Physiol-07A11 Discuss how the body handles a metabolic acidosis.

**Background**

*Metabolic acidosis* = abnormal primary process or condition leading to an increase in fixed acids in the blood

The body responds to the development of metabolic acidosis via:
(1) buffering – short and long term
(2) compensation – via altered ventilation
(3) correction – via renal excretion

**Buffering**

Body is able to rapidly resist large changes to plasma pH via a number of extracellular and intracellular buffering systems.

Main *extracellular* buffer systems include:

(1) **bicarbonate (HCO₃⁻/CO₂)**
- most important buffer in ECF due to abundant bicarbonate ion present (24 mmolL⁻¹ at baseline) and being an open system (*discussed below*)
- pKa 6.1 → reasonable close to baseline plasma pH (7.4)

(2) **phosphate (HPO₄²⁻/H₂PO₄⁻)**
- despite having pKa (6.8) very close to baseline plasma pH, it is not available in large quantities ∴ less important buffer system compared to bicarbonate

(3) **proteins (P⁻/HP)**
- via imidazole residues on histidine groups

Main *intracellular* buffer systems include:

(4) **haemoglobin (Hb/H⁺Hb)**
- most important intracellular buffer of H⁺ (and CO₂)
- Hb present in large quantities within RBCs (140 g/L)
- Hb has large number (38) of histidine groups → serve as effective buffer
- deoxyHb is better buffer for acid when compared with oxyHb due to conformation change

(5) **proteins (P⁻/HP)**
- lower concentration than Hb, less histidine groups → relatively less important buffer system

Long-term buffer (days to weeks)

H⁺ may also be very slowly buffered by bone → via exchange for Na⁺ and Ca²⁺ ions
Respiratory Compensation (hours ~ days)

Metabolic acidosis → H⁺ binds HCO₃⁻ → ↑PaCO₂ → diffuses into CSF → intracerebral acidosis → sensed by medullary respiratory centre → ↑minute ventilation → ↓PaCO₂ → ↑plasma pH (respiratory compensation)

\[ pH = 6.1 + \log \frac{[HCO_3^-]}{0.03PaCO_2} \]
i.e. ↓PaCO₂ → ↑pH

The ability to reduce PaCO₂ (i.e. open system) → significantly increases the buffering capacity of the bicarbonate system

Maximal expected respiratory compensation: PaCO₂ = 1.5 × [HCO₃⁻] + 8 ± 2

Note, respiratory compensation is unable to produce net elimination of fixed acids as every CO₂ eliminated by lungs is equivalent to the removal of both H⁺ and HCO₃⁻

Renal Correction (days ~ weeks)

The kidneys are able to definitively correct metabolic acidosis by:
(1) elimination of fixed acids (H⁺ bound to titratable acid)
(2) reabsorption of HCO₃⁻

1. ↑ Reabsorption of HCO₃⁻
   - in proximal tubule: ↓pH → ↑Na⁺/H⁺ antiport activity → ↑H⁺ secretion → ↑reabsorption of HCO₃⁻
   - in α-intercalated cells of distal tubule/collection ducts: ↑H⁺-ATPase → ↑H⁺ secretion → ↑reabsorption of HCO₃⁻ (stimulated by ↑aldosterone)

2. ↑ Excretion of fixed acids
   - after all HCO₃⁻ ions are reabsorbed (i.e. above mechanism exhausted), the secreted H⁺ is then bound to titratable acids (e.g. HPO₄²⁻) esp. in the distal tubule/collection ducts → excreted

3. ↑ Excretion of ammonium
   - when all titratable acids are exhausted in the tubules → H⁺ is bound to tubular NH₃ → excreted in the form of NH₄⁺
   - NH₄⁺ is synthesised from glutamine deamination, also generating HCO₃⁻, which is absorbed.

Examiner’s comments – 57% of candidates passed this question.

The main points to be covered were a definition of a metabolic acidosis, discussion of extracellular and intracellular buffering systems, respiratory compensation, the renal mechanisms to excrete non-volatile acids (titratable acidity, ammonium and ammonia), and resorption and regeneration of bicarbonate.
Extra marks were awarded for the **mechanism of respiratory compensation**, explaining that **respiratory compensation does not lead to acid excretion**, description of **buffering by long as well as short term mechanisms**, specific details of ammonia and **ammonium production** and **bicarbonate regeneration**, understanding that **H+ ions can not be excreted unbound**, the **amount of acid** that can be **excreted by different renal mechanisms**, and **aldosterone’s effect on H+ excretion**.