aortic and pulmonary thrills
  - Auscultation (ALWAYS time from carotid pulse):
    - Diaphragm and bell at mitral, tricuspid, pulmonary and aortic areas
    - Axilla with diaphragm (mitral regurg if systolic)
    - Carotid arteries (bruit, aortic murmur)
  - To refine murmurs:
    - Left lateral position: Mitral stenosis (bell)
    - Leaning forward, full expiration, parasternal with diaphragm: Aortic regurg, hypertrophic cardiomypathy
    - Tricuspid murmurs: check JVP and pulsatile liver
  - Pulmonary oedema: Percuss and auscultate posterior lung bases. Check sacral oedema

Abdomen Exam (Abdomen only)

- Introduce yourself, wash hands, light, patient at 0º
- Inspection:
  - General: jaundice, pallor, pigmentation, weight/wasting, gynaecomastia, spider naevi, body hair, bruising
  - Abdomen:
    - Scars
    - Distension
    - Veins
    - Striae
    - Hernias, visible masses
    - Pulses (aorta, liver)
- Palpation (warm hands, watch face):
  - Light palpation
  - Deep palpation: test for rebound
  - Percuss then palpate liver (span, firm, nodular, tender, pulsatile). Test for movement on inspiration
  - Percuss then palpate spleen
  - Ballot kidneys
  - Percuss for shifting dullness of ascites
  - Bladder
- Auscultate:
  - Bowel sounds
  - Renal bruit
  - Testicular, PR and inguinal hernias (cough)

Neurology Limb Exam

- Observe:
  - General: alertness, speech
  - Posture
  - Wasting, fasciculations, abnormal movements (tics, tremor, chorea, athetosis)
- Power: compare sides, 0 – 5
- Tone: of all movements: hypo or hyper tonic (rigidity, spasticity), ankle clonus
  - Reflexes:
  - Arm: triceps, biceps, supinator
  - Leg: patellar, ankle, Plantar
- Sensory:
  - Light touch
  - Position sense
  - Vibration
  - Pinprick
  - Temperature (same pathway as pinprick)
- Coordination:
  - Arms: rapid-alternating movements, finger-nose test, drift, flap
  - Legs: heel-shin test, Romberg, heel-toe walking
- Function:
  - Legs: Gait, walk on heels (L5), toes (S1), crouch
  - Hands: identify objects with eyes closed
### Examination of Cranial Nerves

<table>
<thead>
<tr>
<th>Nerve</th>
<th>Examination</th>
</tr>
</thead>
<tbody>
<tr>
<td>2: Ophthalmic nerve</td>
<td>acuity, visual fields, fundoscopy</td>
</tr>
</tbody>
</table>
| 3, 4 and 6: Oculomotor, Trochlear, and Abducens | Pupils: ptosis, corneal light reflex, swinging light test (turn off light), accommodation reflex, squint  
Eye movement: draw H, watch for lag or nystagmus, ask about diplopia |
| 5: Trigeminal | Light touch and pinprick in all 3 divisions  
Corneal reflex  
Motor: Wasting of muscles of mastication  
Jaw opens in midline  
Clench jaw, palpate masseters |
| 6: Oculomotor, Trochlear, and Abducens | Pupils: ptosis, corneal light reflex, swinging light test (turn off light), accommodation reflex, squint  
Eye movement: draw H, watch for lag or nystagmus, ask about diplopia |
| 7: Facial | Wrinkle forehead  
Show your teeth  
Puff up cheeks |
| 8: Vestibulochoclear | Rinne: conductive deafness if mastoid louder  
Weber: hear loudest in good ear if sensori-neural deafness |
| 9 & 10: glossopharyngeal and Vagus | Uvula in midline (say ‘ah’)  
Swallowing and speech (ask about hoarseness) |
| 11: Accessory | Shrug shoulders, turn head against resistance |
| 12: Hypoglossal | Wasting, fasciculation, protrudes in midline, ‘la la la’ quickly, push against inside of cheek |

### Examination of Leg Vasculature

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| Inspection | Colour  
Presence of hairs  
Varicose veins (while standing)  
Dilated superficial veins (DVT)  
Ulcers  
Swelling  
Wasting – compare muscle bulk on each side  
Clubbing of the toes  
Oedema |
| Palpation | Compare size, tenderness and warmth of calves  
Oedema  
Temperature of feet  
Capillary return  
Sensation  
Veins: hard thromboses. Tender thrombophlebitis |
| Peripheral pulses | Femoral: Palpatate and auscultate for bruits  
Palpate popliteal, posterior tibial, dorsalis pedis |
| Buerger’s test | Elevate leg to 45º. Pallor is rapid if poor arterial supply  
Then hand over bed. Cyanosis rapid if poor arterial supply |
| Bed side test | ABI (Ankle Brachial Index): ultrasound comparison of blood flow in the arm and leg |

### Abnormal Menstruation

<table>
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<th>Condition</th>
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| Basic Menstrual History | LMP  
Normal cycle length, days of bleeding, regularity  
How heavy is bleeding (number of pads, clots, etc)  
Associated pain  
Other bleeding: between periods, post-coital  
Age at menarche  
Age at menopause, post menopausal symptoms and any bleeding  
Contraception |
| Amenorrhoea | Primary: Never menstruated. Rare. Turner’s, Testicular feminisation, etc  
Secondary: Pregnancy related: pregnant or breast feeding  
PoP, Depot  
Stress: Anorexia, athlete, disease (↓weight)  
Prolactinoma →↓pituitary function, visual fields, headaches  
Ovarian causes (PCO, tumours): virilisation, ↑weight  
Premature menopause  
Hyperthyroidism |
| Menorrhagia | Young: abnormal menstrual bleeding  
Older: IUCD, fibroids, endometriosis, polyps, cancer  
Infection (any pain, fevers, discharge)  
Hypothyroidism →cold intolerance, weight gain  
Abnormal platelets |
| Intermenstrual | mid-cycle ↓in oestrogen + above factors |

### Gynaecological History

<table>
<thead>
<tr>
<th>Data</th>
<th>Description</th>
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</thead>
</table>
| Introductory data | Age  
Gravidity (pregnancies) + Parity (Deliveries)  
LMP |
| HPC: including details of bleeding, pain, discharge and urinary symptoms |
| Past Gynae History | Age at menarche  
Menstrual history  
Past gynae problems/procedures/abdo surgery  
Sexual history  
Current/past contraception  
Past STDs  
Incontinence  
Smear history  
Past Obstetric history  
PMH |
| Medications |
| FHx: mother or sisters with gynae/obstetric problems |
| Social Hx: Relationship status, sexual activity, alcohol & smoking, occupation, any inter-personal violence or abuse |
### Obstetric History
- Introductory data:
  - Age
  - Gravidity (pregnancies) + Parity (Deliveries)
  - LMP
- Current pregnancy:
  - Due date (check accuracy)
  - Contractions/pain
  - Bleeding
  - Discharge
  - Fetal movements
- Past Obstetric History:
  - When was it
  - Antenatal problems (eg ↑BP, diabetes, etc)
  - Delivered: pre-term, post-term?
  - Delivery: vaginal, C-section
  - Weight of baby
  - Post partum: any bleeding, infection, depression
  - Baby: any problems – how are they now
  - Feeding: breast or bottle
- Past Gynaec history:
  - Previous problems: infection, surgery, etc
  - Contraceptive history
  - Smear history
- PMH: Hypertension, DM, heart disease, asthma, DVTs, infections (esp STIs, Hep B, Tb), depression, endocrine
- Medication: especially folate
- FHx: DVTs, birth defects, multiple births, pregnancy problems
- Social: relationship, smoking & alcohol, occupation

### Pelvic Pain
- Pain with sex = dyspareunia
  - Superficial: eg HSV, atrophy, vaginismus
  - Deep: pelvic disease (eg endometriosis, PID), post-hysterectomy
- Period pain = dysmenorrhoea:
  - Primary: Young, first 2 days of menses, no organ pathology, started at menarche and not getting worse
  - Secondary: Older, prior to and through out bleeding, pelvic disease/infection, PMS
- For > 6 months = Chronic pelvic pain
  - Intermittent (with sex/menses, etc) or continuous
  - Gynae: dysmenorrhoea, endometriosis, adenomyosis, PID, prolapse, post-delivery trauma, etc
  - Non-gynae: UTI, IBS, diverticular, musculo-skeletal

### Sexual History
- Number & duration of relationships
- Previous similar symptoms
- UTI questions: frequency, discharge, abdo pain, testicular pain, joint pain
- Screen for high risk behaviour:
  - Alcohol and drug use
  - Unprotected sex
  - Multiple partners
  - Anal/oral sex

### Psych History
- Identifying data: name, age, occupation
- HPC (including when did you last feel well, what’s your worst worry)
- Systematic enquiry:
  - Anxiety + phobias
  - Mood
  - Psychotic
  - Suicidality
  - Cognitive
  - Neuropsychological: sleep, appetite, weight
  - Alcohol and drug
  - Impulse-control screen
- Medications
- Past psych history
- PMH
- Family: anyone had psych illness, had a breakdown, attempted suicide, had an A&D problem
- Social: including personal history, past difficulties (abuse, legal, relationships, etc)
- Mental state: appearance and behaviour, speech, mood, affect, thought form, thought content, suicidal ideation, perceptual phenomena, cognition, intelligence, insight and judgement, rapport

### Suicide Assessment
- History:
  - Ideation:
    - Do you think a lot about death
    - Do you want to die – or want others to know how bad it is
    - Do you have the means
    - What’s stopped you so far
    - How do you feel about accepting help
  - Past attempts:
    - What did you do
    - Why did you do it
    - What was the final straw
    - Did you leave a note
    - What stop you going through with it
- Risk assessment:
  - Predisposing factors: Family history, psych illness, alcohol and drug problem, suicide exposure, other illness, age and sex, living alone
  - Precipitating factors: Stressful events, current mood, thoughts about the future, mental state, current plans, availability of method
  - Protective factors: cognitive flexibility, social supports, hopefulness, treatment of disorders, responsibility for children
**Shortness of Breath**

- Very sudden:
  - MI: palpitations, pain, anxious, risk factors (hypertension, diabetes, ↑lipids, smoking, previous MI, stroke or claudication, FHx)
  - PE: Palpitations, Leg swelling, immobility, surgery, pregnancy, past or family history
  - Pneumothorax
- Over a few hours:
  - Asthma: night cough, wheeze, previous history. Test peak flow
  - Pneumonia: fevers, sweats, cough, sputum, blood, pain with coughing
- Gradual:
  - Heart failure: oedema, tired, orthopnoea, PND, history or risk factors for IHD
  - Anaemia
  - Carcinoma
- Others:
  - Metabolic acidosis (eg Diabetic ketoacidosis)
  - Psychiatric – eg anxiety
- Remember to ask about medications and smoking
- Investigations:
  - Examine the patient, including BP, pulse & JVP
  - Peak flow
  - Bloods: FBC, Electrolytes, cardiac enzymes
  - ABGs
  - Sputum/blood cultures
  - CXR, ECG
- Treatment: include $O_2$

**Key Differentials**

- Sleepiness/Fatigue:
  - Sleep disturbance/restriction (?anxiety)
  - Sleep apnoea
  - Depression
  - Hypothyroidism
  - Heart failure
  - Anaemia
  - Acute or chronic disease (eg EBV)
  - Drugs: β-blockers, anti-histamines, sedatives, alcohol
- Passing out:
  - Arrhythmia
  - Epilepsy (any aura, witness report, post-ictal state, past head injury)
  - CVA
  - Postural hypotension
  - Vasovagal faint
  - Hypoglycaemia
  - Fall

**ECG Interpretation**

- **Rate** (brady or tachycardia). 300/no of big squares
- **Rhythm**: Relationship of P waves to QRS →sinus arrhythmia, supraventricular arrhythmia, escape beats
- **Cardiac Axis**: Normal if I and II positive
  - Left deviation = I+, II and III –
  - Right deviation = I–, II +/-, III +
- **Description of P wave**:
  - Peaked P: RA hypertrophy
  - Twin peaked P: LA hypertrophy
  - Large P →↓K, small P →↑K
- **Conduction intervals**: Start of P to start of QRS = 3 –5 small squares (0.12 – 0.2 secs)
- **Description of QRS**:
  - Normal <= 3 small squares. > BBB or ventricular
  - **Bundle Branch**: Marrow and William in V1/V6
  - **RV Hypertrophy**: R in V1/2 + S in V5/6
  - **LV Hypertrophy**: S in V1/2 + S in V5/6
- **ST Segment**:
  - Depressed: ischaemia
- **T wave**: Normally inverted in VR and V1. Abnormal if –ive in I, II, V4-6. If not full thickness infarct →T wave inversion but no Q wave. Digoxin: T wave inversion, slopping ↓of ST. ↓K →flat, ↑K →wide, peaked
- **QT interval**

**Paediatric Differentials**

- Quick screen for severity of illness: responsiveness, feeding, urine, colour, breathing
- Fever in a child without clear focus:
  - Infection: UTI, bacteraemia, meningitis
  - Rheumatic Fever
  - Poisoning
  - Leukaemia
  - Drug Fever
- **Gastroenteritis in a child**:
  - Infection: Rotavirus, campylobacter, protozoa
  - Systemic: UTI, Pneumonia, otitis media
  - Surgical: appendicitis, intussusception, obstruction (eg hernia), pyloric stenosis, torsion, secondary to adhesions
  - Other: diabetic ketoacidosis, antibiotic diarrhoea, poisoning
- **PR Bleeding**: necrotising enterocolitis, intussusception, IBD (unlikely), familial polyps
- Abdo pain is likely to be benign if: didn’t know about it till the child said, they’re distractible from it, it is central, no sleep disturbance, no symptoms, intermittent
- **Coma**: hypoxic, epileptic, trauma, infection, poison, renal failure, hypo/hyperglycaemia, hyper/hypo-thermia, hypertension
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