A metabolic alkalosis is a primary acid-base disorder which causes the plasma bicarbonate to rise to a level higher than expected. The severity of a metabolic alkalosis is determined by the difference between the actual [HCO₃] and the expected [HCO₃].

**General**
- The kidney rapidly excretes bicarbonate if the plasma level is elevated.
- This ability of the kidney to rapidly excrete bicarbonate if its level is high is in complete contrast to its powerfull ability to reabsorb all of the filtered load of HCO₃ to a level below normal.
- The persistence of a metabolic alkalosis requires an additional process which acts to impair renal bicarbonate excretion.
- This means that two issues must be considered when analysing a metabolic alkalosis:
  - (i) Initiation: What process is initiating the disorder?
  - (ii) Maintenance: What process is maintaining the disorder?

**The Initiating Process**
- Classification of Initiating Processes for Metabolic Alkalosis
  1. Gain of alkali in the ECF
     - (i) from an exogenous source (eg IV NaHCO₃ infusion, citrate in transfused blood)
     - (ii) from an endogenous source (eg metabolism of ketanoins to produce bicarbonate)
     - 2. Loss of H⁺ from the body
        - (i) via kidneys (eg use of diuretics)
        - (ii) via gut (eg vomiting, NG suction)
     - 3. Excessive intravascular administration of alkali alone will cause a metabolic alkalosis which is only short-lived because of rapid renal excretion of bicarbonate
     - 4. Hepatic metabolism of citrate, lactate, acetate or certain other organic anions to bicarbonate can cause a brief metabolic alkalosis, this may occur after a massive transfusion because of the metabolism of the administered citrate. The kidneys excrete the bicarbonate and the urine will be relatively alkaline.

**Maintenance of Alkalosis**
- Maintenance of the alkalosis requires a process which greatly impairs the kidney's ability to excrete bicarbonate and prevent the return of the elevated plasma level to normal.
- The four factors that cause maintenance of the alkalosis (by increasing bicarbonate reabsorption in the tubules or decreasing bicarbonate filtration at the glomerulus) are:
  - (i) Chloride depletion
  - (ii) Reduced glomerular filtration rate (GFR)
  - (iii) Increased ventilation-perfusion mismatch (as alkalosis inhibits hypoxic pulmonary vasoconstriction)
  - (iv) Peripheral oxygen unloading may be impaired because of the alkalotic shift of the haemoglobin oxygen dissociation curve to the left.

**Adverse Effects of Alkalois**
(i) decreased myocardial contractility
(ii) hyperventilation (due respiratory response to metabolic alkalosis)
(iii) increased ventilation-perfusion mismatch (as alkalosis inhibits hypoxic pulmonary vasoconstriction)
(iv) Peripheral oxygen unloading may be impaired because of the alkalotic shift of the haemoglobin oxygen dissociation curve to the left.
- The body's major compensatory response to impaired tissue oxygen delivery is to increase cardiac output but this ability is impaired if hypovolaemia and decreased myocardial contractility are present.

**Urinary chloride measurements**
- The expected pCO₂ due to appropriate hyperventilation in simple metabolic alkalosis can be estimated from the following formula:
  \[ \text{Expected } pCO₂ = 0.7 \times [HCO₃] + 20 \text{ mmHg} \] (range: +/- 5)
- While it is widely believed that the maximum value of arterial pCO₂ due to compensatory hyperventilation is 55 to 60mmHg arterial pCO₂ can rise higher than this and values up to 80mmHg have been reported in severe cases of metabolic alkalosis.

**Metabolic Alkalois Classification Based on Urinary Chloride**
- 1. Urine Cl⁻ < 10mmol
  - Often associated with volume depletion (increased proximal tubular reabsorption of HCO₃)
  - Respond to saline infusion (replaces chloride and volume)
- 2. Urine Cl⁻ > 20mmol
  - Often associated with volume expansion and hypokalaemia
  - Resistant to therapy with saline infusion
  - Cause: Excess aldosterone, severe K⁺ deficiency
  - Adult causes are steroid dependent Cushing's syndrome
  - Recent diuretic use can acutely elevate the urinary chloride level but as the diuretic effect passes the urinary chloride level will fall to low levels. So seek information on the timing of diuretic use. (This variability in urine chloride levels has been used as an indicator of surreptitious diuretic use)
  - A 'spof' urine chloride may be misleading if bladder urine contains a mixture of urine from different times and after diuretic effect
  - A high urinary chloride in association with hypokalaemia suggests mineralocorticoid excess.
  - The urinary chloride/creatinine ratio may occasionally be useful as it is elevated if there is an extra-renal cause of alkalosis.

**General**
- The commonest causes in clinical practice are those caused by metabolic alkalosis.
- Administration of chloride is necessary to correct these disorders. The two commonest causes of chronic metabolic alkalosis accounting for 90% of cases are loss of gastric juice and diuretic therapy.

(ii) Diuretics
- Diuretics such as frusemide and thiazides interfere with reabsorption of chloride and sodium in the renal tubules. Urinary losses of chloride exceed those of bicarbonate. The patients on diuretics who develop an alkalosis are those who are also volume depleted (increased aldosterone levels) and have a low dietary chloride intake ('salt restricted' diet). Hypokalaemia is common in these patients.
- The effect of diuretic use on urinary chloride levels depends on the relationship of the time of urine collection to diuretic effect. It is high while the diuretic is acting, but drops to low levels afterwards.
- Other causes
  - Villous adenomas typically excrete bicarbonate and can cause a hyperchloremic metabolic acidosis.
  - Sometimes they excrete chloride predominantly and the result is then a metabolic alkalosis.
  - Chloride diarrhoea is a rare congenital condition due to an intestinal transport defect where the chronic faecal chloride loss can (if associated with volume depletion and K⁺ loss as maintenance factors) result in a metabolic alkalosis.