

The **acid-base balance** is vital for normal bodily functions. When this equilibrium is disrupted, it can lead to severe symptoms such as arrhythmias and seizures. Therefore, this acid-base balance is tightly regulated.

The urinary system utilises two methods to alter blood pH. That is, **excretion of hydrogen (H^+) ions** as dihydrogen phosphate or ammonia and production and **reabsorption of bicarbonate (HCO_3^-) ions**.

Excretion of Hydrogen (H^+) Ions

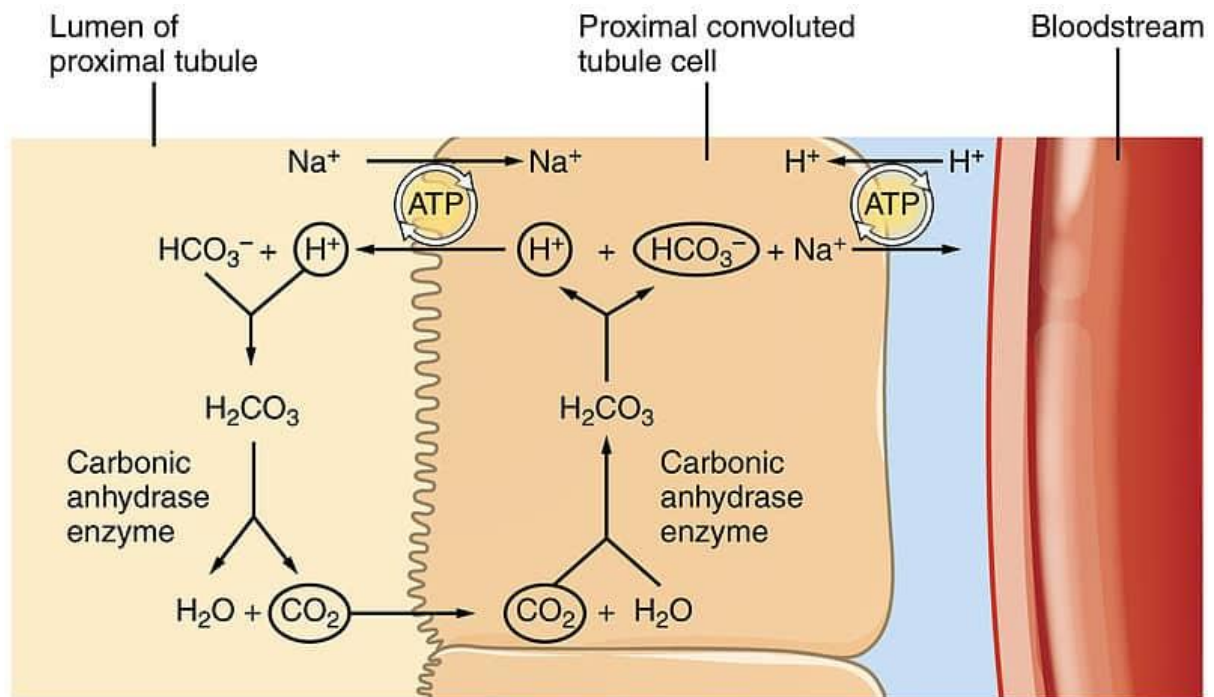
There are 2 methods by which this is achieved:

- Excretion of H^+ ions in the form of **dihydrogen phosphate ($H_2PO_4^-$)** – H^+ ions are actively transported into the lumen via hydrogen-ATPase pumps on alpha intercalated cells. Excess luminal phosphate (only 85% of total phosphate is normally reabsorbed) can bind a large portion of hydrogen ions, buffering them as $H_2PO_4^-$ before excretion. This excretion of H^+ ions increases blood pH.
- Excretion of hydrogen ions in the form of **ammonium (NH_4^+)** – glutamine is converted to glutamate and ammonium in the proximal convoluted tubule (PCT). The ammonium dissociates to ammonia and H^+ ions, allowing it to pass the membrane and enter the lumen. Once in the lumen, it reforms ammonium by picking up a luminal H^+ ion. This allows hydrogen to be excreted as ammonium ions, increasing blood pH. Furthermore, ammonia secreted at the PCT can be used further down to buffer and excrete H^+ ions secreted by alpha intercalated cells in the collecting duct. This is due to its ability to pass membranes and traverse the nephron.

NB: The glutamate created from glutamine can also go on to form bicarbonate (via its conversion to alpha-ketoglutarate) which can then be reabsorbed to further increase pH.

Bicarbonate (HCO_3^-) Reabsorption

Bicarbonate ions can also be reabsorbed in the PCT, which aids in the buffering system. H^+ ions are secreted into the lumen via the **sodium-hydrogen (Na^+-H^+) exchanger** to combine with any filtered bicarbonate. This then forms **carbonic acid (H_2CO_3)**, catalysed by **carbonic anhydrase** on the luminal side. Carbonic acid then dissociates into carbon dioxide and water, which both can diffuse into the cell. Here, the reaction is undone, and carbonic anhydrase inside the cell converts carbon dioxide and water to carbonic acid, which then dissociates into H^+ and HCO_3^- ions. HCO_3^- can then be transported into the blood whilst the H^+ ions can be transported back into the lumen for the cycle to repeat.



Bicarbonate (HCO_3^-) Production

The kidney is also able to produce bicarbonate. The metabolic activity of cells produces large amounts of carbon dioxide. This then reacts with water to produce HCO_3^- ions, which enter the plasma, and H^+ ions to be transported into the lumen. This is useful as it also provides H^+ ions to drive HCO_3^- reabsorption. In addition to this bicarbonate can also be produced from amino acids, which produces ammonium ions which then enter the urine

Metabolic Acidosis

Metabolic acidosis is when the pH of blood < 7.35 i.e. it becomes **acidic**. This is caused by an increase in H^+ ions, lactate and organic acids or by a loss of HCO_3^- . Causes of metabolic acidosis can be divided into **normal anion gap** or **high-anion gap**.

Causes of **normal anion-gap metabolic acidosis** include:

- **Chloride excess**
- **Renal tubular acidosis**
- **Addison's disease**
- **Diarrhoea**

Causes of **high anion gap metabolic acidosis** include:

- **Lactic acidosis**

- **Diabetic ketoacidosis (DKA)**
- **Starvation**
- **Drugs e.g. salicylates, isoniazid, paracetamol**

Symptoms of metabolic acidosis are:

- **Hyperventilation** – lungs try to increase pH by blowing off CO₂ to reduce its concentration in blood. This is classically called **Kussmaul respiration** or ‘air hunger’
- **Confusion**
- **Tachycardia**

Metabolic acidosis is diagnosed through arterial blood gas analysis. Treatment involves correcting the underlying cause of acidosis, however sometimes **sodium bicarbonate** may be given as well. A complication of metabolic acidosis is **hyperkalaemia**, which requires urgent intervention to prevent cardiac arrhythmias.

Metabolic Alkalosis

Metabolic alkalosis is when blood pH > **7.45**, making the blood **alkaline**. This is usually a result of a massive loss of H⁺ ions or increased HCO₃⁻. Metabolic alkalosis can be caused by:

- **Vomiting** – causes loss of stomach acid and therefore H⁺ ions
- **Burns**
- **Milk-Alkali Syndrome** – leads to increased HCO₃⁻ in the blood
- **Diuretic usage**

The symptoms of metabolic alkalosis are:

- **Hypoventilation** – the lungs try to decrease pH by increasing the concentration of CO₂
- **Confusion**
- **Tetany** – particularly if caused by Milk-Alkali Syndrome
- **Tremor** – also more common in Milk-Alkali Syndrome

Like metabolic acidosis, a diagnosis of metabolic alkalosis is made by analysing arterial blood gases. Treatment usually involves correcting the underlying issue, but with some metabolic alkalosis, **chloride replacement** may also be

necessary. Hypokalaemia is usually the main concern in cases of metabolic alkalosis, so this should be dealt with most urgently.