Renal physiology V

Regulation of acid-base balance

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Hydrogen ions (H^+): Concentration and origin

- Concentration

  in arterial blood, resting: $[H^+] = 40\ nM = 40 \times 10^{-9}\ M = 4 \times 10^{-8}\ M$

  $pH = - \log [H^+]$

  $pH = - \log 4 \times 10^{-8} = 7{,}4$

  in resting venous blood: 7,37

- Origin of H^+

  Dissociation of water: $H_2O \rightarrow H^+ + OH^-$

  in pure distilled water:

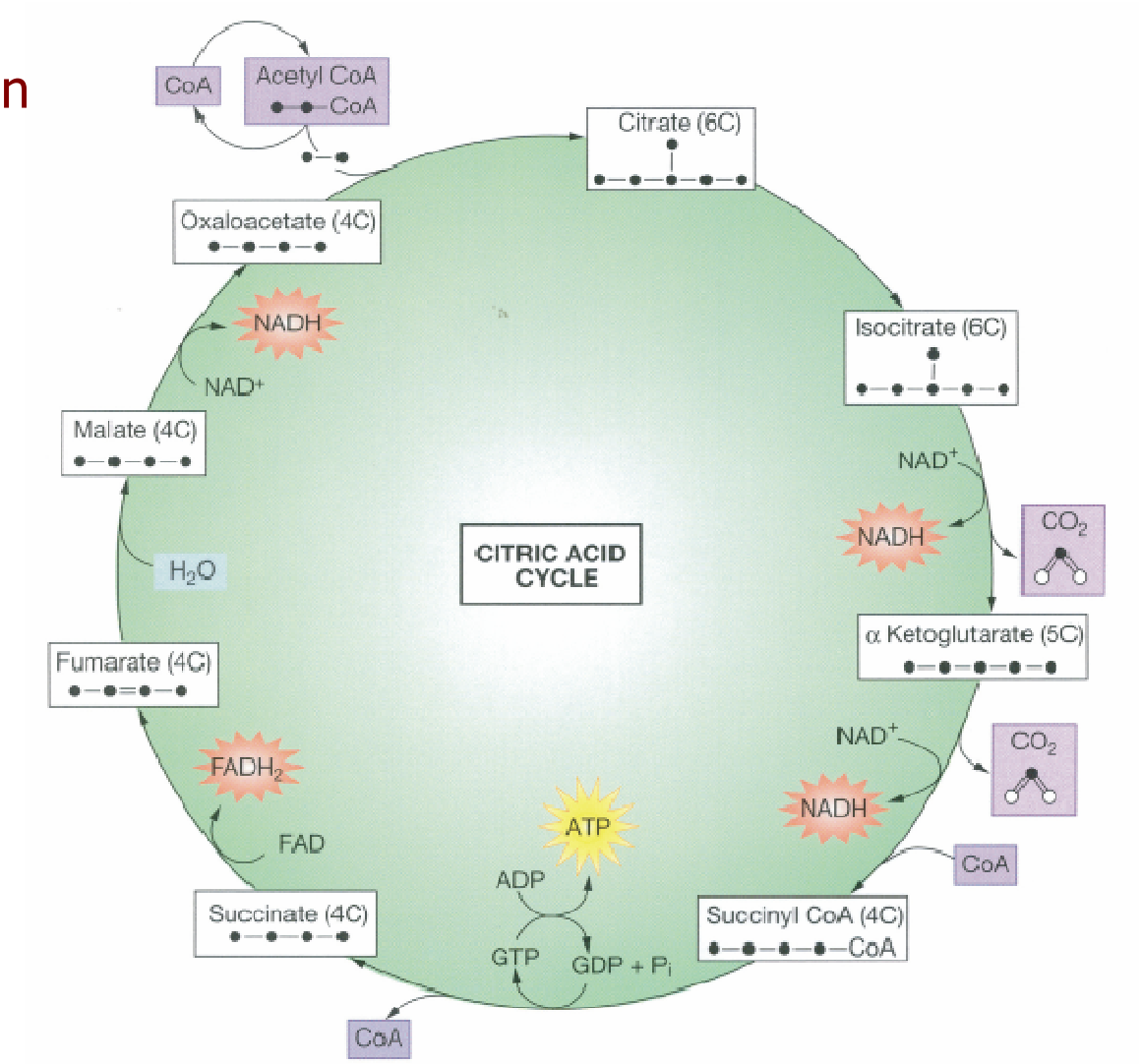
  $[H^+] \times [OH^-] = 10^{-14}$ mole/l and $[H^+] = [OH^-] = 10^{-7}$ mole/l, pH = pOH = 7

  Metabolic origin:

  during muscle action:

  $ATP \rightarrow ADP + P_i + H^+$

From CO_2 production in the Krebs cycle:



Then, in erythrocytes:

$CO_2 + H_2O$

↓ Carbonic anhydrase, Zn^{++}

$H_2CO_3 \rightarrow HCO_3^- + H^+$

- S-containing amino acids, eg., methionine and cysteine are metabolised to H_2SO_4 : $\rightarrow H^+ + HSO_4^-$
- Phosphoproteins and phospholipids are metabolised to phosphoric acid: H_3PO_4: $\rightarrow 2H^+ + HPO_4^{2-}$
- Formation of metabolic acids, eg., lactic acid, acetoacetic acid

Defence mechanisms against fluctuation in pH

A. Buffers:

- a buffer contains a buffer pair: a weak acid and its salt
- Henderson-Hasselbach equation:

$$pH = pKa + \log [salt]/[acid]$$

- Phosphate buffers (5% in ECF, 5% in ICF)

  $HPO_4^{2-} + H^+ \rightarrow H_2PO_4^-$

  anion (salt) acid

  4 : 1

- Bicarbonate buffers (80% in ECF, 15% in ICF)

  $HCO_3^- + H^+ \rightarrow H_2CO_3 \rightarrow H_2O + CO_2$ (volatile)

  anion (salt) acid

  20 : 1

- Protein buffers (80% in ICF, 15% in ECF)

  At body pH, certain amino acids (in proteins) dissociate to form negatively charged anions (NH_2-R-COOH $\rightarrow$ NH_2-R-COO^- + H^+). These NH_2-R-COO^- can then act as hydrogen acceptors. The buffer system is thus:

  $Prot.H \rightarrow H^+ + Prot^-$

  1 : 4

In erythrocytes: Hemoglobin acts as a buffer

(i) Hb is rich in histidine that can also act as a hydrogen acceptor.

(ii) H-HbO_2 is a stronger acid than reduced H-Hb. Thus, when H-HbO_2 sheds its O_2, HHb remains. Because it is a weak acid it does not dissociate easily and the pH does not become too low.

CO_2 transport from tissues into erythrocytes:

(a) NB reactions in gas exchange:

$$HbO_2 \rightarrow Hb$$

$$CO_2 + H_2O \rightarrow H^+ + HCO_3^-$$

(b) Some CO_2 can bind with Hb to form carbamino Hb.

(c) HCO_3^- transported in RBC can be transported into the plasma in exchange for chloride (Hamburger).

B. The lungs:

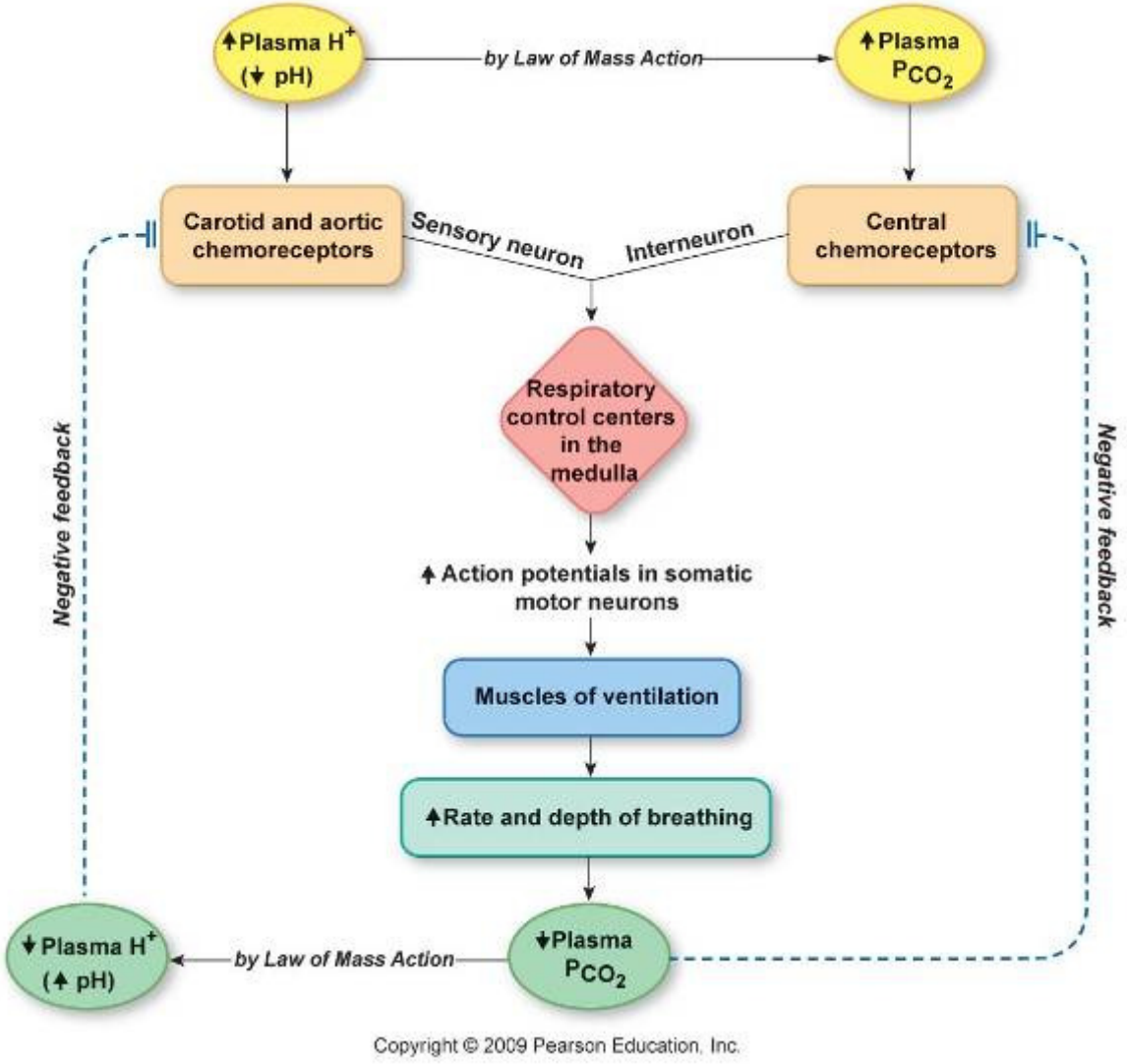
In the erythrocytes in lung capillaries:

- HbO_2 and $HHbO_2$ are formed
- $HHbO_2$ dissociates easily to form free H^+
- $H^+ + HCO_3^- \rightarrow H_2O + CO_2$ (breathed out)
- the lower the bicarbonate in the cells, the more diffuses in from the plasma, in exchange, the plasma gets back its chloride

Indirectly:

- a decrease in pH (?$\uparrow$ pCO_2) stimulates the rhythmic respiratory control center in the medulla oblongata

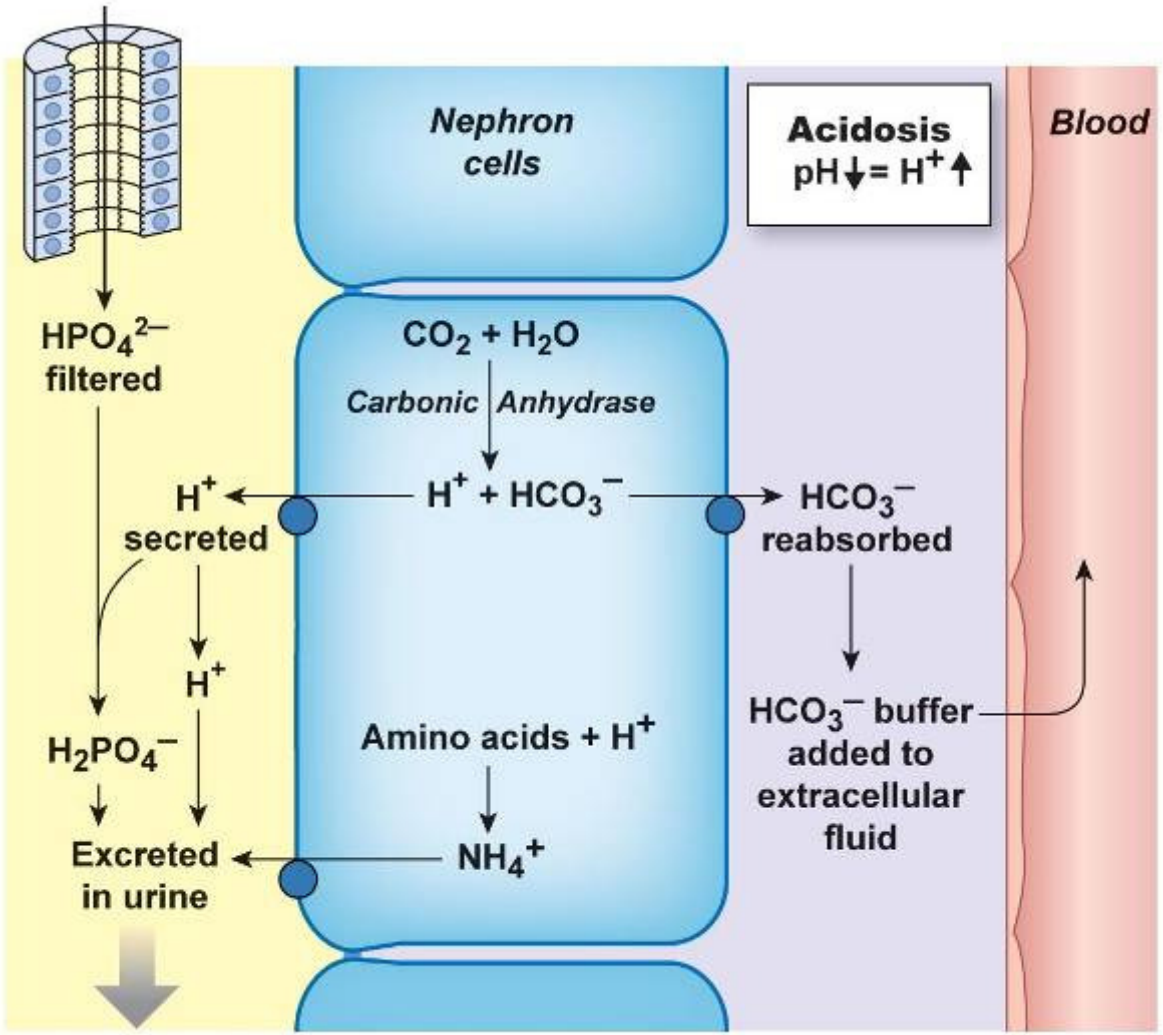
Respiratory compensation for metabolic acidosis



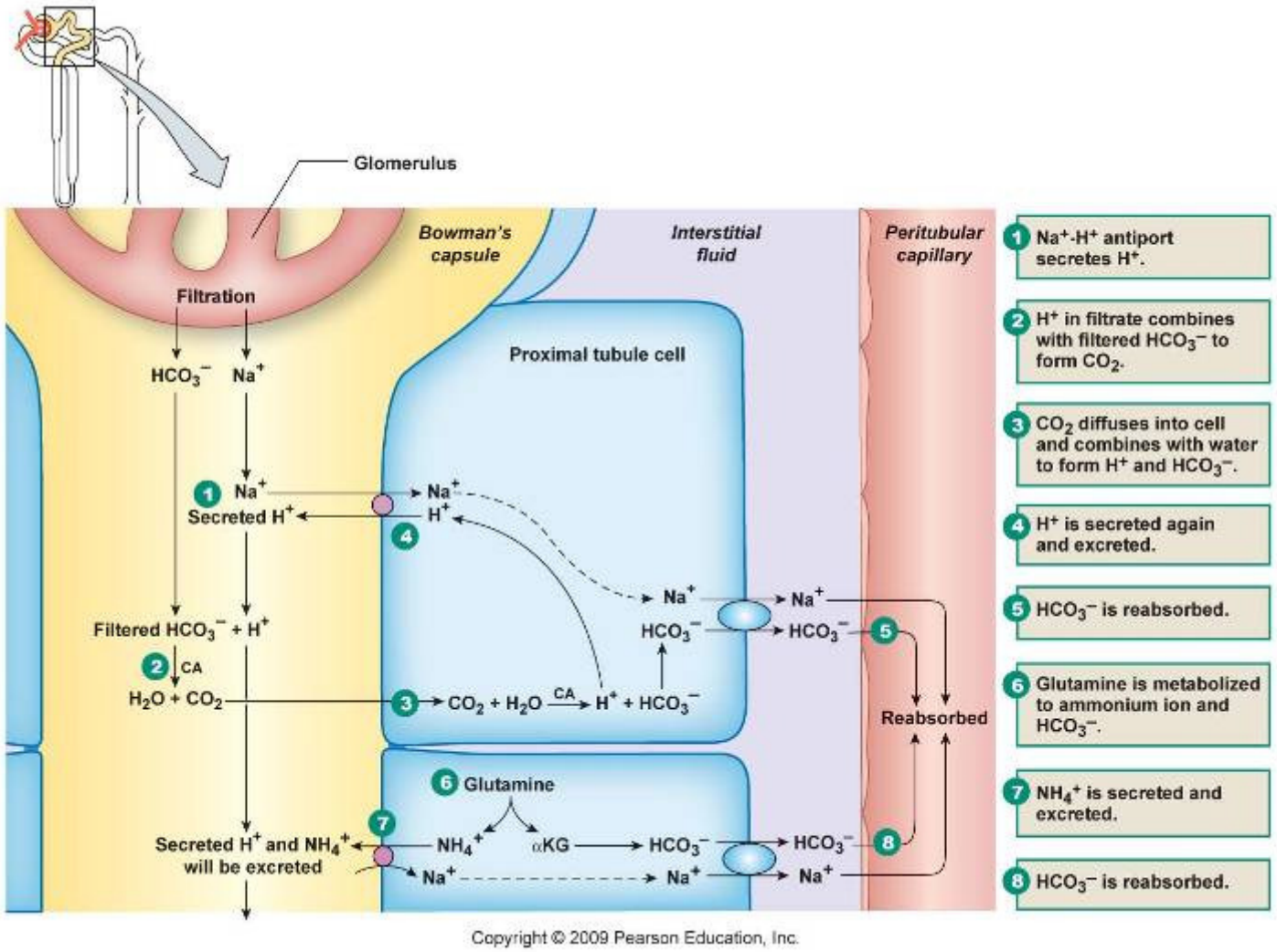
C. The kidneys:

The glomerular filtrate has a pH of 7,4
In proximal tubule: 6,7
In collecting tubules: 5,8-4,5

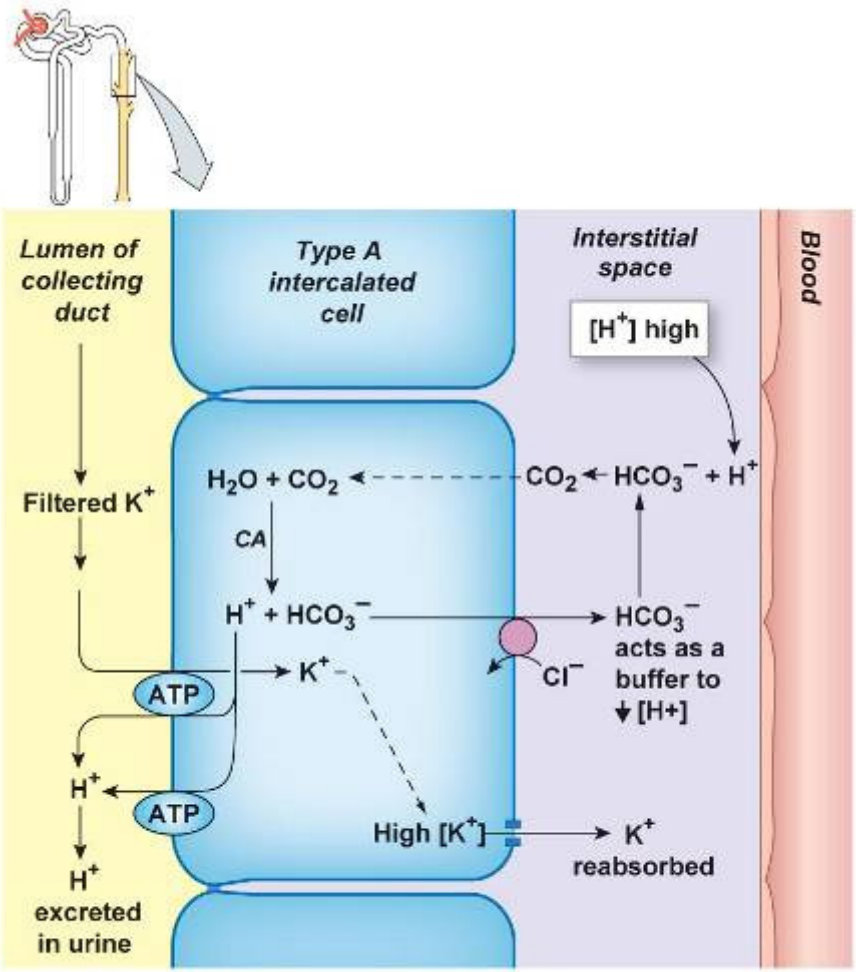
Overview of renal compensation for acidosis



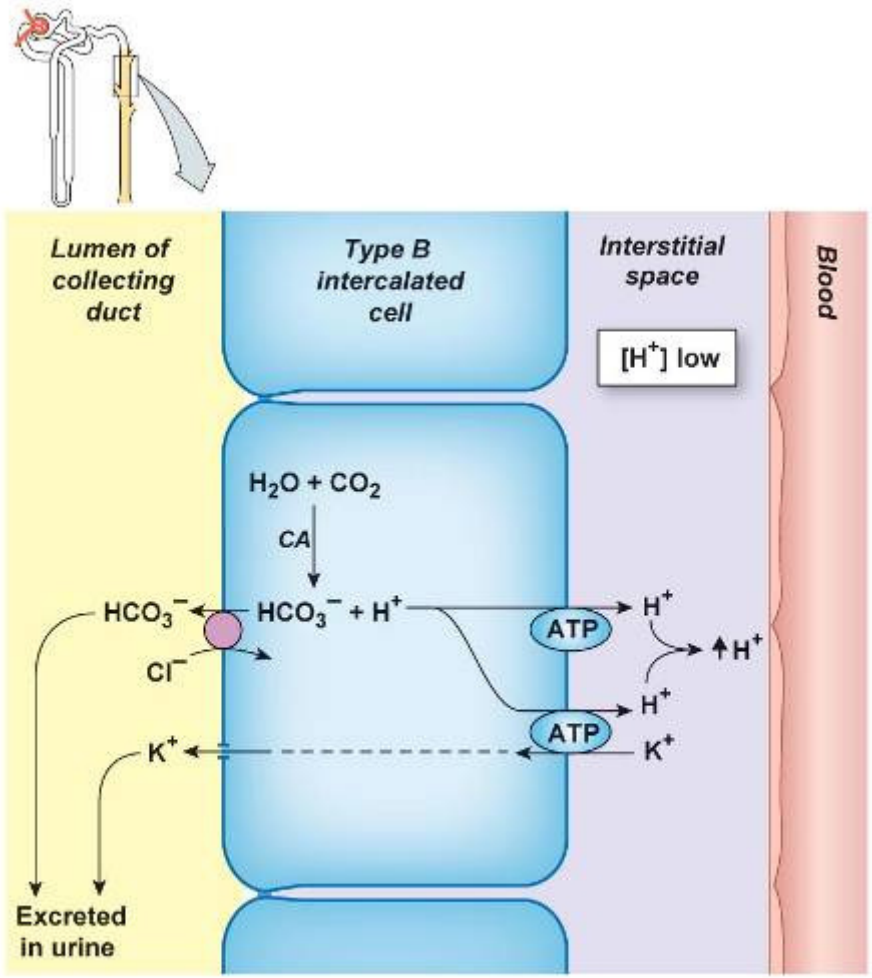
Proximal tubule H^+ secretion and reabsorption of filtered HCO_3^-



Role of the intercalated cells in acidosis and alkalosis



(a) Type A intercalated cell function in acidosis.



(b) Type B intercalated cell function in alkalosis.

- Phosphate buffers in kidneys

  $HPO_4^- + H^+ \rightarrow H_2PO_4^-$

  so that urine pH does not decrease too far

- Gluconeogenesis in kidneys

  the kidney also removes H^+ by the synthesis of new glucose:

  $2\ H_2O + 2\ CO_2 \rightarrow 2H^+ + 2HCO_3^-$ + oxoglutarate (5C) $\rightarrow$ glucose + CO_2

D. The liver:

- removes H^+ mainly by gluconeogenesis:

  $2H^+ + 2\text{lactate} \rightarrow \text{glucose}$

  thus liver pathology can lead to lactic acidosis
- also: $NH_3 + H^+ \rightarrow NH_4^+$
- removes HCO_3^- by urea synthesis:

  $HCO_3^- + NH_4^+ \rightarrow \text{urea}$

E. The skeleton:

- during acidosis H^+ moves into the bone matrix and reacts with calcium phosphate:

  $Ca_3(PO_4)_2 + 2H^+ \rightarrow 3Ca^{2+} + 2HPO_4^{2-}$

- during strong acidosis HPO_4^{2-} is liberated into ECF: $\rightarrow$ helps with buffer action $\rightarrow H_2PO_4^-$

Abnormalities in acid-base balance

Respiratory origin:

Henderson-Hasselbach equation:

$$pH = 6.1 + \frac{[HCO_3^-]}{\log 0{,}031\ pCO_2}$$

thus changes in bicarbonate/pCO_2 lead to changes in pH

Respiratory acidosis: ↑ pCO_2 thus ↓ pH
and ↑ $CO_2 + H_2O \rightarrow \uparrow H^+ + \uparrow HCO_3^-$

Respiratory alkalosis: ↓ pCO_2 thus ↑pH
and ↓ $CO_2 + H_2O \leftarrow \downarrow H^+ + \downarrow HCO_3^-$

Compensation mechanisms:

Acidosis: ↑ ventilation tempo, secretion of H^+ and reabsorption of HCO_3^- in the nephron

Alkalosis: ↓ ventilation tempo, ↓ HCO_3^- reabsorption

Metabolic origin:

Metabolic acidosis:

due to acids stronger than HHb or other buffer acids, eg., lactic acid or aceto-acetic acid

$\uparrow CO_2 + H_2O \leftarrow \uparrow H^+ + \downarrow HCO_3^-$

Compensation:

- $\uparrow H^+$ stimulates ventilation tempo, under pH $\rightarrow$ 6 $\rightarrow$ death
- Kidneys secrete H^+, retain more Na^+ and HCO_3^-

  buffers in the luminal fluid form $H_2PO_4^-$, H_2CO_3 and NH_4^+

Metabolic alkalosis:

due to intake of alkali (sodium bicarbonate or loss of HCl with vomiting)

both the pH and the [HCO_3^-] increase

$\downarrow CO_2 + H_2O \rightarrow \downarrow H^+ + \uparrow HCO_3^-$

Compensation:

ventilation tempo ↓, thus pCO_2 ↑, thus pH ↓

SUMMARY (uncompensated conditions)

NB Normal values: pH = 7,35-7,45

pCO_2 = 35-45 mm Hg, [HCO_3^-] = 22-26 mmol/l

Summary

	ACIDOSIS		ALKALOSIS	
	Respiratory	Metabolic	Respiratory	Metabolic
pH	↓	↓	↑	↑
pCO_2	↑	N	↓	N
HCO_3^-	↑	↓	↓	↑