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# FRACP Clinical Exam Notes

Compiled by David Tripp

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Disclaimer: These are study notes I compiled to help me get through the 2009 RACP Clinical Exam. I share them in the hope they may help. However, I take no responsibilities for mistakes. Learn from them – don't repeat them.

I am also grateful to sources to numerous to name from which I have compiled, cut and pasted in order to learn everything I must know....

These notes, and their companion volume, my RACP Written Exam Notes, can be downloaded from [www.sites.google.com/site/davidtrippnotes](http://www.sites.google.com/site/davidtrippnotes).

Happy Hunting!

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### Long Case Set

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## Long Case Outline

- Time: history and exam in 40 minutes, then map out issues
- With Patient:
  - Introduce yourself, they can tell you anything, there is a lot to get through – I'll need to cut you off sometimes
  - Sketch the problem list (looks at medications for a guide), then go through them in detail (what's most important to you, which symptoms bother you the most)
  - ROS:
    - General (weight), cardiovascular, GI, urinary, neuro, psych, locomotor, haematological, skin
    - Including general screen for HTN, DM, cholesterol, asthma, clots/bleeding, thyroid, kidney, jaundice, arthritis/fractures, epilepsy, vision and hearing, serious infectious(eg TB)
    - Past surgery, anaesthetic problems
    - Mood: depression
  - Medications: all medications (including past ones, when and why stopped), OTC, compliance (“Do you forget to take your pills very often”), allergies, vaccinations
  - Family History
  - Social History:
    - Access to and relationship with GP and other health services
    - Family: ages, health status, problems
    - Supports: Living with you (*is spouse in good health*), employment, financial concerns, hobbies, exercise, support groups, community groups, EPOA
    - ADLs:
      - Barthel (out of 20): dressing, eating/dentures, ambulatory + falls in last 12 months, toileting/continence/hygiene
      - Instrumental ADLs (OARS score): shopping, housekeeping, accounting, food prep, travel
      - Driving
    - Description of house
    - Hobbies
    - Smoking and alcohol (incl forensic history)
    - Sex and contraception, fertility, impotence
- Examination: asked patient if the examiners checked anything else
- Structure of presentation:
  - Summary: Mr/Mrs/ is a (age) who works as/lives with .... and particularly enjoys.... He has a ... year history of .... (or is currently an inpatient for treatment of ....) on a background of the active problems of ... (include social problems) and inactive problems of...
  - Presenting complaint (brief history) – put patients primary concern or presenting problem first
  - “Now detailing each problem”:
    - The aim is a summary with salient highlights, not a long chronology. Eg has a history of severe RA, currently in remission, but with residual significant functional impairment... Also pad it as much as possible with your knowledge – not just what's happened
    - Mr X (illness) was diagnosed in .... :
      - **Original presentation**
      - **Differential**
      - **Risk factors for the illness**
      - **Complications: which do they have, which don't they have**
      - **Investigations** (any they didn't need, any they missed)
      - **Treatment, response to treatment, monitoring, treatment and complications of treatment** (which have they had, which haven't they had)
      - **Current symptoms and function**
      - **Prognosis ie assessment of severity** (and as patient sees it)
    - Include indications of severity, score out of 10, what does this stop you doing, impact on function
    - Don't forget about pain – we often do, patients don't! What works for their pain
    - Active problems first. Whiz through inactive problems at end
  - Medications, allergies, compliance, vaccinations
  - Family history: brief – include where relevant in the problem list
  - Social history

- Examination findings: opening statement (alert and co-operative, ease of positioning, etc), inspection, vitals, relevant positives and negatives. Use unremarkable to cover all the normals
- Issues:
  - “In summary, X is currently [recovering from... stable/mild/severe/active/in remission....]. This patients main problem is ..... In addition she faces the ongoing diagnostic/management problems of .....that I would like to discuss further today.
  - Don’t stop! Launch straight in
  - Start with patient’s main concern if relevant. Include one social problem to show you’re wholistic

	Problem	DDx	Risk Factors/exam findings	Management/Goal
Problem 1				
Problem 2				
Problem 3				

- Diagnostic plans:
    - What is differential given risks and exam
    - Then investigations: for diagnosis, exclude differentials, assess severity, for treatment baselines and any complications
    - “I would order the following diagnostic tests....”
    - “Differentials would be excluded by....”
    - “To assess severity I would ...”
  - Management Plans – be wholistic:
    - **Education**/support: diabetes nurse, cardiac rehab, pulmonary rehab, disease societies
    - Prevention – things patient can do for themselves:
      - **Lifestyle**: quit smoking, dietician, exercise program
      - **Nutrition**: salt, protein, fat....
    - Treatment: of precipitant, of cause, of symptoms, or complications and/or treatment complications
    - **Package of care**:
      - Allied health: SW, OT (aids and modifications), PT, SLT, podiatrist, family meetings
      - GP: primary care package
      - EPOA, support package, benefits, personal alarm, medic alert bracelet
    - Support groups (church, marae, pacific health)
    - Vaccination
    - **Screening**
    - **Follow up**
    - **Assess for or comment on comorbid depression**
    - Formulate specific goals (eg return to work)
    - Any family issues: inheritance issues, screening family members, reproductive
  - Consider “Integration” across all her problems. Good issues could include:
    - Unifying diagnoses
    - Polypharmacy
    - Falls
    - Research issues
  - “Given these problems are going to be long terms issues it’s important that X has a good relationship with her GP and maintains regular contact. I would liase with GP....”
  - “In conclusion, X has .... Problems relating to.... Comment on insight, understanding of problems, level of frustration, impact on life, well-being, relationships, finances, family
- Psychological adjustment to chronic disease (see Lancet 19 July 2008): to promote psychological adjustment, patients should:
    - Remain as active as is reasonably possible
    - Acknowledge and express their emotions in a way that enables them to take control of their lives
    - Engage in self-management
    - Try to focus on potential positive outcomes of their illness
  - Comments:
    - “Number of things that could be done. The most efficacious are...”
    - If you don’t know: “I’m uncertain, on one hand.... On the other hand.... I would find out by ....”
    - Treat him as my patient “I would...”
    - Be yourself

- Try to be fluent
- Don't dig holes for yourself. If you don't know the details, say so, and say you would refer to the appropriate guidelines (you're not expected to know everything)
- Do headings well
- Stop saying "I would like to..."
- You will know more than the examiners – they will have more experience. Make up for this by putting in as much as you know.

### Cardiology

#### *Management of Hypertension*

- History: Chest pain, SOB, claudication, headaches, visual disturbance, family history, high BP during pregnancy
- Risk factors: ↑ weight, ↑ lipids, smoking, DM, inactivity, family history
- Evidence of 2ndary HTN: renal disease, changed appearance, muscle weakness, sweating, palpitations, tremour, erratic sleep, snoring, daytime somnolence, symptoms of hypo-hyper-thyroidism
- Workup:
  - Bloods: FBC (exclude ↑Hb)
  - Identify end organ damage: ECG, fundoscopy, Cr/24 hour urine
- Complications: end organ damage
  - Heart: IHD, LVH, CHF
  - Eyes: retinopathy
  - Renal impairment
  - CVA
  - PVD
- Management:
  - Education: risks and benefits of treatment
  - Set target: <140/90, <130/80 for DM, CRF
  - Non-pharmacologically: Modest but clinically significant differences from each of
    - Diet – low salt/fat, weight reduction (sustained weight loss → ↓BP)
    - Regular aerobic exercise
    - ↓alcohol
    - Stop smoking
  - Pharmacologically:
    - ACEI, β-blocker, Ca blocker, diuretics, α-blockers, ARB
    - Spironolactone: primary aldosteronism, CHF, ascites
    - ALLHAT trial: all classes reduce total and CV mortality – no benefit of ACEI over diuretics as first line
    - Cochrane 2007: evidence doesn't support β-blockers (atenolol most common in trials) as first line treatment for HTN – weak effect to ↓ stroke and no effect on CVD vs placebo
    - If GFR < 30 then loop better than a thiazide
    - SE of β-blocker: sexual dysfunction, ↑ lipids, small weight gain, ↑insulin resistance
    - SE of dihydropyridine CCB (eg felodipine): flushing, headaches (2<sup>nd</sup> to vasodilation), ankle swelling, constipation
    - The future: Aliskiren – oral renin inhibitor (AVOID trial → ↓proteinuria in T2DM), immunisation against angiotensin II
  - Ensure compliance
  - Monitor – 6 – 8 week adjustment
- If adding a second or third agent, or if young, consider secondary causes:
  - Exclude: white coat (no end organ damage), under treatment or poor compliance
  - Most common: Essential HTN
  - Commonly: Renal (parenchyma or vascular), OSA, hyper aldosteronism
  - Rarer:
    - Thyroid, acromegaly, Cushing's,
    - Drugs
    - Alcohol
    - Coarctation
    - Autoimmune: eg scleroderma, SLE
    - Pre-eclampsia
- Management of renal artery stenosis (proximal end of artery, cf fibromuscular dysplasia):
  - Diagnosis: angiography > CT > MRI > US > captopril renogram
  - No evidence that stenting or surgery better than medical management unless < 30 yrs, severe HTN or treatment resistant HTN

- Risk of renal artery thrombosis

### *Management of IHD*

- History: symptoms
- Assess risk factors: HTN, DM, cholesterol, smoking, FHx. Could also check HS-CRP and Coronary Calcium score but no proven change in management from use of these
- Differential:
  - Musculo-skeletal
  - Dissection
  - PE
  - Pericarditis
  - Pneumothorax
  - Esophageal spasm
- Workup:
  - Bloods: FBC (anaemia), Trop, BNP
  - Bloods for other risk factors if indicated: Uric acid, Ca,
  - Exercise tolerance test: did they reach target, interpretation of changes in BP, ST change, stage. Normal treadmill  $\Rightarrow$  medical = CABG. Anormal treadmill  $\Rightarrow$  surgery > medical
  - Imaging: echo, stress echo (more sensitive and specific than ETT), CT angio (needs slow SR, artifacts from stents and Ca)
  - Angiography
- Management:
  - Education: explain condition, GTN protocol, medications
  - Lifestyle: smoking, diet (dietician), exercise (2004 trial of stable single vessel disease: PCI worse than exercise)
  - Medications: aspirin, clopidogrel, b-blocker, statin (target LDL < 2.6), anti-anginals. Monitor for side-effects
  - Percutaneous intervention (BMS/DES, risks of restenosis/thrombosis)/CABG (LMS, 3VD, DM). COURAGE Trial (2008): medical management ~ PCI (NNT for benefit of angina was 17)
  - Cardiac rehab/education
  - Assess for depression
  - Driving
  - GP F/U: monitor symptoms, BP, DM, cholesterol....
- Complications:
  - CHF
  - Arrhythmia
  - Angina
  - Thrombus
  - Other CVS problems: PVD, CVA, RF

### *Management of Arrhythmia*

- Differential of bradycardia (chronotropic incompetence – failure to  $\uparrow$ rate with exercise):
  - Extrinsic: autonomic (eg carotid sinus hypersensitivity), drugs, hypothyroidism, OSA
  - Intrinsic: sick sinus, CAD, rheumatic, amyloid, radiation, Friedreich's Ataxia
- Review medications
- Options for investigation:
  - ECG
  - Bloods: TFTs, electrolytes, K, Mg
  - 24 hour Holter
  - Echo
- Pacemaker:
  - Risks: bleeding, infection, pneumothorax. Longer term pacemaker syndrome
  - Insertion workup: FBC, Coags, CXR
  - Follow up in pacemaker clinic
  - Dual chamber vs single chamber in the elderly with AV block. DAVID trial – no mortality difference, but modest  $\uparrow$  risk of dual chamber worth it due to  $\downarrow$ chronic AF and stroke

### *Management of AF*

- Risks: LA enlargement (MV disease in the young and middle aged), IHD, hyperthyroid, alcohol, post surgery or pneumonia, chronic pulmonary disease

- Investigations: include ETT or walk to assess response to exercise
- Treatment:
  - Rhythm control:
    - Amiodarone – best maintenance agent, no inotropic effect (can use in CHF), SE sun sensitivity, ocular toxicity, pulmonary fibrosis, abnormal LFTs, thyroid toxicity, ↑digoxin concentration, long Qt
    - Sotalol: fatigue, long Qt
    - Flecainide: best in an athlete, ↑mortality with LVF (CAST trial), SE dizziness, visual disturbance
  - Rate control: AFFIRM and RACE Trials – survival and embolic risk the same, including in EF < 35% (AF-CHF Trial 2008)
  - Next research step: test ablation (eg pulmonary vein – if the ectopic focus is there – risks permanent pacing) against rate control
  - Anticoagulation:
    - CHADS Score (age > 75). Warfarin if > 2. Reduces risk to < 1 %. Aspirin halves risk
    - Target 2 – 3. 3 – 3.9 close behind (European Atrial Fibrillation Trial Study Group)
- Recurrent Flutter: ablation (success > 90%) better than medical management

### *Management of Tachyarrhythmias*

- Differential:
  - Inappropriate sinus tachycardia: often after a viral illness. Settles over 3 – 12 months. Titrate βblockers
  - Multifocal atrial tachycardia – think pulmonary disease
  - AV Nodal re-entrant tachycardia – fast and slow pathways in the AV node
  - Associated with Accessory Pathways: WPW. Type A has RAD, Type B resembles LVH
  - VT:
    - non-sustained if < 30 secs
    - 2<sup>nd</sup> to ischaemia (↓ by βblockers), cardiomyopathy, arrhythmogenic RV dysplasia, HOCM. VT storm if active ischaemia or fulminant myocarditis
    - Suggestions of VT (cf SVT with aberrancy): concordance of QRS in all chest leads, large S in V6. Don't give adenosine. May → collapse
    - ICD + sotalol or amiodarone (better tolerated if poor EF). Don't die of SCD, just have severe failure
  - Long QT. QTc > 460 in men, 480 in women. PC Syncope or SCD following exercise
    - LQT1: most common, prolongs with exercise. Responds to β-blockers
    - LQT2: bifid T wave. Triggered by stress or auditory stimulation. Responds to β-blockers
    - LQT3: poor prognosis. Occurs in sleep. Not β-blockers (slows rate in sleep → ↑ risk)
    - Only cardiac condition where genetics recommended for risk stratification
    - ICD if: prior arrest, persistent syncope on beta-blockers (or CI), or QT > 550 without symptoms (esp LQT3 males)
    - Also β-blockers, avoid long QT drugs, avoid extremes of exercise
- NB half life of adenosine prolonged on dipyridamole

### *Management of Congenital Heart Disease*

- ASD: no problems due to ↑ RA till 3<sup>rd</sup> or 4<sup>th</sup> decade. Most common is Secundum (fossa ovalis). Large hole → no murmur (flow murmur in pulmonary area). Fixed splitting. RVH on ECG
- VSD
- Tetralogy: VSD, over-riding aorta, RVOT narrowing (eg pulmonary stenosis), RVH
- Patent Ductus
- Transposition of the great arteries: treated with arterial switch (→ RBBB, RVH, RAD)
- Eisenmenger's Syndrome:
  - Due to VSD, PDA, ASD
  - Measure pulmonary vascular resistance
  - PAH drugs typically don't help
  - Complications: arrhythmias, embolic events, bleeding (↓platelets), clotting (polycythaemia), haemoptasis
  - Treat: heart lung transplant
- Aortic coarction: associated with VSD, aneurysm of the circle of Willis (2<sup>nd</sup> to HTN). Rib notching on xray, radio-femoral delay

### *Management of Hypertrophic Cardiomyopathy*

- Background:
  - AD with variable penetrance
  - Genetically heterogeneous – screening for the 8 most common HCM causing genes has a pick up for 50 – 60%
  - Most common cause of SCD under age 35
  - Signs: jerky pulse, LV impulse, apical systolic murmur which ↑ with valsalva, ↓ with squatting
- Investigations:
  - ECG sensitive not specific
  - Echo: LV wall thickness > 13 mm (can be septal, apical...). Outflow tract obstruction in 25%. Always systolic dysfunction
- Risks of SCD: thickness > 30 mm, FHx of SCD, previous arrest/arrhythmia
- Prognosis: marked variability. Average annual mortality 1 – 3%, most after exercise
- Treatment:
  - Avoid competitive sports
  - ICD easily surpasses other preventative strategies (amiodarone, sotalol) for avoiding SCD
  - Symptom management controversial: CCB/β-blockers to improve diastolic filling
  - Surgery: septal myotomy if resting outflow gradient > 50 mmHg. Mortality 3%
  - Screen first degree relatives: every 2 – 5 years (?annually as a teenager)
  - Genetic counseling

### *Management of Heart Failure*

- Pathogenesis: Index event (may be on-going) → neurohormonal imbalance results to try and restore function → sustained activation → end-organ damage, worsening remodeling → change in LV mass, and shape (elliptical → spherical → worse pump function) → decompensation due to ↓BP, abnormal reflex control, peripheral vasoconstriction, Na retention, ↓organ blood flow
- History:
  - Past RF, MI, arthritis, chemo/rx, HTN treatment
  - SOB, SOBOE, orthopenoea, PND, foot swelling
  - Chest pain/palpitations
  - Fatigue, poor appetite
- Assess risk factors:
  - Depressed EF: IHD, chronic pressure overload (HTN, AS), chronic volume overload (regurgitation), arrhythmia, cardiomyopathy, drugs, radiation, malignancy. Impact of DM unclear
  - Preserved EF: stiffening of the ventricle → ↑pressure to fill it. Causes include: HTN, hypertrophic cardiomyopathies, aging, restrictive cardiomyopathy (infiltrative disorders, storage diseases)
  - 2<sup>nd</sup> to Pulmonary disease
  - High output states
- Exclude reversible causes: thyroid, arrhythmias, reversible ischaemia, anaemia, infection, OSA
- Exam: is he euvolaemia, dry, overloaded
- Review drugs
- Investigations: ECG, **BNP**, Echo (normal EDD is 5.5 cm)
- Assess severity: New York Heart Classification (very subjective but has stuck):
  - I: no symptoms with ordinary physical activity
  - II: Slight limitation of physical activity
  - III: Marked limitation of physical activity
  - IV: Discomfort with any physical activity, symptoms at rest
- Treat underlying diseases: haemochromatosis, ischaemia, HTN, valvular disease, alcohol, smoking
- Treat the failure:
  - Non drug: Low salt (2 – 3 gm/day, but no evidence), fluid restrict (1.5 L per day – but no evidence), exercise. No evidence of benefit from intentional weight loss
  - Pharmacological:
    - β-blocker > ACEI > spironolactone
    - β-blocker: proven in all cause class II – IV, only in post infarct class I. Only bisoprolol, carvedilol and metoprolol shown to ↓ mortality (not atenolol). Tolerated by > 85% (include patients with diabetes, COPD, PVD – only 50% of asthmatics). Diurese before titrating
    - ACEI if EF < 40% (overwhelming evidence) HOPE + PROGRESS Trial – trivial but positive benefit for normal EF

- +/- digoxin: no change in mortality but ↓hospitalization. Not more than 0.125 mg. Toxicity: confusion, anorexia, nausea, visual disturbance, arrhythmia. ↑Levels with antibiotics, amiodarone, diltiazem...
- Symptomatic: diuretics
- In absence of stroke or previous VTE, the value of anticoagulation is not well established (AHA guidelines). ?Treat large anterior MI for 3 months
- Statins only reduce acute coronary events – no difference to the CHF
- N-3 polyunsaturated fatty acids: modest additional benefit
- Device therapy: ICD (class II- III, EF < 30%, expectation of > 1 year survival, ARR of 5% at 5 years) +/- CRT (class III/IV, LVEF < 35%, LVEDD > 60, L conduction delay > 150 msec (mortality benefit not established)
- Multidisciplinary care (evidence from 90s, COACH Study 2008 – no difference from normal followup)
- Transplant: if VO2Max < 10
- Monitor: weight (daily weigh), U&Es, compliance, BP, medication SE
- Supportive:
  - Avoid precipitants: NSAIDs
  - Monitor for depression
  - Vaccinate for influenza
- Research issues: trials of CHF don't match the real world. Trials are typically of much younger people with limited comorbidity and optimal compliance

### *Endocarditis Prophylaxis*

- AHA guidelines (2007) for endocarditis prophylaxis:
  - Recommended for:
    - Prosthetic cardiac valve
    - Previous infective endocarditis
    - Congenital Heart Disease: unrepaired cyanotic CHD, repaired with prosthetic material (but only needed for 6 months), repaired with residual defects
  - Recommended when:
    - Dental procedures involving manipulation of gingival tissues or perforation of the oral mucosa
    - Procedures on the respiratory tracts or infected skin, skin structures or musculoskeletal tissues
    - Not now for genito-urinary or GI tract procedures (except oesophageal dilation)
  - Give: IV or oral amoxicillin 2g, alternative Cefaclor 2 g or clindamycin 600 mg
- NICE guidelines 2007 (controversial): no pre-dental prophylaxis at all – meticulous dental and skin hygiene more important. . Infective endocarditis is much more likely to result from frequent exposure to random bacteraemia than from dental procedures. Prophylaxis prevents an extremely small number of cases of IE (if any). Optimal oral hygiene is more important as it may reduce random bacteraemias

## **Gastrointestinal**

### *Prophylaxis for NSAID Induced Ulcers*

- Indicated in high risk: previous ulcer bleeding, age > 75, concurrent use of steroids, anticoagulants or aspirin
- Uncertain in average risk (1 – 2 % annual incidence of complications): ?H2 receptor antagonists or test and treat for H pylori (depending on pretest probability of H Pylori). PPIs not cost effective

### *Malabsorption*

- Stool fat test. Normal < 6 gm/day on low fat diet
- Differentials:
  - Diarrhoea:
    - Biliary tract disease
    - Cancer
    - Infection
    - Lactase deficiency: H2 breath test following lactase load (not commonly available)
    - Laxative abuse
    - Malabsorption, eg coeliac
    - Hyperthyroidism
    - IBD
    - IBS

- Whipple's: diarrhoea, steatorrhoea, abdo pain, large-joint arthropathy, fever. Tropheryma whipplei. Diagnosis biopsy of affected organ
- Constipation:
  - Drugs: antihypertensive, anticholinergic, antidepressant
  - Endocrine: hypothyroidism, hypoparathyroidism
  - Lead poisoning or porphyria if abdo pain

### *Celiac*

- Antibodies:
  - **IgA** anti-tissue-transglutaminase (tTG) – Highly sensitive, a bit less specific, easy test
  - AGA: Antigliadin antibodies:
  - IgG: 75% sensitive, 80% specific
  - IgA: 85% sensitive, 90% specific
  - EMA: **IgA** antiendomysial antibodies (90 – 95% sensitivity and specificity) – difficult test
  - But 3% of coeliacs have selective IgA deficiency → so test total IgA as well to check or use less reliable IgG tests
  - Will be negative after ~ 3 months on a gluten free diet
  - Absence of HLA-DQ2 (in 90 – 95%, but a very common genotype – 30%, few of them are coeliacs) and DQ8 (in ~ 5%) effectively excludes the diagnosis
- Management:
  - Dietician. Symptoms should start to improve in 2 weeks. Monitor ABs at 6 months (instead of re-biopsying)
  - Screen for folate and iron deficiency. Consider vitamin supplements
  - Bone density with Vit D and PTH if osteoporotic
  - Pneumococcal vaccine due to hyposplenism
  - Consider serology on first degree relatives

### *Inflammatory Bowel Disease*

- Polygenic with multiple subtypes. Loss of tolerance to normal flora
- Diagnosis:
  - No serology
  - Faecal calprotectin (correlates with relapses – highly sensitive)
  - Negative stool for C difficile, ova, parasites
- Severity in CD: initial need for steroids, young age (< 18), perianal disease, fever at diagnosis, weight loss > 5 kg at diagnosis
- Complications:
  - UC:
    - toxic megacolon in 5% attacks, perforation rare but 15% mortality
    - Strictures: need to exclude underlying malignancy
    - Cancer: 10% at 40 years, annual screening from 10 – 15 years
  - CD: weight loss, abscess, perforation, obstruction, fistulas (rectovaginal in 10% women), cancer with long duration (also ↑ risk of haematological malignancy)
- Extraintestinal manifestations:
  - Skin: erythema nodosum, pyoderma gangrenosum (also in MGUS, CML, CTD eg RA)
  - Arthritis: CD > UC
  - Eyes: conjunctivitis, uveitis
  - Fatty liver (chronic illness, malnutrition, steroids), gallstones, PSC
  - VTE
- Management:
  - Steroids don't prevent relapses (always taper)
  - CD:
    - Smoking cessation
    - Low risk: may consider sulfasalazine for mild ileocolonic disease (well controlled negative studies ⇒ stop if not helping. SE allergic reactions, headache, anorexia, nausea). For small intestine tapering steroids, if relapse AZA/methotrexate (3 – 6 months for effect). If relapse then anti-TNFα
    - High risk: Steroids + AXA. If response taper steroids. If no response anti-TNFα (fistulizing > stenosing). Response in 2/3rds, remission in 1/3. Etanercept doesn't work – only infliximab and adalimumab
    - Metronidazole (in CD only) – week 8 remission 38% vs 33%

- UC:
  - Titrate oral and rectal sulfasalazine. Tapering steroids (if needed more than twice a year then ?AZA). If a severe flare then IV hydrocortisone + heparin → surgery or salvage cyclosporin if no response (Tacrolimus increasingly used). Infliximab effective in preventing surgery
  - Pouchitis: in 50%, mainly in first 12 months. Ciprofloxacin, methotrexate and probiotics show efficacy. ↓fertility in females
- Management of complications:
  - Iritis: ophthalmology involvement
  - Bones: malabsorption and steroids
  - Need surveillance colonoscopy as from ~10 years, as per British Gastroenterology Society Guidelines...
  - IHD: ↑risk from inflammation, steroids, etc. Manage cardiovascular risk factors
- Pregnancy:
  - Issues: fallopian tubes scarred, in CD. Sulfasalazine → reversible ↓infertility in men
  - Disease control more important than drugs
  - Consider caesar to avoid peri-vaginal tear → fistula track
  - Management:
    - Folate supplements
    - Sulfasalazine, steroids and AZA safe. Case series only with infliximab
    - Cyclosporin: avoid unless needed to avoid surgery
    - Not methotrexate

### *Liver History*

- Constitutional symptoms: fatigue, weakness, nausea, anorexia, malaise
- Liver specific symptoms:
  - Jaundice, dark urine, light stools, steatorrhea, itching, abdo pain, bloating
  - Jaundice without dark urine → indirect/unconjugated hyperbilirubinaemia (eg haemolytic anaemia)
- Complications of cirrhosis and end stage disease: bruising, haematemesis, encephalopathy (≈ fulminant liver failure)
- Risk factors:
  - Alcohol, medications (including OCP and OTC), sexual activity, travel, exposure to high risk or jaundiced people, IVDU, recent surgery, past blood transfusion, tattoos, needlestick exposure, family history of liver disease
  - Hepatitis risk factors:
    - Sexual transmission common with Hep B, rare with Hep C
    - Vertical transmission:
      - Hep C uncommon, no reliable means of prevention. More common in HIV co-infected mothers
      - Hep B common and prevented by passive and active immunisation at birth
    - Hep C:
      - IVDU the most common risk factor
      - Blood transfusions before 1992
    - Hep B: transfused blood started to be tested for anti-HBc in 1986
    - Hep E: more common in Asia, Africa
    - Tattooing and body piercing: transmission of Hep B and C very rare
    - Hep A: travel important, selfish transmission very rare

### *Alcohol History*

- Current and past ETOH use:

Standard Units per day	Low	Hazardous	Harmful
Male	< 4	5 - 6	> 6
Female	< 2	3 - 4	> 4

- Screen for dependence CAGE (1 yes = needs further assessment, 2 yes has sensitivity of 85% and specificity of 90% for alcohol abuse/dependence):
  - Ever tried to Cut down
  - Do you get annoyed by criticism of your drinking
  - Do you feel guilty about your drinking

- Do you ever have an eye opener
- Questions about alcohol abuse:
  - Failure to fulfill work or social obligations
  - Recurrent use in hazardous situations
  - Legal problems
  - Continued use despite alcohol related social or interpersonal problems
- Features of dependence:
  - Tolerance
  - Withdrawal – details of previous withdrawal episodes – ever had a seizure?
  - Taken in larger quantity than intended
  - Persistent desire to cut down
  - Time spent obtaining, using or recovering from alcohol use
  - Social, occupational or recreational tasks are sacrificed (“primacy” of alcohol)
- Patterns of drinking:
  - Stereotypical drinking: solitary
  - Lifetime history: what caused significant increases
  - Diet: are they malnourished, missing meals
- Comorbidities affecting treatment: physical, social, emotional problems
- Family history of alcohol use
- Finances
- History of complications: gastritis, CNS (poor sleep, blackouts, peripheral neuropathy, depression, anxiety), liver, blood, CVS
- Examination:
  - Poor hygiene
  - Malnutrition
  - Bruising
  - Parotiditis
  - Dupuytren’s
  - Cognitive impairment
  - Signs of liver disease
  - AF
  - CHF
  - Cerebellar signs
  - Peripheral neuropathy
- Labs: GGT > 35 and *carbohydrate-deficient transferrin* (CDT) > 20 both have 70% sensitivity and specificity for heavy alcohol consumption. Also ↑MCV, uric acid, ↓platelets, ↑TGs, AST > ALT. If persisting raised transaminases after 3 months abstinence, and other liver causes excluded than biopsy
- Identify treatment goals:
  - Control drinking if harm not severe:
    - Use non-alcoholic drinks to quench thirst
    - Use spacers: non-alcoholic drinks between alcoholic ones
    - Low alcohol drinks
    - Eat before drinking
    - Count your drinks – keep within the guidelines
    - Have at least 2 alcohol free days per week
    - Don’t drink to cope with stress – try exercise
  - Abstinence if dependent, organ damage, or controlled drinking has failed
- Treatment of alcohol dependence:
  - Predictors of success: high levels of life stability and higher levels of functioning
  - Withdrawal: if mild/moderate, do it at home with support, if severe (or significant comorbidities eg liver disease) then inpatient
  - Brief intervention to increased motivation, including advice to reduce, strategies, empathy (effective in RCTs)
  - Referral for counseling or addiction service
  - Supports, eg AA
  - Pharmacotherapy:
    - Naltrexone: opiate receptor agonist, once daily, start after abstinence. ↑Number of days of abstinence. Not if LFTs > 5 times normal. Additive benefit to psychological intervention demonstrated. SE nausea, headache, dizziness, dysphoria, depression, ↑LFTs

- Acamprosate: GABA agonist, ↓craving. Commence when abstinent, continue for 1 year, rare diarrhoea. Additive benefit to naltrexone suggested in trials
- Disulfiram: ALDH inhibitor. Not if CVD, CVA, DM or HTN. Useful for high risk periods with observed treatment (eg spouse)
- Treatment of alcohol related liver disease:
  - Fatty liver: reversible with cessation
  - Alcoholic hepatitis: tender hepatomegaly, fever, jaundice. Modestly ↑ AST > ALT. Workup: cultures of blood, urine, ascites, IV thiamine and vitamin K, IV cef and met. Treatment: If severe (↑INR, ↓Hb, alb < 25, bilirubin > 137, renal failure) then prednisone for 4 weeks then taper

### *Liver Disease Workup*

- Bloods:
  - Liver inflammation: LFTs, bilirubin (any urine bilirubin will be conjugated/direct ⇒ liver disease. If unconjugated → ?haemolysis, rises later than GGT and ALP, important discriminator of mortality). Isolated ↑ GGT in alcohol, fatty liver, medication (AEDs)
  - Biosynthetic function: albumin, INR, globulins (↑IgG in autoimmune hepatitis, ↑IgM in PBC, ↑IgA in alcoholic disease)
  - Anaemia: ↓folate, hypersplenism, direct toxicity (alcohol), GI blood loss
- Imaging: US if stones. US and CT equally sensitive for detecting duct dilation and fatty liver. US and MRI for vasculature and haemodynamics
- Biopsy:
  - Commonly done for Hep B (if not severe may not start treatment), not for Hep C
  - Value is knowing stage (degree of fibrosis) so you know whether to start cirrhosis management (eg HCC screening)
- Scores:
  - Child-Pugh-Turcotte: bilirubin, albumin, INR, ascites, encephalopathy. Grades A, B, C give 1 year mortality of 29, 38 and 88%
  - MELD: INR, bilirubin, creatinine: accurately predicts short term survival (used in US for liver transplant listing)

### *Hepatitis*

- Hepatitis B:
  - Transmission: 95% risk of vertical transmission, nil from breast feeding
  - Mutations: normal virus is wild type, pre-core mutant doesn't produce e-antigen, YMDD due to resistance to nucleoside analogues
  - Presentation: incubation 45 – 180 days.
  - Treatment:
    - Acute: supportive only. Treatment unlikely to improve rate of recovery
    - Chronic (usually neonatal/infant transmission with immune tolerance):
      - Chronic active hepatitis in 20% → cirrhosis
      - Complications: HCC in 5<sup>th</sup> decade, GN (mesangiocapillary or membranous), mixed cryoglobulinaemia
      - Aim of treatment: Viral suppression, seroconversion (not in pre-core mutants)
      - Options: Nucleoside analogues (lamivudine, adefovir - nucleotide, entecavir, no proven initial combination therapy) or PEG IFNα 2a or 2b (especially young women who won't want antivirals in future pregnancy if fail to seroconvert, not if cirrhosis)
- Hepatitis C:
  - Transmission: 90% by IVDU, sexual contact (high risk 5% per year, monogamous 1.2% per year), 5% maternal transmission
  - Diagnosis: Anti-HCV doesn't appear for 3 months. HCV RNA detectable within 1 – 3 weeks
  - Progression: > 75% progress to chronic infection (higher than Hep B). Cirrhosis in 20% of these
  - Treatment: Want drug free urines in IVDU. Cure in 50%. Genotype 2 & 3 better. IFNα + Ribavirin (ribavirin ↓ virologic relapse, SE: teratogenic, dose dependent haemolysis, not in renal insufficiency, pruritis, gout)
  - Screening: HCC, not αFP
  - Transplant: 65% 5 year survival

### *Autoimmune Liver Disease*

- Autoimmune Hepatitis:
  - Presentation: females, age 40 – 50 with fatigue and ↑ LFTs, limited progression to cirrhosis

- Diagnosis:
  - ↑IgG, ↑aminotransferase (maybe in 1000s, but doesn't correlate with histological severity)
  - Type 1: ↑ANA and smooth muscle antibodies
  - Type 2: Anti-LKM1 (Liver Kidney microsomal)
- Treatment: Prednisone tapering over 12 – 18 months, maybe with AZA as steroid sparing (but not on it's own). Only evidence in is severe disease
- Primary Biliary Cirrhosis (intrahepatic):
  - Presentation: females age 50 with pruritis and fatigue, with xanthelasma
  - Associations: 75% have Sjogren's, 25% have serology of thyroid disease
  - Antimitochondrial ABs, M2 variant specific, ↑ IgM. Not biopsy – patchy disease
  - Treatment:
    - Ursodeoxycholic acid, cholestyramine, or rifampicin for pruritis
    - Bile salt reduction with the above may also reduce hepatocyte damage
    - Steroids, Calcineurin inhibitors, anti-metabolites are used with some success
    - Liver Transplant
  - ↑Cardiovascular risk
- Primary Sclerosing Cholangitis (large bile ducts):
  - Presentation: patient with UC with cholestatic LFTs and pruritis
  - No diagnostic serology (although pANCA often positive). ERCP
  - Treatment: None proven. Steroids, MTX, cyclosporin not effective. UDCA helps itch but not survival
  - Prognosis: cholangiocarcinoma in 10%, ↑pancreatic and colon (if colitis) cancer
  - Transplant: if 2 or more episodes or end stage disease

### *Cirrhosis*

- Assessment of disease and stage. Cirrhosis should be classified (Knodell-Ishak Score) based on:
  - Cause
  - Grade – Necrosis, Portal Inflammation
  - Stage – Fibrosis
- Treat underlying cause,
  - Hepatitis
  - alcohol rehab
  - Fe/ autoimmune
  - NAFLD: weight loss (most evidence in bariatric patients) and exercise, some benefit from metformin
- Management of complications:
  - Nutrition + salt restriction
  - Varices:
    - Scope. If found then propranolol: aim for 25% ↓ in HR, or rate of 60 – 70, whichever is higher. Lower risk of bleed, impact on mortality less clear cut)
    - Acute bleed: Blood and FFP are transfusion priorities, try to avoid lots of crystalloid. Terlipressin or Octreotide. Culture blood, urine and ascites. Ciprofloxacin. If alcoholic then Vitamin K + thiamine
    - Prevention of rebleed: banding + propranolol
  - Ascites: sodium restrict, fluid restrict if dilutional hyponatraemia, target weight, titrate diuretics (frusemide, spironolactone). Large volume paracentesis + diuretics better than diuretics alone. If taking more than 5 litres need plasma expander (?albumin the best)
  - Encephalopathy: treat reversible factors - avoid constipation (lactulose). Aim 3 motions per day
  - Oedema
  - Hepatorenal syndrome: ?2<sup>nd</sup> to severe renal vasoconstriction → hypoperfusion → urinary sodium < 10. Stop diuretics, noradrenaline infusion... (no RCTs)
  - Vaccinate for Hep B and C, influenza and pneumococcal
  - Screening for HCC – controversial. US 6 to 12 months (3 month doubling time). No consensus on αFP
- Transplant: list if CPT stage C. 3 year 80% survival. Matched for ABO blood group and organ size (not HLA). Immunosuppress with Prednisone, Tacrolimus (more potent, ↓rejection, more predictable oral absorption, but more toxic: neuro and nephrotoxicity, HTN, weight gain, T2DM, ↑ risk lymphoproliferative disease), MMF. Valganciclovir for 6 – 12 weeks if CMV D+, cotrimoxazole until prednisone < 10 mg for PCP, lamivudine long term for Hep B
- Measures to prevent transmission

## Rheumatology

### Rheumatoid Arthritis

- High clinical suspicion if:
  - $\geq 3$  tender or swollen joints
  - MCP or MTP squeeze test positive (sensitive for MRI proven synovitis not otherwise clinically evident)
  - Morning stiffness  $> 30$  minutes
- Diagnosis: American College of Rheumatology Guidelines (1987): 4 or more of 7 criteria:
  - Morning Stiffness:  $> 1$  hour before maximal improvement
  - Arthritis of 3 or more of 14 joint areas observed simultaneously: Left or Right PIPs, MCPs, MTPs, wrist, elbow, knee, ankle
  - Arthritis of hand joints: wrist, MCP or PIPs
  - Symmetric arthritis: involvement of the same joints on both sides of the body
  - Rheumatoid nodules
  - Positive RF (ie *don't* have to be RF positive)
  - Radiographic changes typical of RA on posterior hand and wrist films
- Poor prognosis in RA
  - Systemic features
  - RF +ve
  - Nodules
  - Insidious onset
  - Bony erosions
  - Activity of disease  $> 12/12$
- History. Include:
  - Extra-articular manifestations: skin, lungs, eyes, nervous system, blood, renal
  - Medical management and complications
  - Surgery
  - Current function
  - Signs of current disease activity (morning stiffness, number of tender/inflamed joints, ESR, constitutional symptoms)
- Complications:
  - Atlanto-axial instability
  - CVD: premature
  - Infection
  - GI bleeding
  - Prednisone complications
- Education
- Allied health:
  - PT: exercise and splinting of joints to prevent deformity
  - OT: orthotic and assist devices
- Treatment:
  - Drugs: Start early (Tight Control for RA study – TICORA):
    - Prednisone almost always helpful. Pred pulses for flares
    - Less aggressive: methotrexate monotherapy – maximal effect by 6 months, effective in 75%
    - Early aggressive disease if risks for progressive disease (RF/anti-CCP, multiple joints, ESR/CRP, erosions, persistent synovitis):
      - Triple therapy (methotrexate with two of Leflunomide, sulphasalazine, prednisone, AZA, gold, hydroxychloroquine [monitor eyes])
      - AZA: level of 6-GTN corresponds to clinical response. 6-MMPR  $\rightarrow$  hepatotoxicity. Homozygotes for in active TPMT (phase 2 metabolism)  $\rightarrow$  severe pancytopenia. Avoid allopurinol  $\rightarrow$  inhibits metabolism
      - Early biologics
  - Analgesia: NSAIDs. PPI as precaution to DU
  - Biologics:
    - Anti-TNF:
      - Infliximab and Adalimumab (monoclonal Ab against TNF)

- Etanercept (fusion protein that is antagonist of TNF receptor)
- 60% response, rapid onset 1 – 2 weeks, halves structural progression of methotrexate – clear benefit as initial treatment
- Also CTLA-Ig, IL-6, IL-1,
- Pregnancy: hydroxychloroquine, AZA, prednisone (but gestational DM), Salazopyrin (?↓fertility), intra-articular steroids
- Surgery: hips, knees, shoulders (↓pain and ↓disability)
- Monitor: FBC, LFT, urine for proteinuria (Drugs, Amyloid)
- Prevention:
  - CVD risk factor modification
  - Bone protection
- Precaution before GA or endoscopy: C-spine XR to rule out atlanto-axial subluxation

### *Spondyloarthropathies*

- Have in common:
  - Inflammatory back pain: Defined by at least two of the following:
    - Morning stiffness > 30 minutes
    - Improvement with exercise not by rest
    - Awakening with pain only in the 2<sup>nd</sup> half of the night
    - Alternating buttock pain
  - Involvement of spine and sacroiliac joints (= axial arthritis): *Radiologic progression is very slow* (ie don't xray any more frequently than every 2 years)
  - Usually asymmetrical large joint mono or oligo-arthritis:
    - 4 or fewer inflamed joints
    - Asymmetric
    - Disease activity assessed by number of tender/swollen joints and ESR, CRP
  - Inflammation then calcification of tendon insertions (enthesopathy)
  - Dactylitis: Diffuse fusiform swelling of a toe or finger due to inflammation of the flexor tendon sheath. Most common in psoriatic arthritis and reactive arthritis (also in sarcoidosis and gout)
  - Extra-articular manifestations:
    - Uveitis: unilateral, acute, eye pain, photophobia, blurring of vision with redness at the scleral-corneal junction
    - Skin: psoriasiform lesion: keratoderma blenorrhagica, circinate balanitis
    - Enteric mucosal lesions: up to 60% have a colonic lesion, only 10% have clinical disease
    - Aortic regurgitation (rare – due to aortic valve fibrosis)
    - Upper zone pulmonary fibrosis
  - Familial tendency: HLA-B27 +ive predisposition (8% in the general Caucasian population)

### *Ankylosing Spondylitis*

- Risk: insidious ↓ in spinal mobility
- Most common pattern: persisting symptoms with superimposed flares. Average diagnostic delay 5 – 8 years
- Modified New York Criteria for Definite AS (eg used for original TNF studies):
  - Radiographic findings of bilateral sacroiliitis  $\geq$  grade 2, or unilateral  $\geq$  grade 3, and at least one of
  - Inflammatory back pain
  - Reduced spinal mobility in 2 planes
  - Reduced chest expansion
- Other complications:
  - Half AS patients have a T score < -1.0
  - Amyloid
- Markers of severity: juvenile onset, poor response to NSAIDs, dactylitis, oligoarthritis, smoking, hip arthritis
- Bloods: fewer than half have ↑ESR/CRP
- Assess current state (Bath Ankylosing Spondylitis Activity Index)
- Physiotherapy: exercises to maintain spinal mobility, esp hyper-extension of the spine
- Medical treatment:
  - Exercise & physio
  - NSAIDs: Indomethacin. Regular better than symptomatic. Little or no disease modifying effect
  - Intra-articular steroids
  - DMARD

- Sulfasalazine/Methotrexate (for peripheral disease)
- Anti TNF(for **axial** disease) – good morbidity response, long term safety and cost effectiveness data lacking
- Wedge osteotomy for severe disease
- **Genetics:** HLA B27 +ve pts' siblings have 30% chance of developing
- Prognosis:
  - 40% severe spinal restriction
  - 20% significant disability
  - Peripheral joint involvement (particularly hip) = worse prognosis
- Driving with bamboo spine
  - Increased whiplash injury
  - Restricted lateral vision
- Differentials:
  - RA: but spine rarely affects, and small joints rarely affected in AS
  - Osteitis Condensans Iliis: bilateral sclerosis of the lower SIJ in multiparous women
  - Diffuse Idiopathic skeletal hyperostosis: Calcification and ossification of the anterior longitudinal ligament – older males, 20% with T2DM

### *Gout*

- Distribution: MTP of big toe in 75%, ankles and knees after recurrent attacks, fingers, wrists and elbows late
- Tophi: urate deposits with inflammatory cells in avascular areas: pinna, infra-patella and Achilles tendons, joints, eyes
- Differential: septic arthritis, other crystal arthropathies, palindromic RA, psoriatic arthritis
- Causes:
  - ↓ renal excretion: primary gout, renal failure, HTN, DM, hypothyroidism, drugs (frusemide, thiazides)
  - ↑ cell turnover: lymphoma, leukaemia, haemolysis, disorders of purine synthesis
- Complications: urate nephropathy
- Assessment: aspiration – do it – the only definitive diagnosis and may be on pills for life
- Treatment:
  - Stop thiazides
  - Acute: NSAIDs, Colchicine (max bd) and Steroids. Also IA Steroids
  - Long term Tx if recurrent attacks or tophi, or chronic arthritis or renal disease
    - Life style modifications-Weight loss, low alcohol and reduced food with high purine content
    - Allopurinol max 900 mg with colchicine or NSAIDs cover while starting it. Treat to target (will ↓flares, ↓tophi, ↓intra-articular crystals). Check uric acid monthly till target reached. SE rash in 2% (stop quickly given TEN in 0.1%). If rash only can do allopurinol desensitisation over 15 – 18 days, effective in 80%
    - Uricosuric therapy if urinary excretion of uric acid is less than 1g/day – probenecid (if Cr < 200)

### *Psoriatic Arthritis*

- NSAIDs for pain (may worsen skin lesions)
- Steroid injects for local synovitis
- Not prednisone – can get rebound psoriasis rash
- DMARDs: much less data, methotrexate, leflunomide and sulphasalazine
- All 3 TNF $\alpha$  inhibitors: prompt improvement and delayed progression

### *Osteoarthritis*

- Patient education and support
- Weight reduction
- Physical therapy: exercise programme, range of motion exercises, walking aid
- Analgesia: paracetamol, NSAIDs
- Joint treatment: steroid injection – but no more than 3 – 4 per year
- Consider surgery: arthroscopic, joint replacement, arthrodesis

### *Systemic Lupus Erythematosus*

- Pathology: immune dysregulation, activation of innate immunity, ↓activation threshold for adaptive immunity cells, abnormal clearance of apoptotic cells due to ineffective phagocytosis → nuclear

antigens persist. Homozygotes for ↓Ca, C2, and C4 (rare) → SLE ⇒ low complement important in sustaining SLE

- Diagnostic criteria – American College of Rheumatology: 4 of the following 11 simultaneously or serially:
  - Skin features (note each is a criteria on its own):
    - Malar rash: erythema tending to spare the nasolabial folds
    - Discoid rash: erythematous raised patches with keratotic scaling, atrophic scarring in older lesions
    - Photosensitivity: skin rash in response to sun light
    - Oral or nasopharyngeal ulcers: usually *painless*, observed by a physician. If painful think Behcet's
  - Arthritis: *non-erosive* arthritis of 2 or more peripheral joints with swelling or effusion. I.e differential of symmetrical polyarthritis
  - Serositis: pleuritis or pericarditis
  - Renal disorder: persistent proteinuria > 0.5 gm/day or cellular casts
  - Neurologic disorder: Seizures or psychosis
  - Haematologic disorder (one criteria even if you have them all): haemolytic anaemia, leukopenia (< 4 on 2 occasions) or lymphopenia (< 1.5 on 2 occasions) or thrombocytopenia (< 100) in the absence of offending drugs
  - Immunologic disorders: Positive antiphospholipid antibody, Anti-DNA, Anti-Sm, or false positive VDRL (confirmed by Treponema pallidum immobilisation or fluorescent treponemal antibody absorption test)
  - Antinuclear antibody in the absence of drugs causing drug lupus
- Lupus nephritis: asymptomatic – monitor urine and Cr. Proliferative glomerular damage → haematuria and proteinuria, nephrotic syndrome and HTN. Only biopsy if expecting class 4 (diffuse proliferative) – benefit of immunosuppression established for this.
- Investigations:
  - FBC – anaemic, C3, C4
  - ESR > 20, CPR often low
  - Antibodies: ANA -ive, dsDNA +ive in 40 – 60%, anti Sm, VDRL false positive in 30%
  - Cerebral lupus: CSF for raised CSF to serum Ig. Oligoclonal bands. MRI sensitive
- Treatment:
  - Conservative: sun blocks, analgesia, hydroxychloroquine for skin and joints, RCT showing ↓ flares. Annual eye check. NSAIDs: but care of kidneys. Supervised exercise. Bone and CHD protection.
  - Flares: prednisone pulses effective within 24 hours. No improvement in renal function
  - Proliferative nephritis: Cyclophosphamide established (bladder cancer). MMF unless significant renal failure (not demonstrated there). Rituximab – case series in CNS disease. *Anti-TNF not effective* in case series (associated with ↑ANA and drug lupus)
- Pregnancy: fertility rates normal. Hydroxychloroquine safe. Higher fetal loss if flare, antiphospholipid antibodies or nephritis

### *Management of Antiphospholipid Syndrome*

- Diagnosis requires (Sapporo Criteria):
  - Arterial or venous clotting and/or repeated fetal loss (3 losses at < 10 weeks or 1 > 10 weeks or preeclampsia < 34 weeks) and/or thrombocytopenia
  - 2 positive tests for aPL 12 weeks apart: IgG anticardiolipin (more sensitive) and lupus anticoagulant (more specific). May also be positive for β<sub>2</sub>-glycoprotein I antibodies (strongly associated with thrombosis, but not formally in diagnostic criteria)
- Treatment:
  - Heparin in pregnancy
  - Plasma exchange, steroids, immunoglobulin used in treatment. Not cyclophosphamide
  - Long term anticoagulation indicated after a thrombotic event (less clear if no prior clot):
    - INR 2 – 3 if one episode of venous clotting
    - INR 3.0 – 3.5 if recurring clots or arterial clotting, especially in the CNS

### *Management of Sjogren's Syndrome*

- Dry mouth, eyes and maybe other exocrine glands. Raynaud's. Secondary Sjogren's with RA, scleroderma, polymyositis, graft vs host, AIDs
- Extra glandular manifestations: arthritis, hypothyroidism, peripheral neuropathy, pulmonary fibrosis, interstitial nephritis, vasculitis

- Investigations:
  - Schirmer test: < 10 mm of filter paper under the lower eye lid is wet after 5 minutes
  - Slit-lamp examination of the cornea with rose Bengal staining → punctuate ulcerations
  - Lacrimal gland biopsy – or small piece of oral mucosa on inside of lip – contains salivary glands
  - ↑ESR & CRP. May have normal CRP (can get this in most CTDs, but not RA)
  - 100% have RF
  - ANA positive in 60 – 70%
  - Anti-Ro (SSA) and Anti-La (SSB) present in 70% of primary, and 10% of secondary. Associated with worse prognosis. NB Ro and La antibodies cross the placenta causing congenital heart block
- Treatment:
  - Symptomatic relief: Artificial tears and saliva
  - Avoid drugs that reduce secretions: diuretics, antihypertensives, anticholinergics and antidepressants
  - Hydroxychloroquine (good for arthralgia and lymphadenopathy)
  - Visceral involvement: More problems with steroids (periodontal disease/candidiasis). AZA, MTX, ?MMF
- Differentials:
  - Hep C (can look like SS except for serological tests), head/neck radiotherapy, sarcoidosis, graft vs host disease, HIV, Human T-lymphotropic virus type 1 (HTLV-1)
  - Bilateral parotid gland enlargement:
    - Viral infection: mumps, influenza, Epstein-Barr, Coxsackie, CMV, HIV
    - Sarcoidosis
    - Amyloidosis
    - Endocrine: acromegaly, gonadal hypofunction
    - Metabolic: DM, chronic pancreatitis, hepatic cirrhosis
    - Alcohol
- Complications: malignant lymphoma (~ 6%). Most are extra-nodal, low-grade marginal zone B cell lymphomas

### *Management of Systemic Sclerosis and Scleroderma*

- “Always” Raynaud’s → sclerodactyly (not dactylitis – that’s psoriasis)
- Diffuse/Systemic Sclerosis:
  - Widespread skin + early visceral involvement → kidney, proximal myopathy, lung and GI fibrosis.
  - Renal crisis: abrupt onset of marked HTN. Obliteration of renal cortical arteries → aggressive ACEI
- Limited: hands, face and neck, digital pitting scars (probably initial presentation of CREST). Anti-centromere +ive
- CREST (probably very different to diffuse): calcinosis, Raynaud’s, oesophageal dysmotility (give PPI), sclerodactyly, telangiectasia. Scl-70 (Topoisomerase-1) positive
- Pulmonary disease:
  - HRCT and PFPs
  - Interstitial disease: cyclophosphamide → ↑survival (modest benefit but nothing else works)
  - Pulmonary HTN: ↓DLco but no change in FVC. Monitor with 6 minute walk. Treatment trial as for PHTN: bosentan, Sildenafil

### *Polymyositis, Dermatomyositis, Inclusion Body Myositis*

- Voluntary muscle inflammation → insidious proximal muscle weakness, only rare facial involvement, never eye muscles, dysphagia
- IBM most common, usually diagnoses as PM until patient doesn’t respond to treatment
- Differential:
  - Muscular dystrophy
  - Endocrine: thyroid, ↑Ca, ↓K,
  - Neurological: MND, GBS, MG
  - Drugs
- Investigations: ↑ESR, ↑CRP, ↑CK, ANA, RF, EMG, biopsy
- Treatment: tapering steroids, immunosuppression (never tried in RCTs), IVIg or plasmapheresis 3<sup>rd</sup> line but rapid improvement

### *Vasculitis*

Vessels	Signs/Symptoms	Investigations	Treatment
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Giant Cell	Extracranial and carotid branches	Jaw claudication, visual loss	ESR, biopsy showing granuloma, giant cells	Pred
Takayasu's	Aorta and large branches (esp subclavian)	Arm claudication, HTN (renal artery stenosis)	ESR, angiography showing stenosis	Pred +/- MTX
PAN	Medium (not small)	Renal artery stenosis, neuropathy, abdo pain. Not lungs	ESR, beaded pattern on angiography, necrotizing vasculitis without granuloma, no GN. 30% Hep B	CycloP + Pred
Wegner's	Small	Upper & lower Resp tract. Renal	cANCA, granulomatous, pauci-immune focal segmental GN	CycloP + Pred. AZA maintenance, MTX if intolerant
Microscopic polyangiitis	Small	Renal, haemoptysis, neuropathy (like Wegner's but no URT or pulmonary nodules)	pANCA, necrotising vasculitis without granuloma, pauci immune	CycloP + Pred. AZA maintenance, MTX if intolerant
Churg-Strauss	Small	Asthma, rhinitis, neuropathy	ANCA 50%, marked eosinophilia	Pred
HSP	Small	Purpura, arthritis, abdo pain, renal	Skin biopsy: IgA deposition	Pred for GI/arthritis symptoms only
Cryoglobulinaemia	Small	Purpura, arthritis, neuropathy	Cryoglobulins, Hep C, Myeloma. Biopsy: immune complexes. Renal: membranoproliferative	Underlying disease
Leukocytoclastic Vasculitis/Hypersensitivity Angiitis	Small	Purpura, necrotic papules, ulcers, urticaria	Skin Biopsy. Drugs, SLE, Hep B related	NSAIDS, antihistamine, dapsone, colchicine, thalidomide
Behcet's	Large-small	Oral + genital ulcers, eyes, acquired blindness	Pathergy test (sterile pustules at phlebotomy sites in some)	NSAIDS, antihistamine, dapsone, colchicine, thalidomide

### Amyloid

- Fat is 80% sensitive and easy to FNA
- Types:
  - AL (light chain) from clonal B cell marrow disorder. Nephrotic range proteinuria, cardiac involvement, peripheral sensory neuropathy, macroglossia. Treat as for myeloma: Cyclic oral melphalan + pred or dex.
  - AA (secondary amyloidosis): serum amyloid A protein in chronic inflammatory illness. Eprodisate beneficial in RCT.
  - Aβ2M: if on dialysis for years
  -

## Respiratory

### Management of Asthma

- History. Include:
  - Family history
  - Symptoms, including night symptoms
  - Triggers, incl exercise, allergens, infection, *occupational*, emotional
  - Occupational asthma – caused by work agents, work-related asthma – worsened by work – takes time to be sensitised

- Smoking
- Medications
- Hospital/ICU admissions
- PEFr
- Do they have an action plan
- What is their follow-up
- Impact on function
- Differential: reversibility with  $\beta$ -agonists most specific, can also test NO ( $> 50$  and  $< 25$  ppb identify patients who do, and do not, need long term steroids)
  - COPD: less variability of symptoms, less response to  $\beta$ -agonists
  - LVF
  - Infection: mycoplasma, chlamydia
  - Reflux
  - Eosinophilic pneumonias ( $\uparrow$ eosinophils, no airways hyperresponsiveness, try Aspergillus precipitins) and systemic vasculitis (eg Churg Straus)
  - Conversion disorder
  - Airway obstruction: tumour, laryngeal oedema
  - Hyper/hypothyroidism can worsen asthma
- Management: Evidence doesn't translate into practice – significant tolerated limitation in ADLs. Often rely on  $\beta$ -agonists (as they work) – so combine with something that prevents (eg steroid)
  - Education
  - Assess severity: symptom diary
  - Avoid triggers
  - Action plan: Level 1 evidence  $\rightarrow$  fewer days off work,  $\downarrow$ ED attendances
  - Medication:
    - ICS. SE hoarseness, oral candidiasis
    - LABA
    - Anticholinergics: slower onset, small incremental benefit, little systemic absorption ( $\rightarrow$  dry mouth, urinary retention)
    - Theophylline: Inhibits phosphodiesterases. Narrow TI. SE nausea, headaches, palpitations
    - Antileukotrienes: montelukast. Modest incremental benefit
    - Anti-IgE (Omalizumab). If  $\uparrow$ IgE and skin prick positive to aeroallergens.  $\downarrow$ exacerbation and  $\downarrow$ steroids in severe asthma. Expensive
  - Regular review

### *Management of COPD*

- Differential:
  - Smoking related
  - $\alpha$ 1AT deficiency (ZZ or Z-null). Diagnosed by  $\downarrow$  serum  $\alpha$ 1AT then genotype. Treatment supportive. Liver transplant curative
  - Asthma: if  $> 400$  ml response to bronchodilators, or to 2/52 of 40 mg prednisone, or significant symptom variability
- Assessment:
  - 6 minute walk
  - LFTs: FEV1  $< 80\%$  predicted, FEV1/FVC  $< 0.7$ ,  $\downarrow$ DLCo. FEV1 Mild  $< 80$ , moderate  $< 50$ , severe  $< 30\%$ . Correlates poorly with SOB/exercise capacity
  - CT doesn't change management unless consider differential or assessment for surgery
  - If acute, pH on ABG
- Treatment:
  - Only evidence in terms of mortality for smoking cessation, O2 therapy and LVRS in selected patients
  - **Pulmonary rehab**: demonstrated  $\downarrow$ morbidity
  - Vaccinate
  - Nutrition
  - Inhalers:  $\beta$ -agonists (incl LABA) + anticholinergic agents  $\rightarrow$  add in ICS (no benefit on disease progression, use if FEV1  $< 50\%$  and 2 exacerbations in a year, NICE guidelines, TORCH study)  $\rightarrow$  add in tiotropium (if FEV1  $< 60\%$ , UPLIFT study)
  - O2: only of benefit in those with severe resting hypoxaemia (PO2  $< 60$ )
  - Surgery

- LVRS if upper lobe dominant emphysema. Reduces RV, increases FEV1, improved quality of life and exercise capacity. Not if FEV1 < 20%, diffuse disease or DLco < 20% (all → ↑harm)
- Single lung transplantation – does not increase survival but increased quality of life.  
Indications:
  - End stage lung disease
  - <60 with life expectancy of > 12/12
  - No underlying cancer or other systemic illness
- Exacerbations:
  - Bacterial infection implicated in > 50%. Common bugs Haemophilus, moraxella, strep pneumonia. Amoxil ineffective against many strains of the first two
  - Steroids: ↓LOS and ↓ relapse
  - Titrate O2 to maintain sats 85 – 92%. > 92 associated with acidosis in up to half hypercapnic patients
  - Ventilation: BiPAP – patient triggered, pressure limited ventilation. → ↓mortality and ↓intubation (but can delay necessary intubation). (CPAP – which is just about alveoli recruitment → ↑O2)

### *Smoking Cessation*

- Assess smoking dependence: Smoke after waking, in forbidden areas, how many, smoke when sick
- Assess willingness to quit
  - Not ready/thinking about/ready to quit
  - If not ready, give brief advice of risks, rewards, and repeat this often
- If ready to quit (Brief advice OR 1.7, absolute difference 2.5%):
  - Review past attempts
  - Review high risk situations
  - Relapse prevention
  - Set quit date
  - Involve family/friends for support
  - Post-quit encouragement
- Approaches:
  - Cold turkey has worst quit rate, < 5% at one year
  - Medication: bottom line – everyone should get NRT
    - Nicotine replacement therapy: patches down titrating over 6 weeks. 50% get local skin reaction, 5% don't tolerate it. 12% vs 6% at 2 years
    - Bupropion/Zyban (NA/Dopamine reuptake inhibitor): CI in seizure disorders and HTN. Start before quit date and continue for 2 months. Not subsidised, costs same as smoking. At 1 year placebo 16%, Zyban 30%, Zyban + patches 35%
    - Varenicline: blocks nicotinic AcH receptor. Better than bupropion SE nausea, insomnia
  - Requires systemic support: smoke free legislation, taxes, etc
- Relapse is high – it is a chronic disorder

### *Management of Bronchiectasis*

- Differentials:
  - Childhood infection: measles, pertussis
  - Haemophilus (→ epithelial injury), viruses, necrotising bacteria, TB
  - Impairment of host defences: Ig deficiency, ciliary disorders, CF
  - Non-infectious: foreign body, aspiration, α1AT deficiency
- Complications of Bronchiectasis
  - Pneumonia
  - Empyema/lung abscess/disseminated infection
  - Deteriorating lung function
  - Cor pulmonale
  - Sinusitis
  - Haemoptysis
  - Brain abscess
  - Amyloidosis
- Treatment
  - Education
  - Physiotherapy
  - Elimination of any identifiable reversible causative process

- Aerosolized recombinant DNAase to aid removal of secretions (only proven in CF)
- Antibiotics for acute exacerbations
- Bronchodilators
- Surgical removal of affected area if localised
- Bronchial arterial embolisation in significant haemoptysis
- Lung transplant:
  - FEV1 30%
  - Respiratory failure of any nature
  - Significant recurrent haemoptysis
- Flu vaccine, ?pneumovax

### *Management of Cystic Fibrosis*

- Diagnosis: Sweat test. < 40 meq/L normal. > 80 CF. > 140 then error. Genetics for CFTR gene, chromosome 7. Most detected neonatally. 5% present after 18 years of age.
- Typical progression of bugs: common → staph → pseudomonas (non-mucoid the mucoid strains) and Burkholderia (formerly pseudomonas cepacia) → opportunistic mycobacteria (eg MAC)
- Complications:
  - Sinusitis/polyps
  - Colonisation/infection
  - Deteriorating lung function
  - Obstructive lung function → type 2 failure → BiPAP
  - Pulm HTN → Cor pulmonale
  - Intestinal obstruction syndrome
  - Focal biliary cirrhosis
  - DM
  - Azoospermia (95%), anovulation (20%)
- Treatment:
  - Education: CF society, family needs education too
  - Nutrition
  - Allied health: physio, dietician
  - Chest:
    - Intensive chest clearance physiotherapy: breathing exercises, postural drainage, flutter valves, percussion
    - β-agonists for associated bronchospasm
    - Inhaled hypertonic saline → ↓exacerbations (NEJM 2006)
    - Human recombinant DNAase to reduce sputum viscosity (very expensive)
    - Macrolide Abs: orally 3 times weekly preserves lung function
    - Inhaled tobramycin in some patients prophylactically
    - Intravenous antibiotics for infective exacerbations, tobramycin and ceftazidime for Pseudomonas. Ciprofloxacin only in combination (otherwise rapid resistance). European consensus guidelines recommend IV ABs every 3 months – little evidence.
    - Haemoptasis: Treat infection, check coags (biliary obstruction → liver impairment), embolisation
  - If pancreatic insufficiency: pancreatic enzyme replacement + fat soluble vitamin replacement + insulin (late complication) +/- PEG
  - Lung ± heart transplant (CF does not recur in transplanted lung). > 2 year survival 60%. Indications FEV1 < 30%, paO2 < 55, paCO2 > 50

### *Management of Pneumonitis*

- Hypersensitivity pneumonitis:
  - Cell mediated hypersensitivity, can → granulomas. Acute → chronic presentations
  - Diagnosis: ↑inflammatory markers, RF, not eosinophilia, suspected serum antigens, CT, LFTs (reversible restriction or obstruction after exposure stops), BAL (lymphocytic alveolitis), lung biopsy
  - Avoid antigens. If progressive then → steroids
- Eosinophilia: Causes: fungal (aspergillus), parasites, drug induced (sulphonamides, penicillin, thiazides), Hypereosinophilic syndromes
- Environmental lung disease: restrictive LFTs. Asbestos (long latency), silicosis (“crazy paving” on HRCT), Coal dust (~ 15 years), beryllium, organic dusts (cotton, grain)

### *Management of Idiopathic Interstitial Pneumonia*

- Interstitial Lung Disease is old term
- Not usually episodic (consider eosinophilic, hypersensitivity, vasculitis, etc)
- Types:
  - Idiopathic pulmonary fibrosis: usual interstitial pneumonia on histology – steroids don't work. Consider steroids +/- immunosuppression (cyclophosphamide/AZA) in the rest
  - Non-specific interstitial pneumonia
  - Cryptogenic organising pneumonia
  - Smoking related: Desquamative interstitial pneumonia and respiratory bronchiolitis interstitial lung disease
  - Lymphocytic interstitial pneumonia
- Diagnosis:
  - Bloods: rheumatoid screen, ANCA, HRCT can be specific enough to avoid biopsy/BAL in IPF, sarcoid, hypersensitivity, asbestosis, and several other rarer ones
  - LFTs usually restrictive
  - 6 minute walk best test of global function
- Good Prognostic factors
  - Reversible aetiology
  - Young age of onset
  - Female
  - Predominantly ground glass changes on imaging
  - Lung biopsy results
- Management
  - Prednisone 40mg OD for 6 weeks which is continued based on results of investigations and response
  - Cyclophosphamide on patients with specific aetiologies or predominant neutrophils on bronchial lavage
  - Remove any underlying causes
  - Lung transplant
- Complications:
  - Interstitial lung disease gives a tenfold increase of bronchial carcinoma
- Diffuse parenchymal lung disease of known cause:
  - Drugs
  - CTD: Scleroderma (fibrosis, PAH), SLE (pleuritis +/- effusion, pneumonitis, haemorrhage), RA (ILD, PAH)
  - Other: Lymphangiomyomatosis – proliferation of smooth muscle cells
  - Syndromes with diffuse alveolar haemorrhage: Goodpasture's, Wegner's, SLE

### *Management of Sarcoidosis*

- Non-caseating granulomas, hypergammaglobulinaemia. Acute onset → usually self-limiting. Insidious onset predicts progressive fibrosis
- Presentation: fatigue, night sweats, arthralgia (esp knees), cough, SOB
- Findings: skin, eye, liver, bone, cardiac and spleen lesions
- Workup:
  - Bloods:
    - ↑Ca (restrict Ca intake, no Vit D supplements, avoid sunlight, low dose steroids)
    - Serum ACE. Elevated in 60% active disease. Also in leprosy, hyperthyroidism, miliary Tb. ACE in lymphoma is usually ↓
  - CXR, HRCT, LFTs with DLco (most sensitive test of interstitial lung disease)
  - Biopsy
- Differential: Tb and fungal infection, malignancy
- Treatment: based on symptoms only. If only cough then ICS. Prednisone (most trials in lung disease). Hydroxychloroquine for skin. Infliximab works (etanercept doesn't – same as Crohn's)

### *Management of Pulmonary Artery Hypertension*

- Differential:
  - Lung: COPD, ILD, sarcoid
  - Heart: LVF, MR/MS
  - Other: WTE, OSA, Sjogren's, Drugs, idiopathic, portal HTN

- Diagnosis: mean pulmonary artery pressure > 25 mmHg at rest (severe > 50) or > 30 with exercise, and the absence of lung or cardiac disease
- Investigations to exclude other causes:
  - ECHO/ECG for heart
  - CXR/PFTs: emphysema, fibrosis
  - CTPA for PE
  - Auto-antibodies
  - HIV
- Then: exercise test, RH catheterisation, vasodilator test (→ responders and non-responders to vasodilators)
- Predictors of prognosis: BNP, uric acid (sign of hypoperfusion), Trop
- Medications:
  - Calcium channel blockers (eg high dose diltiazem) in responders only
  - Prostacyclins → ↑cAMP mediated vasodilation. Continuous infusions. Iloprost can be inhaled
  - Endothelin Receptor antagonists: Bosentan
  - Sildenafil: oral cyclic GMP phosphodiesterase type 5 inhibitor – numerous studies show benefit
- Heart Lung transplant

### *Other Respiratory*

- OSA:
  - Differential: Pain, insufficient sleep, depression, hypothyroidism, restless legs, central sleep apnoea (eg Cheyne Stokes 2<sup>nd</sup> to CHF or neurologic disease)
  - Measure Epworth Sleepiness Score and sleep study for Apnoea + Hypoxia index (< 20 mild, >60 severe)
  - Treatment: CPAP, mandibular reposition splint, surgery in specific cases (eg jaw advancement)
  - Driving restrictions
- Restless legs:
  - Exclude fe deficiency, neurological disorders, pregnancy, uraemia, drugs (TCA, SSRI, lithium)
  - Treat: dopamine agonists (eg simemet, ropinirole). ?benefit from clonazepam, codeine, carbamazepine

## **Renal**

- Give the patient information about the kidney foundation

### *Polycystic Kidney Disease*

- Complications:
  - Chronic kidney disease leading to ESRF
  - HTN: occurs prior to significant renal impairment
  - Nephrolithiasis
  - Haematuria
  - Pain: mass effect, infection, bleeding into cysts
  - Diverticular disease
  - Liver and pancreatic cysts – usually later and less clinical significance
  - Mitral valve prolapse
  - Dilation of aortic root
  - Intracranial aneurysm (screen only if family history)
- Management:
  - Treat hypertension
  - Lifestyle modification
  - Pain management
  - Renal replacement therapy

### *Management of Chronic Renal Failure*

- Stage 3: GFR 30 – 59, 4: 15 – 29, 5: < 15
- History:
  - Symptoms: Proteinuria, haematuria, oliguria, oedema, sore throat, sepsis, rash, haemoptysis, kidney stones, uretic reflux, diabetes, HTN
  - Other illnesses: CTD (SLE, scleroderma), Hep B/C, Hodgkins (→ minimal change), solid tumours (→ membranous), myeloma, drugs
  - Treatments: biopsy, access problems

- Aware of prognosis
- Treat any reversible causes
- Management of factors worsening renal function:
  - Stop smoking
  - Watch drugs
  - Aggressive BP control: if proteinuria target 125/75 + salt restriction (blunts ACEI). If Cr ↑ by 30% check for renal artery stenosis. Stop if K > 6 despite dose reduction, dietary restriction and diuretics. ACEI + ARB better control in DM and non-DM – delay in RRT not (yet) demonstrated, Larger trials awaited on triple blockade with spironolactone
  - Diabetes control
  - CHF
  - Hypercalcaemia
  - Hyperuricaemia
  - Obstruction
- Complications of CRF (usually with GFR < 20):
  - Uraemia:
    - Symptoms: *fatigue, restless less, anorexia, nausea, pruritis, impotence, pericarditis*
    - Monitoring: Cr & urea affected by malnutrition, Cr falsely elevated at low levels due to some tubular excretion. Watch anaemia, albumin (negative acute phase reactant → ↓ with ↑CRP), HCO<sub>3</sub>
    - Prone to constipation (worsening by phosphate binders and Fe). ↓Protein may help nausea
  - Phosphate:
    - Dietary restriction
    - Phosphate binders (CaHCO<sub>3</sub> → ↑Ca, Mg less effective, Al → toxicity) – awaiting new ones eg non absorbable cationic polymer Sevalamer
    - Vit D – Calcitriol, aim for PTH 1.5 – 3.5 times normal (ie once PO<sub>4</sub> normalised, control ↑ PTH with Vit D)
    - Calcimimetics: alter set point for Ca sensing receptor. Good control of Ca/PO<sub>4</sub>, no outcome data on mortality
    - Parathyroidectomy if Ca persistently > 3, PTH > 10 \* normal, falling BMD
  - Renal osteodystrophy (↑PTH, ↓Vit D, dialysis related amyloid, acidosis):
    - Diagnosis: xray, ↓Ca and ↓Vit D levels, ↑ALP, ?bone biopsy, DEXA
    - NaCO<sub>3</sub> – aim for HCO<sub>3</sub> > 22. Watch for ↑Na load
  - ↑K: ↓dietary intake and ion exchange resins, check medications
  - Anaemia: near universal by stage 4. Exclude Fe deficiency (loss it in dialysis), poor nutrition (eg folate), blood loss, chronic disease, EPO. Uraemia is a chronic inflammatory state → ↑IL6. Care with blood transfusions (complicates future transplant). Want ferritin > 200 and transferrin saturation > 25%, EPO once Hb < 100 with a target of < 120. Give folate as well. Check in 4 weeks if poor response then ↑dose, if no response in 8 weeks then non-responder
  - Fluid overload. Na and fluid restriction, daily weigh, frusemide
- Minimise diseases worsened by renal failure:
  - Protein: Epidemiology ⇒ assoc with high protein and progression, Modification of Diet in Renal Disease did not show restriction retards progression, some meta-analysis do (but many trials pre-ACEI). Don't want malnutrition. Balance.
  - *Cardiovascular risk factors* (CKD equivalent to diabetes)

### *Management of Dialysis*

- Death: 50% by CVD, 15% by infection
- Absolute indications (with other management failed):
  - Uraemia
  - Overload
  - K
  - Pericarditis
- Ask about: where, how often, for how long, relief of symptoms, shunts, weight monitoring, emergency plans, followup
- Measure of adequacy:
  - Transfusion dose – KT/V
  - PO<sub>4</sub> control
  - Fluid control
- General:

- Strict fluid restriction
- CV risks:
  - Statins controversial. Very low LDH → ↑mortality. Treat Ca and PO<sub>4</sub> for the heart
  - BP targets unclear. Benefits of treatment unclear. Aim for 140/95 (both high and low bad). Control with dialysis. BB better than CCB and ACEI
- Peritoneal:
  - Pros: more independence, smooth removal, cardiac friendly, no heparin but ↓DM control/weight gain, infections, protein loss, inefficient, easier to learn, access via Tenckhoff (contraindications previous perforation)
  - Initial dose: 2L of 1.5% dextrose for 2.5 H with 3 day time exchanges and 1 overnight. Do peritoneal equilibrium test in 2 months → high transports loose albumin with long dwells
- Haemodialysis:
  - Pros: more efficient than peritoneal, but intermittent (fluctuating fluid), need good heart, uses heparin, access problems
  - Survival critically dependent on hours per week on dialysis (50% 12 month survival > 85)

### *Management of Transplanted Kidney*

- History:
  - What sort of kidney disease, infections, if long term ?reflux nephropathy
  - Compliance
  - Do they know the signs of rejection (fever, swelling, and tenderness over the graft, oliguria)
- Pre-transplant issues:
  - Education:
    - Signs of acute rejection: fever, swelling, tenderness of graft site
    - Avoid nephrotoxic drugs
    - Treat urinary infections aggressively
    - Risks of infection and cancer
  - Issues of recipient selection: living > cadaver, related > unrelated
  - Criteria for listing (ie no contraindications):
    - Life expectancy > 5 years
    - No cancer
    - Screen for infection: HIV, Hep B, Hep C, Tb, CMV
  - Tissue typing: ABO, HLA (A, B, and DR) and antibodies to HLA Class 1
  - Surgical risk
  - Pregnancy (?egg/sperm banking)
- Immunosuppression:
  - Principles: multiple agents → ↑efficiency and ↓toxicity, tailor to risk of acute rejection (start high, taper to ↓CAN), watch for drug interactions (CsA/Tacrolimus metabolised through 3A4 – eg macrolides, CCB)
  - Typical regime: CsA or Tacrolimus for 3 – 6 months + AZA/MMF (ongoing with downwards titration) + prednisone (7.5 – 10 mg, titrate down over 3 – 6 months, maintenance dose for chronic rejection) and basiliximab up front
  - SE of immunosuppression:
    - CsA: nephrotoxic, HTN, ↑lipids, IFG, hirsutism, hyperplasia of the gums, ↓Mg, *tremour*, rare haematological malignancy
    - Tacrolimus: More nephrotoxic than CsA, HTN, more diabetes, less hirsutism/gum hyperplasia
    - AZA: Inhibits purine synthesis. marrow suppression, jaundice and alopecia (and avoid allopurinol)
    - Mycophenolate: diarrhoea, liver toxicity, marrow suppression
    - Sirolimus: non-calcineurin immunosuppressor, mTOR inhibitor → IL-2 co-stimulation. ↑Lipids, ↓platelets, poor wound healing, anaemia, mouth ulcers, diarrhoea
- Pregnancy: best 2 years post transplant, frequent pre-eclampsia, most experience with AZA, CsA and prednisone. MMF contraindicated. Breast feeding controversial. If Cr < 125 no long term decline. If Cr 125 – 250 30% have irreversible decline
- ?Rejection: measure drug levels, nuclear scans, ultrasound, biopsy. Acute rejection in 1 in 4 or 5 kidneys. Need biopsy. Treat with 3 pulses of prednisone, + OKT3 or ALG (antilymphocyte globulin) if severe
- Complications:
  - Monitor: change in Cr, LFTs (↑2<sup>nd</sup> to CsA or CMV), WBC (↑in infection, ↓in AZA)
  - Infection:

- Most common in 1<sup>st</sup> 6 weeks is common bacterial infections (eg UTI)
- Valgancyclovir for CMV D+, R- for 3 months + co-trimoxazole for PCP
- Early risk from CMV, PJP, legionella, Hep B & C
- Late: fungal, BK polymavirus
- If infections, blood culture + aggressive search
- CV risk protection. HTN. Start with CCB then ACEI
- T2DM: 10% get it within 1 year
- Bones: calcitriol + Ca (1993 study on asthma patients on steroids)
- Anaemia – monitor
- Tumours: non-melanoma skin most common. Solid organ 2 fold higher risk. Regular cervical smears. Post-Transplant Lymphoproliferative disease, usually < 2 years later, especially in EBV +ive. Treatment: ↓immunosuppression, rituximab, CHOP
- Disease recurrence:
  - GN: 1 in 10 risk your graft will fail in 10 years. Highest risk in FGS, also in IgA
  - Lupus and vasculitis < 10%
  - DM: graft loss common after 10 years

## Endocrine

### *Management of Diabetes*

- Diagnosis:
  - Type 1:
    - Risks: small family risk, identical twins 50%, geographic variation
    - Antibodies – one or more elevated in > 75%: Glutamic acid decarboxylase (GAD), Tyrosine phosphatase (IA2), Insulin autoantibody (IAA)
    - All prevention trials unsuccessful (tried with insulin, cyclosporine, AntiCD3 antibodies, immunisation with GAD)
  - Type 2:
    - Screen if > 55 or younger with risk factors (IFG, IHD, gestational diabetes, PCOS, BMI > 30, first degree relative, HTN)
    - Impaired fasting glucose → 40% risk of DM over next 2 years
    - DM if FPG > 7, 2 hr post prandial > 11.1 *on 2 occasions*
    - Peripheral insulin resistance, excessive hepatic production of glucose (2<sup>nd</sup> to hepatic insulin resistance) and ↓insulin secretion
  - C-peptide doesn't distinguish between T1 and T2 but determines need for insulin
  - Latent autoimmune Diabetes of the Adult: phenotypic T2 (except younger and thinner) but antibodies – plan to escalate treatment quickly, check other autoimmune conditions
  - MODY: AD disorders of β-cell function – glucokinase gene (mild) and transcription factor (progressive)
- History:
  - Assess severity, symptoms (change in weight)
  - Lifestyle and other risk factors: exercise, CVS
  - Current and past treatment
  - BSL control and HbA1C (spurious readings in CRF, Fe deficiencies, haemoglobinopathies & pregnancy)
  - How do they monitor, urine tests
  - Medications (caution with thiazides and beta blockers)
  - Hypos and hypers – symptoms – treatment – consequences
  - Who follows up
- Plan:
  - Allied health
    - Diabetes nurse educator
    - Dietician
    - Podiatry
  - Treatment of type 1:
    - HBAIC target 7% - less than this → ↑hypos. Anaemia and uraemia may interfere with the result
    - Trials in T1:

- Diabetes Control and Complications Trial (DCCT): ↓hyperglycaemia → ↓microvascular complications
- Epidemiology of Diabetes Intervention and Complications (EDIC): Followed DCCT – intensive group slipped in control but maintained benefit – legacy effect
- Monitoring: continuous glucose monitoring → ↓HbA1C but not ↓hypos
- Continuous pumps: ↓hypos, downside is cost, infection and dislodgement (→ DKA)
- DKA: nausea, vomiting, abdo pain → +ive ion gap metabolic acidosis. β-hydroxybutyrate better indicator of ketones but not tested by nitroprusside urine strips
- Treatment of type 2:
  - Prevention:
    - Diabetes Prevention Programme: Diet + exercise prevented/delayed T2 by 58% cf placebo, metformin by 31%
    - Ramipril + statin reduced new cases in cardiovascular trials (not primary endpoint)
    - DREAM trial: Rosiglitazone prevented progression, small ↑ CHF
  - Trials in Type 2:
    - UK Prospective Diabetes Study (UKPDS): each 1% ↓ in HbA1C → ↓35% in microvascular complications, ↓21% in diabetes related deaths, non-significant ↓ in MI but more weight gain
    - Legacy effect: microvascular benefits persisted, macrovascular complications emerged and ↓ death from any cause. No legacy effect from lowered BP
    - ACCORD and ADVANCE trials: does tighter control → ↓macrovascular complications. ADVANCE showed ↓mortality, ACCORD showed ↑ (more rosiglitazone)
    - ADOPT trial: head to head showed rosiglitazone better than metformin better than glibenclamide for failure of monotherapy, but worst for weight. Glibenclamide best for CVD
  - Medication:
    - Insulin: inhaled versions coming. Adding a basal insulin more effective than meal time (Treating to Target in Type 2 DM – 4-T Trial)
    - Insulin Secretagogues: sulphonylureas: stimulate secretion. Best in recently diagnosed, obese and residual insulin production. SE hypos. Avoid in renal and hepatic failure. Interacts with alcohol, warfarin aspirin
    - Biguanides: ↓hepatic glucose production, ↑insulin sensitivity. No hypos, modest weight loss. SE nausea/diarrhoea, not if Cr > 133 men > 124 women (accumulates rapidly)
    - Thiazolidinediones (pioglitazone in NZ): Insulin sensitiser: PPARγ agonists. OK in renal impairment. Small weight gain (subcutaneous not visceral), ↑oedema
    - Acarbose: ↓absorption. GI flatulence and diarrhoea. Not in renal/liver disease or IBD
    - Incretins: Add on with metformin or sulphonylurea. Exenatide sc. Not with insulin. No outcome trials. GLP-1 receptor antagonists (GLP-1 stimulates β-cells and slows gastric emptying). Sitagliptin oral DPP-4 inhibitor.
  - Vaccination
  - Monitor for depression
  - Sick day regime:
    - Test BSL 2 – 4 hourly and record all results. If BSL > 15 test ketones each time PUing
    - Take at least usual dose of insulin
    - Have plenty to drink
    - Find cause of illness – seek early treatment
    - Emergency review if: vomit > 3 times, > a trace of ketones, BSL > 15 twice, infection or fever
    - Watch for signs of ketoacidosis: nausea/vomiting, “fruity smell” on breath, SOB, drowsiness, abdo pain
  - Hypoglycaemia plan:
    - Sympathoadrenal response < 3.5 but blunted with repeat hypos
    - Neuroglycopenic response (eg confusion) < 2.5
  - Complications:
    - ADA Targets:
      - BP < 130/80, <120/75 if retinopathy
      - LDL (trials in T2 only, not T1) < 2.6 (no CVD), < 1.6 (with CVD), TG < 1.7, HDL > 1.0 (men), 1.3 (women)
    - Microvascular:
      - Eye: ?had photos taken, 2 yearly review

- *Kidney*: dysuria, nocturia, oedema, HTN. Normal albumin:creatinine ratio is < 2.5 (m), 4.5 (f). BP target < 130/80 without proteinuria, < 125/75 with. Drug specific benefit independent of BP shown with ACEI in type 1 and ARB in type 2
- Peripheral and autonomic (fainting, erectile) *neuropathy*
- *Feet*
- Macrovascular risk factors: MI, CVA, PVD
- Infections

### *Management of diabetic foot*

- Assess risk: peripheral neuropathy, PVD, previous ulceration, foot deformity, glycaemic control
- General:
  - Manage diabetes
  - Treat infection
  - Consider revascularization if needed, ABI etc
- Low risk: general foot care and advice, annual review (incl monofilament)
- High risk:
  - Education
    - Avoid smoking
    - Avoid walking barefoot
    - Stepping into a bath without checking the temperature
    - Trim toenails
  - Inspect feet daily looking between and underneath the toes and at pressure areas for skin breaks blisters, swelling, or redness
  - Wash feet daily + moisturise
  - Podiatrist - appropriate shoes
- Ulcer:
  - Debridement, wound care
  - Podiatrist – offloading footwear
  - Evaluate for ABs
  - Evaluate for PVD with ABI
  - Exclude osteomyelitis

### *Management of Lipids*

- Bottom line:
  - No evidence for trying to raise an isolated ↓HDL
  - Statins: ↓LDL
    - Many Trials: Scandinavian Simvastatin Survival Study (Men with CHD), Treat to New Targets (atorvastatin 80 vs 10, ↓CV events, ↑non-cardiac deaths including haemorrhagic strokes, no mortality difference)
    - Stable patients. Mortality benefit. Minimal survival benefit for higher over lower dose, but reduction in nonfatal events and revascularisation
    - Unstable/high risk: aggressive lipid lowering as survival benefit
  - Fibrates – no survival benefit proven. Use as additional therapy to statins or if high TG
  - Ezetimibe: no endpoint data for survival. Minimal drop in LDL as sole drug, useful in combination for further ↓LDL or if statin intolerant
  - Combination of fibrate and a statin has never been tested against either a statin or fibrate alone in reducing cardiovascular events
  - Resins: further ↓LDL or if statin intolerant, pregnant/breastfeeding, but not if ↑TG
  - Niacin: most effective drug for ↑HDL, also ↓TG, but watch side-effects. Use in combination with statin if ↑LDL and ↓HDL is primary abnormality
  - Fish oils if high TG, often in combination with fibrates
  - For severe, refractory (usually genetic) ↑LDL can get LDL apheresis (a haemo-dialysis sort of treatment)

### *Management of Obesity*

- Reversible causes:
  - Drugs: steroids, progestogen
  - PCOS
  - Hypothyroidism
- Assess comorbidities:

- IHD
- DM
- OSA
- Lipids
- HTN
- Assess Complications:
- OA
- Gallstones
- Stress incontinence
- Gout
- Assess psychological factors: readiness to change, supports, potential barriers
- Treatment approach:
  - Diet: calorie restriction (1 – 1,200 kcal/day for women, 1,200 – 1,600 kcal/day for men) with < 30% fat
  - Exercise: 30 mins moderate exercise on most days of the week, eg walking bus stops, taking stairs
  - Behavioural therapy: attitudes to weight, weight loss, expectations. Risky situations, precipitants, alternatives
  - Pharmacological: 3 - 6 months of lifestyle first. Then ?orlistat, sibutramine ( $\beta$ 1 adrenergic and 5HT receptors, SE dry mouth, insomnia, HTN)
  - Surgery: if BMI > 40, or > 35 with complications. Average loss of 30kg sustained over 2 years. Swedish Obesity Study at 15 years 30% reduction in mortality (6.3 vs 5.5%)

### *Management of Pituitary Problems*

- History:
  - Gonadal failure → amenorrhoea, weight gain, vaginal dryness
  - Thyroid deficiency: weight gain, cold intolerance
- Exam: hormone and space occupying effects
- Assessment of pituitary function
  - Screening:
    - PRL – if very high then prolactinoma. Exclude hypothyroidism, pregnancy/breastfeeding, antipsychotics, metoclopramide, renal failure, sarcoid. Treat with Cabergoline weekly or bromocriptine (nausea)
    - TFT for TSH
    - IGF-1 for GH. NB to diagnose acromegaly screen with  $\uparrow$ IGF-1 then oral glucose tolerance test (GH should fall if normal). Txt trans-sphenoidal surgery, radiation, somatostatin analogues (octreotide but gut complications). GH receptor antagonists (not funded)
    - If 9 am cortisol is normal than pituitary insufficiency of ACTH unlikely
    - Overnight metyrapone → blocks cortisol production →  $\uparrow$ ACTH if pituitary normal
  - Tests of pituitary sufficiency: Triple test (not in HD or epilepsy): inject insulin (aiming for BSL < 2.2), TRH and GnRH. Look for  $\uparrow$  GH,  $\uparrow$ Cortisol,  $\uparrow$ TSH,  $\uparrow$ PRL (due to  $\uparrow$ TSH)
  - Imaging: incidentalomas in up to 10% of MRIs. Only image if hormonal abnormality
- Differential:
  - Radiation
  - Functional or non-functional adenoma
  - Other tumours, mets
  - Infection: TB
  - Sarcoid
  - Vascular
  - Exclude: depression, dementia
- Replacement: hydrocortisone (K will drive mineralocorticoids. Start before T4 otherwise may → Addisonian crisis), T4 (follow T4 not TSH), testosterone in men, for women oestrogen till 45, then HRT till 55. GH not funded

### *Cushing's Workup*

- Cushing's Syndrome:
  - Screening tests: 24 hr urinary free cortisol, midnight salivary or serum cortisol
  - Low dose dexamethasone suppression tests: 1 mg at midnight, check at 8 am. False positives with depression, alcohol, obesity and drugs affecting cortisol metabolism (phenytoin)
  - Measure ACTH (on 2 separate days) to determine if primary or secondary
  - ACTH dependent (~ 80%)

- High dose dexamethasone suppression test: If pituitary some but not normal suppression of cortisol, adrenal and ectopic tumour won't
- MRI of pituitary – but lots of incidentalomas
- Inferior Petrosal sinus sampling
- ACTH independent: Undetectable ACTH. Exogenous corticosteroids, adrenal gland adenoma
- Addison's Disease:
  - Failure of gluco- and mineralocorticoids
  - Differential: idiopathic (autoimmune), Mets (eg lymphoma), TB (fungal in immunocompromised), drugs, congenital adrenal hypoplasia
  - Testing: 8am cortisol < 83 rules it in, > 500 rules it out, in between → short Synacthen
- Adrenal incidentalomas:
  - > 6 cm excise
  - < 4 cm monitor
  - History of prior malignancy – must consider metastasis
  - Biochemical evaluation: low dose overnight dexamethasone for pre-clinical Cushing's, ARR if hypertensive, exclude pheo before FNA
- Multiple Endocrine Neoplasia:

	PTH	Pancreas	Pituitary	MTC	Pheo	Other
MEN1 – MENIN tumour suppressor gene. Consider if ↑PTH less than 30	↑	↑	↑			?↑gastrin
MEN2A – mutation in RET proto-oncogene	↑			↑	↑	
MEN2B – mutation in RET proto-oncogene				↑	↑	Mucosal neuromas
VHL – tumour suppressor involved in angiogenesis		↑			↑	Clear Cell Ca

### Thyroid Workup

- Exam: normal gland 12 – 20 gm. Check down thyroglossal track for ectopic tissue
- Bloods:
  - TFT
  - Antibodies: against thyroid peroxidase and thyroglobulin
  - Thyroid stimulating Igs (TSIs) stimulate TSH-R in Graves – not measured often
- US: is it nodular or diffuse enlargement. Not for thyroid dysfunction, just masses
  - If ↓TSH then US – will alter management between Graves (suppression) and nodular (radio- ablation)
  - If ↑TSH and no nodules then treat and observe
  - If TSH N and nodules then FNA
- Radio-iodine scan: gland size and uptake. Not if amiodarone (already lots of iodine in the body)
- Differential:
  - Graves
  - Autonomy: TMG, adenoma, functioning carcinoma
- Assessment of a thyroid nodule:
  - If < 1 cm don't need to FNA unless other concerning features. Up to 5% > 1 cm contain carcinoma
  - Risk factors: < 20, > 50, men, past neck irradiation, family history (including MEN)
  - If ↓TSH then radioiodine scan as a hot nodule is almost never malignant
  - Otherwise FNA

### Treatment of Thyrotoxicosis

- β-Blocker for symptom relief
- Anticoagulation if AF
- Eye disease:
  - Congestive ophthalmopathy or ocular myopathy
  - Smoking and radioiodine risk factors for progression
  - Steroids if significant Grave's ophthalmopathy only
- Choice of anti-thyroid drugs or radioactive iodine for Grave's: Carbimazole or propylthiouracil
- Surgery for severe disease, Nodular disease, or Amiodarone induced where the anti-arrhythmic is a necessity
- NSAIDs for viral thyroiditis

### *Management of Polycystic Ovary*

- PC: infertility (anovulation), menstrual irregularity, androgen excess
- Differential:
  - Idiopathic hirsutism
  - Cushing's
  - Non-classical CAH: rare
  - Androgen secreting tumour: rare
- Associations:
  - Obesity
  - T2DM
  - High lipids
  - HTN and OSA – unexplained by obesity alone
- Pathogenesis: ↑non-cyclical oestrogen → ovarian hyperplasia, ↓FSH (↓follicular maturation and no menses)
- Workup:
  - Serum testosterone, LH and DSH. Testosterone and LH high
  - Fasting glucose and lipids
  - Ultrasound > 10 follicles
  - Rare: PRL for prolactinoma, DHEAS for androgen tumour, 17-hydroxyprogesterone for CAH
- Treatment:
  - Weight loss → ↓peripheral oestrogen and androgens, ↓insulin resistance
  - Combined OCP: ↓risks of unopposed oestrogen
  - Metformin
  - Cyproterone (anti-androgen) for hirsutism and acne

### *Differential of Calcium disorders*

- Low calcium:
  - Symptoms: tetany, prolonged QTc
  - Hypoparathyroidism: abscess/gland destruction, ↓Mg, resistance to PTH (pseudo)
  - ↓Vit D (→ ↓Ca and ↓PO<sub>4</sub>): renal failure, malnutrition, drugs (phenytoin, rifampicin, steroids)
  - Rarer: Genetic Ca sensing receptor abnormalities, acute pancreatitis, excess citrate from blood transfusions
- High calcium:
  - ↑PTH: primary (adenoma, ↑PTH → ↑Ca, ↓PO<sub>4</sub>), secondary or tertiary, lithium, immobilisation
  - ↑Vit D: nutritional, ↑conversion (sarcoid)
  - Thiazides → ↑Ca reabsorption
  - Paraneoplastic: PTHrH (→high RANKL:OPG ratio), bone mets, myeloma
  - Dehydration
  - Symptomatic treatment: rehydrate, correct ↓K and ↓Mg, frusemide, pamidronate
- Workup: test Ca, PO<sub>4</sub>, Mg, **ALP**

### *Management of Prednisone Complications*

- What is prednisone history. Has down titration been attempted?
- Bone protection.
  - Check Ca, Vit D **and ALP**. Greatest bone loss happens early
  - If course may be prolonged, start Ca and Vit D from the outset
  - Do DEXA scan. Z score < 2.5 start bisphosphonates. If > -2.5 not funded otherwise although still of benefit. Only drug shown to prevent fracture risk
  - Stop smoking
  - Reduce alcohol
- Monitor and treat HTN (mineralocorticoid effect)
- Metabolic:
  - ↑TG – measure lipids and treat
  - ↑BSL – monitor FPG
- Peptic ulcer disease: consider PPI
- Immunosuppression: Vigilance for infection. Consider TB and PCP risks
- Other complications:
  - Adrenal suppression
  - Weight gain

- Cushing's
- Steroid myopathy
- Poor sleep
- Skin atrophy

### *Management of Osteoporosis*

- Rule out reversible causes:
  - Hypothyroidism
  - Hyperparathyroidism ( $\uparrow$  Ca)
  - $\downarrow$  Vit D
  - Hypogonadism
  - Drugs: especially steroids, also methotrexate, AZA, phenytoin, carbamazepine, omeprazole
  - Exclude myeloma
- Risks:
  - Age, low body weight
  - Maternal history
  - Current cigarette smoking
  - Alcoholism
  - Steroids
  - Many comorbidities: COPD, Amyloid, RA, endocrine disorders
- Test: **Ca, Vit D, ALP, TFTs, renal function**
- Exacerbating causes:
  - Ca intake
  - Sunlight exposure
- Have they ever fallen. Risks for falls: eye sight, safety at home
- Therapeutic interventions:
  - Non-drug:
    - Weight bearing exercise
    - Aerobic exercise: no gain in bone mass but prevents loss
    - Nutrition
    - Vertebroplasty
  - Drug:
    - Ca: if history of kidney stones 24 hour urinary Ca first
    - Vitamin D: no evidence that analogues (eg calcitriol) are any better than Vit D
    - Women's Health Initiative: Vit D and Ca in healthy women made no difference to bones but  $\uparrow$  kidney stones
    - HRT:  $\downarrow$  risk of hip (NNT 1,700 in WHI) and clinical spine #, but  $\uparrow$  MI,  $\uparrow$  CVA,  $\uparrow$  breast Ca (little risk if  $<$  5 years) and  $\uparrow$  VTE. Should use for txt of postmenopausal symptoms only
    - Bisphosphonates (check for swallow problems)
    - Other:
      - PTH sc
      - SERMS – not as potent as bisphosphonates
      - Calcitonin: poorer quality evidence
      - Denosumab: mab inhibiting RANK pathway – same effect as osteoprotegerin.  $\uparrow$  BMD, # data awaited
  - No established guidelines for monitoring treatment

## **Neurology**

### *Management of Stroke*

- Differential:
  - Ischaemic stroke
  - Haemorrhagic stroke
  - Embolic stroke
  - Dissection (associations: Marfan's, cystic medial necrosis, fibromuscular dysplasia, spinal manipulative therapy)
  - Hypercoagulable disorders (incl post partum and SLE): usually venous clots – non-specific, headaches. Signs papilloedema, CN 3,4 and 6 impingement from cavernous sinus
  - Vasculitis: GCA, PAN, cerebral SLE. Do WBC, CRP, ESR, ANA, ENA, dsDNA

- Infection: syphilis, TB, others if immunocompromised
- Space occupying lesion
- MS: do oligoclonal bands on CSF and MRI
- Rapid assessment. ABCD2 score if TIA
  - High risk if > 4, crescendo TIA, or AF
  - Low risk if ABCD2 score < 3 or presentation > 1 week (most have had consequential strokes in this time)
- Investigations:
  - Bloods:
    - FBC: polycythaemia, ↑platelets
    - ESR/CRP: giant cell arteritis, vasculitis
    - Renal Function
    - Cholesterol
    - Glucose
  - ECG: AF, MI
  - CT/MRI
  - Carotid imaging if Anterior circulation symptoms (dysphasia, unilateral weakness) and fit for surgery. If symptomatic and > 50% refer for surgical assessment for treatment within 2 weeks
- Acute treatment of stroke:
  - Stroke Unit + MDT care. Assess function with a modified Rankin score
  - tPA: NNT 18 to prevent one death/disability, 7 to see improvement. Little difference between experienced and inexperienced centres in studies. Short window: NNT to see improvement < 1 hour = 3, < 3 hours = 7, < 4.5 hours = 14
  - Aspirin (IST and CAST Trial)
  - Decompressive surgery (if young and oedema – saves lives but ↑ disability)
  - Lower malignant HTN
  - Poor glucose control → worse outcome, but no evidence for tighter control
  - No evidence for neuroprotective strategies
- Secondary prevention:
  - Aspirin immediately (in stroke patients subsequent shown to have bleed not shown to cause harm) +/- dipyridamole (in NZ 150 mg BD funded – evidence is for 200 mg bd – significant drop out due to headaches, reduced by od for one week then bd). Clopidogrel (CAPRIE aspirin vs clopidogrel, CURE aspirin + clopidogrel, PROFESS aspirin + dipyridamole vs clopidogrel)
  - Warfarin if AF
  - Lifestyle: low fat, low salt diet, weight reduction, increased exercise (Grade A evidence), ↓ alcohol
  - HTN lowering meds – absolute target uncertain, but “normal” is defined as 120/80. Don’t drop suddenly. Strong evidence for ACEI/ARB for lowering below traditional targets
  - Statin – 40 mg, target LDL < 2.5 (evidence is in those with cardiovascular risk factors)
  - Carotid endarterectomy if > 60% stenosis, and age < 75. 1.2% annual risk reduction
  - Smoking cessation
  - Tight control of blood glucose not proven
- Other:
  - No driving for 1 month after a single TIA
  - Refer to Stroke Foundation

### *Management of Intracranial Haemorrhage*

- CT more sensitive than MRI for acute blood
- Subarachnoid (eg blood in CSF space):
  - Rupture or saccular aneurysm the most common cause. If asymptomatic surgical risk >> bleeding risk
  - LP: blood and xanthochromia
  - Delayed deficits due to rebleed, hydrocephalus, vasospasm (nimodipine), hyponatraemia
  - Management:
    - BP below 170/110
    - If ↓LOC or haematoma > 3 cm then neurosurgery – although supratentorial bleeds haven’t been shown to benefit from surgery
    - Aspirin: ↑risk of recurrent ICH by 40%, absolute ↑ of 0.8% per year. Give aspirin for 1 month after an MI
- Intraparenchymal haemorrhage:
  - Most common. Deficits worsen over 30 – 90 minutes

- Surgery of benefit if < 1 cm from surface (STICH Trial)
- Acute reduction in BP showed ↓clot size but no difference in outcome (INTERACT Trial)

### Management of Migraine

- Warning signs:
  - Worsening over months
  - New of different headache
  - Any headache with maximum severity at onset
  - New onset > 50
  - Headache precipitated by a valsalva
  - Suggestion of a systemic disorder, neurologic signs or seizures
- Treatment:
  - Supportive: quiet room, hydration, caffeine
  - Aspirin, paracetamol, ibuprofen
  - Anti-nausea: metoclopramide, prochlorperazine, chlorpromazine
  - Serotonin agonists: 5HT<sub>1B</sub> and 1D – constrict cerebral vessels, inhibit trigeminal neurons and block transmission
    - Triptans: eg sumatriptan sc
    - Ergots: more side effects
    - CI: IHD, PVD, pregnancy
  - Prophylaxis:
    - Symptom diary
    - Avoid triggers: alcohol, ↓sleep, relationship with menstrual cycle
    - Beta-blocker: several proven effective, amitriptyline (limited evidence)
    - Not closure of patent foramen ovale: MIST trial

### Management of MS

- Risks: 25% twin concordance, latitudinal gradient for first 15 years of life
- Presentation: first demyelinating event optic neuritis (40%) or transverse myelitis (30%, exclude para-infectious, cord ischaemia) preceded by fatigue
- Diagnosis (McDonald Criteria):
  - Clinical – 2 lesions separated in time and space
  - CSF: mononuclear cell pleocytosis in 25%, ↑total IgG, oligoclonal IgG
  - MRI: hyperintense areas on T2, new lesions are gadolinium enhancing
  - Visually evoked responses. Non-specific
  - Exclude differentials: ESR, B12, ANA, VDRL. Also ADEM, PML, HIV, Lyme, neoplasm (eg Lymphoma), Sarcoid, CTD (Sjogren's, vasculitis, APS, SLE)
- General: Education, support, physio, OT
- Patterns: RRMS (initially 85%), SPMS (after 15 years in 50%), PPMS, PRMS
- Acute relapse:
  - Exclude pseudo-relapse due infections
  - IV methyl pred 500 mg for 3 days
- Chronic treatment:
  - Relapsing remitting:
    - IFN-1 $\beta$ , sc every 2<sup>nd</sup> day. SE flu-like, depression, LFTs. Not in pregnancy. ↓relapse, ↓progression
    - Glatiramer acetate: sc daily. Chest tightness, flushing, SOB, palpitations
  - Secondary progressive: IFN, rarely methotrexate
  - Primary progressive: ?Mitoxane
  - Biologics: ant-TNF worse. Rituximab in trials → ↓lesions. Natalizumab ( $\alpha$ 4 integrin adhesion molecule antagonist) NNT 10 for ↓disease progression
- Symptomatic treatment:
  - Spasticity: drugs (baclofen 10 – 20 mg TDS, don't stop abruptly) only in association with physio + splints. Also BZD, gabapentin
  - Constipation: high fibre, exercise, hydration
  - Lethary: exclude depression (fluoxetine), occupational counselling, rest after lunch, amantadine 100 – 200 mg
  - Impotence: Viagra, prostaglandin injections, counsellor
  - Urgency:
    - Exclude infection and constipation

- Detrusor instability: frequent bladder emptying, anticholinergic (eg oxybutinin)
- Hypotonicity (retention) or detrusor/sphincter incoordination → refer for urodynamics
- Pain: carbamazepine, clonazepam, TCAs
- Tremour: BZD, carbamazepine (100 – 300 mg bd)
- Immunisations: essential ones only
- Depression: can be exacerbated by βIFN and baclofen (GABA analogue)

### *Management of Epilepsy*

- Workup:
  - Diagnosis: Was it a seizure. Identify syndrome → accurate prognosis, specific treatment, proper genetic counselling
  - Differential: syncope, psychogenic seizures, metabolic, infection, tumour, toxic, CVD
  - Tests:
    - Bloods incl U&E, LFTs (treatment baseline), urine toxicology screen
    - EEG
    - MRI (do without only if EEG diagnostic) – 15% yield. Especially if adult or focal onset. FLAIR sequence for Mesial Temporal Sclerosis. Emerging role for PET if refractory
- Treat underlying disease: alcohol, mesial temporal sclerosis
- Avoid precipitating factors: sleep deprivation, alcohol
- Drug therapy: aim – monotherapy
  - Common SE: sedation, ataxia, diplopia. Less common: rash, blurred vision, bone marrow suppression, hepatotoxicity
  - Multiple drug interactions, including OCP
- Support:
  - Education about seizure management
  - Driving (if chronic need 2 yrs seizure free)
  - Safety issues at work
  - Management of social stigma
  - Epilepsy association
- Fertility:
  - ↓OCP with AEDs
  - ↓levels with pregnancy, teratogenicity (but greater harm from seizures). Folate 5 mg for prior to conception and 1<sup>st</sup> trimester
  - Vit k for 2/52 pre delivery
  - Encourage breastfeeding
- Withdrawal of txt: after 2 years ↓dose by 3<sup>rd</sup> every 2 weeks

### *Diagnosis and Management of Dementia*

- Definition:
  - An acquired deterioration without reversible cause in memory and at least one of:
    - Impairment of abstract thinking
    - Impairment in judgement
    - Personality change
    - Other disturbance of higher cortical thinking
  - that impairs the successful performance of ADLs or relationships
- Progression: benign forgetfulness → Mild Cognitive Impairment (MMSE usually normal)
- Pathology:
  - Major degenerative dementias associated with the abnormal aggregation of a specific protein:
    - α-synuclein:
      - Multiple System Atrophy (early urinary incontinence, postural hypotension, and dysarthria)
      - Parkinson's
      - Dementia with Lewy Bodies (but early hallucinations – especially drug induced – and disturbances of behaviour)
    - Tauopathies
      - Progressive Supranuclear Palsy (early imbalance and falls)
      - Frontotemporal dementia. 3 repeat Tau (Pick bodies) in Pick's variant
    - Amyloidopathies: Alzheimer's – plaques of amyloid (Aβ42), also tangles (Tau) and Lewy bodies (α-synuclein)
    - Prion related protein: CJD

- Workup:
  - MMSE < 24: poor sensitivity, good specificity
  - Bloods: low yield: TFTs, B12, FBC, electrolytes,
  - Imaging: CT (rule out), MRI (rule in). Must image if < 60, rapid decline, significant trauma, unexplained neurological symptoms, anticoagulants. PET useful in Dementia with Lewy Bodies
- Consider:
  - Alcohol
  - ?Infection: HIV, ?VRDL, prion, TB
  - Psychiatric: depression, schizophrenia
  - Degenerative: Huntington's, PSP, MSA, MND, MS
- Management;
  - Alzheimer's:
    - Acetylcholinesterase inhibitors: donepezil, rivastigmine. 12 week trial. SE nausea, diarrhoea, vomiting, bradycardia
    - Memantine: neuroprotective NDMA antagonist
    - Supportive: carer training, memory aids, make life comfortable, uncomplicated and safe
  - Monitor for comorbid depression
  - Neuropsychiatric side effects:
    - Assess of medical and environmental causes first
    - Behavioural interventions
    - Assess for depression
    - Consider drugs last. Antipsychotics:
      - Block D2 receptors. Benefit for aggression not agitation (Cochrane)
      - SE: EPS (dystonia, akathisia, Parkinsonism), Tardive Dyskinesia, sedation, anticholinergic effects, neuroleptic malignant syndrome

### *Management of Parkinson's*

- Diagnosis:
  - Cardinal clinical manifestations
  - Response to dopaminergic therapy
- Features suggesting an alternative diagnosis:
  - Early falls
  - Poor response to levodopa
  - Symmetrical motor signs
  - Rapid progression
  - Lack of tremor
  - Dysautonomia
  - History of encephalitis
  - History of repeated head injury
  - History of recurrent strokes and stepwise progression of parkinsonism
  - Antipsychotic drug treatment at the onset of symptoms
  - Presence of neoplasm or hydrocephalus on neuro-imaging
  - Cerebellar signs
  - Supranuclear gaze palsy
  - Dementia preceding or occurring concurrently with parkinsonism
  - Babinski sign
  - Presence of apraxia
- Treatment:
  - Goals
    - Maintain function and quality of life
    - Avoid drug-induced complications
    - Prevention of secondary disability
  - Response:
    - Bradykinesia, tremor, rigidity, and abnormal posture respond well
    - Cognitive symptoms, hypophonia, autonomic dysfunction, and imbalance don't
  - Program of physical exercise – maintains function, doesn't affect progression
  - Drugs as soon as function impaired:
    - Initiation - either dopamine agonist (Ergot alkaloids pergolide and Cabergoline SE rare heart valve disease, impulse control disorders) or levodopa. SE of dopamine agonists:
      - Nausea

- postural hypotension
- psychiatric symptoms
- daytime sedation
- Side effects of levodopa: motor fluctuations, (On and Off, overflow), reduced response (wearing off), dyskinesias, neuropsychiatric toxicity (eg hallucinations)
- Levodopa Augmentation:
  - MAO-B Inhibitors [selegiline]: SE - insomnia
  - COMT Inhibitors entacapone: SE – gastrointestinal, sleep, dyskinesia
  - Anticholinergics for tremor
  - Amantadine for dyskinesias. SE - n/v headaches, oedema, erythema, and livedo reticularis
- Drugs don't affect non-motor features: balance, gait, swallow, mood, sleep disturbance, cognitive impairment, autonomic (postural instability)
- Therapy of Non-Motor Symptoms:
  - Depression – TCA/SSRI
  - Confusion - anticholinergics and amantadine should be eliminated first.
  - Psychosis – Clozapine/Quetiapine
- Surgical Treatments - Deep brain stimulation

### *Management of Myasthenia Gravis*

- Caused by antibodies to acetylcholine receptor on the post synaptic junction
- PC: Painless weakness, including chewing, speaking, swallowing, rapid fatigue, early involvement of extra-ocular muscles (diplopia and ptosis, maybe for years). No wasting. Normal reflexes. Exacerbated by infection, stress, pregnancy
- Testing: edrophonium, AntiAChR radioimmunoassay, repetitive nerve stimulation
- Investigations: CT for thymus, tests for other autoimmune disease + TFTs (either ↑ or ↓ worsens) + glucose
- Differential: Lambert Eaton (absent reflexes, ↑ response on repetition), hyperthyroidism, botulism, MND, muscular dystrophy
- Treatment:
  - Pyridostigmine (anticholinesterase) → immunosuppression (prednisone, improvement in 1 -3 months, +/- AZA +/- cyclosporin if refractory), + thymectomy if generalised (85% get improvement)
  - Crisis (eg precipitated by infection): ICU + plasmapheresis/IVIg +/- neostigmine

## **Oncology/Haematology**

### *Chemotherapy Agents*

- Direct DNA interacting agents:
  - Alkylating agents: Cyclophosphamide: haemorrhagic cystitis 2<sup>nd</sup> to acrolein (prevent with mesna), pulmonary fibrosis, alopecia, nausea, marrow suppression
  - Platinum:
    - Cisplatin: myelosuppression, nephrotoxicity, neuropathy, hearing loss
    - Carboplatin: ovarian cancer. Very myelosuppressive, less nausea
    - Oxaliplatin: Colorectal cancer: neuropathy and cold related dysaesthesia
  - Antitumour antibiotics: bleomycin: little myelosuppression, rarely pulmonary fibrosis (requires regular LFTs)
- Indirect DNA interacting agents:
  - Methotrexate: inhibits dihydrofolate reductase. High dose regimes with folinic acid rescue. Collects in 3<sup>rd</sup> spaces → prolonged myelosuppression, pulmonary toxicity, neuro and nephro toxic
  - 5-FU: diarrhoea, vasospasm (care in angina), endothelial toxicity (VTE, PE, MI), rare cerebellar toxicity
  - Capecitabine: metabolised to 5-FU. Palmar-plantar erythrodysesthesia, mucositis, diarrhoea
  - 6-Mercaptopurine: treatment of AML
  - Gemcitabine: NSCLC, bladder and ovarian. Pulmonary toxicity, thrombocytopenia.
  - Hydroxyurea: inhibits ribonucleotide reductase → S phase block
- Mitotic spindle inhibitors:
  - Spindle assembly: Vincristine: powerful vesicant, glove and stocking neuropathy
  - Spindle disassembly: Taxanes (Paclitaxel and docetaxel) in ovarian, breast, lung. Common hypersensitivity, alopecia, short duration myelosuppression

- Topoisomerase interacting agents (stop DNA uncoiling and super-coiling):
  - Active against Topo I: Irinotecan
  - Active against Topo II: Etoposide and Doxorubicin (myelosuppression, alopecia, mucositis, CHF)
- Targeted therapies:
  - Anti-VEGF (anti-angiogenesis):
    - Avastin/bevacizumab: in renal, colon, lung and breast ca (not recurrent breast). Poor wound healing, HTN, proteinuria, haemorrhage, VTE
    - Sorafenib, sunitinib. Target multiple receptor tyrosine kinases
  - Epidermal growth factor receptor family ( $\rightarrow$   $\uparrow$ angiogenesis,  $\uparrow$ cell proliferation,  $\downarrow$ apoptosis):

### *Complications of Chemotherapy Treatment*

- Depression ~ 25%
- Malnutrition
- Diarrhoea
- Mucositis
- Alopecia
- Gonadal dysfunction
- Alopecia
- Pulmonary toxicity
- Myelosuppression
- Neurotoxicity
- Nephrotoxicity
- Infection
- Nausea
- Hypercalcaemia
- Tumour Lysis  $\rightarrow$  acute urate nephropathy,  $\uparrow$ PO<sub>4</sub>  $\rightarrow$   $\downarrow$ Ca ( $\rightarrow$  tetany, arrhythmia)
- Recurrence: breast, melanoma, lung, colon and lymphoma – no evidence of the benefit of monitoring. Asymptomatic relapses are not more salvageable than symptomatic relapses

### *Management of Lung Cancer*

- Cancers of respiratory epithelium
- Screening: not proven or recommended even in high risk
- PC: clubbing (30%, HPOA in 1 – 10%), cough, phrenic nerve paralysis ( $\uparrow$ hemidiaphragm), Horner's, Pancoast's, SVC obstruction (also in NHL, mediastinal mets, non-malignant causes)
- Diagnosis;
  - Sputum: exclude TB
  - CT for staging: include liver and adrenals. Brain in small cell (10% have mets)
  - 18fluro-deoxyglucose PET scan 85% sens and spec, Standardised uptake value  $>$  2.5 highly suspicious. False negatives in diabetes, concurrent infections (eg TB) and small lesions. Main role is to guide mediastinal biopsy
  - MRI better than bone scan for mets
  - Need biopsy: different natural history's
- Treatment:
  - Surgery: contra-indications: MI in last 3 months, poor pulmonary function or pulmonary HTN
  - Metastatic disease: chemo extends survival by 4 – 6 months over supportive care
  - Supportive care: Evidence for:
    - Treatment of depression
    - Early referral to palliative care
    - O<sub>2</sub> is dyspnoea
    - Bisphosphonates for bony pain
- Small cell:
  - Doesn't cause clubbing
  - Presents centrally with early mets. Mets in 95% at diagnosis
  - Initially good response to chemo and radiotherapy but relapse, prophylactic intracranial radiotherapy
  - Limited stage: confined to one hemithorax and regional lymph nodes (one radiotherapy field)
  - Extensive stage disease: not safe for radiotherapy
- Non-small cell:
  - Mets at diagnosis in 50% squamous, 80% adenocarcinoma
  - Adenocarcinoma: exclude other primary

- TNM staging with CT and PET then surgery +/- adjuvant chemo, or radiotherapy if not surgical candidate
- Emerging evidence for VEGF (but not in squamous → ↑bleeding) and EGFR (big response in the small group with the relevant mutations)
- Treatment complications: oesophagitis, radiation pneumonitis, spinal chord injury
- Management of a solitary lung nodule:
  - Little evidence basis
  - Low risk: serial HRCT 3 monthly for 1 year, 6 monthly for 1 year then stop
  - Intermediate: PET then transthoracic FNA
  - High risk: surgery with intraoperative frozen section and → lobectomy if malignant

### *Management of Colorectal Cancer*

- Risks:
  - Hereditary:
    - FAP: AD cancer due to mutation in APC on 5q21. Cancer by 40. Treatment: proctocolectomy with anal pouch in teens. Screen family members for serum APC then genetic typing
    - HNPCC/Lynch Syndrome: Amsterdam criteria: 3 or more relatives with colon ca, one < 50 and 2 successive generations affected. < 20 polyps but accelerated transformation. Also endometrial and ovarian cancer
    - Another 20% have familial loading, gene not identified
  - Age
  - IBD
  - Small ↑ risk: smoking, obesity, T2DM,
- Prevention: Regular exercise. Small ↓ risk from HRT, regular aspirin (NNT 1250 after 10 - 20 years)
- Screening:
  - FOBT: ↓incidence after 13 years but ↑↑ colonoscopies, and false negatives
  - Colonoscopy: CT vs normal. 5 yearly colonoscopy for moderate risk
- Prognosis:
  - TNM staging. Young is worse. Preoperative ↑CEA predicts recurrence
  - Toxicity from treatment: ECOG and albumin < 30 (prospectively validated)
- Presentation: anaemia, obstructive symptoms, and if distal PR bleeding and tenesmus
- Investigations: Whole bowel colonoscopy. Risks perforation 1 in 2,000, bleeding from removed polyp, over sedation
- Treatment:
  - Not radiation for colon (used for rectal)
  - Adjuvant chemo from stage III/Dukes C. 3 year disease free survival is validated surrogate for overall survival. Folfox4 (5FU + oxaliplatin) or Capecitabine (standard of care if wouldn't tolerate folfox). Adjuvant chemo controversial for stage 2
  - Mabs: EGFR benefit a small group – those who don't have k-ras mutations – test and give to wild type k-ras only. Acne like rash correlates with efficacy. VEGF also modest improvement in survival
  - 30 – 40 have mets at diagnosis. 20% with isolated liver mets are suitable for resection. If early metastatic disease and asymptomatic, no benefit from treatment till symptomatic. EG Capecitabine, folfox
  - Screening: some evidence of survival benefit from US/CT screening, interval unclear. Stage 1 and 2: 3 monthly CEA. 3 – 5 % risk of new cancer → 3 yearly colonoscopy

### *Management of Hepatocellular Carcinoma*

- PC: decompensating cirrhosis (jaundice, variceal bleeding, ascites, etc) or found on screening
- Screening: US – but not shown to save lives
- Diagnosis:
  - Tumour markers: αFP in 50% (so not good for screening)
  - Biopsy: core preferred over FNA but ↑ risk bleeding
- Treatment: managing 2 diseases – cirrhosis and cancer
  - Resistant to chemo, and many chemo agents hepatotoxic
  - Treatment: resection, local ablation, injection, or transplant
  - Experimental: Selective internal radiation therapy
- Prevention: Hep B vaccination, interferon for Hep B

*Management of Prostate Cancer*

- Screening: PSA (free lower in cancer, also PSA velocity) – level at which to do a biopsy not defined, DRE (most cancers peripheral → palpable). Detects early cancers but doesn't differentiate between benign and lethal. DRE and PSA together still miss more cancers than they find
- Risks: family risk, SNPs found which ↑ risk, tomatoes and statins protective
- Prevention: 5α-reductase inhibitors block conversion of testosterone to DHT. Proven to ↓incidence of prostate ca over 7 years – but most prevented were benign
- Diagnosis: TRUS guided biopsy – want 12 – 14 cores for good yield. Boney mets are sclerotic
- Treatment:
  - Prostate Cancer Prevention Trial: radical prostatectomy slight ↓mortality over watchful waiting. Advised if life expectancy > 10 years. Equivalent to external beam radiotherapy but more bowel problems
  - Adjuvant therapy: Unclear whether hormonal or radiotherapy ↑OS
- Metastatic disease:
  - Treating symptom-free PSA relapse – controversial. ↑OS but ↑SE
  - Androgen depletion: ↓symptoms in 70 – 80%, small ↑OS:
    - Castration: ↓libido, erectile dysfunction, hot flushes, gynaecomastia, ↑body fat, ↓anaemia, ↓BMD
    - Testosterone lowering: GnRH/LHRH agonists (but testosterone surge so not if obstructive symptoms), estrogens (→ ↓LH → ↓testosterone), GnRH antagonists
    - Antiandrogens: receptor blockers: eg flutamide – nipple tenderness, gynaecomastia,
  - Chemical or surgical androgen depletion → will become androgen independent in time (median survival is then 10 -12 months – slight ↑OS from some chemo regimes)

*Management of Testicular Cancer*

- Never biopsy
- Non-seminomatous: 3<sup>rd</sup> decade, embryonal, secretes αFP, hCG or both. Early mets. Orchiectomy. Lower stages: intensive surveillance, chemo or RLND. High stages: chemo – cisplatin, etoposide +/- bleomycin – one or two cycles
- Seminoma: 4<sup>th</sup> decade, more indolent. αFP and βHCG usually normal. Small nodes: radiation. Large nodes: chemo

*Management of Breast Cancer*

- Risks:
  - Age > 50
  - FHx: 10 – 20% have family history but only 5% attributable to BRAC1 or 2. BRAC 1 also risk of ovarian (and prostate in male). BRAC2 ovarian only. Li Fraumeni (rare, p53 mutation). Ataxia Telangiectasia (100% risk of NHL, also breast, ovarian and GI). No evidence of screening for ovarian
  - Prior irradiation
  - Young age at menarche
  - Nulliparous and/or no breast feeding
  - HRT
  - Regular physical exercise is protective against post-menopausal breast cancer
- Screening: breast-self examination – no change in mortality. Mammogram effective but misses 10 – 20% of breast cancer. For age 40 – 49, benefit from 10 – 12 years. Age 50 – 59 25 – 30% reduction in risk of dying for breast cancer
- Diagnosis:
  - Mammography → ultrasound → biopsy. US distinguishes cysts from solid tumour. Mammography is to screen the rest of the breast before biopsy is performed
  - MRI – detects more tumours but more false positives
  - Tumour markers: CA 15.3 and 27.29
- Treatment:
  - Lumpectomy (if < 5 cm, don't involve the nipple and single quadrant) +/- mastectomy same as mastectomy +/- radiation – higher recurrence but 10 yr survival the same
  - Sentinel node biopsy. If positive then axillary clearance for prognostic purposes
  - Adjuvant chemo: 30% relative risk reduction

	Node negative		Node positive	
	HR+	HR-	HR+	HR- (nasty)
Pre-menopausal	Hormone	Chemo 1 <sup>st</sup> – 2 <sup>nd</sup>	Chemo	Chemo: 2 <sup>nd</sup> – 3 <sup>rd</sup>

	?chemo (?main benefit early menopause) ?Ov suppression (GnRH analogue)	generation	Hormone ?Ov Suppression (controversial)	generation
Post-menopausal	(best prognosis) Hormone	Chemo 1 <sup>st</sup> – 2 <sup>nd</sup> generation	Hormone ?chemo	Chemo: 2 <sup>nd</sup> – 3 <sup>rd</sup> generation

- Chemo usually anthracycline (eg doxorubicin with cyclophosphamide) + taxane (eg paclitaxel)
- Neo adjuvant in locally advanced disease → downstage to breast conserving
- Adjuvant hormone therapy:
  - Aim: ↓ oestrogen activity in breast, uterus and ovary, ↑ in bone and CVS
  - Tamoxifen: SERM. If ER positive. No benefit beyond 5 years. SE not effective in 2D6 poor metabolisers. Not with 2D6 inhibitors (eg paroxetine). Hot flushes, small ↑ endometrial ca, stroke, PE and cataracts. ↑ bone density.
  - Aromatase inhibitors: block conversion of androgens to oestrogen in post menopausal women. Must be ER +ive. ↑ risk osteoporosis, diarrhoea, arthralgias, cataracts
  - Herceptin (trastuzumab): EDRF receptor inhibitor → ↓ cell cycle progression. Only in node positive. SE infusion related fevers/chills. Care in CHF
- Non-invasive malignancies:
  - Ductal carcinoma in situ (now ductal intraepithelial neoplasia): 1/3 will develop invasive cancer within 5 years. Lumpectomy + radiation. Tamoxifen helps
  - Lobular intraepithelial neoplasia. Not a pre-invasive lesion. Marker of increased risk

### Management of Anaemia

- Fe deficiency:
  - Ferroportin negatively regulated by hepcidin (deficient in most haemochromatosis)
  - Losses: GI (ulcers, gastritis, malignancy, diverticulitis), menstruation, diet, poor absorption
  - Labs: ↓Fe, ↑transferrin (↓ in chronic disease)
- B12 deficiency:
  - Problem anywhere in the absorption process, most commonly pernicious anaemia. Test IF and parietal cell antibodies.. Also consider diet, gastrectomy, Crohn's disease, uncommonly in PPIs.
  - No consensus or gold standard for diagnosis. Can measure methylmalonate
- Haemoglobin disorders:
  - α-thalassaemia: H bodies in Haemoglobin H disease (αα-). Due to gene deletions
  - β-thalassaemia: mutations → phenotypic spectrum (β+ or β0) → ↓HbA but not HbA2. Splenomegaly if ↑ transfusion requirement. Test with high performance liquid chromatography
  - Sick Cell Anaemia: Mutation in 6<sup>th</sup> amino acid on β-globulin chain. If βsβs then severe haemolytic anaemia with painful venoocclusive crisis
- Haemolytic Anaemias:
  - PC: pallor, jaundice, urobilinogen, splenomegaly, skeletal changes if congenital
  - Labs: **blood film**, reticulocytes, LDH, haptoglobin, **bilirubin**/LFTS, +/- Combes
  - Intravascular causes:
    - Red cell fragmentation: TTP and HUS, mechanical, toxic (eg cisplatin, lead poisoning)
    - Paroxysmal nocturnal haemoglobinuria: intermittent coca cola urine. Acquired deficiency of PIG-A gene → ↓CD59 and CD55 (test with flow cytometry)
    - Paroxysmal cold haemoglobinuria: kids or 2<sup>nd</sup> to syphilis
  - Extravascular causes:
    - Immune mediated: Combes test:
      - Warm AIHA: IgG. Idiopathic or second to autoimmune disease, lymphoproliferative disease, infection, drugs (penicillin, cephalosporin). Treatment. Prednisone effective in 50%, may need more immunosuppression, splenectomy if persistent, ?rituximab
      - Cold c3b, IgM: Cold Agglutinin Disease: IgM antibody related to Waldenstrom macroglobulinaemia. Do PEP. Rituximab promising
      - Mixed (eg SLE) IgG and c3b
    - RBC membrane defects: spherocytosis
    - RBD enzyme defects: G6PD (X linked, bite and blister cells and Heinz bodies)
    - Haemoglobinopathies
- Complications of haemolytic anaemia:
  - Fe deficiency if intravascular

- Fe overload if extravascular (both from ineffective erythropoiesis or transfusional overload). Chelation with desferoxamine. Poor compliance. Oral chelators now available
- Bone marrow suppression during acute inflammatory illness, including plastic crisis (eg parvovirus B19)
- Gallstones
- Folate deficiency
- If splenomegaly then → thrombocytopenia/neutropenia

### *Management of Bone Marrow Failure Syndromes*

- Aplastic anaemia:
  - Mostly idiopathic. Also radiation, drugs (eg chloramphenicol), viruses, immune mediated (thymoma, Graft vs Host)
  - BM: fat on aspirate, ↓CD34 stem cells
- Pure red cell aplasia: idiopathic (responds to prednisone) or acquired (thymoma, CTD, Parvovirus B19, EPO)
- Myelodysplasia: clonal disorder → ↑apoptosis → bone marrow failure. Fever and weight loss suggest a myeloproliferative process. Refractory to treatment. Thalidomide good in MDS with isolated del 5q

### *Management of Myeloproliferative diseases*

- Education:
  - Explain disease
  - Risk of transformation to AML
- Complications:
  - Hyperviscosity: vertigo, tinnitus, headache, visual disturbances, TIA
  - Systolic HTN
  - Venous or arterial thrombosis: cerebral, cardiac, mesenteric, hepatic vein
  - Vascular stasis: digital ischaemia, epistaxis, GI haemorrhage
  - Gout
  - Pruritis: increase cytokines and histamine release
  - Splenic infarction
  - Myelofibrosis
  - AML: risks - ↑ age, exposure to chemo/radiotherapy. Poor cytogenetics. Poor response to treatment
  - Aspirin: caution - ↑ risk haemorrhage secondary to acquired vWD
- Polycythaemia Vera:
  - Exclude dehydration, hypoxia, renal artery stenosis, drugs (eg EOP)
  - PC: splenomegaly, hyperviscosity, HTN, VTE, ↓EPO
  - Treatment: phlebotomy to induce Fe deficiency. Allopurinol. Hydroxyurea. Splenectomy if necessary
- Essential thrombocytosis:
  - Symptomatic treatment
  - Caution with aspirin: TIA, CVD risk
  - Rarely: hydroxyurea/interferon to bring count down
- Myelofibrosis:
  - Polyclonal proliferation of fibroblasts, extramedullary erythropoiesis
  - PC: may include night sweats and weight loss
  - Labs: ↑ALP and LDH, Osteosclerosis on xrays, cytogenetics to exclude CML Hydroxyurea to control splenomegaly. Allogenic bone marrow transplant if young
  - Treatment:
    - Symptomatic
    - Splenectomy, splenic irradiation
    - Allogenic transplant
- Chronic Myeloid Leukaemia:
  - ↑ number of full spectrum of myeloid cells
  - PC: ↑neutrophils, ↑platelets and anaemia
  - Labs: Philadelphia chromosome positive – t(9:22) translocation → BCR-ABL
  - Inevitable transition to AML (sometimes ALL)
  - Treatment: imatinib (in the past have used hydroxyurea, allogenic transplant, IFN-α). Splenectomy if symptomatic and treatment resistant. Emergency leukapheresis

### *Management of Acute Myeloid Leukaemia*

- Median age 60
- PC: splenomegaly, hepatomegaly, lymphadenopathy, sternal tenderness. Maybe gum/skin infiltration
- Labs: WBC may be  $< 5$  or  $> 100$ . Often  $\downarrow$ platelets. Check clotting. Blood film (Auer rods), bone marrow, flow cytometry, cytogenetics
- Classification: WHO and FAB
- Small percentage are secondary: trisomy 21, myeloproliferative syndromes, radiotherapy with alkylating agents (after ~ 5 years) or topoisomerase 2 inhibitors (after 1 -2 years)
- Treatment:
  - Assess for infection
  - Replace blood components
  - Monitor urea
  - Induction: Cytarabine (s-phase antimetabolite), intensified with etoposide. Aim to achieve normal marrow
  - Consolidation: cytarabine, autologous SCT or high dose combination chemo with allogeneic SCT
- APL:
  - t(15:17) translocation. Can present with DIC and pancytopenia.
  - Induction: anthracycline + ATRA  $\rightarrow$  induces differentiation (SE ARDS like syndrome)

### *Management of Acute Lymphoid Leukaemia*

- Mainly kids and young adults (biologically a different disease)
- Risks: Trisomy 21 and radiation
- Labs: must include LP to exclude CNS involvement
- Classification: main one is T-cell, mature B-cell or B-cell precursor
- Induction (anthracycline, prednisone, vincristine)  $\rightarrow$  consolidation  $\rightarrow$  intensification  $\rightarrow$  maintenance  $\rightarrow$  +/- allotransplant – complex schedule over 12 – 24 months

### *Management of Chronic Lymphoid Leukaemia (CLL)*

- Usually mature B cell
- PC: asymptomatic, lymph nodes or immune problems
- Investigations:
  - Labs: FBC, major organ function, bone marrow
  - AIHA in 15 – 30%: consider Coombs, LDH, uric acid, calcium
  - Blood film: smudge cells
  - Prognosis: LDH and  $\beta$ 2microglobulin
  - Cytogenetics: some prognostic information (eg ZAP70)
  - CT to exclude lymphadenopathy (worsens prognosis)
- Complications: anaemia 2<sup>nd</sup> to marrow infiltration, autoimmune or hypersplenism
- Rai and Binet staging systems
- Management:
  - Treatment  $\rightarrow$  remission (complete response + molecular remission)  $\rightarrow$  relapse. Cure very rare
  - Only marrow involvement and  $\uparrow$ lymphocytes: median survival 10 years. Observe
  - Bone marrow failure: median survival 1.5 years. Treat:
    - Chlorambucil for 2 -4 months and/or fludarabine (purine analogue) +/- predmospme +/- rituximab
    - Other regimes: CHOP or CVP
    - Anti-CD52
  - Consolidation difficult

### *Management of Lymphoma*

- Presentation: painless, rubbery lymph nodes, hepatosplenomegaly, night sweats, weight loss, fatigue, involvement of skin, CNS, GI, salivary glands
- Differential: reactive atypical lymphoid hyperplasia: drugs (eg phenytoin), RA, SLE, CMV, EBV
- Education:
  - A type of cancer
  - HL cure rate ~ 75%, NHL cure ~ 40%. HL spreads node to node, NHL spreads to any node in the body
  - Chemo and complications
  - Use of blood products and risks
  - Involve Cancer Society

- Staging:
  - Bloods: FBC, ESR, major organ function, uric acid, Ca, HIV (risk factor for HL), LDH,  $\beta$ 2microglobulin, PEP
  - Biopsy
  - CT
  - BM
  - Echo prior to anthracyclines
  - PET of some use in assessing response to treatment in aggressive NHL
- Staging systems:
  - Ann Arbor in NHL, including A for no systemic symptoms, B if symptoms
  - NHL: international prognostic index – age, serum LDH, performance status, Ann Arbor III or IV, > 1 site of extranodal involvement
- Treatment:
  - NHL:
    - Low grade: Radio therapy +/- CVP (cyclophosphamide, vincristine, prednisone) +/- rituximab
    - Higher grade: CHOP (= CVP + adriamycin) +/- rituximab
    - Types:
      - Follicular: indolent. Median survival 8 – 10 years. 5% pa transformation to diffuse large B cell. Treatment: may observe. Stage 1 and 2: radiotherapy
      - Diffuse Large B cell (most common). Bad. CHOP \* 6 + rituximab (now proven) +/- involved field radiotherapy
      - HIV lymphoma: EBV associated. Treat as for NHL. Dose reduction often required
    - HL: Radiotherapy +/- ABVD (adriamycin, bleomycin, vincristine, dacarbazine)
    - Rituximab: optimal dose not established. Infusion related chills/nausea. Rare bronchospasm and hypotension. Tumour lysis
    - Autologous stem cell transplant – can't do it in refractory disease – needs to be chemo responsive to give induction chemo
  - Allied health: coping strategies
  - Complications:
    - Myelosuppression
    - Infection with attenuated responses → check temperature
    - Infertility, esp if total body irradiation
    - 2<sup>nd</sup> malignancy: solid malignancy, acute AML, squamous cell (skin, cervix)
    - Radiotherapy: hypothyroidism and premature IHD. Aggressive treatment of risk factors. Lhermitte's syndrome in 15% (electric shock on neck extension, also in MS, spinal chord tumours)
  - Prevention: mammogram and cervical smears

### *Management of Stem Cell Transplant*

- Conditioning regime:
  - Eradicate tumour and immunosuppress host to permit engraftment
  - Complications:
    - Early: mucositis, hairloss, profoundly neutropenic, venoocclusive disease
    - Late:
- GVHD: Inversely proportional to relapse
  - Acute: rash, diarrhoea,  $\uparrow$ LFTs – needs biopsy. Treat with steroids, anti-thymocyte globulin, anti-T monoclonal antibodies
  - Chronic: resembles an autoimmune disease: malar rash, sicca symptoms, arthritis, BOOP. Treat: prednisone. Usually settles over time

### *Management of Myeloma*

- Differential of paraproteins:
  - MGUS: survival 2 years shorter than age matched controls. 1% pa transformation to MM
  - Myeloma
  - Waldenstroms (IgM): epistaxis, visual disturbances, neurologic symptoms more common. IgM interferes with clotting factors → INR and APPT
  - Primary amyloidosis
  - Rarely Lymphoma
- Incurable except rarely by autotransplant (in highly selected patients)
- Myeloma: > 20% marrow plasma cells
- Presentation:

- Hypercalcaemia: lytic lesions and bone pain. Doesn't show up on bone scan
- Renal failure: due to high calcium, light chains causing cast nephropathy, amyloidosis, urate nephropathy, NSAIDs for bone pain, recurrent infection
- Fatigue/anaemia
- Also recurrent infections and neurological symptoms, hyperviscosity
- Workup:
  - Bloods: PEP, Igs, serum free light chains (may save a BM), ALP usually normal (little osteoblast involvement)
  - Bone Marrow: cytogenetics for prognosis
  - MRI for bone involvement. PET not established
  - Prognostic markers: serum  $\beta$ 2microglobulin (can substitute for staging), albumin, LDH, CRP, cytogenetics
- Treatment:
  - 10% indolent: treat when symptomatic
  - Melphalan (nephrotoxic, alkylating agent, toxic to stem cells) + prednisone
  - Thalidamide + dexamethasone: cyto-reduction in 2/3rds SE constipation, painful neuropathy, DVT
  - SCT if under 65, doubles survival but doesn't alter cure. Induction  $\rightarrow$  autologous transplant  $\rightarrow$  maintenance prednisone
- Supportive:
  - Pamidronate:  $\downarrow$ decreases skeletal progression and bone pain. Ca and vit D suggested not proven
  - Radiotherapy
  - Plasmapheresis effective but controversial
  - Pneumococcal vaccines

### *Differential of Thrombocytopenia*

- Bone marrow damage: Drugs (acyclovir, amiodarone), MDS, hep C, alcohol
- Immune:
  - ITP: chronic in adults, acute in kids. Mucosal bleeding. Check retina. Associated with AIHA, CLL, RA, SLE, drugs. BM only if elderly or unusual features. Exclude HIV, Hep C, SLE, do PEP and Ig levels, and Combes if anaemic. Treatment: prednisone. IVIg is severe. Rituximab. Splenectomy.
  - Heparin: platelets don't drop below 20, thrombosis risk. Antibody to platelet factor 4 and heparin. Switch to fonaparinux
  - Also HIV, CMV, Hep C, CMV, mycoplasma
- DIC
- Thrombotic Thrombocytopenia Purpura: haemolytic anaemia, very low platelets, neurologic manifestations. Deficiency of, or antibodies to ADAMTS13 which cleaves vWF multimers  $\rightarrow$  endothelial damage  $\rightarrow$  microangiopathic haemolysis. Coagulation and fibrinogen normal (cf DIC)

## **Infectious Diseases**

### *Management of Tb*

- Droplet transmission
- Risk factors: HIV, post-transplant, jejunioileal bypass, dialysis, immunosuppression
- Presentations:
  - Primary TB: kids < 4 and immunocompromised
  - Secondary/post-primary/latent TB
  - Extra pulmonary disease: lymph nodes, pleural, genitourinary, skeletal, meningitis
- Investigation:
  - Sputum, gastric lavage, CSF, no serology
  - Diagnosis of latent:
    - Tuberculin skin testing (Mantoux): lacks species specificity, subjective interpretation, can't differentiate between latent and active, false negatives if immunocompromised
    - Quantiferon Gold Assay/IFN $\gamma$  release assays – better correlation in low incidence settings, works OK in immunocompromised
- Treatment:
  - Combination therapy. Most common cause of failure is poor compliance
  - 2 month bactericidal phase  $\rightarrow$  longer sterilising phase
  - Isoniazid: Rash 2%,  $\uparrow$ LFTs in 20%, hepatitis in 1%. Only monitor if at risk or abnormal LFTs. Good CSF penetration

- Rifampicin: rash 0.8%, flu-like symptoms, transient ↑LFTs, haemolytic anaemia 1%. Lots of interactions
- Pyrazinamide: small risk liver toxicity, hyperuricaemia. Lowest safety profile in pregnancy
- Ethambutol: neuritis → ↓visual acuity. Not in little kids given difficulty of testing vision
- 2<sup>nd</sup> line: flouroquinolones
- Immune reconstitution reaction – in HIV, steroid txt proven in meningitis and maybe pericarditis
- Treatment of latent TB → reduce risk of active disease Isoniazid for 9 months or rifampicin for 4 months

## HIV

- History:
  - When, how and why diagnosed
  - Risk factors (currently having unprotected sex?), ↑ risk with concurrent STD, IVDU (key in western heterosexual spread), maternal transmission (20 - 30 %),
  - Other comorbid diseases: STIs, Hepatitis, syphilis
  - Diagnosis: HIV EIISA then Western Blot, HIV plasma viral load testing
  - Baeline testing:
    - FBC, U&Es, BSL, lipids, LFT, CK, amylase
    - Infection: syphilis, Hep A, B, C, toxoplasmosis, CMV
    - Cervical screening
    - Mantoux, CXR, ECG, MMSE
  - Complications:
    - Infectious
    - Autoimmune: often early, eg GBS, CIDP, sjorgren's
    - AIDS defining illnesses: candidiasis, cervical cancer, cryptococcosis, CMV, prolonged herpes simplex, lymphoma, Tb, PJP. US defn includes CD < 200, Australian doesn't
    - Liver disease: 3<sup>rd</sup> deaths due to this. Hep B/C coinfection common
    - Other: bone marrow suppression, neurologic (infections, neoplasm, due to HIV), wasting
  - Current:
    - Quality of life
    - Constitutional symptoms: weight loss, sweats, etc
    - CD4 count/viral load
  - Treatment
    - Treatment, past changes and the reason (? Resistance)
    - Compliance
    - Treatment complications (esp mucocutaneous as these are socially distressing)
  - Thought about long term prognosis
- General treatment:
  - Education: infection risk, importance of compliance
  - EPOA
  - Contact tracing
  - Immunisation: Hep B, Hep A, influenza (not in egg allergy), s pneumonia before count < 200, HPV. Never BCG or oral polio. ?Varicella and MMR if CD > 200
- Treatment principles:
  - Initiate if acute HIV, all pregnant women, symptomatic disease, asymptomatic disease and CD count < 200 – 350
  - Routine start pack in NZ: Efavirenz (NNRTI, rash, drowsiness, dreams, depression, teratogenic, interferes with methadone), tenofovir (nucleotide RTI, renal toxicity) and lamivudine (NRTI, hepatotoxicity). Newer NRTI sparing regimes...
  - Watch for immune reconstitution syndrome. Treat opportunistic infections first
  - Drugs:
    - RTIs: block RNA dependent DNA synthesis. Hepatic steatosis and lactic acidosis NNRTI don't have mitochondrial side effects
    - Protease inhibitors: lipodystrophy: fat redistribution, ↑ lipids, ↑BSL. Augment with ritonavir
    - Entry inhibitors: CCR5 inhibitors – injections reactions in nearly 100%
    - Integrase inhibitors: block integration into host genome. Safe and potent
  - Prophylaxis:
    - Cotrimoxazole for PJP when count < 200
    - Azithromycin for MAC when count < 50
    - Cryptococcus, toxoplasmosis and CMV if prior disease

- TB if infection or close contact
- Treatment complications:
  - Lipodystrophy. Pravastatin
  - Drug interactions
  - Also ↑MI, hepatotoxicity (multifactorial)
- Resistance: viral load repeatedly detectable despite treatment
  - Role of resistance testing not established
  - HIV-2 (West Africa, India) intrinsic resistance to non-nucleoside RTI
  - CCR5 virus → CXCR4 over time

## Transplant

- Contraindications:
  - Alcoholism and compliance issues
  - Smoking
  - HIV/active infection
  - Other organ failure
  - Malignancy
  - Advanced age (relative)
  - BMI >130 or <70% (relative)
  - Osteoporosis (relative)
  - Diabetes mellitus (relative)
- Investigations
  - ABO, HLA typing
  - UEC, LFTs, FBC, Coags
  - Fasting lipids and glucose
  - CXR and lung function tests
  - Cardiac work up- ECG, echo, (angio)
  - DEXA scan
  - Swabs for MRSA
  - Mantoux test
  - Hep A,B,C, toxoplasmosis, CMV, EBV, HIV, HSV, VZV
  - Dental check
  - SW and psych consult
- Transplant History
  - Cause of organ failure
  - Symptoms – before and after
  - Time on waiting list/time since transplant
  - Prophylaxis – PCP, CMV, pneumonia, anti-fungal
  - BP and cholesterol control
  - Malignancy – screening
  - Investigations – before and after
  - Complications – post-op, early and late
- Complications:
  - Immunosuppression:
    - Infection
    - Cancer – skin, PTLN, solid organ
    - Drug side effects
  - Rejection
  - Recurrence of disease
- Transplant Exam:
  - ?Cushingoid
  - BP
  - Candida
  - Scar and wound healing
  - Evidence of infection, recurrence, malignancy, rejection
- Issues fodder: talk about ethical issues given organ shortage:
  - Issues of increasing supply:
    - Taking organs without family consent if patient has agreed

- Selling organs: would increase supply but commodification of organs, incentives for those with occult badness to sell them, victimising of the poor by the rich
- Issues of organ donation in Maori communities – esp cadaveric transplants where the organ is tapu
- Issues of allocation:
  - Who do you give an organ to – next in the line, most able to benefit (eg do you discriminate on grounds of age or other comorbidities), who decides, etc
  - Conflict for a doctor between advocating for a patient and having to decide between patients
  - Issues of paternalism vs autonomy: Making decisions for patients (eg won't give you a new liver because you might continue using IV drugs)
- In stem cell transplants, “saviour siblings” – turning people into commodities, etc

	<b>Indication</b>	<b>Contraindications</b>	<b>Investigations</b>	<b>Prognosis</b>
<b>Heart</b>	<ol style="list-style-type: none"> <li>1. Refractory end-stage heart failure</li> <li>2. Arrhythmia</li> </ol>		<ol style="list-style-type: none"> <li>1. EF by gated blood pool scan.</li> <li>2. Angio and R) heart catheter with reversibility testing</li> <li>3. 24 holter</li> <li>4. Cardiac biopsy</li> <li>5. Fe studies</li> <li>6. Serology (coxsackie, echovirus, adenovirus, influenza)</li> </ol>	<p>1yr – 90% (infection)  5yr – 75% (IHD)  10yr – 50%</p> <p>If stenosis &gt;40% then 2yr = 50%. Once MI occurs 2yr = 10-20%.</p>
<b>Lung</b>	<ol style="list-style-type: none"> <li>1. COPD – FEV1&lt;25%, PaCO2 &gt;55mmHg</li> <li>2. CF – FEV1&lt;30% or haemoptysis, cachexia or PaCO2 &gt;50 PaO2&lt;55</li> <li>3. ILD – VC, DLCO&lt;60%</li> <li>4. Pulm HTN – NYHA III/IV, PaO2&lt;60, pressure&gt;55mmHg</li> </ol>	<ol style="list-style-type: none"> <li>1. Atypical Tb infection</li> <li>2. Age &gt;65 (unilateral)</li> <li>3. Age &gt;60 (bilateral)</li> <li>4. Age &gt;55 (heart+lung)</li> </ol>		<p>1yr – infection (CMV, pseudomonas, aspergillus)  5yr – bronchiolitis obliterans in &gt;50% (major late cause of death, Starts after 2yrs)</p>
<b>Kidney</b>	<ol style="list-style-type: none"> <li>1. Stage 5 CRF</li> </ol>			<p>1yr graft survival &gt;90% (acute rejection)  20yrs = 50% if completely matched.  Late graft loss = CAN  Late death = CVS disease</p>
<b>Liver</b>	<ol style="list-style-type: none"> <li>1. MELD score</li> <li>2. Child-Pugh &gt;6</li> <li>3. Episode of variceal bleeding, SBP or stage II encephalopathy in acute failure</li> <li>4. HCC</li> </ol>	<ol style="list-style-type: none"> <li>1. Portal vein thrombosis</li> </ol>	<ol style="list-style-type: none"> <li>1. US and CT scan to determine anatomy and exclude HCC</li> <li>2. ERCP to determine biliary anatomy</li> </ol>	<p>1yr – 85% (infection)  5yr – 60%</p>

## Integrative Topics

- Differential of fatigue/weight gain:
  - Anaemia
  - Depression
  - Drugs
  - Hypothyroidism
  - OSA
  - Cushing's
  - PCOS
  - Pregnancy
  - Chronic disease
  - Chronic fatigue

### *Management of Falls*

- Background: Only 2% falls result in a #NOF, 5% in any # (but 40% NOFs are from rest homes)
- History:
  - Past falls
  - Fear of falling
  - Syncope
- Risk factors:
  - Age
  - Cognitive impairment
  - Weakness (eg disuse from arthritis, balance problems)
  - 4 or more medications of psychotropic medications
  - Arthritis
  - Past stroke (no such thing as "no residual symptoms")
  - Dizziness, postural drop
  - OA: risk of injury from falls
  - Environment: probably not a strong contributor
- Exam: vision, postural drop, gait, balance, sensory, strength, joint stability
- Investigations:
  - Geriatric bloods: ↓Cr, ↑PTH and ↓Vit D are independent risk factors for falling
  - ECG: ?arrhythmia
  - Head CT if indicated
  - CK if prolonged lie on the ground
  - Bone Protection: DEXA scan, Ca, Vit D and ALP
- Prevention:
  - Best evidence is from multiple risk factor interventions
  - Exercise: supervised muscle strengthening and balance retraining, Tai Chi
  - Home hazard assessment by a trained person, only evidence for secondary not primary prevention
  - Vit D supplements, with or without Ca – soft evidence → ↓fractures and ↑ strength
  - Stop psychotropic drugs: John Campbell's study: 66% reduction in falls in intervention group, 46% resumed psychotropics after one month
  - Cochrane 2004: best interventions → ↓20% RRR, ↓9% ARR, NNT to prevent one fall of 11
  - Bone protection
- Unknown effectiveness: correcting visual deficiency, walking stick (no RCT), giving them a list of exercises (→ ↑falls). No evidence that ↓ falls → ↓fractures. Hip protectors don't work

### *Diagnosis of Depression*

- Consider in every chronic disease. It's they don't have it, say you screened for it and there were no current signs, but you'd continue to monitor
- Handy mnemonic:
  - S:** Sleep
  - A:** Appetite and weight
  - D:** Dysphoria and anhedonia
  - F:** Fatigue
  - A:** Agitation/retardation
  - C:** Concentration

E: Esteem

S: Suicide

- 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:
  - Depressed mood, most of the day, nearly every day (either self report or observed by others)
    - Markedly diminished interest or pleasure in all, or all most all, activities (exclude grief reaction)
    - Significant weight loss/gain or ↓/↑ in appetite (exclude cancer, Tb, hypothyroid)
    - Insomnia/hypersomnia nearly every day (exclude sleep apnoea)
    - 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?
    - Fatigue or loss of energy nearly every day
    - 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?
    - Diminished ability to think or concentrate, or indecisiveness, nearly every day
    - 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. Eg what difficulties have all these symptoms caused?
  - Exclude depression if symptoms:
    - Are due to physical illness, medication or street drugs
    - 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
- Also review risk factors:
  - 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

### *Managing Insomnia*

- Sleep history:
  - Pattern of sleep
  - Adequacy of sleep: wake refreshed, daytime somnolence
  - Partner's sleep pattern, corroborative history
- Exclude secondary causes:

- Medical: eg CHF, pain, polyuria, SOB, reflux, OSA, restless legs
- Psychiatric: anxiety, depression
- Medications: decongestants, diuretics, antidepressants, alcohol, caffeine, nicotine
- Sleep diary
- Sleep hygiene:
  - Reduce light, noise and extremes of temperature
  - Ensure physical security
  - Avoid caffeine, nicotine and alcohol before bedtime
  - No heavy meal for 2 hours beforehand, but have a light snack if hungry
  - Regular exercise last in the afternoon/early evening, but nothing vigorous for 3 hours beforehand
  - Allow one hour of quiet activity before bedtime (reading, TV, music)
  - Develop a bedtime ritual, cleaning teeth, reading, etc
  - Don't go too early (ie before you feel sleepy)
  - Don't stay in bed if you are awake. If not asleep within 15 – 20 minutes (estimate – don't use a clock), get up, go elsewhere and do something mundane until you feel sleepy again
  - Get up at the same time in the morning: don't sleep in in weekends or after late nights. This helps train your body clock
  - Don't nap during the day
  - Don't worry if you can't get to sleep at night: worry will delay sleep even more
- Hypnotics only for temporary insomnia

### *Managing compliance/polypharmacy*

- Issues in the elderly:
  - Comorbidities that impact on prescribing: renal failure, ↓hepatic blood flow → ↓clearance, ↓lean body weight, impaired homeostatic response
  - Evidence: most trials exclude the elderly and those with comorbidities
  - Adverse reactions more common
- Strategies to reduce polypharmacy:
  - Single prescriber, single dispenser
  - Medication Review (Cochrane 2006):
    - Clinical pharmacist review: RCT showed ↓ reduction in medications without change in outcome
    - Pharmacist education
- Non-compliance is multi-factorial:
  - Rapport with doctor
  - Not knowing how to take them
  - Not understanding their importance
  - Anticipation or experience of side effects
  - Forgetfulness
  - Impaired physical function
- To improve compliance (concordance is a better term – do the doctor's and patients agendas align)
  - Determine understanding of their illness and treatment
  - Education:
    - About drugs and side effects
    - Provide written information: spoken instructions are quickly forgotten
  - Involve carers
  - Prescribe the least complex schedule
  - Use daily routines as a medication prompt
  - Drug diaries/medication charts
  - Dose-dispensers/blister packing, large print labels
  - Return or destruction of old drugs
  - Monitor response
- Drug interactions:

	Substrate	Inhibitor	Inducers
CYP3A4/5 No PM's identified Chromosome 7	CCB: diltiazem, felodipine, nifedipine, verapamil Antiarrhythmics: lidocaine, quinidine Carbamazepine (??)	CCB: Verapamil, Diltiazem (NB also substrates) Amiodarone Azoles: Ketoconazole & Itraconazole	Rifampicin Anticonvulsants: Carbamazepine, Phenytoin ART: Efavirenz,

	<p>Statins: Simvastatin (?), atorvastatin (not pravastatin)</p> <p>Macrolides: clarithromycin, erythromycin</p> <p>Cyclosporin, tacrolimus</p> <p>NRTI and PIs</p> <p>Midazolam</p> <p>Losartan</p> <p>Sildenafil</p> <p>Warfarin (r-enantiomer – less clinical relevance)</p> <p>Oestrogen</p> <p>Methylprednisone</p> <p>Cisapride was withdrawn because of Torsade with concurrent inhibitors</p>	<p>Macrolides: Erythromycin, clarithromycin NB also substrates (not azithromycin)</p> <p>Ritonavir</p> <p>Large quantities of grapefruit juice</p> <p>Fluoxetine (small effect, nil from paroxetine)</p>	<p>nevirapine</p> <p>St John's Wort</p> <p>Chronic alcohol</p> <p>Dexamethasone</p> <p>Activate PXR (nuclear receptor) which binds to the CYP3A4 promoter</p>
<p>CYP2D6*</p> <p>PM in 7% Europeans &amp; Africans</p> <p>1% UM</p>	<p>Betablockers: Metoprolol, carvedilol, propranolol, timolol (→ systemic β blockade if inhibited)</p> <p><i>Codeine</i></p> <p>Flecainide (also renally excreted, so little impact)</p> <p>TCA: Nortriptyline, amitriptyline (in part)</p> <p>Fluoxetine, paroxetine</p> <p>Simvastatin (note also 3A4)</p> <p>Haloperidol</p> <p>Venlafazine</p> <p><i>Tamoxifen</i> (transformed to active metabolite)</p>	<p>Quinidine (even a ultra-low doses)</p> <p>TCA: Clomipramine</p> <p>Fluoxetine, (larger effect, but ?clinical significance), trace from paroxetine, (NB also substrates)</p> <p>Neuroleptics: chlorpromazine &amp; haloperidol</p>	
<p>CYP2C9*</p> <p>1 – 3% PM</p> <p>Little expression at birth</p> <p>Chromosome 10</p>	<p><i>Warfarin</i> (S-enantiomer – which has the greatest anticoagulant effect – PM's require only ~ 1mg/d)</p> <p>Phenytoin</p> <p>Glipizide</p> <p>Losartan (transformed to active metabolite)</p>	<p>Amiodarone</p> <p>Fluconazole, miconazole</p> <p>Celecoxib</p> <p>Cimetidine and omeprazole impair R-enantiomer of warfarin → less effect</p>	<p>5' regulatory region has an PXR-RXR element, so CYP3A inducers also induce CYP2C9 (→ warfarin effect)</p>

- = Clinical significant genetic variants described

#### *Ethical Issues given Resource Limitations*

- Taken from NZ Medical Council Statement on safe practice in an environment of resource limitation
- Eg Discussions about patients who have a high cost of care
- Principles:
  - Care of the patient is first concern
  - Responsibility to provide the best care within the resources available
  - Resource limitation is a reality
  - Doctors have a responsibility to the population at large for the proper use of resources and must balance this duty of care with the duty of care to the patient
  - In all roles, doctors should use evidence from research and audit to make best use of the resource
  - This implies doctors will make and communicate prioritisation judgements to patients and populations for whom they have a duty of care
- Application to practice:
  - Doctors should support research and discussion so that resource use is rational
  - Should try not to acutely withdraw treatment due to resource limitation, take care the discharges to create beds are not left unsupported, and patients should be informed of the reasons for decisions
  - A service should only offer treatment that it is able to deliver (eg outpatient appointments)
  - Prioritisation systems should be fair, systematic, consistent, evidence based and transparent

- When a potentially beneficial service is not funded:
  - Doctors should inform patients it is in their interests
  - Doctors should outline the rationale for the treatment being limited
  - Doctors should not allow their financial interests, nor those of their employer, to override their responsibility to patients
- Excessive workloads: Doctors should not put their own health at risk

## General Short Case

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- Check comfort
- Position and expose
- Inspect
- Exam
  
- State findings. “These are consistent with ....” Eg these findings are consistent with an extrapyramidal disorder, the differential of which is .....” Don’t say “this is so-and-so”
- Differential
- State:
  - What aspects of history would be useful and why
  - I would examine .... for further features of ....
- Investigations
- Management (if time)
  
- Tips:
  - Never make up a sign – you’re digging yourself a big hole. Can say “I would have expected a collapsing pulse given aortic regurgitation, but the pulse was of normal character”
  - If unsure (ie is there clubbing) say “equivocal – I don’t think the sign is clearly present but it is not normal”
  - If a Maori person, ask if it’s OK to touch their head before doing so

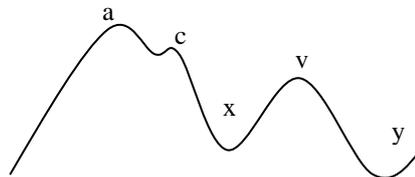
## General Cardiovascular Exam

- General inspection
- Hands:
  - right & left radial pulses
  - clubbing
  - signs of infective endocarditis: splinters, Osler's nodes (red raised nodules on the pulps of fingers), Janeway lesions, non-tender red macular-papular lesions containing bacteria
  - Cyanosis
  - xanthomata – eg affecting tendons on dorsum of hand
- **Pulse – bilaterally, is it regular? Character**
- **Collapsing Pulse**
- **Blood pressure**
- Face:
  - Eyes:
    - Cornea (arcus cornea),
    - Sclera (pallor, jaundice)
    - Pupils (Argyll Robertson, small, irregular, react to accommodation, not light – aortic regurgitation, also syphilis and rare in diabetes)
    - Xanthelasma – xanthoma affecting the eye lids
  - Malar flush (mitral stenosis, pulmonary stenosis)
  - Mouth: cyanosis, high arched palate (Marfan's), dentition
- Neck:
  - JVP:
    - Examine *then palpate, obstruct, position and hepato-jugular reflex*. If elevated > ear lobe, raise arm and check basilic vein
    - Elevation in RVF, TS or TR, pericardial effusion or constrictive pericarditis, SVC obstruction, fluid overload, hyperdynamic circulation (fever, anaemia, thyrotoxicosis, pregnancy, exercise, hypoxia)
    - A wave: Atrial contraction. Dominant in TS, PS, PAH. Cannon in complete HB.
    - V wave: Atrial filling. Dominant in TR
  - Carotid pulse character: **palpate them both** one after the other
    - Anacrotic: small volume, slow uptake (AS)
    - Plateau: slow upstroke (AS)
    - Bisferiens: anacrotic and collapsing (AS & AR)
    - Collapsing: AR, PDA, peripheral fistula, arteriosclerotic aorta, hyperdynamic circulation
    - Small volume: AS and pericardial effusion
    - Alternans: LVF
    - Jerky: hypertrophic cardiomyopathy
- Precordium:
  - Inspect: scars, deformity, apex beat, pulsations, pectus excavatum (Marfan's)
  - Palpate:
    - Apex beat:
      - Pressure loaded: forceful and sustained (eg AS, HTN)
      - Volume-loaded: forceful but unsustained (AR, MR)
      - Tapping: MS (a palpable first heart sound)
      - Dyskinetic: previous large MI
      - Double or triple apical impulse in hypertrophic cardiomyopathy
    - Heel of hand for L parasternal heave (RV hypertrophy or LA enlargement)
  - Auscultate **while feeling pulse**:
    - Bell at apex, diaphragm at apex, tricuspid, pulmonary and aortic areas
    - L lateral position: listen for MS with bell
    - Lean forward: listen for AR with bell at LSE 4<sup>th</sup> intercostals space and feel for thrills at LSE at base in full expiration
    - If an ESM, exclude:
      - Pulmonary flow murmur of ASD by listening carefully for fixed splitting

- HOCM with valsalva
- Dynamic manoeuvres : if you hear a murmur:
  - L sided murmur loudest on expiration
  - R sided murmur loudest on inspiration
  - Valsalva → ↓preload → ↑MVP and HOCM
  - Handgrip (isometric exercise) → ↑afterload → ↓MVP and HOCM
- **CAROTID BRUIT**
- Focused posterior chest exam:
  - INPSECT, percuss and auscultate lower lung fields. *If dull to percussion also do vocal resonance so you can differentiate effusion from pulmonary oedema*
  - Listen for coarctation murmur
- SACRAL OEDEMA
- Abdomen:
  - AAA
  - Listen for bruit
  - Hepatomegaly and ascites: RVF
  - Pulsatile liver: TR
  - Splenomegaly: endocarditis – if so look at fundi for Roth’s spots and check fingers and toes again for splinters
- Legs:
  - Femoral pulses, radio-femoral delay, **auscultate**
  - Foot pulses, oedema, clubbing of toes, splinters, achilles tendon xanthomata, calf tenderness
- Urine analysis (haematuria in endocarditis), temperature (endocarditis), fundi (HTN change and Roth’s spots)

### *Jugular Venous Pressure (JVP)*

- Pressure waves in atria:



- a wave: atrial contraction at end of diastole → ↑atrial pressure. Coincides with first heart sound and precedes carotid pulse. Closely followed by ...
- c point: bulging of AV valves into atria during systole → ↑atrial pressure. Not usually visible
- x descent: atrial relaxation between S1 and S2
- v wave: End of atrial filling during systole – venous inflow into atria with AV valve closed → ↑atrial pressure
- y descent: rapid ventricular filling following opening of the AV valve
- Height:
  - Rises with 10 seconds pressure on the liver (hepatojugular reflex). A rise is normal. If it remains raised then ventricular failure
  - Causes of ↑ height: Right ventricular failure, 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:
  - 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

## Differentials

- Cardiac failure:
  - Ischaemic
  - Valvular disease
  - Arrhythmia
  - Cardiomyopathy
  - High output: anaemia, B1 deficiency, thyrotoxicosis, AV fistula, Paget's
- Cardiomyopathy:
  - HTN
  - Ischaemic
  - Endocrine: hypothyroid, acromegaly, ?DM
  - Hypertrophic, arrhythmogenic RV dysplasia, restrictive, dilated
  - Infective
  - Haemochromatosis
  - CDT: SLE, RA, PAN
  - Infiltration: amyloid, sarcoid, malignancy
  - Toxic: alcohol, chemo, radiotherapy
  - Peripartum
- Hypotension:
  - Hypovolaemia
  - Cardiogenic
  - Distributive (septic, anaphylactic, ↓adrenal)
- Aneurysm:
  - Degenerative/atherosclerosis
  - Cystic medial necrosis
  - Volume or pressure load (eg Hypertension)
  - Infective: syphilis, TB
  - Trauma

## Murmurs

### *Presentation*

- Exam
- Description of findings including grade of murmur
- Differential – which murmurs would fit the findings – state what you think it is
- Severity – what sign's of severity are present, which are not
- What are the causes of this murmur
- Investigations you'd like to review, and what you'd expect to find: ECG, CXR, Echo
- Indications for surgery

### *Grading Murmurs*

- Grade 1/6: very soft
- 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 5/6: very loud, thrill easily palpable
- Grade 6/6: audible without stethoscope
- For diastolic: Usually graded 1 to 4

### *Management*

- Who needs an echo:
  - Symptoms: SOB, chest pain, VTE, syncope, endocarditis
  - Abnormal ECG or CXR
  - Murmurs: diastolic, continuous or murmur > grade 3
- Mortality Rates for surgery:
  - AVR isolated 2.8%
  - MVR isolated 5.3%

- AVR + CABG 5.2%
- MVR + CABG 10.3%
- AVR + MVR 8.8%
- Valve replacements:
  - Bioprosthetic:
    - Xenograft: porcine or bovine (eg in some with religious objections to pigs)
    - Allograft: cadaveric, autologous
  - Metallic:
    - Tilting disk
    - Bi-leaflet (St Jude's)
    - Ball in cage

### 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 1 <sup>st</sup> degree heart block) or failure of leaflets to close properly (eg mitral regurgitation), delayed LV systolic (eg LBBB)
S2	Splitting	Most often due to right bundle branch block
	Loud	Loud aorta in patients with hypertension and congenital aortic stenosis (→ forceful closure). Pulmonary closure loud in pulmonary hypertension
	Soft	Aortic calcification or regurgitation → leaflets don't close well
	Increased Splitting	If abnormal ⇒ delay in right ventricular emptying, eg right bundle branch block, pulmonary stenosis, pulmonary hypertension, ventricular septal defect (→ ↑right ventricle filling). Also mitral regurgitation → earlier aortic valve closure
	Fixed splitting	Doesn't change with respiration ⇒ atrial septal defect and both atria have equal volumes
	Reversed splitting	P2 occurs before A2, and gap increases on expiration. Due to delayed left ventricular emptying (left branch bundle block, severe aortic stenosis, coarctation of the aorta, or large patent ductus arteriosus)

### Extra Heart Sounds

	Description	Cause
<b>S3</b>	Low-pitched mid-diastolic sound. Called Gallop Rhythm	?Caused by tightening of mitral or tricuspid muscle at the end of rapid ventricular filling. Normal in children and young people. Pathological when ↓ ventricular compliance, so get S3 even when filling is not rapid
Left Ventricular S3	Louder at apex than at sternal edge, and louder on expiration	Normal under 40 years and in pregnancy. Otherwise, left ventricular failure, also aortic regurgitation, mitral regurgitation, ventricular septal defect and patent ductus
Right Ventricular S3	Louder at sternal edge than apex, and louder with inspiration	Due to right ventricular failure or constrictive pericarditis
<b>S4</b>	Late diastolic sound, higher pitched than S3. Can sound like a gallop rhythm.	Always abnormal. Due to high-pressure atrial wave reflected back from a poorly compliant ventricle. Doesn't occur in AF as it requires atrial contraction
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

### Murmurs

Murmur	Nature	Cause
Pan systolic	Pan-systolic: extend from S1 to S2, loudness and pitch vary during systole	Ventricular leakage: Mitral or tricuspid regurgitation, ventricular septal defects
Ejection (mid) systolic	Intensity greatest in early to mid-systole then wanes	Turbulent flow through an orifice: Aortic or pulmonary stenosis, hypertrophic cardiomyopathy, atrial septal defect (this one is a pulmonary flow murmur)
Late systolic	Noticeable gap between S1 and murmur, and continues to S2	Mitral valve prolapse or papillary muscle dysfunction
Early Diastolic	Begins with S2 and fades (decrescendo). High pitched.	Regurgitation through a leaky valve: Aortic or pulmonary regurgitation.
Mid Diastolic	Begin after S2, may extend to S1. Lower pitched.	Impaired flow during filling: Mitral or tricuspid stenosis
Pre Systolic	Just before S1	Atrial systole increases blood flow across the valve: Mitral or tricuspid stenosis
Continuous murmurs	Through systole and diastole	Communication where there's a permanent pressure gradient: Patent ductus, numerous malformations or fistulas
Combined systolic and diastolic murmurs		Aortic stenosis and aortic regurgitation
Pericardial friction rub	Superficial scratching sound at any time in the cycle. Intermittent. May varies with respiration and posture	Pericarditis

### Aortic Stenosis

- History: fatigue, angina, syncope during or after exercise, SOB
- Differential: pulmonary stenosis, HOCM, ASD
- Clinical signs of severity:
  - Narrow pulse pressure
  - Plateau pulse
  - Aortic thrill
  - Length, harshness and lateness of peak of murmur
  - 4<sup>th</sup> HS
  - No 2<sup>nd</sup> heart sound or paradoxical splitting of 2<sup>nd</sup> HS

- LVF – late sign
- *Not* the loudness – this is related more to cardiac output and turbulence, not valve size
- Causes:
  - Age: Calcified valve
  - Rheumatic
  - Congenital bicuspid valve
- Investigations:
  - History: angina, SOB, syncope
  - ECG: LVH (Sokolow-Lyan Criteria: S in V1 + R in V5 or V6 > 35 mm, 32 % sensitive, 95% specific, the other 5% are tall and thin) and LV strain, LAD, conduction abnormalities due to calcification of conducting tissues
  - CXR: LVH and valve calcification, post stenotic dilation of the aorta
  - *Not* ETT: safety concerns. If asymptomatic may do to check for ↓BP
  - Echo
    - Doppler for gradient
    - Valve mobility
    - LVH
    - LV dysfunction
  - Severity on echo: Valve area normally 1.5 – 2.0 cm<sup>2</sup>. Severe stenosis < 1 cm<sup>2</sup> with mean gradient > 40 mmHg and aortic jet velocity > 4.0 m/sec
  - Angio or coronary-CT to exclude IHD prior to valve surgery
- Indications for surgery:
  - Severe AS and symptomatic (angina, syncope, SOB)
  - Severe AS with reduced EF (< 50%) even if asymptomatic (controversial)
  - Expanding aortic root (> 4.5 cm, or >0.5 cm/year)
- Choice of Valve:
  - Tissue if > 65 (will fail in 15 years)
  - Young – mechanical (needs warfarin)
  - Balloon valvuloplasty only for those unable to tolerate surgery

### *Aortic Regurgitation*

- Differential: pulmonary regurgitation (or the mid diastolic murmurs of mitral or tricuspid stenosis)
- Clinical signs of severity
  - Collapsing pulse
  - Wide pulse pressure
  - Long murmur
  - 3<sup>rd</sup> HS
  - Soft A2
  - Austin Flint Murmur (diastolic rumble caused by limitation to mitral inflow by the regurgitant jet)
  - LVF
  - May have systolic flow murmur (ie ESM may be this not AS)
- Causes: chronic
  - Valvular
    - Rheumatic
    - Congenital (e.g. bicuspid)
    - Endocarditis
  - Aortic Root
    - Marfan's
    - Aortitis
    - Dissecting aneurysm
    - Old age
    - Syphilis
    - Ankylosing spondylitis
- Investigations:
  - ECG: LVH and LV strain
  - CXR: LVH/LVF and valve calcification
  - Echo
    - LV dimension and function
    - *Size of regurgitant jet exceeds 65% of outflow tract, regurgitant fraction > 50%*
    - Aortic root dimensions

- Valve thickening/prolapse
- Vegetations
- Indications for Surgery
  - Symptoms
  - Worsening LVF
  - LVSD  $> 5.5\text{cm}$  or EF  $< 55\%$

### *Mitral Regurgitation*

- Differential: TR, VSD, (also ESM of AS, PS, HOCM or ASD)
- Clinical signs of severity:
  - Small volume pulse (very severe)
  - Displaced apex beat + signs of failure
  - Soft S1
  - Early A2 (LV contents all going to the LA so early A2)
  - 3<sup>rd</sup> HS (not always reliable)
  - Apical thrill
  - Signs of PAH: **↑a wave in JVP, RV impulse, loud P2, PR, TR**
- Causes:
  - Chronic
    - Ischaemic disease
    - Dilated cardiomyopathy
    - Secondary to Mitral valve prolapse
    - Infective endocarditis
    - Rheumatic heart disease
    - Collagen diseases such as SLE, Marfan's
    - Congenital
    - HOCM
  - Acute
    - Ischaemic event with papillary muscle rupture
    - Failure of prosthetic valve
- Investigations:
  - ECG: P Mitrale if in sinus rhythm, LVH, AF. RV Hypertrophy (Prominent R in V1 – R  $>$  S and R  $>$  5 mm – also happens in RBBB, posterior MI, pre-excitation – and deep S in V6, RAD, with ST change in V1 – V3 = strain pattern)
  - Xray: Cardiomegaly
  - Echo severity: EF  $<$  60%  $\Rightarrow$  significant dysfunction, area of regurgitant jet relative to atrial size ( $>$  40%), Regurgitant volume  $>$  55%
- Management:
  - Warfarin for all those in AF (18x stroke risk in RHD)
  - ACE and Hydralazine are best trialled in chronic MR
  - Consider endocarditis prophylaxis
- Indications for surgery
  - NYHA II – IV regardless of ejection fraction, or NYHA I + LV dysfunction
  - EF  $<$  60% regardless of symptoms
  - LVESD  $<$  45 mm regardless of symptoms
  - PAH  $>$  50 mm H<sub>2</sub>O

### *Mitral Stenosis*

- Differential: TS (or the early diastolic murmurs of AR or PR)
- Clinical Signs of severity
  - Narrow pulse pressure
  - Early opening snap (↑L atrial pressure)
  - Long diastolic murmur
  - Thrill at apex (rare)
  - Signs of PAH (↑a wave in JVP, RV impulse, loud P2, PR, TR)
  - Features of subsequent right heart failure (Graham-Steel Murmur, TR, V waves)
- Other clinical signs:
  - Malar facies
  - Tapping apex beat (only occurs in MS or TS)
  - Mid-diastolic rumbling murmur: Absent in severe disease but increases in duration up to this point

- Causes
  - Rheumatic Heart disease. More commonly affects the mitral valve in women. Chronic turbulence leads to calcification of valve which exacerbates problem
  - Congenital
  - Rarely SLE, RA
- Investigations:
  - History: SOB, pulmonary oedema, haemoptysis
  - ECG: AF, P Mitrale (if in sinus rhythm), AF (a soft sign of advanced disease), evidence of right heart changes (RV overload, RAD, severe disease)
  - Chest x-ray: Mitral Valve calcification, double left atrial shadow, evidence of pulmonary hypertension
  - Echo severity: Normal 4 – 6 cm<sup>2</sup>, severe < 1 cm<sup>2</sup>, gradient > 15, PCWP > 18
- Management:
  - Warfarin for all those in AF (18x stroke risk in RHD MS)
  - Rate control in AF or heart failure associated tachycardia to prolong diastole and therefore ventricular filling time.
  - Prophylactic antibiotics for all patients
- Indications for surgery or balloon valvotomy
  - Progressive dyspnoea
  - Massive haemoptysis
  - Pulmonary oedema

#### *Mitral Valve Prolapse (systolic click-murmur syndrome)*

- Signs: mid systolic click followed by **late** systolic high pitched murmur
- Auscultation: Valsalva → ↓preload → longer murmur, earlier click. Handgrip → ↑afterload or squatting → ↑preload → shorter murmur
- Echo: prolapse > 1 cm abnormal, less than this normal variant
- Associations: Marfan's, ASD, anorexia, Poly Cystic Kidney Disease
- Complications: MR (more common with men with MVP), infective endocarditis (rare)

#### *Tricuspid Regurgitation*

- Clinical Signs
  - Prominent V waves in JVP
  - Distended JVP if right ventricular failure present (usually would be)
  - Right ventricular heave
  - Pan systolic murmur at base:
    - ↑ by inspiration
    - ↓ by valsalva manoeuvre
  - Pulsatile liver
  - Peripheral oedema and ascites
- Differential: MR
- Clinical signs of severity:
  - Onset of TR secondary to PVH may cause improvement of pulmonary congestion (features of PVH with development of raised venous pressure symptoms)
  - Cardiac output decreases as TR becomes more severe
- Causes of chronic:
  - Usually secondary to right ventricular dilatation:
    - Left heart failure and pressure overload
    - Pulmonary artery hypertension
    - Right ventricular infarct
  - Infective endocarditis (rare)
  - Rheumatic heart disease usually secondary to TS (rare)
  - Congenital (Ebstein's anomaly with right atria ventricularisation and associated with WPW and ASD – Can be secondary to in-utero first trimester lithium exposure)
- Investigations:
  - ECG: P Pulmonale, RVH
  - CXR RA and RV enlargement
  - Echo
- Management: Reducing venous pressures (diuretics, hydralazine) and maintain cardiac output
- Indications for surgery (complicated by valve thrombosis)

- Surgery is usually not indicated as:
  - Isolated TR is well tolerated
  - Correction of left sided or pulmonary disease reduces right ventricular pressures and therefore improves normal tricuspid morphology
- TR secondary to rheumatic heart disease
- Occasional cases of Ebstein's anomaly and other congenital disorders

### *Coarctation*

- Commonest site – just distal to origin of L subclavian
- Clinical signs:
  - Better developed upper body
  - Radio-femoral delay
  - HTN in arms only
  - Collateral vessels
  - Mid-systolic murmur over chest and back
  - Fundi – changes of HTN
  - May have Turner's
- Investigations:
  - ECG: LVH
  - CXR:
    - LVH
    - Enlarged subclavian
    - Dilated ascending aorta with indentation
    - Rib notching – 2<sup>nd</sup> to 6<sup>th</sup> and over inferior border
  - Echo
    - LVH
    - Coarctation
    - Abnormal flow patterns

### *Eisenmenger's syndrome*

- Conditions required for the diagnosis
  - Underlying heart defect that allows passage of blood between left and right heart
  - Pulmonary hypertension
  - Polycythaemia
  - Shunt reversal
- Clinical signs
  - Features of either ASD, VSD or PDA
  - Cyanosis
  - Clubbing
  - Features of pulmonary hypertension
  - Consequent features of right ventricular hypertrophy
- It is important to detect pulmonary hypertension to differentiate Eisenmenger's from Tetralogy of Fallot where Pulmonary Stenosis is partly the cause of the right ventricular changes.
- Defining the level of shunt: Based on auscultation of the second heart sound:
  - Wide Fixed-splitting (ASD)
  - Single sound (VSD)
  - Normal (PDA – look for evidence of isolated lower limb clubbing)

### *HOCM*

- Clinical signs
  - Pulse – sharp, rising and jerky (rapid ejection followed by obstruction)
  - Prominent a wave: forceful atrial contraction against a non-compliant ventricle
  - Apex: double or triple impulse owing to pre-systolic ventricular expansion
  - Auscultation:
    - Ejection systolic murmur
    - Pansystolic murmur
    - 4<sup>th</sup> HS
    - NB – no diastolic murmur
  - Dynamic manoeuvres: louder with valsalva and isotonic exercise (eg jogging), softer with squatting, raising legs and isometric exercise (eg handgrip)

- Investigations:
  - ECG:
    - Higher sensitivity than echo in detecting affected individuals in family studies, but low specificity in screening
    - LVH
    - Deep Q waves
    - Conduction defects
  - CXR: LVH/LVF with hump along border
  - Echo:
    - Asymmetrical hypertrophy of septum, LV wall thickness > 13 mm in an adult
    - Systolic anterior motion of anterior valve leaflets
    - MR
    - LV outflow tract obstruction with increased gradient in ~ 25%
- Management:
  - Major risks for SCD (any one qualifies for an ICD):
    - LV wall thickness > 30 mm
    - FHx of sudden death < 35
    - Previous cardiac arrest/ventricular tachycardia
    - Risks factors (if > 2 of them then consider ICD): HTN, haemodialysis, elite athletes, aortic stenosis, cardiac amyloidosis, cardiac thrombus. *ICD easily surpasses other preventative strategies* (amiodarone, sotalol) for avoiding SCD
  - Symptom management (controversial): Ca blockers, beta-blockers (improve diastolic filling, reduce contractility → ↓outflow obstruction), diuretics (no impact survival)
  - Surgery:
    - Septal myotomy if resting outflow gradient > 50 mmHg – will reduce it to < 10 mmHg in 90%. Mortality 3%
    - Alcohol septal ablation (ie cause an MI in the septum)
  - Screen first degree relatives (ECG, echo) every 2 – 5 years (maybe annually as a teenager – usually develops following growth spurt). No established role for genetic testing (yet) – although cause found in 50 – 60%
  - Genetic counselling

## Hypertensive Exam

- Inspect: Cushing's, acromegaly, polycythaemia, uraemia
- Inspect hands: vasculitic changes, fistula
- Pulse: radial-radial and radial-femoral
- Measure BP: *both arms, lying and standing* and legs in young people
- Neck: consider circumference for OSA
- CV exam: LVF and coarctation. 4<sup>th</sup> HS present if severe. Listen between scapula for coarctation
- Abdo exam:
  - Renal masses (?PCKD), adrenal masses, AAA
  - Renal bruit (fibromuscular dysplasia or atheroma)
- Legs: peripheral pulses, oedema
- Eyes:
  - Injected sclera (polycythaemia)
  - Fundi:
    - Grade 1: silver wiring
    - Grade 2: above + AV nipping
    - Grade 3: above + haemorrhages (flame shaped), soft exudates (cotton wool spots due to ischaemia), hard exudates (lipid residues)
    - Grade 4: above + papilloedema
- Note signs of stroke 2<sup>nd</sup> to HTN
- Comment: would check BP again at the end when patient more relaxed
- Investigations:
  - Bloods: U&E, FBS (polycythaemia), TSH, Ca
  - ECG, CXR, echo
  - Urinalysis: protein, blood, casts
  - Consider: ARR, 24 hr urine cortisol and catecholamines, IGF-1

## Differential

- Most common: essential
- Common:
  - White coat
  - Suboptimal medical therapy/poor compliance
  - Exclude drugs: eg NSAIDs
  - Renal:
    - Renal artery stenosis
    - Parenchymal disease: HTN, DM or GN
  - Hyperaldosteronism (Conn's, main presentation is with normal K)
  - OSA
- Uncommon:
  - Endocrine – Cushing's, CAH, Pheo, Acromegaly, Thyroid (either ↑ or ↓)
  - Coarctation
  - Neurological: autonomic dysregulation, acute ↑ICP
  - Polycythaemia
  - Familial

## Constrictive pericarditis

- Causes:
  - Post-viral pericarditis
  - Tuberculosis
  - Post surgical
  - Radiation therapy to the mediastinal area
  - Chronic renal failure with uraemic pericarditis
  - Connective tissue disorders
  - Neoplastic infiltration
  - Previous infective (Fungal, parasitic, bacterial) pericarditis
  - Post MI (Dressler's Syndrome)
  - Associated with Asbestosis
- Pathophysiology: Constrictive 'shell' around the heart. During inspiration, right ventricular pressures rise causing bulging of the septum into the left ventricle, reducing inspirational left ventricular volume → pulsus paradoxus (accentuation of normal physiological feature with a drop in BP of > 10 mm Hg during inspiration), and distended (occasionally paradoxical) JVP. During expiration the reverse occurs with bulging of the septum into the right ventricle.
- Clinical features:
  - Low blood pressure with pulsus paradoxus
  - Raised JVP with prominent x and y descents
  - Impalpable apex
  - Kussmaul's sign (JVP increasing on inspiration) is seen but rare
  - Distant heart sounds with a 3<sup>rd</sup> sound
  - Pericardial knock heard early in diastole (rapid ventricular filling abruptly halted)
  - Features of right heart failure – ascites, hepatomegaly, oedema
  - Features of underlying aetiology
- Investigations
  - CXR:
    - Pericardial calcification and pleural effusions
    - Evidence of aetiology
      - Radiation exposure
      - Pulmonary TB
      - Asbestosis
      - Neoplasm
      - Previous surgery
  - Echo defines pericardial disease and effusion if present
  - CT and MRI can further evaluate the pericardium
- Management:
  - Treatment of underlying disease if possible
  - Treatment of active tuberculosis if found
  - Diuretic therapy to reduce venous pressures

- Surgical stripping of pericardium has a mortality of 5 – 15 %. Mortality is lower earlier in the disease process

## Marfan's

- CV exam looking for:
  - Aortic murmur
  - Mitral valve prolapse is common and may be associated with mitral regurgitation
  - Aortic root disease which may manifest as aortic regurgitation, aortic dissection, or coarctation of the aorta. Check blood pressure in both arms and radial-femoral delay
  - Dysrhythmias
- Also:
  - Tall
  - Dolichostenomelia: Thin tall body with long slender limbs, Arm span > height
  - Arachnodactyly (spider fingers) and joint hypermobility
  - Face: lens dislocation, blue sclera, high arched palate
  - Chest: pectus excavatum (can cause respiratory compromise), percuss and auscultate for pneumothorax which is more common in Marfan's Syndrome
  - Back: kyphoscoliosis
  -
- Management: serial echo for progressive aortic root dilation (which can → dissection)
- Pathophysiology: Autosomal dominant condition caused by mutations in FBN-1 gene on chromosome 15. Normal gene codes for fibrillin-1 which appears to be fundamental in maintenance of normal extracellular matrix, by inhibiting the action of TGF-β. Disease shows variable expression but likely complete penetrance
- Diagnostic Criteria: **Ghent** criteria (not 100% sensitive):
  - Family history + 1 major organ criteria + 1 other organ system involvement
  - 2 major organ criteria + 1 other organ system involvement

## Cyanotic Heart Disease

- Cyanotic, clubbed?
- Pulmonary HTN:
  - 2<sup>nd</sup> heart sound single: VSD
  - 2<sup>nd</sup> heart sound split: ASD
  - Normal: ?PDA
- No pulmonary HTN: Tetralogy (with pulmonary stenosis), or other corrected missing chamber defect

## Oedema

- Inspect:
  - Where is the oedema
  - Nutrition: hypoalbuminaemia and B1 deficiency → oedema
- Lower limb:
  - Legs: Asymmetric calves for DVT, scars from vein grafting, varicose veins (→ oedema), inguinal nodes
  - Abdo: abdo wall oedema, abdo wall veins (IVC obstruction), ascites, masses, liver disease (including pulsatile ⇒ TR)
  - Heart for RV failure
  - Examine all nodes
  - *Delayed ankle jerks: hypothyroidism*
  - Ask for urine analysis, exclude vasodilating drugs (cause oedema)
  - Non-pitting oedema: lymphoedema (malignant infiltration, filariasis), myxoedema
- Differential of bilateral oedema:
  - CHF
  - ↓albumin: Liver failure, malabsorption, malnutrition etc
  - Nephrotic syndrome
  - Vascular compression: eg IVC
  - Bilateral lymphatic obstruction
- SVC obstruction:
  - Appearance: Cushingoid from tumour or steroid treatment
  - Face appearance: cyanosis, periorbital oedema, exophthalmos and conjunctival injection, Horner's syndrome from chest mass

- Fundi: venous dilation
- Raised JVP
- Check for thyroid mass
- Supraclavicular nodes
- Tracheal stridor
- Chest for extended collaterals

## General Respiratory Exam

- Inspection: sputum mug, type of cough, rate and depth of respiration, **accessory muscles** or respiration, audible wheeze, *paradoxical* chest or abdominal *movement* with inspiration (sucks in rather than expands – suggests obstruction/hyperinflation)
- Hands:
  - Clubbing – if present check **wrist tenderness** for hypertrophic pulmonary osteoarthropathy
  - **Cyanosis** (requires > 30 g/L deoxygenated haemoglobin)
  - Nicotine
  - Wasting and weak **finger abduction** (lower trunk injury)
  - Flapping tremour
  - Pulse and count respiratory rate
- Face:
  - Horner’s (look at pupils), jaundice, anaemia
  - Tap Sinuses
  - Mouth: **central cyanosis**
  - Voice: hoarseness
- **Trachea:** tug, displacement
- Forced expiratory time – if prolonged then obstruction
- **Cough**
- Posterior Chest (get them to sit on opposite side of the bed):
  - Inspect: shape, scars, radiotherapy marks, prominent veins, upper lobe expansion (look over their clavicles)
  - Palpate:
    - Cervical and submandibular lymph nodes – take time
    - Expansion, vocal fremitus
  - Percuss (with elbows in front to out wing scapulae – “bring your elbows together”)
  - Auscultate: breath sounds, vocal resonance
- Anterior Chest:
  - Inspect
  - Palpate: supraclavicular nodes, vocal fremitus, axillary nodes
  - Auscultate
  - Pemberton’s sign
  - **Percuss and auscultate axilla – must lift arm**
- Lymph nodes: cervical, submandibular, supraclavicular, axilla – take time
- Cardiovascular: JVP, apex, PAH (↑JVP, loud P2, RV heave), Cor pulmonale
- Other:
  - If effusion check for malignancy (breasts, abdomen, rectal, lymph nodes)
  - Pemberton’s sign: SVC obstruction – hold arms over head → facial plethora, inspiratory stridor and ↑JVP
  - Check liver for mets 2<sup>nd</sup> to lung Ca and for ptosis (displaced downwards in emphysema)
  - Feet check for oedema (pulmonary HTN) and DVT
  - Temperature

### Exam Differentials

- Bronchial breath sounds: lobar pneumonia, localised fibrosis or collapse, above a pleural effusion, large lung cavity
- Reduced breath sounds (not “air entry”): emphysema, large lung mass, collapse, fibrosis or pneumonia, pneumothorax
- *Raised hemidiaphragm:* dull, no air-entry, no added sounds
- Crackle:

Disease	Early Crackle	Late Crackle
Congestive Heart Failure	Very Common	Common
Obstructive Lung Disease	Present	Absent
Interstitial fibrosis	Absent	Present
Pneumonia	Absent	Present

- Common presentations:

	Expansion	Percussion	Breath sounds	Vocal Resonance	Trachea
Consolidation	↓	Dull	↑, Bronchial, coarse crackles	↑	-
Effusion	- or ↓	Stony dull	↓	↓	-
COPD	Hyper-expanded	Hyper-resonant	Wheeze	-	-
Pneumothorax	- or ↓	Hyper-resonant	↓	↓	Deviated if tension
PE	-	- (unless effusion)	-	-	-
Fibrosis	↓	- or dull	Crackles	↑	Depends
LV Failure	↓	Dull	Fine crackles	-	-
Collapse	↓	Dull	↓	↓	Deviated

### Investigations

- ECG: Sinus tachy, tall R in V1 – R heart strain, S1Q3T3
- CXR
- Bloods
- Sputum
- Lung Function Tests
- ABG – for hypoxia
- V/Q or CTPA

### Pleural Effusion

- 500ml of pleural fluid enough for clinical detection
- Clinical signs:
  - Inspection
    - Decreased movement on affected side
    - Aspiration marks
  - Tracheal deviation to opposite side
  - Percussion – stony dullness - causes for this:-
    - effusion – decreased AE and vocal resonance, tracheal deviation
    - consolidation/collapse – creps, increased AVR or in collapse tracheal deviation towards lesion, bronchial BS in consolidation
    - pleural thickening – no tracheal deviation with audible BS
    - raised hemidiaphragm
  - Auscultation: decreased AE and VR, bronchial breath sounds
- Differential:
  - Exudate:
    - Malignancy – primary and mets
    - TB
    - Pneumonia
    - RA/SLE
    - Pulmonary infarction
  - Transudate:
    - CHF
    - Nephrotic syndrome
    - Liver failure
    - Hypothyroidism
- Investigations:
  - CXR – obliteration of costophrenic angles, may need lateral decubitus film
  - Pleural tap
    - Protein, albumin, LDH & glucose with simultaneous serum levels
    - pH
    - M,C & S
    - Cytology – eosinophils benign, lymphocytes worrying (TB and Ca)

- AFB or mycobacterial cultures (may also get adenosine deaminase for TB)
- Cholesterol – increased in malignancy
- Amylase – pancreatitis/oesophageal rupture/adenocarcinoma
- RF/ANA
- Chylothorax (increased fat) - malignancy
- Pleural biopsy – for mycobacterial cultures or to pathology
- US – to confirm site of aspiration, to locate loculated lesions, differentiates between fluid and thickening
- CT
- MRI less useful
- Testing pleural fluid:

### *Pleural fluid testing*

- Diagnosis:
  - low pH with low glucose poor prognostic indicator in Ca
  - low pH, low glucose and high LDH in empyema, RA, SLE, Ca, TB
  - parapneumonic effusion – drain if glucose <4 and pH <7
- Light's Criteria for exudates (100% sensitive but 70% specific especially in CHF)
  - Pleural protein: Serum protein > 0.5
  - Pleural LDH: Serum LDH > 0.6
  - Pleural LDH > 2/3 of upper limit of normal serum LDH
  - Serum-effusion albumin gradient (ie serum alb – pleural alb) **more specific**. Gradient of <1.2 = exudate

## **Bronchiectasis**

- Examination
  - Copious purulent sputum in cup
  - Finger Clubbing
  - Cachexia
  - HPOA if secondary to carcinoma
  - Lymphadenopathy
  - Course late inspiratory crepitations which may be bilateral or localised if secondary to obstruction
  - Comment on kyphoscoliosis if present as impacts on clearance
  - Check for splenomegaly as evidence of amyloidosis in longstanding bronchiectasis
- Causes of Bronchiectasis
  - Post Infection
    - Bacterial pneumonia
    - Measles
    - Pertussis
    - Tuberculosis
  - Mechanical bronchial obstruction
    - Tuberculosis
    - Carcinoma
    - Extrinsic compression
  - Cystic Fibrosis
  - Allergic bronchopulmonary aspergillosis
  - Immunoglobulin deficiency (Gammaglobulin)
  - Immobile cilia syndrome (Kartagener's, Young's)
  - Idiopathic
- Investigations
  - Xray may show prominent cystic spaces, tram tracks, and ring shadows
  - CT confirms changes (HRCT 90% sensitive) and shows cygnet ring changes
  - Sputum culture

## **Interstitial Lung Disease**

- Heterogeneous group of diseases characterised by either inflammation and fibrosis, or granulomatous changes.
- Examination
  - Likely to be asked to examine the respiratory system and proceed
  - Clubbing

- Central cyanosis
- Tachypnoea
- Fine end-inspiratory crepitations which do not clear on coughing, and become quieter on leaning forward
- Fibrosis causes the following signs
  - Tracheal deviation to affected side
  - Reduced expansion on affected side
  - Dull percussion note
  - Bronchial breathing may be present
- Proceed
  - Examine hands for evidence of RA or Systemic sclerosis
  - Examine face for SLE, Dermatomyositis, Systemic sclerosis
  - Lupus Pernio, VII nerve palsy of Sarcoid
  - Parotid swelling of Sarcoid, Sjogren's
  - Mouth for evidence of Aphthous ulcers (Crohn's), Sjogren's
  - Cardiac examination to look for evidence of pulmonary hypertension
- Causes
  - Occupational exposure and pneumoconiosis
  - Extrinsic allergic alveolitis (pets)
  - Connective tissue disorders
  - Granulomatous diseases including TB, Sarcoid, Wegener's
  - Drugs
  - Radiotherapy
  - Chronic pulmonary oedema
- Types of interstitial pneumonitis that are seen prior to fibrosis
  - Usual interstitial pneumonitis (UIP): Mean survival of 3 years with a poor response to steroids.
  - Desquamative interstitial pneumonitis (DIP): Mean survival of 12 years. 2/3 respond to steroids
  - Non-specific interstitial pneumonitis (NSIP): Mean survival is 14 years. 2/3 respond to steroids
- Investigations
  - Chest xray reveals reticulonodular shadowing with honeycombing
  - ABG reveals hypoxia
  - PFTs show restrictive disease with reduced DLCO/VA
  - HRCT reveals ground glass changes in inflammation
  - DPTA scanning reveals slow clearance in patients with irreversible interstitial changes and thus negates treatment in some
  - Lung biopsy
  - Bronchial lavage – Lymphocytes predicts steroid response. Neutrophils – Cyclophosphamide
  - Investigations into specific aetiologies

## Cystic Fibrosis

- Autosomal recessive mutation of CFTR gene on chromosome 7 (most common is  $\Delta 508$  mutation) causing abnormal cellular chloride channel
- Systems affected
  - Bronchiectasis
  - Pancreatic insufficiency
  - Associated diabetes
  - Bile duct obstruction with cirrhosis
  - Malabsorption syndrome
  - >95% infertility in males (20% of females)
- Clinical Features
  - Muscle wasting and stature: a good marker of severity
  - Clubbing
  - Nasal polyps (Uncommon)
  - Acanthosis Nigricans
  - Reduced breath sounds with crackles and wheeze
  - Evidence of right heart failure and pulmonary hypertension
  - Evidence of bile duct obstruction
    - Jaundice
    - Itch marks

- Evidence of chronic liver disease
- Hepatomegaly
- Abdominal tenderness and mass due to faecal loading
- Meconium ileus equivalent with distal bowel obstruction due to secretions
- Investigations
  - Family history
  - Sweat test (98% sensitive) with pilocarpine iontophoresis on 100mg of sweat
    - >70 mmol/l in adults
    - >60 mmol/l in children
    - <50 mmol/l normal
    - Causes of high sweat test
      - Most autoimmune endocrine insufficiency diseases
      - Nephrogenic DI
      - Glycogen storage disease
      - G6PD disease
  - Sputum culture
    - H. Influenzae and S. Aureus in young
    - E. Coli and Proteus spp follow
    - Pseudomonas colonisation usually by 10 years of age
  - Blood tests may reveal evidence of fat soluble vitamin malabsorption
  - Chest xray reveals mostly upper lobe changes (98%) with cysts, mucous plugs, and atelectasis
  - CT or HRCT reveals typical Bronchiectasis changes
  - Pulmonary function tests

## Sarcoidosis

- Pathophysiology: Chronic granulomatous condition with unknown aetiology. There is an excess of Th1 cells at sites of disease, and macrophages within the granulomatous hydroxylate vitamin D causing hypercalcaemia.
- Clinical Features
  - General:
    - Clubbing if fibrosis is present
    - Pulse for evidence of conduction system disease
    - Generalised lymphadenopathy
    - Erythema Nodosum particularly on lower limbs
    - Maculopapular eruptions of < 1cm diameter
    - Lupus Pernio – swollen purple nodules particularly on the nose, cheeks, eyelids
    - Evidence of non-deforming arthritis
  - Eyes:
    - Uveitis – Redness of the eye with blurred vision and pain
    - Yellow conjunctival nodules
    - Papilloedema secondary to optic nerve sarcoidosis
  - Parotid swelling: Uveoparotid syndrome (Heerfordt-Waldenstroem syndrome)
  - Fever
  - Facial nerve palsies
  - Chest:
    - Inspiratory crepitations if fibrosis present
    - Occasional pleural effusions
    - Evidence of infiltrative heart disease and failure
  - Abdomen: Hepatomegaly (20%)
  - Splenomegaly (40%)
  - Lofgren's Syndrome: Fever, Erythema Nodosum, Arthritis, BHL - self limiting over 6 weeks
- Investigations
  - Blood tests
    - Lymphopenia
    - Raised serum ACE (65% sensitive) also elevated in PBC, Mycobacterial infections including TB, Leprosy, Atypical, Hyperparathyroidism
    - Hypercalcaemia with low PTH
    - Pituitary (particularly ADH) abnormalities
  - Urine for hypercalciuria (more common than hypercalcaemia)

- Chest X-ray classifies the disease
  - Stage 1 – BHL
  - Stage 2 – BHL and pulmonary infiltrate
  - Stage 3 – Pulmonary fibrosis
- Management
  - Stage 1 has 80% remission rate without treatment
  - Stage 2 has 50% remission rate but should be managed with steroids if restrictive PFT's
  - Steroids (1mg/kg over 6 weeks – tapered over 1 year)
  - Steroid sparing agents (Azathioprine, Methotrexate) when problems
  - Infliximab (TNF- $\alpha$  inhibitor) in severe disease (TB reactivation)

## Differentials

- SOB:
  - Respiratory
  - CVS
  - Neuromuscular
  - Acidosis
  - Anaemia
- Acute Respiratory Failure in COPD
  - Infection
  - Asthma
  - LVF
  - Pneumothorax
  - Lack of drive – exhaustion/drugs
- Asthma Triggers
  - Allergens
  - Infections
  - Environmental
  - Occupational
  - Exercise
  - Pharmacologic
  - Emotional
- Bilateral Hilar Adenopathy
  - Sarcoidosis
  - Lymphoma
  - Cancer
  - Tb
  - Brucellosis
  - Coccidioidomycosis, Histoplasmosis, toxoplasmosis, berilliosis
- Bronchiectasis
  - Idiopathic
  - Infection – pneumonia, Tb, MAC, measles, pertussis, flu
  - Immunocompromise – CF, ciliary dyskinesia, IgA, IgG and CVID
  - Inflammation – ABPA, RA, Sjogren's
  - Mechanical – foreign body, adenoma
- Cough – persistent with normal CXR
  - Pertussis
  - Post-nasal drip
  - Asthma
  - Reflux
- Eosinophilia with Pulmonary Infiltrates
  - Idiopathic:
    - Acute and Chronic eosinophilic pneumonia
    - Hypereosinophilic syndrome
    - Churg-Strauss syndrome
  - Known cause:
    - Parasitic infections – esp filarial
    - Allergic bronchopulmonary mycoses
    - Drug reactions

- Interstitial Lung Disease
  - Idiopathic interstitial pneumonia:
    - Subacute/acute – COP, NSIP, DAD
    - Chronic – IPF, DIP, LIP
  - Inorganic dusts (pneumoconiosis)
  - Hypersensitivity pneumonitis
  - Drug or radiation induced
  - Connective tissue disorder/ part of multisystem disorder
  - Oddities:
    - LAM
    - Pulmonary alveolar proteinosis
    - Idiopathic granulomatous disease
    - Sarcoidosis
    - Langerhans granulomatosis
    - Lymphocytic granulomatosis
    - Eosinophilic pneumonia

### General Abdominal exam

- Inspection: jaundice, pigmentation (haemochromatosis), xanthoma (biliary obstruction), mental state (encephalopathy)
- Hands:
  - Clubbing, leuconychia (white nails). If clubbing check for HPOA with wrist squeeze
  - Palmar erythema
  - Dupuytren's contractures
  - Arthropathy
  - Hepatic flap: Asterixis – hands/fingers repeatedly drop then recover due to a momentary loss of tone
- Arms:
  - Spider naevi: >5 in adults is probably pathological. Refill from central arteriole when compressed)
  - Bruising
  - Wasting
  - Needle tracks
  - Scratch marks (chronic cholestasis)
  - Tattoos
- Face:
  - Eyes: sclera (jaundice, anaemia, iritis), cornea (Kayser-Fleischer rings)
  - Parotids (alcohol)
  - Mouth: use tongue depressor
    - Breath: fetor hepaticus
    - Lips: stomatitis, telangiectasia
    - Gums: gingivitis, bleeding, hypertrophy, pigmentation, candida
    - Tongue: atrophic glossitis, leukoplakia, ulceration
- Cervical/axillary lymph nodes
- Chest: gynaecomastia, spider naevi, hair loss (alcohol)
- Abdomen (crouch beside bed):
  - Inspect: scars, distension, prominent veins, striae, bruising, localised masses, peristalsis. *Watch while taking some deep breaths*
  - Abdominal veins:
    - Accessing direction of flow: place two fingers on the vein, move second away to squeeze the blood out of a section, release second finger and see if it refills. Repeat with release of the first finger to test flow from the opposite direction
    - Caput Medusae (literally “head of Medusae” – mythical character whose hair turned to snakes). Rare. Portal HTN → flow to umbilicus then out across the superficial abdomen. So flow is toward the legs below the umbilicus
    - IVC obstruction : Flow is always upwards, so is to the head below the umbilicus
  - Palpate:
    - Ask about pain, superficial then deep palpation
    - Murphy's sign: two fingers over liver and take a deep breath. ↑pain as a gallbladder pushes against hand. Courvoisier's law: ‘in painless jaundice, if the gallbladder is palpable, the cause is not gallstones’ and the acute distension is more likely to be due to an obstructive mass
    - Liver:
      - Enlarged or ptosis. Normal span in 11 - 12.5 cm in males, 10 – 11 cm in females. Lots of inter-observer variation
      - Liver edge: always comment – pulsatile/non-pulsatile, tender/non-tender, smooth/irregular, hard/soft
    - Spleen:
      - Percuss for spleen from LIF side of naval (including in 11<sup>th</sup> intercostal space in mid axillary line – dullness is apparently sensitive for hypersplenism)
      - Palpate: grasp lateral rib cage and pull towards you – displaces spleen downwards. Take deep breaths while feeling spleen
      - Role 30o onto right side for spleen

- Differentiating spleen from polycystic kidneys: spleen has no upper border, a notch, moves inferiomedially on inspiration, is not resonant, is not ballottable, may have a friction rub
- If palpable spleen then also do:
  - Lymph nodes for haematological malignancy
  - Nails (splinters) and fundi (Roth spots) for endocarditis
  - Ask for temperature chart
- Percuss for ascites (shifting dullness)
- Auscultate: bowel sounds, bruits (over the liver  $\Rightarrow$  HCC or acute alcoholic hepatitis), hums (portal HTN), rubs (spleen  $\Rightarrow$  infarction)
- Groin: genitalia, lymph nodes, hernia (stand up and cough)
- Legs: bruising, oedema, neurological (alcohol)
- Assess for Portosystemic encephalopathy:
  - Fetor
  - Trail-making test
- Other:
  - Rectal: inspect and palpate
  - Urine analysis
  - Blood pressure
- Proceed: if signs suggestive of alcohol:
  - Peripheral neuropathy
  - Proximal myopathy
  - Cerebellar syndrome
  - Bilateral sixth nerve palsy
  - Recent memory loss/confabulation – Korsakoff's

#### *Investigations to look for cause*

- Bloods:
  - Liver function tests
  - Viral Serology
  - Autoimmune Antibodies (ANA, Anti-SM, Anti-LKM)
  - Anti-Mitochondrial (M2)
  - Iron and Ferritin
  - Wilson's: Low serum Cerulo-plasmin and  $\uparrow$  urinary copper (treatment: zinc, transplant curative)
  - $\alpha$ 1-antitrypsin levels
  - HIV serology (PSC)
  - Carbohydrate-deficient transferrin (CDT)  $> 20$  for alcohol
- Ascitic fluid analysis (see below)
- Imaging: US/CT abdomen
- Liver Biopsy (Can be transjugular if locally available)

### **Jaundice**

- Usually only visible when the bilirubin  $> 40 - 50$  mmol
- Likely, if the patient is obviously jaundiced, to be either asked to examine the abdominal system or the abdomen directly and proceed
- Examination
  - Be seen to check for Murphy's sign (2 fingers over gallbladder on inspiration – pain is sign of cholecystitis)
  - Heart to exclude mechanical heart valve
  - Lymphadenopathy to consider autoimmune haemolysis in the context of haematological malignancy
  - Skin for evidence of purpura etc which could point to a haemolysis in the context of microangiopathic haemolysis ie TTP
- Differential of Jaundice
  - Pre-Hepatic: Haemolysis including membrane defects, immune haemolysis, sickle cell, Mechanical
  - Hepatic
    - Conjugation defects (Gilbert's, Crigler-Najjar)
    - Excretion defects (Dubin-Johnson, Rotor syndrome)
    - Any form of cirrhosis

- Any form of hepatitis
- Liver metastases
- Post-Hepatic
  - Gallstones
  - Gallbladder/Bile duct pathology
  - Pancreatic pathology
- Investigations
  - Liver function tests
  - Conjugated/unconjugated fraction (rarely performed)
  - Urinalysis: Absence of bilirubin points to unconjugated types (Pre-Hepatic)
  - Haemolysis studies (Reticulocytes, Haptoglobin, Coomb's testing)
  - Viral serology
  - Other tests for cirrhosis causes
  - US abdomen if obstructive jaundice suspected

## Haemochromatosis

- Possible stems: examine the abdomen”, “patient has recently become diabetic”, “notice a change in his appearance”
- Pathology: HFE C282Y defect. Biopsy if age > 40 and ferritin > 500 for staging (↓↓ risk of cirrhosis otherwise). Otherwise phlebotomy. Family screening
- Hands:
  - Signs of CLD including flap
  - Arthropathy: esp 2<sup>nd</sup> and 3<sup>rd</sup> MCPs – ROM, note protrusion when making a fist
  - Proximal myopathy
- Axillary hair
- Diabetic eyes
- Chest: ↓hair, gynaecomastia and ↓muscle bulk
- CVS for cardiomyopathy, lungs for failure, sacral, pedal oedema
- Abdomen: HSM, ascites
- Testicular atrophy (hypopituitarism)

## Differentials

- Differential of liver disease
  - Viral: Hep B, C, HIV
  - Non-alcoholic fatty liver disease
  - Toxic: alcohol, drugs
  - Autoimmune: AIH, PBC, PSC
  - Metabolic: Haemochromatosis, Wilson's,  $\alpha$ 1AT, Porphyria
- Hepatomegaly:
  - Malignancy: Cancer mets, hepatoma
  - Alcohol with fatty infiltration
  - Haematological: myeloproliferative disease (eg CML), lymphoma
  - RHF
  - Metabolic: haemochromatosis, fatty liver
  - Infective: hepatitis, hydatid disease, HIV
  - Biliary obstruction, amyloid, ischaemia
  - Character:
    - Irregular: cirrhosis, mets, hydatids, amyloid, cysts
    - Tender liver: hepatitis, RHF
    - Pulsatile liver: TR, hepatoma, vascular abnormalities
- Splenomegaly:
  - Differential of massive splenomegaly:
    - Myeloproliferative: Myelofibrosis, CML, Polycythaemia
    - Lymphoproliferative: Lymphoma, CLL, Hairy cell leukaemia
    - Sarcoid
    - Autoimmune haemolytic anaemia
    - Malaria
  - Differential of mild splenomegaly:
    - Mechanical: Portal HTN 2<sup>nd</sup> to:
      - Cirrhosis

- Portal vein thrombosis
  - Pancreatic problems causing portal HTN
  - Post-hepatic obstruction (eg Budd Chiari)
- Other myeloproliferative or lymphoproliferative
- Other infection: EBV, endocarditis, Dengue fever
- Amyloid
- Fealty's syndrome: In patients with chronic RA, splenomegaly, neutropenia +/- anaemia/thrombocytopenia
- Differential of Ascites
  - Prehepatic:
    - CHF
    - Budd-Chiari Syndrome
    - IVC obstruction
  - Hepatic: decompensated cirrhosis with portal HTN
  - Intra-abdominal causes:
    - Abdominal
    - Nephrotic syndrome
    - TB peritonitis
    - Chylous ascites
    - Pancreatitis
  - Grading:
    - Grade 1 — mild ascites detectable only by ultrasound examination
    - Grade 2 — moderate
    - Grade 3 — large or gross ascites with marked abdominal distension.
  - Investigations:
    - USS – to confirm ascites
    - Paracentesis to:
      - Diagnose its cause
      - Exclude infection
    - Ascitic Fluid Tests:
      - Cell count and differential - polymorphonuclear count  $250/\text{mm}^3$  = infection
      - Serum-to-ascites albumin gradient
      - Total protein concentration
      - Culture/Gram stain
      - Cytology
- Acute abdomen:
  - Surgical if: fever, hypotension, acidosis, peritonism
  - Major threat to life:
    - Necrotic viscus (pancreatitis, bowel, intussusception, volvulus, hernia)
    - Perforated viscus: PUD, bowel perforation
    - Ascending cholangitis
    - Haemorrhage: AAA, ectopic, spleen, liver
- Malabsorption:
  - = steatorrhea. Exclude lactose intolerance and IBS
  - Malnutrition
  - Pancreatitis → lipolysis defects
  - Micelle defects: liver disease, biliary obstruction, bacterial overgrowth
  - Mucosal defects; coeliac, Whipple's, parasites (giardia), amyloid, HIV, hypogammaglobulinaemia, lymphoma, resection
- Upper GI bleed:
  - Erosive (gastritis, ulcer)
  - Portal HTN
  - Trauma/MW tear
  - Tumour
- Pancreatitis:
  - Stones
  - Alcohol
  - ERCP
  - Drugs: NRTIs, azathioprine, steroids

- Tumour
- Mumps
- Autoimmune (PAN, SLE)
- Endocrine: ↑TGs, ↑Ca
- Hereditary

## Differentials

- Renal failure:
  - Pre-renal
  - Intra-renal – vessels, tubules, glomeruli, interstitium
  - Post-renal
- Glomerulonephritis:
  - Non-proliferative
    - Minimal change
    - Membranous
    - FSGS
  - Proliferative
    - Mesangiocapillary GN
    - IgA
    - Immune
      - Linear – Anti-GBM disease
      - Granular – post-strep
      - Pauci – Wegner's, microscopic polyangitis
    - SLE
- Glomerulonephritis – causes:
  - I infections
  - N eoplasm – paraprotein, paraneoplastic
  - D rugs
  - I diopathic
  - A utoimmune disorders
- Heavy proteinuria:
  - GNs - Non-proliferative and MCGN
  - DM
  - Paraprotein
  - Amyloid and sarcoid

## Chronic Renal Failure

- General:
  - Mental state
  - Hyperventilation [acidosis]
  - Hicups
  - Hydration
  - Cushingoid
- Hands:
  - Terry's nails
  - AV fistulas
  - Asterixis
  - Neuropathy
  - Gout
- Arms:
  - Bruising
  - Pigmentation
  - Scratch marks
  - Urea frost
  - Myopathy
- Skin – BCC [complication of transplant]
- **Blood pressure**
- Neck: LN + elsewhere – CV access
- Face:
  - Eyes: ocular nerve palsy [aneurysms], anaemia, jaundice, fundi
  - Rashes (vasculitis)
  - Hirsutism (CsA)

- Saddle nose: Wegner's
- Mouth: dryness, fetor, candida [immunosuppression]
- Chest: **Pericarditis and pleural effusion** (2<sup>nd</sup> to uraemia), valve problems in PKD [mvp - 26%, also AR]
- Abdomen:
  - Scars from dialysis, nephrectomy, transplant, Tenckhoff catheter sites (is it infected?)
  - Bladder
  - Hepatomegaly: from cysts or amyloidosis
  - Ascites, bruits
- Legs: oedema (nephrotic syndrome, CHF), bruising, pigmentation, gout, neuropathy
- Back: spina bifida scar

### *Investigations in Renal Failure*

- Renal function:
  - 24 hr Cr clearance and protein
  - Urine analysis and culture
  - Bloods: incl glucose, Ca, PO<sub>4</sub>, uric acid, Alb
- Renal structure: US (including ?reflux)
- Underlying disease processes: Hep B/C, HIV, ANA, complement, protein electrophoresis
- Complications of renal failure: FBC, ferritin, Ca, PO<sub>4</sub>, PTH

### **Palpable Kidneys**

- Stem – examine this patient's abdomen and proceed
- Aim: Look for CRF and complications, differentials, immunosuppression
- You find: one or two large kidneys
  - Causes of unilateral enlarged kidney:
    - Polycystic kidneys
    - Renal cell ca
    - Hydronephrosis
    - Renal cyst
    - Hypertrophy of a solitary functioning kidney
  - Causes of bilateral enlarged kidneys:
    - Polycystic kidneys
    - Bilateral hydronephrosis
    - Bilateral renal cell ca
    - Amyloid kidneys
  - Proceed looking for findings associated with the above differentials and features of chronic renal failure

### **Transplanted kidney**

- Similar to palpable kidney but...
  - Examine graft for tenderness/pain, **bruit**
  - Look for reasons why person has had a transplant – diabetes, HTN, Vasculitis [GN]
  - Look for complications of transplant therapy:
    - Skin cancers
    - Cushing's, other complications of steroid therapy
    - Hirsutism (cyclosporin)
    - Gums
  - HTN
  - Infections: lungs, mouth (candida)
  - CVD/PVD
  - Lymphomas
  - Gouty tophi

## Haematological

- Lie flat
- Inspect:
  - Bruising: petechiae, ecchymoses (if palpable then vasculitis, bacteraemia)
  - Pigmentation (lymphoma)
  - Rashes and infiltrative lesions (lymphoma)
  - Ulceration (neutropenia)
  - Cyanosis (polycythaemia)
  - Plethora (polycythaemia)
  - Jaundice (haemolysis)
  - Scratch marks (myeloproliferative disease)
  - Racial origin
- Hands:
  - Nails – koilonychia (haematological)
  - Palmar crease pallor (anaemia, if < 90)
  - Arthropathy (haemophilia, secondary gout, drugs)
- Arms:
  - Epitrochlear nodes
  - Axillary nodes (central, lateral, pectoral and subscapular groups): axilla has 4 sides (medial, lateral, posterior, anterior) – be seen to check them all
- Face:
  - Sclera: jaundice, pallor
  - Mouth: gum hypertrophy (AML, scurvy), ulceration, infection (candida), atrophic glossitis (Fe, B12 or folate deficiency), angular stomatitis (iron and vitamin deficiencies)
  - Tonsil enlargement (lymphoma)
- Cervical nodes: sitting up and from behind. 7 groups:
  - Submental
  - Submandibular
  - Jugular chain: running down SCM
  - Posterior triangle: posterior to SCM and round to the spine
  - Post-auricular
  - Preauricular
  - Occipital
- Bony tenderness: sternum, clavicles, shoulders, spine
- Abdomen: and genitalia
- Inguinal nodes
- Legs: Vasculitis, bruising, pigmentation, ulceration, neuro signs (subacute combined degeneration, peripheral neuropathy)
- Other:
  - Fundi (hyperviscosity, haemorrhages, infection)
  - Temp
  - Urine analysis: haematuria, bile
  - Rectal exam (blood loss)
  - Hess test: inflate BP cuff to 10 mmHg above diastolic for 5 mins, deflate, wait 5 mins, look for > 5 petechiae per cm<sup>2</sup> around wrist and antecubital fossa

- Differentials:

- Decreased counts:

	↓Production	↑Destruction
Hb	Fe, B12, folate, BM disorder (Pure Red Cell Aplasia, MDS), chronic disease, renal failure, endocrine (↓testosterone, hypothyroidism)	Haemolysis, thalassaemia, sickle cell, spherocytosis
WCC	BM infiltration BM dyscrasias (MDS)	Immune, drugs, sepsis
Platelets	BM infiltration BM dyscrasia (MDS)	Immune, TTP, DIC
Pancytopenia	BM infiltration	Immune, drugs, sepsis

BM dyscrasia  
Aplastic anaemia

Increased counts:

	Reactive	Clonal
Hb	Hypoxia, ↑EPO	Polycythaemia Vera
WCC	Infection, inflammation	Eg CML, CLL
Platelets	↓Fe, infection, inflammation, splenectomy	Essential thrombocythaemia
Eosinophils	Vasculitis, drugs, parasites, lymphoma, malignancy	Chronic eosinophilic leukaemia

Macrocytosis:

- Alcohol
- B12/folate deficiency
- Drugs
- Hypothyroidism
- Liver disease
- Bone marrow failure: aplastic anaemia, myelodysplasia
- Pregnancy

Thrombocytopenia:

- ↓production: marrow/fibrosis/infiltration, liver disease, Fe/B12, folate deficiency
- Hypersplenism of any cause
- ↑consumption:
  - Autoimmune (SLE, vasculitis, APS)
  - Infection: EBV, CMV, HI, toxoplasmosis
  - Drugs: heparin, penicillins, sulfonamides
  - Other: ITP, TTP/HUS, DIC

Splenomegaly:

- Infection: EBV, CMV, HIV, endocarditis, malaria, hydatids
- Haematological:
  - Myeloproliferative: CML, myelofibrosis, PCV, ET
  - Lymphoproliferative: CLL, leukaemia, lymphomas, hairy cell disease
  - CVID
  - Haemolytic anaemia
- Mechanical: portal HTN, splenic vein thrombosis, infiltration (amyloid, sarcoid), storage disease
- Autoimmune: RA, SLE, PAN
- Lymphadenopathy: Lymphoma (rubbery and firm), CLL, ALL, malignancy (very firm), infection (CMV < HIV, EBV, TB, Toxoplasmosis), RA/SLE, Sarcoid, drugs (phenytoin)
- Intravascular anaemia: DIC, TTP, HUS, Valve, bongo drummers

- LOOK, FEEL, MOVE, Special tests, joint above and below, distal pulses, neurology

## Hand Exam

- Principles
  - Look
  - Feel
  - Move
  - Special tests and neurology
  - Function
- General Inspection
  - *Cushing's*
  - Weight
  - Iritis
  - Obvious joint disease
- **Look on pillow:**
  - Nails: Pitting ( $\Rightarrow$  psoriasis), ridging, onycholysis
  - Muscle wasting
  - Synovitis
  - Dactylitis: isolated sausage finger, due to tenosynovitis, suggests any spondyloarthropathy
  - Deformity:
    - Fingers: Boutonniere, Swan neck,
    - MCP: Subluxation, Ulnar deviation of fingers
    - Z deformity of the thumb
    - Wrist: Radial deviation and subluxation
  - Nodes: Heberden's, Bouchard's
  - Hold hands out (tremour, drift)
- Feel (*ask if any pain before doing so*):
  - Temperature on arms compared with hands, heat of any particular joint
  - All joints: Tenderness, effusion
  - **MCP squeeze**
  - Thickened palmar tendon – feel while asking patient to make a fist, test grip strength
- Move:
  - Wrist and fingers: Flexion/extension
  - Flexion of distal phalanx (flexor profundis) & proximal phalanx (flexor superficialis) tests
  - Thumb: Flexion/extension, abduction/adduction, opposition
  - Quick nerve tests:
    - Ulnar: little finger abduction
    - Median: sensory over 2<sup>nd</sup> digit, weak thumb abduction
    - Radial: extension of fingers, sensory over anatomical snuffbox
  - Make fist
  - Carpal tunnel test – Phalen's for 30secs
  - Prayer sign
- Function:
  - *Opposition strength*
  - Unscrew jar
  - Key grip
  - *Undo a button*
- Proceed:
  - Feel skin up arms and chest
  - Feel proximal muscles for bulk and tenderness
  - Rheumatoid nodules at elbow (an Achilles tendon)
  - Psoriatic rash: *extensor elbow*, hairline, naval, natal cleft
  - Tophi on ears
  - FROM of neck
  - Eyes and mouth for Sjogren's: xerostomia and keratoconjunctivitis sicca
  - Lungs for fibrosis
  - Spleen for Fealty's Syndrome

- Feet
- **If Sjogren's or SLE always do BP**

## Raynaud's Syndrome

- General inspection
- Hands: arthritis, loss of pulp, digital ulcers, scleroderma changes (calcinosis, telangiectasia), Gottron's papules
- Arms:
  - R-R delay
  - BP – bilaterally
  - Proximal myopathy
- Head: Alopecia, Scleroderma, telangiectasia, butterfly or heliotrope rash, conjunctivitis.
- Neck: Palpate for cervical rib.
- Chest, Abdo and Resp and legs as per SLE and systemic sclerosis exams
- Differential:
  - Primary (> 3 years without other disease)
  - Secondary:
    - Autoimmune: SLE, DM, SLE, RA, MCTD
    - Arterial: PAN, atherosclerosis
    - Drugs: eg  $\beta$ -blockers
    - Other: Cryoglobulins, vibration
- Investigations
  - UE, LFTs, FBC, ESR, total Ig and electrophoresis
  - ANA, RF, ENA
  - Nail-fold capillaroscopy – drop of oil and look with fundoscope – capillary loop drop out is the most sensitive test of progression
  - Urinalysis
  - CXR and Hand Xray

## Back

- Inspect : while standing, undress to underpants
  - From back
  - From side
  - Looking for – loss of kyphosis, lumbar lordosis, skin changes – hair tufts, step deformities
- Walk
- Feel
  - Each vertebrae for tenderness
  - *Paravertebral muscles for spasm*
  - Skin rolling for fibromyalgia
- Move while standing:
  - Lumbar spine: extension/flexion/lateral flexion
  - Schoeber's test normal increase 7cm
  - Occiput to wall distance
- "Sit on bed"
  - Test thoracic spine
    - Cross your arms and place hands on shoulders
    - Test rotation
  - Test C-spine
    - Flexion – chin to chest
    - Extension – look up
    - Lateral flexion – put ear on shoulder
- "Lie on your back"
  - Test the SI joint: Patient lying on back
    - press down on hips on both sides
    - Knee to shoulder test - push knee towards opposite shoulder
- Neurologic testing
  - Quickly exclude spinal chord compression
  - Femoral stretch – patient on front – extend hip with knee flexed – positive if pain down anterior thigh

- Proceed :
  - Test hips knees shoulders
  - Ank spond: Chest expansion, apical fibrosis, AR, MVP, uveitis
  - Sero -ve: Achilles tendonitis, plantar fasciitis, psoriasis
- Evaluation for malignancy (breast, prostate, lymph node exam) when persistent pain or history strongly suggests systemic disease

## Hip Exam

- Inspection
  - While standing:
    - Observe gait
    - Walking: on toes (tests S1), on heels (test L5)
    - Observe from front and do Trendelenberg's test: thumb on each ASIS while they alternate standing on one leg. Sagging to contra-lateral side is Trendelenburg positive (ie lack sufficient abductor strength to stabilise pelvis)
    - 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
    - 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
      - Apparent leg length discrepancy: measure umbilicus to medial malleolus. If discrepancy but no real leg length discrepancy then postural cause
- Palpation:
  - Groin: lumps: hernias, lymph nodes, femoral artery aneurysm ⇒ pain is not hip pain
  - Check for ilio-tibial band pain over the greater trochanter ⇒ pain is not hip pain
- Range of motion: always state start and end: from X to Y degrees (eg adduction from 0 to 30 degrees)
  - Compare sides
  - 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
  - Test flexion
  - To test adduction (0 - 20°) and abduction (0 - 50°), stabilise hip by holding hand across both ASIS 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
- Finally check:
  - Leg pulses → relevant to operative risks
  - Joint above: did this while standing
  - Joint below: check knee

## Knee

- Look
  - Ask patient to walk to and from you
  - Heel-Toe walk
  - Ask patient to squat to assess function and meniscal injury
  - Quadriceps wasting
  - Effusions
  - Scars from injuries/procedures
  - Skin changes suggestive of inflammation
  - Fixed flexion deformity
  - Varus (OA) or Valgus (RA) deformity
- Feel

- Quadriceps and other muscle wasting
- Temperature of joint
- Patellar tap
- Medial and lateral bulge test
- Synovial thickening
- Feel tone if neurology exam also required
- Move
  - Passive
    - Flexion (normal up to 135°): do with hand on patella to check for crepitus
    - Extension (normal to 5°)
    - Collateral (Normal 5 – 10°)
    - Cruciate (Normal 5 - 10°): feel for end point. ↑ anterior movement = ACL, ↑ posterior movement - PCL
    - Patellar apprehension test: push patella laterally while slowly flexing the leg
  - Active flexion and extension with assessment of power if neurology exam required
- Roll onto back
  - Evidence of Baker's cyst
  - Appleby's grind test to look for meniscal injury – knee extended to 90o
  - McMurray's test for meniscal integrity: flex/extend knee while internally/externally rotating the tibia
- Function
  - Assess walk
  - Stand from sitting position
- Investigations
  - AP and lateral films
  - Joint aspiration

## Rheumatoid Arthritis

- General points
  - Joints involved
    - Wrists: subluxation
    - PIP (swan neck and boutonniere) & MCP (ulnar deviation and volar subluxation)
    - Thumb: Z deformity
    - Neck
    - MTP
    - Knees
  - Nodules (usually over elbow) = more severe disease
    - Other sites of nodules
      - Flexor & extensor surface of hands
      - Achilles tendon
      - Sacrum
      - Sclera
      - Lungs
      - Myocardium
- Complications:
  - Skin lesions caused by vasculitis
  - Amyloidosis
  - Anaemia
  - Pulmonary
    - Pleural effusions and pleurisy
    - Nodules
    - Fibrosis
    - Caplan's syndrome – rounded fibrotic nodules
  - Eyes
    - Episcleritis
    - Scleritis
    - Keratoconjunctivitis sicca
    - Sjogren's
  - Palindromic RA

- Recurrent episodes with symptoms lasting hours to days
- Rx – Hydroxychloroquine
- Neurology
  - Peripheral glove and stocking neuropathy
  - Mononeuritis multiplex
  - Carpal tunnel
  - Atlanto-axial
- Sjogren's
  - Keratoconjunctivitis sicca & xerostomia
  - Schirmer test
  - Anti-Ro and La Abs
  - Rx with artificial tears/saliva
- Investigations:
  - Bloods: RF and Anti-CCP
  - Imaging: Xray, US (detects more erosions than xray), MRI

## Ankylosing Spondylitis

- Signs (remember 4 As – AR, apical fibrosis, ant. uveitis, Achilles tendonitis)
  - Loss of lordosis
  - Kyphoscoliosis
  - Loss of spinal movements
  - Increased occiput to wall distance
  - Schoeber's test < 5cm
  - Reduced chest expansion < 5 cm
  - Other systems:
    - Eyes: iritis (acute red sclera) and anterior uveitis
    - Heart: AR
    - Lungs: restrictive disease, UL fibrosis
    - Feet: *Achilles tendonitis, plantar fasciitis*
- Differential (other seronegative arthropathies):
  - Reactive arthritis
  - Psoriasis
  - Intestinal arthropathy
- Investigations:
  - AP & lateral XR
    - Erosions & sclerosis of SI joints
    - Syndesmophytes later
    - Lastly 'bamboo spine'

## Gout

- Basic Exam:
  - Start with feet: MTP and Ankle exam:
    - Look for asymmetric swelling, deformity
    - Tophi, esp over Achilles tendon and other tendons
  - Knee exam
  - Quick look at fingers, wrist and elbow-usually late involvement
  - **Look for Tophi** elsewhere: Ear, olecranon bursa, extensor surface of forearm
- **Look for secondary causes of Gout:**
  - Myeloproliferative
  - Lymphoma/Leukaemia
  - Renal disease
  - Hypothyroid
  - Ask for: Thiazide use, alcohol use, cyclosporin
  - Also look for associations: DM/HTN/IHD
- Look for complications: urate nephropathy/carpal tunnel
- Investigations:
  - Joint or tophi aspiration-negatively birefringent needle shaped crystals
  - Serum uric acid in serum

- X-ray for chronic damage

## Systemic sclerosis

- General inspection:
  - Cachexia
  - Expressionless (bird like) facies
- Hands:
  - Run hands down from arms to hands – note coldness of hands
  - Start with dorsum and do standard rheumatological hand exam
  - Skin:
    - Sclerodactyly: shiny smooth, tight, (thick) skin
    - Calcinosis
    - Telangiectasia (comment on absence as a pertinent negative)
    - Atrophy of pulps
    - *Ulcerations, infarcts* and auto-amputations
  - Joints: synovitis
  - Deformity: contractions
  - Nails: *dilated capillary loops*
  - Turn over to see palmer surface
    - FEEL:
      - warmth, synovitis and tenderness
      - skin thickening-map to the most proximal part
      - contractures
      - calcinosis
  - At this point skip neurology and passive movements if it is suggestive of scleroderma
  - Move:
    - Fingers: fist, extension, opposition
    - Wrist: flexion (prayer sign), extension (backs of hands)
  - **Function:**
    - Grip
    - Key holding and bottle opening
    - Undo a button
    - Writing
  - **Proximal myopathy**
- Test skin tightness up the arms – what is the limit
- **Blood pressure (forget it and fail!)**
- Face:
  - Wrinkles
  - Pinched face
  - Telangiectasia (on hands face and neck)
  - Skin thickening
  - Eyes for closing and dryness
  - Mouth-3 finger test and xerostomia (dry mouth)
  - **Swallow water**
- Chest: Skin
- Respiratory: Percussion and auscultations (looking for interstitial fibrosis and pulmonary hypertension)
- CVS: JVP, apex, heave, heart sounds with loud P2, pericardial rub (pericardial effusion)
- Legs:
  - Same as hands, but more specific to scleroderma
  - Skin thickening, telangiectasia, calcinosis, and soft tissue atrophy
  - **Vasculitis** rash or ulcers
- Differential:
  - Limited scleroderma: skin to mid forearms and fact
  - Diffuse: other places (upper arms and chest)
- Investigations:
  - **Urinalysis**
  - Bloods: ESR, FBC (anaemia), ↑Ig, ANA, RF (anti-centromere and AntiScl70)

- CXR and **spirometry** (DLCo)
- ECG and Echo
- History/investigations for PBC

## Dermatomyositis

- Signs
  - Skin:
    - Gottron's papules (erythema over knuckles with sparing over phalanges c.f. SLE which is opposite)
    - Heliotrope rash
    - Periungual erythema
    - Mechanics hands
  - Muscle
    - Proximal weakness
    - Tenderness
    - Tell examiner would like to ask pt. about dysphagia & dysphonia
- Differential (for myopathy with high CK):
  - Inclusion Body Myositis
  - Myopathy secondary to Rx – e.g. statins
  - Secondary to steroids (without raised CK)
  - Sarcoid myositis
  - Infectious
- Investigations:
  - If patient over 40 tell examiner would like to exclude underlying neoplasm
  - CK (shows disease activity)
  - Anti Jo
  - EMG – myopathic changes
  - Muscle Bx

## Differentials

- Differential for thickened skin:
  - CREST
  - Systemic sclerosis
  - MCTD
  - Eosinophilic fasciitis
  - Morphea
  - Chemical insult
  - GVHD
- Differentials of chronic arthritis:
  - Monoarthritis: OA, seronegative arthritis, chronic infection (TB), metastasis, trauma
  - Polyarthritis:
    - RA
    - Seronegative:
      - Ankylosing Spondylitis
      - Psoriatic
      - Reactive (check for conjunctivitis and ask for infectious and sexual history)
      - Inflammatory Bowel Disease
    - OA
    - Gout, pseudogout or hydroxyapatite arthropathy
    - CTD (eg SLE)
    - Haemochromatosis
    - Haemophilia
    - Infection: Lyme disease, Gonococcal
  - By distribution:
    - Small joints: RA, SLE, Psoriatic arthritis
    - Asymmetric large joint: sero-negative spondyloarthropathies: AS, reactive, psoriatic, arthritis of IBD
- Eye signs in arthritis:
  - Anaemia

- Scleritis: RA. An elevated white or purple-red lesion (a type of rheumatoid nodule) and is usually surrounded by intense redness of the injected sclera
- Iritis (acute red sclera) and Anterior Uveitis: Ank Spond (*not* RA)
- Cataracts: Steroid use
- Conjunctiva: Reactive arthritis
- Sjogren's: Keratoconjunctivitis sicca – dry eyes
- Causes for anaemia in inflammatory arthritis:
  - Chronic disease
  - NSAIDs → bleeding → Fe deficiency
  - Macrocytic anaemia: AZA, folate ↓ with MTX
  - Fealty's Syndrome: pancytopenia in RA

## Thyroid

- Stem:
  - Thyrotoxic patient: Likely to be asked to examine the neck and proceed, the eyes (Grave's) and proceed, the pulse and proceed, or the hands (tremor)
  - Hypothyroidism: Likely to be asked to examine the neck or the pulse and proceed
- General:
  - Note any restlessness, nervousness
  - Comment on evidence of weight loss
- Sitting up
- Inspection: If hypothyroid
  - face (anaemia)
  - Weight gain
  - Loss of outer third of eyebrows
  - Carotenaemia
  - Puffy lower eyelids
  - Xanthelasma
  - Hair loss or coarsening
- Neck:
  - Inspect: scars, swelling, prominent veins, swallow (glass of water)
  - Palpation (from behind with neck flexed):
    - Enlargement: size, shape, consistency, borders (can you get below it), mobility – single, multinodular (normal volume = 20 mls)
    - Tenderness (subacute thyroiditis)
    - Thrill
    - Cervical nodes
    - Horse voice
  - Palpation (from in front):
    - Thyroid as above
    - Carotid arteries (if absent ?malignant infiltration)
    - Supraclavicular nodes
    - Trachea position
    - Sternomastoid function (?malignant infiltration)
  - Percuss sternum for retrosternal extension
  - Auscultate: thyroid ( $\Rightarrow$ thyrotoxicosis) and carotid bruit
  - There are 4 things in the neck that get blocked. Check:
    - Oesophagus: swallow
    - Trachea: Pemberton's sign
    - SVC obstruction: plethora,  $\uparrow$ JVP
    - Horner's Syndrome
- Hands:
  - If hyperthyroid:
    - Shake hands to note warmth
    - Thyroid Acropachy (This *is* clubbing but is termed this is thyroid disease)
    - Tremor (Place paper on outstretched hands)
    - Onycholysis (loosening of the nail distally from the bed causing increased whiteness)
    - Vitiligo
    - Palmar Erythema
    - Pulse (Comment on AF)
  - If hypothyroid:
    - Brittle fingernails
    - Absent cuticles
    - Bradycardia
    - Yellow tint of carotenaemia
    - Dry skin
    - Carpal Tunnel Syndrome
- Eyes of hyperthyroid:

- Exophthalmos/ Proptosis: looking from above and behind
  - Presence of sclera below the cornea when looking straight ahead
  - Lid retraction: sclera above the cornea
  - Lid lag – follow finger descending quickly
- Test eye muscles for ophthalmoplegia – inferior oblique is lost first
- Fundi for atrophy (late sign)
- Check for scars of tarsorrhaphy (suturing of eyelids to prevent dryness)
- Chest
  - JVP for SVC
  - Cardiac exam especially noting AF
  - Gynaecomastia
  - If female and age is appropriate, assess for signs of recent pregnancy eg caesarean scar
- Lower limbs
  - Hyperthyroid:
    - Hyperreflexia
    - Pre-tibial myxoedema
  - Hypothyroid:
    - Proximal myopathy
    - Delayed ankle jerks
- Proceed
  - Examine briefly for other autoimmune features
    - Vitiligo
    - Fundoscopy for diabetic retinopathy
    - Dorsal column signs due to pernicious anaemia
    - Rheumatoid arthritis
  - If evidence of thyroidectomy check for features of hypocalcaemia
    - Chvostek's Sign – Tapping of facial nerve at angle of jaw causes ipsilateral mouth and nose twitch
    - Trousseau's Sign – Sphygmomanometer 20 mmHg above systolic BP for 3 minutes causes *main d'accoucheur* (Wrist/finger flexion, with extension of IP joints)
- Differential:
  - Thyrotoxicosis:
    - Increased uptake on radioiodine scan
      - Grave's disease
      - Nodular Goitre (Only becomes active in later life)
      - $\beta$ -HCG related thyrotoxicosis
    - Decreased uptake
      - Thyroiditis
      - Viral (De Quervain's)
      - Post-Partum
      - Early Hashimoto's
    - Factitious thyrotoxicosis
  - Hypothyroidism:
    - With Goitre: Hashimoto's, Iodine deficiency, drug induced (amiodarone)
    - Without Goitre: atrophic thyroiditis, post surgical, post radiation
- Investigations:
  - TSH and thyroid hormones
  - Check for Thyroid stimulating (Ts) antibodies
  - Check for Anti-TPO (Microsomal) antibodies
  - ECG if tachycardic
  - US of gland to evaluate nodule, and to guide treatment in amiodarone induced
  - Radioiodine uptake scan
  - FNA of node if no uptake on radio-iodine scan as this could indicate tumour
- Treatment of hypothyroidism: Thyroxine based on TSH. Elderly or those with IHD should start on 25mcg

## Diabetes

- Inspection: weight, hydration, endocrine facies (eg Cushingoid, acromegaly), pigmentation (eg haemochromatosis)

- Legs (start here):
  - Skin: hair loss, infection, pigmented scars
  - Injection sites
  - Muscle wasting (eg quadriceps from amyotrophy)
  - Temperature of feet
  - Peripheral pulses (auscultate femorals) and capillary return
  - Oedema
  - Neuro: proximal muscle power (femoral nerve mononeuritis), reflexes, peripheral neuropathy
- Arms: pulse
- Eyes: visual acuity, fundi – cataracts, retinal disease, 3<sup>rd</sup> nerve palsy (is pupil sparing – infarction affects inner more than the outer fibres, as opposed to compressive which affect out first → pupil affected first)
- Mouth and ears: infection
- Neck: carotids: palpate and auscultate
- Chest: signs of infection
- Abdo: liver: fat infiltration, hypertrophy from injection sites
- Other:
  - BP lying and standing
  - Urine analysis

## Diabetic foot

- Look :
  - Deformity
  - Claw toes
  - Collapse of the arch
  - Small muscle wasting
  - Skin - cracked/infected/erythema/callus/gangrene/absent sweating
  - Ulcers
  - Look between the toes and under the metatarsal heads
- Feel:
  - Temperature of skin
  - Pulses
  - Plantar response and ankle jerk
  - Vibration sensation 128-Hz tuning fork
  - Pressure sensation (10-g) monofilament
  - Pain or temperature
  - Joint position sense
- Move:
  - Joint mobility/hyper mobility? Charcots
  - Gait and balance
- Patterns:
  - Neuropathic – dry, warm, reduced sensation, plantar ulcers, absent reflexes
  - Ischaemic – cold, pulseless, heel/toe ulcers
  - Mixed
- Investigations:
  - Glucose and HBA1C
  - FBC to exclude infection
  - B12/folate to exclude other causes of neuropathy (also alcohol)
  - XR

## Panhypopituitarism

- Inspection:
  - Hair loss
  - Chest: ↓hair, gynaecomastia, pale skin
  - Short stature (↓GH before puberty), 2ndary sexual characteristics
  - Wrinkles round eyes: ↓GH
  - Feel for facial hair
  - Hypophysectomy scar: inner eye, above hair line
- Genitals: ↓pubic hair, testicular atrophy

- Eyes:
  - Visual fields (bitemporal hemianopia) and fundi (for optic atrophy and papilloedema)
  - Nerves 3, 4, 6 (for ocular palsies) and V1 (extension into cavernous sinus)
- ↓ankle jerks in TSH deficiency
- Standing and lying BP: ACTH deficiency
- Note: Hormone production lost in the following order: GH-Prolactin-FSH/LH-TSH-ACTH
- Differential:
  - Sheehan's syndrome
  - Pituitary tumour
  - Craniopharyngioma
  - Iatrogenic- Surgery and radiotherapy
  - Head injury
  - Granulomatous disease
  - Idiopathic
- Investigations:
  - Pituitary stimulation test
  - MRI head to r/o mass lesion causing neuro issues
  - Pituitary hormones
- Treatment:
  - If mass effect-surgery
  - If not-Hormone replacement.

## Cushing's

- Stem: weight gain or HTN
- Inspection/standing:
  - Look for front, sides, behind
  - Central obesity, thin limbs, *skin atrophy*
  - Pigmentation (rare ACTH tumour, or bilateral adrenalectomy)
  - Poor wound healing
  - Arms: purple striae, proximal myopathy
- Sitting:
  - Face:
    - Plethora, hirsutism, acne, telangiectasia → plethora
    - Moon shape
    - Eyes: visual fields, fundi (atrophy, papilloedema, HTN, diabetes)
    - Mouth: thrush
    - Neck: fat pad over the supraclavicular fossa, acanthosis nigricans
  - Back: buffalo hump, kyphosis and vertebral tenderness (osteoporosis)
  - Legs: squat (proximal myopathy), purple striae (thighs and shoulders), bruising, oedema
  - Mental state: depression, psychosis, irritability
- Lying flat:
  - Abdomen: purple striae, adrenal masses, adrenalectomy scars, liver (tumour deposits)
  - Genitalia: virilisation in women/gynaecomastia in men suggests adrenal carcinoma more likely
- Blood pressure
- Comment on signs of asthma, RA, SLE, fibrosing alveolitis: treated with chronic steroids
- Others: urine analysis (glycosuria, renal stone disease), signs of ectopic lung tumour
- Note: Hirsutism is not common in exogenous steroids as they suppress adrenal androgen secretion

## Acromegaly

- Stem: changed facial appearance
- General Inspection: diagnostic facies
- Hands: shape, sweat, can they remove rings, Phalen's test (prolonged wrist flexion – put back of wrists together) or Tinel's (percussion over carpal tunnel – not as good as Phalen's)
- Ulnar nerve: thickened
- Proximal myopathy
- Axillae: skin tags (also neck), acanthosis nigricans, greasy skin

- Face: frontal bossing (also in rickets or Paget's), hirsutism, macroglossia, prognathism (protrusion of jaw – over bite), teeth spacing, hoarseness
- Eyes: **visual fields**, CN 3, 4, 6, 5, fundi
- Neck: thyroid goitre (if found then check for thyrotoxicosis)
- Heart: failure: JVP, apex
- Abdomen: organomegaly
- Lower limbs: OA and pseudogout of hips and knees, heel pad thickening
- Other: BP, glycosuria, sleep apnoea

### Addison's

- Stem: weakness, anorexia, weight loss
- Pigmentation: palmar creases, elbows, gums, buccal mucosa, vitiligo (autoimmune association)
- Postural blood pressure

### Gynaecomastia

- A benign proliferation of the glandular tissue of the male breast caused by an increase in the ratio of oestrogen to androgen. It is unilateral or bilateral. Palpable mass usually under the nipple
- Causes:
  - Physiologic/Puberty
  - Drugs – many:
    - CVS - spironolactone, nifedipine, digoxin, ACEI
    - GI - cimetidine omeprazole, antiandrogens
    - Anti-infectives – ketoconazole, HAART, isoniazid
  - Cirrhosis
  - Hypogonadism
  - Hyperthyroidism
  - CRF
  - Pituitary disease
  - HCG producing tumours - Germ cell, HCC, lung,
- Differential:
  - breast cancer
  - pseudogynaecomastia
  - fat
- Examination:
  - Klinefelter's
  - Absence of body hair
  - Clubbing, cachexia
  - AF
  - CHF
  - Visual fields
  - signs of liver disease
  - signs of kidney disease
  - testicular size testicular mass
- Investigations:
  - hCG, LH, FSH, testosterone, oestradiol, PRL, TFT
  - Testicular ultrasound for mass
  - CXR – lung ca
  - chromosomal analysis

### Differentials

- Acanthosis nigricans: due to insulin resistance:
  - Obesity
  - Endocrine: DM, acromegaly, Cushing's, PCOS, not Addison's
  - Cancer: gastric adenocarcinoma
- Amenorrhoea (secondary):
  - Ovarian
  - Pituitary
  - Hypothalamic
  - Thyroid

- Androgen excess (PCOS, adrenal)
- Anion gap:
  - Increased:
    - Methanol, ethanol, salicylates, uraemia, ketones
    - Lactate: Hypoxia/tissue damage, DM, malignancy (usually liver involvement), alcohol, HIV or NRTIs, drugs (metformin), mitochondrial disease, pheo
  - Decreased: ↓albumin, myeloma
  - Normal (loss of HCO<sub>3</sub>): acetazolamide, RTA and some renal failure, diarrhoea, pancreatic loss
- Hypercalcaemia:
  - Exclude dehydration, cuffed sample and raised albumin
  - ↑PTH
  - Malignancy
  - Renal failure
  - High bone turnover: Paget's, immobilization, hyperthyroid, ↓adrenal
  - ↑intake: vitamin D, milk alkali
  - Drugs: thiazides
- Hypocalcaemia:
  - ↓PTH
  - ↓Mg
  - ↓Vit D
  - Burns, sepsis
  - Tumour lysis and haemolysis
- Osteoporosis:
  - Endocrine: cortisol, testosterone, thyroid, PTH
  - Metabolic: osteomalacia, renal failure, liver disease
  - Blood: myeloma, marrow infiltration, leukaemia, lymphoma
  - CTD: RA, AS, Marfan's, congenital
  - Drugs: alcohol, steroids, heparin, anticonvulsants
- Osteomalacia:
  - ↓Vit D: malabsorption, renal (CRF, nephritic syndrome, peritoneal dialysis), inadequate sunlight
  - ↓PO<sub>4</sub>: phosphate binders, Fanconi syndrome, hereditary
- Hirsutism:
  - PCOS
  - POEMS
- Impotence:
  - Psych
  - Neurogenic
  - Vasogenic
  - Drugs
  - Endocrine: acromegaly, ↑PRL

- Abulia: loss of will power, initiative or drive – inability to make decision
- Acalculia: inability to do mathematical calculations
- Anosognosia: lack of awareness that a deficit exists
- Apraxia: inability to perform a familiar task despite normal sensory and motor function
- Ataxia: inability to coordinate movement
- Finger agnosia: loss of ability to indicate one's own or another's fingers
- Eyes:
  - Ptosis: drooping of upper eye lid
  - Exophthalmos: protrusion of the eye
  - Mydriasis: dilation of the pupil
  - Miosis: contraction of the pupil
- Movement problems:
  - Akathisia: motor restlessness, as seen in reactions to phenothiazines
  - Athetoid: slow writhing movements
  - Chorea: Ceaseless rapid, jerky, involuntary movements
  - Dyskinesia: impairment of voluntary movement
  - Dystonia: impairment of muscle tone – sustained muscle contractions causing twisting movements of abnormal posture

### Presenting

- State:
  - Findings
  - Severity
  - Comment on function

### Where is the lesion

- Think: cortex, basal ganglia, cerebellum, brainstem, cord, nerves, NM junction, muscles
- Lower: weakness, wasting, hypotonicity, ↓reflexes, fasciculation
- Upper: Spasticity, clonus, ↑reflexes, all groups weak but more so in:
  - Upper limb: shoulder abductor and elbow and wrist extensor muscles → flexion contractures
  - Lower limb: Hip and knee flexion and ankle dorsiflexion → extension contractures
- Differential of multiple CNS Lesions:
  - MS
  - SLE, Sjogren's, Behcet's
  - Acute disseminated encephalomyelitis
  - Syphilis
  - Sarcoid
  - Lyme disease
  - Multi emboli of any source
- Differential of diffuse Upper Motor Neuron process:
  - Degenerative
  - Ischaemic
  - Demylinating
  - Metabolic

### Cranial Nerves

- Inspection: head and neck, craniotomy scars (behind hairline), facies (Cushing's, acromegaly), ptosis, proptosis (= forward bulging, when referring to the eye = exophthalmos), pupil inequality
- Smell (Olfactory): "Can you smell normally". Only if not then:
  - Test each nostril separately
  - Differential: URTI, meningioma, trauma, hydrocephalus, congenital (eg Kallman's syndrome)
- Ophthalmic:
  - Visual acuity (with glasses on)
  - Visual fields: confrontation with red tipped pin (detects earlier loss), use fingers if poor visual acuity
  - Check fundi:

- Papilloedema: space occupying lesion, hydrocephalus, benign intracranial hypertension (OCP, Addison's, steroids, lateral sinus thrombosis, head trauma), HTN, central retinal vein thrombosis
- Optic neuropathy: glaucoma, ischaemia, MS, drugs (ethambutol), EBV
- Cataract: old age (senile cataract), DM, steroids, glaucoma, irradiation, trauma
- Test for enlarged scotoma (blind spot) if MS suspected or abnormality on fundoscopy
- Oculomotor, Trochlear, Abducens:
  - Ptosis Differential: MG, myotonic dystrophy, thyrotoxicosis, senile, Horner's, 3<sup>rd</sup> nerve lesion (with dilated pupil). Muscle that holds open the eye lid is *levator palpebrae*
  - Pupil:
    - Light reflex has no cortical involvement. Accommodation does. Argyll Robertson pupil = midbrain lesion with accommodation but no light reflex – including syphilis, DM, alcohol
    - Constriction: *Horner's*, Argyll Robertson, pontine lesion (often bilateral but reactive to light), narcotics, old age
    - Dilation: *third nerve lesion*, atropine, mydriatics, cocaine, trauma, surgery
    - Pupillary reaction: afferent defect – affected eye won't dilate but will dilate when torch swung to other eye
    - Accommodation: look at distance then focus on finger at 15 cm
  - Eye movements: ask about diplopia. If any lesion test each eye separately – show fixing eye
  - Third nerve lesion:
    - Complete ptosis, eye “down and out”, unreactive pupil to light and accommodation. Exclude 4<sup>th</sup> nerve lesion – can they look down and in on the affected side – Trochlear intorts the eye *when it's adducted* (when it's abducted, 3<sup>rd</sup> nerve is the depressor via inferior rectus)
    - Differential: vascular (brain stem infarction, aneurysm of posterior communicating artery), tumour, trauma, idiopathic
    - MR palsy only → intranuclear ophthalmoplegia (MS of CVA)
  - Sixth nerve lesion:
    - Failure of lateral movement (lateral rectus). Diplopia maximal on looking to affected side
    - Differential:
      - Bilateral: trauma, Wernicke's, ↑ICP, mononeuritis
      - Unilateral: vascular, tumour (cerebellar pontine angle lesion), Wernicke's, DM, etc
  - Assess saccadic eye movements and smooth pursuit both horizontally and vertically:
    - Hypometric saccades: undershoots and catches up
    - Hypermetric saccades: overshoots and corrects back
  - Nystagmus:
    - Horizontal:
      - Vestibular, cerebellar (both cause nystagmus to the side of the lesion)
      - Internuclear ophthalmoplegia: Nystagmus in the abducting eye, failure of adduction in the other eye. If young, MS, if old then brain stem CVA
    - Vertical: brain stem lesion, toxic (phenytoin)
    - Bilateral or unilateral with afferent pupillary defect: MS (also red eye with optic neuritis) or bilateral cerebellar lesion
  - Supranuclear Palsy:
    - Loss of vertical upward gaze and sometimes downward gaze – differentiate from nerve palsies as both eyes affected, pupils often unequal, no diplopia, reflex doll's eye movements (on flexing and extending neck) intact
    - Loss of upward gaze can be normal in old people, loss of downward gaze more sensitive for pathology
    - Progressive supranuclear palsy: associated with pseudobulbar palsy, long tract signs, extrapyramidal signs, dementia and neck rigidity, no tremour
  - Causes of ophthalmoplegia (CN 3, 4, 6):
    - Vascular: infarct, aneurysm, cavernous sinus
    - Infiltrative
    - Myopathy – thyroid, amyloid, sarcoid
    - MG
    - GBS
    - ↑ICP
    - Wernicke's
    - Supranuclear palsy
- Trigeminal:

- Light touch and pin-prick in ophthalmic, maxillary and mandibular divisions
- Motor 5<sup>th</sup>: jaw opening in midline (tests pterygoids – jaw deviates to side of lesion), clench jaw and palpate masseters
- Differential: vascular, tumour, syringobulbia, MS, aneurysm, fracture of the middle fossa, thrombosis. *Also Sjogren's and SLE*
- Corneal reflex (cornea not conjunctiva) – once on each side – should blink both sides simultaneously and should actually feel it (V component – if ipsilateral 7<sup>th</sup> nerve then no blink on that side)
- *Jaw jerk: increased in UMN lesion (eg pseudobulbar palsy)*
- Facial nerve:
  - Look for asymmetry – droop, flattened nasolabial fold, LMN lesion if forehead affected (bilaterally innervated):
    - Mouth is orbicularis oris
    - Eye is orbicularis oculi
  - Open eyes wide, tight closed and *try to open each eye.*
  - “Show me your teeth”. Puff out cheeks – can they form a seal with their lips
  - If lower motor lesion check ear and palate for herpes zoster vesicles
  - Taste on anterior not usually tested
  - Differential of facial nerve palsy:
    - UMN (supranuclear); vascular, tumour
    - LMN:
      - Bell's palsy
      - Otitis media
      - Tumour (eg acoustic neuroma), meningioma
      - Syringobulbia
      - MS
      - Fracture
      - Ramsay Hunt Syndrome (zoster with eruption on the external ear canal and tympanic membrane)
      - Parotid enlargement: sarcoid, lymphoma
      - Leprosy
      - Vascular lesion
- 8th nerve: Vestibulochoclear
  - Whisper a number in each ear – mask other side with rustling
  - Rinne's: 256Hz Tuning fork on mastoid process, when it's no longer heard put it outside the external meatus. Normal: still heard there. Nerve deafness: still heard there (air conduction better than bone). Conduction: not heard outside meatus
  - Weber's: Tuning fork on forehead. Normal – sound in the middle. Nerve deafness – sound is transmitted to the normal ear. Conductive deafness – hear louder in the abnormal ear
  - Rinne's and Webber not very accurate
  - If abnormal check ears (wax the most common cause of conductive loss)
  - Differential:
    - Sensorineural: degeneration (Presbycusis), trauma (eg noise exposure), toxic, infection, tumour (acoustic neuroma), brain stem
    - Conductive: wax, otitis media, otosclerosis, Paget's disease of the bone
- Glossopharyngeal and vagus:
  - Uvula, say ahh. In 10<sup>th</sup> lesion moves to unaffected side
  - Gag reflex: 9th is sensory, 10<sup>th</sup> is motor – can they feel it, do they gag
  - Speaks: hoarseness, cough (listen for bovine cough)
  - Taste on posterior not usually tested
- Accessory: shrug for trapezius, shake for SCM, neck flexion. Palpate SCM while doing it.
- Hypoglossal (12): look at tongue while in the mouth first for wasting and fasciculation before protruding. Deviates to affected side. Most muscles bilaterally innervated so detecting unilateral LMN lesions difficult
- Discretionary:
  - If lateral medullary: check peripheral
  - Multiple lower cranial nerve palsy's, check nasopharynx for tumour
  - Auscultate for carotid bruits, take BP, urine for sugar

### *Other Differentials*

- Differential of bulbar palsy:
  - Botulinism, diphtheria
  - MND
  - MS
  - MG, Lambert Eaton
  - Jugular foramen syndrome
  - Cerebello-pontine lesion
  - Vascular lesion
  - Pseudobulbar palsy: bilateral upper motor neurone lesions of the 9<sup>th</sup>, 10<sup>th</sup> and 12<sup>th</sup> nerves
  - If bilateral: GBS, bilateral parotid disease
- Causes of multiple CN lesions:
  - Nasopharyngeal carcinoma (think cancer first): check nasopharynx
  - Chronic meningitis: TB, sarcoid
  - GBS (spares I, II and VIII)
  - Brain stem lesions, trauma, Arnold-Chiari malformation

### *Eyes*

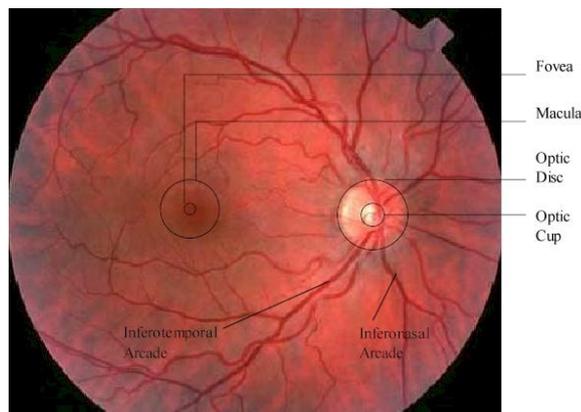
- Look broadly – may be a spot diagnosis
- General inspection: facies
- External eye:
  - Orbits: Palpate – tenderness, brow (loss of sweating)
  - Ptosis
  - Exophthalmos: from behind and above
  - Eyelids (Xanthelasma)
  - Lid lag (hyperthyroidism)
  - Fatigability – look up at pin for ½ a min (myasthenia)
- Cornea:
  - Arcus: cholesterol if young, senile if old
  - Band keratopathy (hypercalcaemia), Kayser-Fleischer rings
- Sclera: jaundice, pallor and injection
- Neuro:
  - Acuity
  - Fields
  - Fundi (low yield)
  - Pupils: shape size, symmetry, light reflex, accommodation
  - Eye movement (as per cranial nerves)
  - Corneal reflex
- Visual Field defects:
  - Tunnel vision: glaucoma, papilloedema, syphilis
  - Unilateral central scotomata optic nerve to chiasmal lesion (demyelination, toxic, vascular, nutritional)
  - Unilateral field loss: optic nerve lesion (vascular, tumour)
  - Bitemporal hemianopia: optic chiasm
  - Homonymous hemianopia: lesion anywhere from optic tract to the occipital cortex
  - Upper quadrant homonymous hemianopia: temporal lobe lesion
  - Lower quadrant homonymous hemianopia: parietal lobe lesion
- Differential of bilateral ptosis and diplopia:
  - MG
  - Thyroid
  - Miller Fisher
  - Mitochondrial disorders
- **Horner's Syndrome:** if partial ptosis and a constricted pupil which reacts normally to light:
  - Difference in sweating over each brow with back of finger (only occurs if lesion is proximal to carotid bifurcation)
  - Check:
    - Hoarseness (recurrent pharyngeal nerve lesion)
    - Clubbing. Finger abduction to screen for a lower trunk brachial plexus (C8, T1) lesion

- If any → respiratory, focusing on apices including axillary lymphadenopathy and tracheal deviation
- Neck for lymphadenopathy, thyroid carcinoma
- Carotid bruit or aneurysm
- Exclude lateral medullary syndrome – present if:
  - Ipsilateral cerebellar signs including nystagmus to the side of the lesion
  - Ipsilateral 5<sup>th</sup> (pain and temperature), 9<sup>th</sup>, 10<sup>th</sup>
  - Contralateral pain and temperature loss over the trunk and limbs
- If unilateral nystagmus then cerebellar exam

### Assessment of Diplopia

- Patient may fixate with either eye – either the weak or normal eye, and can alternate
- Diplopia will be greatest looking in the direction of the action of weak muscle
- The peripheral image comes from the eye with paretic muscle
- Examination:
  - Ask if the double vision is above or beside
  - Watch for head turning or tilting to reduce the diplopia
  - Cover each eye and ask which one gives the ghost or peripheral image – that is weak eye
  - What if eyes move with covering – that will tell you which is the fixing eye
- Vertical diplopia:
  - Problem will be the depressor of the higher eye or the elevator of the lower
  - Check whether alignment is worse in up or down gaze identifies the weak muscle
  - Head tilt test identifies and confirms superior oblique weakness (the usual case): tilt head to abnormal eye, gets worse with alternating cover test
- Exclude restrictive ophthalmopathy (eg thyroid eye disease)

### Eye Fundoscopy



- Definitions:
  - Optic disc: ~ 1.5 mm in diameter and with sharp margins.
  - Physiologic cup: white area located centrally. Normally 1/3 the diameter of the optic disc
  - Retinal veins are thinner and darker than arteries
  - Macula is ~ 5mm diameter and contains the highest concentration of cone cells. The macula receives its blood supply from the choroid vessels rather than the retina.
- Examining the fundi
  - Find the red reflex (Absence of this implies cataracts or retinoblastoma)
  - Follow the red reflex to the eye
  - Focus on the optic disc and note the diameter, margins, colour and presence of vessels
  - Find the physiologic cup and note the cup to disc ratio
  - Follow each of the four arcades to the peripheries (Supertemporal, Superonasal, Inferotemporal, and inferonasal)
  - Ask the patient to look directly at the light and inspect the macula noting it's size and colour
- Optic Disc
  - Papilloedema
    - Swelling of the optic nerve head
    - Signs

- Blurring of the disc margins
- Hyperaemia of the disc
- Retinal vein engorgement (earliest manifestation)
- Loss of the physiologic cup
- Bulging of the disc (evidenced by difference in dioptre of focus at peripheral and central disc)
- Enlargement of the blind spot
- Reduced visual acuity
- Causes
  - Raised intracranial pressure of any cause (BIH, mass lesion)
  - Cerebral oedema
  - Hypercapnea
  - Thyroid eye disease
  - Guillain-Barre Syndrome
  - Central retinal vein occlusion
  - Polycythaemia
  - Vitamin A intoxication
- Papillitis
  - Swelling of the optic nerve head due to inflammation of the optic nerve itself
  - Signs
    - Unilateral features
    - Markedly reduced visual acuity
    - Marked colour vision loss
    - Features otherwise may be similar to Papilloedema
    - Relative afferent papillary defect is present (Marcus-Gunn pupil)
  - Causes
    - Demyelination (early sign of CN II involvement in MS)
    - Vascular disorders including GCA
    - Leber's optic atrophy
    - Malignant infiltration
    - Drugs: ethambutol
- Optic Atrophy
  - Irreversible loss of optic nerve fibres
  - Signs
    - Pale disc with clearly defined margins
    - Relative afferent papillary defect
    - Central scotoma ie enlargement of physiological scotoma due to optic nerve
  - Causes
    - Multiple Sclerosis
    - Compressing lesion
    - Glaucoma
    - Toxins including tobacco and lead
    - Ischaemia from vasculitis or central retinal vein occlusion
    - Friedrich's ataxia
    - Paget's disease
    - Vitamin B12 deficiency

### *Central Scotoma*

- A scotoma is an island of abnormal or absent vision surrounded by normal vision. The blind spot is a normal scotoma
- Examine
  - Likely to be asked to examine the patients visual fields or vision
  - Ask patient if they can see all of your face on direct confrontation with each eye closed
  - Visual field testing
  - Measure scotoma
  - Comment on whether the lesion crosses the horizontal or vertical midline
    - Optic nerve lesions cause complete scotomas
    - Vascular lesions of retina do not cross the horizontal midline
    - Optic pathway defects do not cross the vertical midline

- Comment on whether the scotoma involves the normal blind spot
- Check opposite eye
- Proceed:
  - Fundoscopy specifically looking for retinal lesions, or evidence of optic neuritis
  - Neurological examination for other signs of MS (concentrate on cerebellum as next most likely affected area)
  - If homonymous hemianopia pattern suggested examine the relevant cortical functions
  - Examine posterior columns for evidence of subacute combined degeneration of the cord
  - Examine for evidence of GCA
- Causes
  - Multiple Sclerosis
  - Optic Nerve compression
  - Glaucoma
  - Toxins
  - Ischaemia
  - Paget's Disease
  - B12 deficiency
- Differential: upper or lower red desaturation: ischaemic optic neuropathy (eg Giant Cell arteritis, arterial atheroma)

### *Lateral Medullary Syndrome*

- Vascular lesion to the lateral medullary area causes:
  - Ipsilateral palsies of V<sup>th</sup> through XI<sup>th</sup> nerves
  - Ipsilateral Horner's Syndrome
  - Ipsilateral cerebellar signs with limb ataxia (Inferior cerebellar peduncle)
  - Contralateral spinothalamic limb signs (dissociated loss)
  - Hiccups
- Site of lesion
  - Posterior inferior cerebellar artery
  - Vertebral artery
  - Superior, middle or inferior lateral medullary arteries
- Exam cases
  - Likely to be asked to examine cranial nerves
  - If you have been asked to examine the cranial nerves as opposed to vision, and a Horner's syndrome is present, think lateral medullary syndrome
  - Presence of Horner's syndrome and contralateral dissociated sensory loss in limbs will be this syndrome

### **Higher Centres**

- Lying or sitting
- Ask about handedness
- General inspection:
  - Shake hands (94% of R handed and 50% of L handed have a dominant L hemisphere)
  - Diagnostic facies
  - Obvious cranial nerve or limb lesions
  - Ask about handedness, level of education
- Orientation: time, place, person
- Speech:
  - Repeat a phrase
  - Name objects
  - One and two step commands (point to the ceiling but first take off your glasses, touch your chin then your nose then your ear)
  - Reading and writing if problems found
- Other: blood pressure
- Abbreviated Mental Test:
  - Age
  - DOB
  - Time
  - Address for recall
  - What year

- Name of this place
- Recognise two people
- World War 2
- Prime Ministers
- Count 20 → 1

### *Frontal Lobe*

- Test for frontal lobe involvement if
  - Evidence of hemispheric infarct i.e. Above the internal capsule. Frontal lobe signs will be contralateral to the motor features (Left sided paresis usually will not result in aphasia)
  - Dementia
  - Anosmia
  - Expressive dysphasia (Broca's Area – Left lobe in 96%)
- Frontal release signs – Re-emergence of primitive reflexes
  - Snout reflex: tap above upper lip → pout – non localising
  - Grasp reflex: contralateral lesion
  - Palmar-mental reflex – Ipsilateral movement of chin on stroking palm with key
- Ask to assess smell
- Assess speech to look for expressive dysphasia (Say British Constitution)
- Proverb interpretation: rolling stone gathers no moss
- Four legged animals
- Have a brief conversation with the patient to assess disinhibition, appropriateness of emotions, perseveration
- Hemiparesis
- Limb apraxia: ask patient to copy simple hand movements, and by asking patient to mime action such as slicing bread
- Contralateral motor features if lead to problem via other stem
- Fundi and visual fields
- *Gait*- feet glued to floor → shuffling gait
- Other symptoms: Incontinence of urine and faeces

### *Parietal Lobe*

- Test for parietal lobe function if:
  - Evidence of stroke within the MCA territory
  - Homonymous hemianopia or inferior quadrantanopia (lesion is opposite to VFD)
- Decide which lobe is affected
- Dominant Signs (Left-sided lesion in most)
  - Acalculia: mental arithmetic
  - Agraphia: writing
  - Left-Right disorientation: show L hand then R, touch L ear with R hand
  - Finger agnosia: name fingers
  - Dysphasia (usually receptive)
- Non-Dominant signs
  - Dressing Apraxia: turn jersey inside out
- Parietal signs which may occur on either side
  - Contralateral sensory and visual neglect/inattention: wiggle L finger, wiggle R, then both – R sided parietal lesion → L sided inattention and visa versa
  - Contralateral spatial neglect: draw a clock face
  - Contralateral Astereognosis: inability to recognise an object by feel (parietal lobe lesion → deficit on the other side)
  - Constructional apraxia: draw a house, draw a five sided star
  - Agraphaesthesia: can't appreciate numbers drawn on the hand
  - Quadrantanopia

### *Temporal Lobe*

- Test for temporal lobe function if
  - Differential of conductive nerve deafness on CN exam
  - Receptive aphasia is present
  - Short and long term memory loss
- Remember 3 objects (eg chair, apple, shirt) and then recall 5 minute later

- Recall dates of world wars, previous PM's etc
- Assess CN VIII and note any conductive deficit (Rinne's, Weber's localises to abnormal side)
- External examination of ear including otoscopy to exclude other causes of conductive deafness
- Assess speech and comprehension
- Examine visual fields looking especially for a contralateral homonymous or superior quadrantanopia

### *Occipital Lobe*

- Test for occipital lobe function if
  - Appropriate visual field defect
  - Visual abnormality that suggests cortical lesion (bilateral, denial)
- Signs and symptoms
  - Total loss of vision bilaterally (Cortical Blindness)
  - Congruent Homonymous Hemianopia due to PCA lesion
  - Denial of loss of vision (Anton's Syndrome)
  - Visual Agnosia – The inability to recognise an object despite being able to see (propragnasia when applied to faces)
  - Visual Hallucinations

### **Gait**

- Examination:
  - Ask to walk in the corridor (probably won't be allowed to but helpful if you can)
  - Observe rising from chair
  - Observe gait walking towards and away from you: (do they need to look at their feet)
    - Posture – trunk stability
    - Initiation
    - Arm swing
    - Centre of gravity
    - Speed
    - Turning
    - Do they veer to the left or right
  - Walking on heels (L5) and toes (S1)
  - Heel-toe
  - Squat: test of proximal muscle strength L3/L4
  - Romberg's: Positive if ↑ instability on closing eyes – a sign of proprioceptive loss. Instability with eyes open is either cerebellar or vestibular
  - Proceed to Lower Limb exam: focus on tone, power, reflexes, coordination, and proprioception/vibration
- Differentials:
  - Weakness (LMN):
    - Proximal myopathy: *Waddling* gait – lordosis, swinging of hips (waddle), also difficulty in getting up, positive Gower's sign
    - *High stepping* gait: unilateral foot drop or bilateral (eg peripheral motor neuropathy)
    - Myasthenic gait: normal initially, progressive difficulty, developing foot drop
    - Motor Neuron: amyotrophic lateral sclerosis: death of LMN motor nerves and upper (cortico-spinal). Eyes and bladder spared. Asymmetric limb weakness (flexor > extensor), spasticity, bulbar weakness. EMG → chronic denervation. Survival benefit from Riluzole, BiPAP, PEG feeding
  - *Spastic* gait (UMN): stiff, no flexion at hips/knees, circumduction (bring leg round the side)
    - Bilateral. ↑Tone, eg MS, Cerebral palsy, Hereditary Spastic Paresis. If severe then *scissor* gait (feet cross midline)
    - Hemiplegic gait: unilateral spasticity
  - Sensory neuropathy: *Stamping* or *slapping* gait: heel-toe not good – can correct if watching feet, Romberg's +ve
  - Ataxic:
    - Wide based drunken gait, worse when feet close together/heel toe, gait not made worse by closing eyes, truncal ataxia. Difficulty turning. *Power, tone and reflexes usually normal.* Tone may be subtly ↓. No spasticity
    - Cerebellar: including
      - Paraneoplastic

- Hereditary: Cerebellar Spinal Ataxias, FA (staggering gait, ↓tendon reflexes, vibration, proprioception, dysarthria, nystagmus, cardiomyopathy), AT (telangiectasia, nystagmus, lymphoma), Wilson's, Mitochondrial disease
- Vestibular (abnormal VOR)
- Apraxia
- Hydrocephalus
- Parkinson's gait: Rigidity/bradykinesia
- Choreiform gait
- Functional gait
- Combination of above

## Speech

- Examine this patient's speech and proceed
- Introduce yourself
- Ask if they can hear you OK
- "Can you tell me what you have been doing this morning?" (ie just get them to say something)
- State name, address, age
- Then ask to say
  - "British Constitution"
  - Me – lips
  - Tuh – front of tongue and palate
  - Kuh – soft of palate
  - Aaah – further back
- → decide if dysphasia, dysarthria or dysphonia
- **Dysphasia:**
  - Receptive:
    - If fluent but imperfect or disorganised content then receptive or nominal aphasia. Can't understand questions. Dominant hemisphere lesion in the posterior part of the first temporal gyrus (Wernicke's area):
      - Name objects (?Nominal aphasia)
      - Repeat a statement
      - Paraphasic errors 'Treen' for 'train'
      - Follow commands: 'Shut your eyes', "Touch left ear with right hand"
      - Comprehension: "If a lion ate tiger – which is alive?", "Do you put your shoes on before your socks?"
      - Read and write if these are abnormal
      - Proceed to dominant parietal lobe tests (see page 108)
  - Expressive:
    - If slow and hesitant non-fluent responses but understands then likely to be expressive. Same procedure but assess for hemiparesis - power, vision, parietal, frontal memory + look for causes of CVA, carotid bruits
    - Lesion in the dominant 3<sup>rd</sup> frontal gyrus (Broca's area). Aware of deficit – often frustrated. Ask: "Describe this picture for me"
  - Nominal dysphasia: can't name objects but can use long sentences fluently. Can't be reliably localised
  - Conductive: can't repeat statements or name objects, but can follow commands. Lesion of the arcuate fasciculus
- **Dysarthria:**
  - Disorder of articulation, no problem with speech content ⇒ proceed with CN exam then cerebellar exam
  - *Cerebellar disease*: Scanning speech: Slow, jerky, slurred and often explosive speech, or broken up into syllables.
  - Upper Motor Neuron:
    - Pyramidal (*Spastic*) dysarthria: slow, laboured, tight sounding, patient is trying to squeeze out the words from tight lips (eg pseudobulbar palsy)
    - *Extrapyrarnidal* disease, eg Parkinsonism: Monotonous speech. Bradykinesia and muscular rigidity
    - *Apraxic* speech: prefrontal motor dysfunction. Individual muscles OK but can't translate idea of speech into muscle movements (can't "construct" the complex actions)

- *Lower Motor Neuron*: nasal (air escapes into nasopharynx) and flaccid. Eg MG, MND with lower motor neuron signs, bulbar palsies. Facial muscle weakness → slurred speech
- **Dysphonia**: huskiness with decreased volume. Laryngeal disease (eg URTI) or recurrent laryngeal palsy. Assess cough
- Presenting: Describe findings in terms of:
  - Hearing/dysarthria
  - Comprehension
  - Is speech comprehensible?
  - Fluency
  - Awareness
  - Type of aphasia – conduction/expressive/receptive/nominal
  - **Impact**
  - Other signs: eg disinhibition

## Cerebellar Exam

- Cerebellum control tone → unconscious control of posture in complex movements of the trunk, limbs, eye movements and of speech. Gives ipsilateral signs
- Stem: eg Falling to one side
- **Gait**:
  - Observe: Truncal ataxia → wide based gait, truncal titurbation, lurching/over-correcting
  - Deviated with walking to affected side
  - Heel-toe walk is poor (differential is posterior column loss)
  - Walk on toes and heels is normal (test of power)
  - Romberg’s negative (a sign of proprioception). If unsteady with eyes open, and no difference with eyes closed then cerebellar or vestibular problem
- **Eyes**:
  - Check all positions, pursuit and saccades
  - Horizontal nystagmus: increased amplitude on affected side gaze
  - VOR normal (caused by brain stem, not cerebellar defect)
- **Speech**: Dysarthria with scanning speech: jerky, explosive and loud-“British constitution”. Due to incoordination of tongue and face muscles
- **Limbs**: *power normal, may be subtle ↓tone. Reflexes will be normal and plantars down going.* Tremour with testing coordination will be:
  - Coarse: comes from incoordination of proximal muscles
  - Intention: gets worse on approaching target (as opposed to postural/action tremour which is worse on sustained posture)
  - **Upper Limb**:
    - Pronator drift: Affected side arm drift upwards. Test rebound
    - Finger nose: Intention tremor and past pointing
    - Dysdiadochokinesis
  - **Lower Limb**:
    - “With your toe touch my finger”
    - Dysdiadochokinesis: rapid tapping of foot
- Consider:
  - Testing CN 5, 7 and 8
  - Looking for lateral medullary syndrome.
  - Looking at fundus for papilloedema and optic atrophy: MS is a common cause
- Differentials:
  - Only LL: Alcoholic cerebellar degeneration
  - Unilateral: Space occupying lesion, CVA, MS, Trauma
  - Bilateral: Phenytoin toxicity, alcoholic cerebellar degeneration, hereditary ataxias, hypothyroid, paraneoplastic, MS, Arnold-Chiari
  - Midline/Truncal-Paraneoplastic, Midline tumour

## Peripheral neuropathy

- Peripheral neuropathy:
  - Drugs and toxins: alcohol, lead, isoniazid, vincristine, phenytoin, amiodarone
  - Amyloid
  - Metabolic: diabetes, uraemia, hypothyroidism, porphyria

- Immune: GBS and CIDP
- Tumour: lung
- B12, B1, B6 deficiency
- Idiopathic and Infectious: HIV (CIDP following seroconversion, cf more rapid polyneuropathy from nucleoside analogues with lactic acidosis), syphilis, botulism (pupillary activity lost early), polio (fever and meningism), CMV if immuno-suppressed
- CTD: SLE, PAN (neuropathy in 50%), Sjogren's
- Hereditary motor and sensory neuropathy (CMTD 1 – demyelinating and 2 – axonal loss – sensory symptoms rarer) – pes cavus (short, high arched feet with hammer toes), distal atrophy, absent reflexes, little sensory loss, rarely optic atrophy
- Predominantly motor neuropathy:
  - GBS/CIDP
  - CMT
  - DM
  - Lead
  - Consider MND, NM junction disorders
- Predominantly sensory neuropathy: unusual and → sensory ataxia:
  - Carcinoma
  - Paraproteinaemia, paraprotein, myeloma (esp in osteosclerotic myeloma – POEMS)
  - Sjogren's
  - DM
  - Syphilis
- Painful peripheral neuropathy: DM, alcohol, B12/B1 deficiency
- Mononeuritis multiplex:
  - Acute: DM, PAN, SLE, RA
  - Chronic: Compressive, sarcoid, acromegaly, leprosy, Lyme, idiopathic
- Spinal Lesion:
  - Compressive: trauma, neoplasm, abscess, disc
  - Vascular: infarction (eg APS)
  - Inflammatory: MS, sarcoid
  - Infective: viral, etc
  - Developmental: syringomyelia, tethered chord
  - Metabolic: B12

### *Grading power*

- 0 = paralysis
- 1 = flicker
- 2 = movement with no gravity
- 3 = able to overcome gravity only (any resistance stops movement)
- 4 = movement with gravity plus some resistance
- 5 = Normal

### *Muscle Weakness*

- Features specific to proximal myopathy
  - Weakness of flexor and extensor proximal muscles
  - Difficulty standing from sitting position (check by asking patient not to use hands)
  - Gower's sign is using hands to climb up legs when rising from floor
  - Waddling gait
- Proceed:
  - The gait and proceed
  - The neurological system in the lower limbs and proceed
  - Full endocrine exam
  - Look for evidence of dermatomyositis
  - Other features of hereditary muscular dystrophies
- Differential of proximal muscle weakness:
  - Myopathic:
    - Hereditary muscular dystrophy:
      - Duchenne's: only males, early proximal weakness, preserved reflexes, progressive kyphoscoliosis, ↑Cr, dilated cardiomyopathy
      - Becker's: less severe than Duchene

- Others
- Dystrophia myotonica/Myotonic dystrophy: frontal baldness, weak facial muscles (ptosis, smooth forehead), cataracts, weak neck flexion 2<sup>nd</sup> to ↓ SCM, expressionless/wasted face, grip myotonia (difficulty releasing a grip), dysphagia (oesophageal involvement), impotence (gonadal atrophy). Also cardiomyopathy and cardiac conduction defects. Develops in 3<sup>rd</sup> or 4<sup>th</sup> decade, displays anticipation over generations (ie gets worse)
- Acquired:
  - Alcohol
  - Endocrine (hypothyroid, hyperthyroid, Cushing's, acromegaly, hypopituitarism)
  - DM: diabetic amyotrophy. Asymmetrical proximal pain and weakness with absent knee reflexes. Resolves with better control
  - Drugs: steroids, AZT, statins
  - Sarcoid
  - Osteomalacia
  - IBM, PM or DM
  - Carcinoma - paraneoplastic
- NM Junction: MG, LES
- Myopathy and peripheral neuropathy: alcohol, CTD, paraneoplastic
- Investigation
  - CK is raised in most myopathies but the level is variable
  - CK is not elevated in steroid induced myopathy or thyrotoxicosis
  - Specific tests to exclude endocrine cause
  - EMG, EEG
  - Muscle Biopsy

### *Myasthenia Gravis*

- Examination:
  - Eyes and Face:
    - Ptosis
    - Range of motion and diplopia
    - Sustained up-gaze – how long till fatigue
    - Peek sign – close eyes as tight as possible. Within 30secs you can see the lower sclera
    - Smile – may produce snarling expression
  - Test neck strength – neck flexion especially weak (and also excludes spinal cause of weakness and neck flexion is cranial nerves)
  - Test for muscle fatigue: Hold arms out in forward flexion while counting backwards from 100 (checks for nasal speech from bulbar fatigue at the same time).
  - Check sternum for thymectomy scar.
  - Check lung expansion and for paradoxical breathing
  - Upper limb neuro:
    - Tone, reflexes, coordination and sensation should be normal
    - Muscle wasting is rare and a late severe sign.
  - Lower limb weakness
    - Rise from chair unaided
    - Squat
    - Gait
    - Lower limb neuro
- Associations: Myasthenia gravis is associated with thyrotoxicosis, DM, RA, SLE and thymoma
- Myasthenia gravis may be worsened by fatigue, exercise, infection and drugs (aminoglycosides, morphine, quinine)

## **Upper Limb**

### *Shoulder*

- Look: Inspect for asymmetry, scars, swelling (large anterior swelling = ?effusion), deltoid wasting
- Feel from SC joint, down arm, bulk of muscles, down the spine, test axillary nerve sensation
- Move: stand behind with hand on AC joint
  - Passively: abduct to 90o, extend
  - Actively: internal and external rotation, flexion, adduction
  - Rotator cuff: pain on internal rotation (doing up bra)

- Apprehension test: abduct to 90°, external rotation, and push on humerus from behind
- Neurological shoulder girdle exam:
  - Eg Muscular dystrophy or a root lesion
  - From the back:
    - Trapezius: XI, C3, C4 – elevate shoulders against resistance, look for winging of the upper scapula
    - Serratus anterior: C5-7 (protraction of scapula) – push hands against a wall and look for winging of the scapula
    - Rhomboids: C4-5 (retraction of the scapula) – pull shoulder blades together with hands on hips
    - Supraspinatus: C5-6 – abduct arms against resistance (starting from < 15°)
    - Infraspinatus: C5-6 – rotate upper arms externally against resistance
    - Teres major and subscapularis: C5-7 – rotate upper arms internally against resistance
    - Latissimus dorsi: C7-8 – ask patient to cough and palpate on both sides
  - From the front:
    - Pectoralis major/clavicular head: C5-8 – lift upper arms above the horizontal and push forward
    - Pectoralis major/sternocostal part: C6 – T1 and pectoralis minor: C7 – adduct upper arms against resistance
    - Deltoid: C5-6 – abduct arms against resistance starting from > 15°

### *Upper Limb*

- Shake hands (if they can't let go then dystrophia myotonica)
- Inspection: Facies (Parkinson's, CVA), scars, skin (neurofibromata, café-au-lait), abnormal movements
- Motor (sit on bed facing you):
  - Inspect arms, shoulder girdle – extend both arms:
    - Wasting, fasciculation, tremour
    - **Drift** (with eyes closed):
      - Drift downwards ⇒ weakness ⇒ ?UMN
      - Drift upwards ⇒ hypotonia ⇒ cerebellar
      - Any direction owing to joint position sense loss ⇒ ?posterior column loss
  - Palpate: muscle bulk, tenderness, fasciculation (= LMN)
  - Tone: wrist, elbow
  - Power:
    - Shoulder: abduction: C5/6, Adduction: C6/8
    - Elbow: flexion: C5/6, extension: C7/8
    - Wrist: flexion: C6/7, extension C7/8
    - Fingers: flexion C7/8, extension C7/8, abduction C8/T1
  - Reflexes: biceps C5/6, triceps C7/8, supinator C5/6, finger C8
  - Co-ordination: finger-nose test (intention, past pointing), dysdiadochokinesis, rebound
- Sensory:
  - Pain/pinprick and temperature (usually not tested): spinothalamic
  - Vibration (128 Hz): test on thumb IP joint then at ulnar head – if can't feel it test elbow and shoulder
  - Proprioception: DIP joint in each hand. If negative wrist and elbows
  - Light touch
  - "Cape" sensory loss (neck, shoulders, arms) ⇒ syringomyelia, "shield" loss (front of chest) ⇒ ?syphilis
- Other:
  - Thickened nerves (wrist, elbow) – hereditary neuropathy, acromegaly, CIDP, amyloid, leprosy
  - Axillae, neck, lower limbs, CN, urine analysis
  - If ?MND check lower limbs and tongue
  - If ?C5/C6 then neck for cervical spondylosis

### *Weakness of the upper limbs*

- Rapid assessment of which peripheral nerve involved:
  - Radial: test for wrist drop
  - Ulnar: grasp paper with thumb and index finger (thumb adduction)
  - Median: weak thumb movements except adduction
- Differential for wasting of small muscles of hand:

- Unilateral:
  - Ulnar nerve
  - Proximal median nerve injury: Benediction sign: fail to flex thumb and terminal phalanx of the index finger when making a fist
  - Brachial plexus injury/infiltration (Pancoast's)
    - Upper Trunk (Erb, C5/C6): ↓shoulder movement, ↓elbow flexion (→ waiter's tip position), ↓sensation lateral arm and forearm
    - Lower Trunk (Klumpke, C8/T1): claw hand (↓all intrinsic muscles), ↓sensation medial arm and forearm, Horner's
- Bilateral:
  - RA
  - Old age
  - GBS
  - Hereditary motor and sensory neuropathy (Charcot-Marie-Tooth)
  - Anterior horn cell disease: MND, polio, spinal muscular atrophies
  - Myopathy: dystrophia myotonica, distal myopathy
  - Spinal chord lesion: syringomyelia, C8 cervical spondylosis, other (tumour)
- Cervical cord lesions:
  - C6 Radiculopathy: Weakens elbow flexion and wrist extension. Sensory loss of dorsolateral forearm, thumb and index finger
  - C7 Radiculopathy: pain from neck, shoulder, arm and forearm. Weakness of elbow, wrist and finger extension
  - T1 root lesion: Weakness of small hand muscles, sensory loss on medial arm and often Horner's Ulnar nerve palsy
- Differentiating ulnar/C8/lower trunk lesions:
  - C8 sensory loss extends proximal to the wrist
  - Ulnar doesn't include thenar muscles
  - C8 or lower trunk – Horner's suggest lower trunk

### *Ulnar Nerve Palsy*

- Findings:
  - Claw hand deformity: flexion at IP joints of ring and little finger with hyperextension of MCP. NB other fingers not affected as lateral 2 lumbricals supplied by median
  - Wasting of interossei
  - Weakness of finger but not thumb abduction (that's median)
  - Weakness of all movements of the little finger
  - Thumb adduction weak (paper test for adductor pollicis. Test by asking pt. to grasp paper with thumb and index finger)
  - Sensory loss to little finger
  - Weakness of long flexors (flexor digitorum profundus) of 4<sup>th</sup> and 5<sup>th</sup> fingers – hyperextension of MCP joints and flexion of IP joints
  - Weakness of flexor carpi ulnaris (flexes and ulnar deviates wrist)
- Proceed:
  - Often pressure palsy at elbow. Look at elbow for scars or for OA
  - Assess function of hand – key, buttons
- Differential:
  - RA
  - Leprosy
  - Trauma
- Where is the lesion?
  - If above cubital fossa – flexor carpi ulnaris involved
  - If at wrist – adductor pollicis involved
- Causes:
  - Wrist – compression in Guyon's canal (between pisiform and hamate)
  - Elbow – compression in cubital tunnel

### *Median Nerve Palsy (Carpal Tunnel Syndrome)*

- Findings:
  - Wasting of thenar eminence (abductor pollicis brevis and flexor pollicis brevis)
  - Weakness and wasting of opponens pollicis

- Weakness of flexion, extension, abduction and opposition of thumb
- Decreased sensation of lateral 3.5 fingers (palmar aspect)
- Proceed:
  - Look for scars at wrist
  - Tinel's/Phalen's sign
  - If you have time look for and tell examiner you would like to look for associated conditions:
    - RA
    - Acromegaly
    - Myxoedema
- Other associated conditions:
  - Pregnancy
  - OCP
  - CRF (due to  $\beta_2$  microglobulin)
  - Sarcoid
  - Hyperpara
  - Amyloid
- Investigations:
  - Nerve conduction studies (increased latency) (**NOT** 100% sensitive)
  - Investigate for associated conditions if none found
- Rx:
  - Diuretics
  - Splint
  - Steroid injection (proximal tunnel and not into tunnel)
  - Surgical decompression

### *Radial Nerve Palsy*

- Anatomy:
  - Posterior branch of brachial plexus – from 5<sup>th</sup>, 6<sup>th</sup>, 7<sup>th</sup> & 8<sup>th</sup> cervical nerve roots
  - Enters forearm and becomes posterior interosseous nerve
  - Supplies: Triceps, brachioradialis, finger and wrist extensors
- Findings:
  - Weakness of extension at wrist & elbow
  - Apparent weakness of finger abduction and adduction but this is not the case when hand placed on pillow/table
- Proceed:
  - Test brachioradialis – look at brachioradialis upon flexion at elbow against resistance (lesion at middle 3<sup>rd</sup> of humerus if weakness present)
  - Test triceps (lesion above middle 3<sup>rd</sup> of humerus)
  - Decreased sensation in 1<sup>st</sup> dorsal interossei (only part with exclusive sensory input from radial nerve)

## **Lower Limbs**

- Inspection: Facies, scars, skin, catheter, upper limb girdle wasting
- Gait – **walk them first**
- Motor:
  - Inspect:
    - Wasting, fasciculation (benign – most common, MND, root compression, malignant..), tremour
    - Feet: claw toes and pes cavus (high arch) suggests Charcot Marie Tooth
  - Palpate: muscle bulk, muscle tenderness
  - Tone and clonus: knee (push patellar down – clonus = UMN) and ankle (clonus with knee bent and hip externally rotated)
  - Power:
    - Hip: flexion: L2/3, **Extension: L5, S1/2, Abduction: L4, S1/2**, Adduction L2/3/4
    - Knee: **flexion L5/S1**, L3/4
    - Ankle: plantarflexion S1, dorsiflexion L4,5
    - Foot: **eversion L5/S1, inversion L5**
  - Reflexes:
    - Cremasteric: L1
    - Knee:L3/4

- Ankle: S1/2
- Plantar: S1
- Coordination: heel-shin, **toe-finger**, foot tapping
- Sensory: if loss then establish level on abdomen
  - Do vibration and proprioception first
  - Pain
  - Light Touch
- Saddle region sensation
- Anal reflex
- **Back:** deformity, scars, tenderness, bruits
- Other: upper limbs, CN, urinalysis
- Common Lesions:
  - **Tarsal Tunnel Syndrome:** Just posterior to medial malleolus from ankle sprain, ill fitting footwear, etc. Pain on sole of foot when walking, weakness of toe plantars
  - **S1 Radiculopathy:** Pain in back, buttock, thigh, leg, and foot, numbness of the lateral border of the foot. Mild weakness of eversion and dorsiflexion, depressed ankle jerk
  - **L5 Radiculopathy:** Pain in back, buttock, 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	OK

### *Foot Drop*

- Causes of foot drop:
  - Common peroneal nerve palsy
  - Sciatic nerve palsy
  - Lumbosacral plexus lesion
  - L4, L5 root lesion
  - Peripheral motor neuropathy
  - Distal myopathy
  - MND
  - Spinal chord lesion
- Walk
- Do full leg neuro
- Unilateral foot drop:
  - Ankle jerk absent:
    - Loss of sensation/power below knee: sciatic nerve
    - Loss of sensation in dermatomes: cauda equina, lumbosacral plexus
  - Ankle jerk present:
    - Inversion absent: L5 root lesion (with weak big toe extension)
    - Inversion present:
      - Sensory loss only between 1<sup>st</sup> and 2<sup>nd</sup> toe: Deep peroneal branch of common peroneal
      - Sensory loss over lateral foot/leg: common peroneal – check fibular head
- Bilateral:
  - Reflexes normal: ?myopathy, distal neuro
  - Reflexes ↑: ?spinal chord

### *Paraplegic patient*

- Sensory level:
  - Chord compression → loss of all modalities bilaterally below the level involved, and radicular pain + LMN weakness at the level of spinal compression
  - Transverse myelitis

- Anterior Spinal artery occlusion (posterior column function is spared – discriminative sensation) – spinothalamic tract (pain and temp cross over and ascend anteriorly), lateral corticospinal (pyramidal tract ascends laterally)
- Brown-Sequard syndrome (hemi-section of the spinal cord):
  - Motor signs: UMN below the hemi-section and LMN at the level of the hemi-section *on the same side as the lesion*
  - Sensory changes: ↓pain/temperature on the opposite side, ↓vibration/proprioception on the same side, light touch is often normal
  - Differential: MS, mass lesion, trauma, myelitis, post-radiation
- Back examination: deformity, tenderness
- Differential of acute myelopathy (ie spinal chord):
  - Acute: demyelination, infarction, systemic disease (SLE, Sjogren's, sarcoid), infection (Tb, HIB, HSV, EBV), radiation, idiopathic
  - Chronic: vascular malformation, infection, syringomyelia, familial, MS, spondylitis, B12 deficiency, paraneoplastic
- Arms involved: Consider
  - Cervical spondylosis, MND, MS
  - Syringomyelia: loss of pain/temp over neck/shoulders/arms (cape distribution), amyotrophy (weakness, atrophy and areflexia of the arms), UMN signs in lower limbs)
- CN lesions: consider MND, MS
- Peripheral neuropathy: consider:
  - Friedreich's ataxia, syphilis, carcinoma, hereditary
  - B12 deficiency (subacute combined degeneration of the cord): ↓vibration/position sense → ataxic gait, symmetrical UMN lower limb signs with ↓ankle jerks, mild sensory neuropathy, optic atrophy, dementia (occasionally)
- Cerebral lesion

## Movement Disorders

### *Multiple Sclerosis*

- Cranial nerves:
  - Eyes: ↓visual acuity, optic atrophy, papillitis, central scotomata
  - Internuclear ophthalmoplegia: weakness of adduction in one eye, and nystagmus in abducting eye due to damage to medial longitudinal fasciculus (also in SLE, Sjogren's, brain stem CVA or tumour)
  - Charcot's triad: nystagmus, intention tremor and scanning speech
- Lhermitte's syndrome: electric shock in limbs on neck flexion (also caused by other cervical spine disorders)
- Spastic paresis
- Posterior column sensory loss
- Cerebellar signs

### *Chorea*

- Examination:
  - Irregular, jerking and unpredictable movements
  - Pt. clumsy
  - Milk-maid's grip – ask patient to squeeze fingers, a squeezing/relaxing motion occurs
  - Ask pt. to stick tongue out – 'jack in the box'
  - Reflexes – pendular
  - Ask examiner you wish to test higher mental functions
- Differential:
  - Inherited: Huntington's chorea and Wilson's
  - Rheumatic fever: Sydenham's chorea
  - Autoimmune: SLE and vasculitis
  - Polycythaemia
  - Following CVA
  - Drugs: OCP, L-Dopa, phenytoin
  - Other: senility, pregnancy, thyrotoxicosis

## *Tremour*

- Differential of Tremor
  - Resting tremor:
    - Parkinsonian: does not produce tremour of the whole head
    - Midbrain tremor: Presence of other cerebellar findings, ptosis and long tract signs
    - Wilson's disease
    - *Thyrotoxicosis*
  - Postural or action tremor: Worse with increased muscle tone (eg holding arms in front of face), but finds target OK on finger-nose
    - Physiologic tremor
    - Essential tremor – not legs
    - Large fibre peripheral neuropathy GBS/CIDP
  - Intention tremor:
    - Cerebellar disease: large amplitude/course due to involvement of proximal muscles. Worst at the termination of goal-directed activity
    - Multiple sclerosis
    - Midbrain stroke/trauma
  - Restless legs: Idiopathic, familial, Fe deficiency, dialysis, pregnancy, DM peripheral neuropathy, RA (Treatment: small dose of levodopa/bromocriptine/ropinirole)
- Examination:
  - Gait:
    - Parkinsonian, ataxic
    - Test balance – stand on one leg, give them a pull
  - Hands:
    - Observe with hands resting on lap
    - Look for rest tremor in hands:
      - Ceases with changes in limb posture but quickly reappears following repositioning
      - Activated by repetitive movements of the opposite hand, walking, and distraction
      - Thyrotoxicosis – fine tremor – warm moist palms, tachy, do thyroid exam
    - Open and close hand quickly for bradykinesia, clap
  - Arms:
    - Limb fully supported at rest
    - Outstretched hands – for postural and action tremors.
    - Hands below nose, elbows raised
    - Finger-to-nose test
  - Face:
    - Eyes : ? KF rings
    - Voice - prolonged note
  - Drinking or pouring from a paper cup
  - Check plantars
- Check for cerebellar signs
- Investigations: Thyroid function. Exclude Wilson's, heavy metals, brain imaging

## *Parkinson's Disease*

- Parkinson's is not hard to spot – the exam is about excluding things that can look like Parkinson's
- Differential diagnosis:
  - Essential tremor —can also affect the head, voice, chin, trunk, and legs. Test with outstretched arms
  - Parkinson's Disease: asymmetric, no eye signs, autonomic (eg BP urinary) 2<sup>nd</sup> only to medication
  - Secondary parkinsonism:
    - **Drugs** (antipsychotics, metoclopramide)/Toxins
    - Head trauma
    - Structural brain lesions
    - Wilson's disease
    - Post-encephalitis (rare)
    - Vascular parkinsonism – small vessel disease of the basal ganglia
  - Dementias/Neurodegenerative conditions:

- Red flags for something more than Parkinson's: early bulbar/sphincter/autonomic signs, up-going plantars, abnormal eye movements
- Dementia with Lewy bodies: visual hallucinations, behavioural change, fluctuating cognition, falls, syncope, autonomic dysfunction, neuroleptic sensitivity
- Corticobasal degeneration: apraxia, alien limb, aphasia, absence of tremor, absence of levodopa response
- Multiple system atrophy: Cognitive function preserved. Two patterns:
  - MSA-P: MSA with *symmetric* Parkinson's features of rigidity, but pyramidal signs, absence of tremor, poor response to levodopa
  - MSA-C: MSA with *dysautonomic* and *cerebellar* involvement (Shy-Drager)
- Progressive supranuclear palsy = Steele Richardson Olszewski syndrome. *Vertical supranuclear palsy*, rigidity, postural instability, falls, apathy, disinhibition, dysphoria, anxiety, no tremor, pseudobulbar palsy, frontal lobe-like dementia, poor, response to levodopa
- Communicating hydrocephalus
- Examination:
  - Observe:
    - Lack of facial expression
    - Paucity of movement
    - Resting tremor
    - Reduced blinking
    - Speech – soft, monotonous
  - Gait:
    - Test gain, turning, start/stop
    - Look for – difficulty turning, flexed posture, difficulty initiating, shuffling (↓stride length), freezing, arm swing (unilateral onset), *not* wide based
    - Test – retropulsion (“I’m going to pull you backwards – try not to fall – ready 1 – 2 – 3 pull”), propulsion
  - Hands:
    - Tremour: accentuate with distraction – get them to tap the other hand
    - Wrist: cog-wheel, lead pipe – with reinforcement
    - Test finger-nose – resting tremor may diminish but action tremor increases
    - Bradykinesia – fast big movements – open and close both hands repeatedly
    - Foot tapping – each side in turn
    - Ask patient to write a sentence
  - Face
    - Inspect: mask like
    - Glabellar tap (from behind to patient can't see)
    - Ocular movements:
      - PSP: impaired voluntary upward gaze but dolls eye normal
      - MSA: cerebellar signs, eg nystagmus
    - Voice: cerebellar in MSA, dysphonia in PSP
  - Arm: *Postural hypotension* (MSA or L-Dopa)
  - Other
    - Check reflexes and plantars
    - Test for dementia: especially frontal in DLB and PSP
    - *Ask about family history especially if young*
- Investigations:
  - LFTs/eye exam to exclude Wilsons
  - MRI to exclude specific structural abnormalities (eg, hydrocephalus, tumor, or lacunar infarcts)

## Macroglossia

- Differential:
  - Hypothyroidism
  - Acromegaly
  - Amyloidosis
  - Pseudomacroglossia: small mandible- Down's syndrome
  - Mass effect: Lymphangioma/hemangioma/Cystic hygroma/thyroglossal ducts/sarcoma/lymphoma
  - Acutely: Angioedema
- Inspect:
  - Tongue:
    - At rest, protruding past teeth. Look for teeth indentation.
    - Ulcers.
  - Observe for weight loss, tachypnoea, impaired speech-all functional issues 2<sup>nd</sup> to large tongue.
  - Assess swallow.
- Exam for differentials: especially hypothyroidism and then acromegaly

## Turners Syndrome

- Stem: primary amenorrhoea, patient looks short=> think turners
- Observe: female, height, carrying angle of elbow, facies, short neck with webbing
- Arms: Lymphoedema of hands, short 4<sup>th</sup> metacarpals, hyperplastic nails, increased carrying angle
- BP: hypertension
- Face: Small chin, epicanthic folds ptosis, hypertelorism, fish like mouth, deformed or low ears
- Mouth: High arched palate
- Hearing: Impaired
- Neck: Webbing, low hair line, redundant skin at back of neck
- Chest: Shield like, wide spaced nipples, multiple moles
- Leg: Lymphoedema
- Other: Colour blindness, strabismus and ptosis
- CVS exam: Coarctation-radio femoral delay and systolic murmur between scapula, septal defects and AS
- Other associations: Osteoporosis, mental retardation, intestinal telangiectasia, DM and Hashimotos thyroiditis, Horseshoe kidney
- Investigations: Karyotype, LSH/FH will be high, Investigations for complications