Functions of the kidney

1. Excretion of nitrogenous waste, urea & uric acid
2. Regulation of body fluid compartments - homeostasis of arterial blood pressure
3. Production of hormones

- renin, erythropoietin, Vit D etc

4. **Acid-base balance**

Acid - proton (H^+) donor

e.g. HCl

Base - proton acceptor

e.g. $NaOH$

Conseqences of acid-base imbalance

Acidosis (pH < 7.4) : depression of CNS $\longrightarrow$ disorientation $\longrightarrow$ coma $\longrightarrow$ death

Alkalosis (pH > 7.4) : hyper-excitability of nerve and muscle $\longrightarrow$ convulsion $\longrightarrow$ tetany

Normal range of acid in the body fluid

	H+ (Eg/L)
Normal	3.8x10-7
Range	1.0x10-8 - 1.0x10-7
Vital limit	1.58x10-8 - 1.58x10-7

pH concept

$$pH = Log \frac{1}{H^+} = - Log\ H^+$$

	H+ (Eg/L)	pH
Normal	3.8x10-7	7.4
Range	1.0x10-8 - 1.0x10-7	7.37 - 7.43
Vital limit	1.58x10-8 - 1.58x10-7	6.80 - 7.80

Extracellular fluid - 7.4
Intracellular fluid - 6.0 - 7.4, average 7.0

Our body is an acid producer

1. Volatile acid

H_2CO_3 ~ 10,000mM of H^+

↑during exercise and trauma

2. Non-volatile or fixed acid

H_3PO_4 - breakdown product of phosphoprotein, phospholipid, phosphoglyceride & cysteine

H_2SO_4 - breakdown product of methionine and cysteine

50 - 100 mM H^+

Excessive acid is produced
in some pathological situations

e.g. diabetes mellitus

pH $<$ 7.4 - acidosis

pH $>$ 7.4 - alkalosis

Responses to acid-base disturbance

1. Buffer

2. Respiratory

3. Renal

Renal defense

1. Secretion of H^+ and reabsorption of HCO_3^-

2. Production of NH_4^+

3. HPO_4^{2-} / HPO_4^- buffer

Reabsorption of bicarbonates in the renal tubules

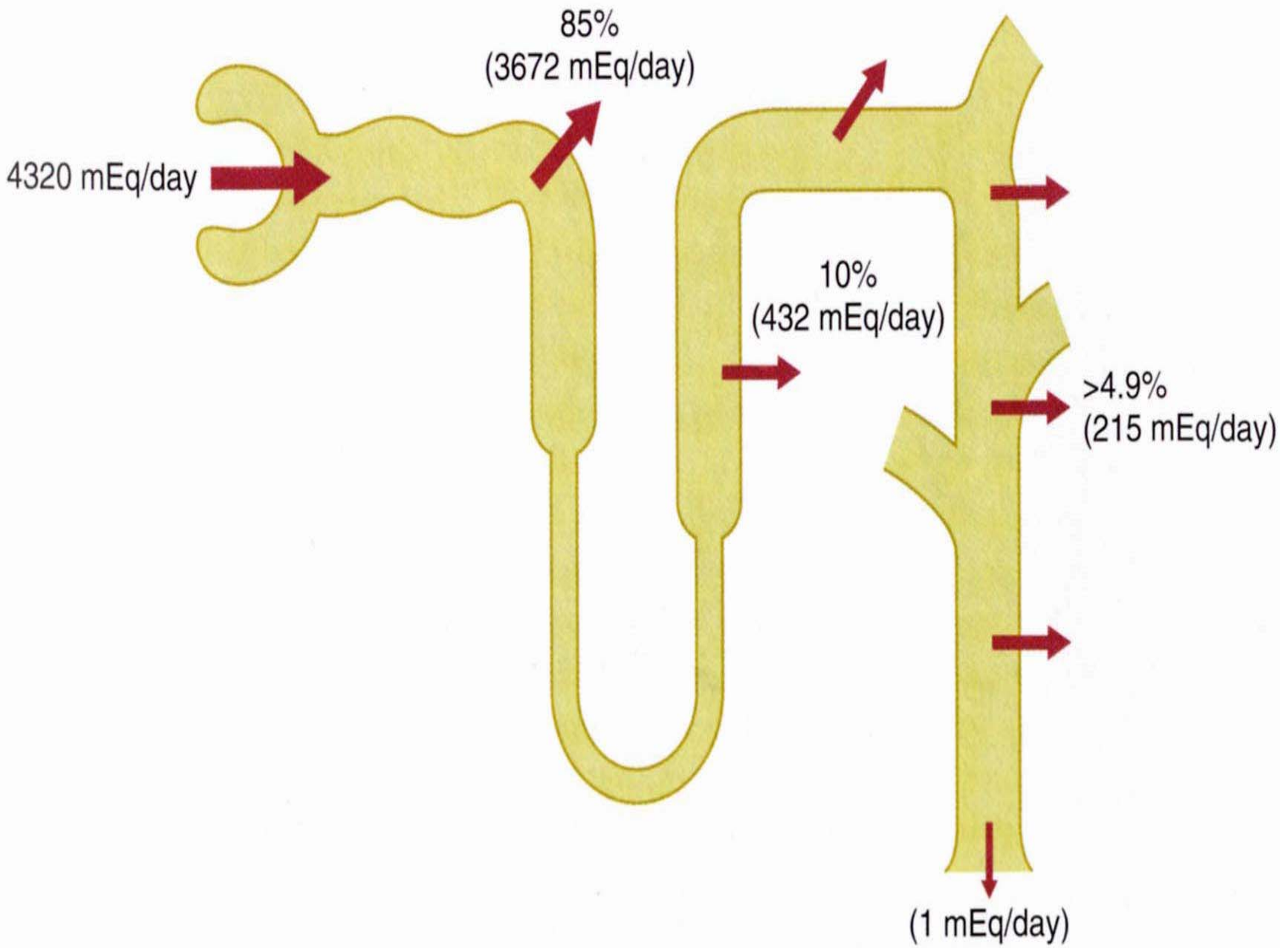
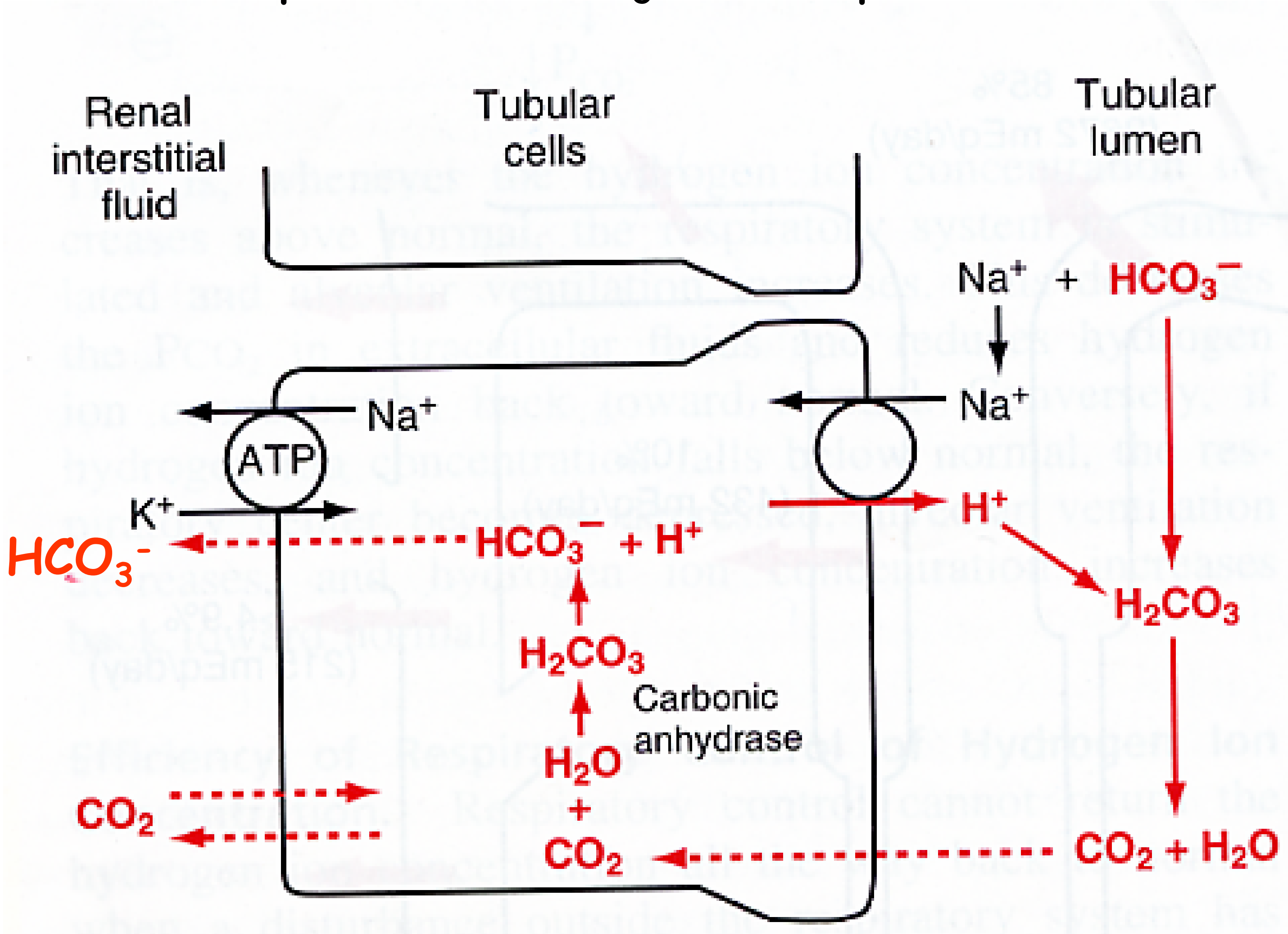


Figure 30–4

Reabsorption of bicarbonate in different segments of the renal tubule. The percentages of the filtered load of bicarbonate absorbed by the various tubular segments are shown, as well as the number of milliequivalents reabsorbed per day under normal conditions.

Renal reabsorption of HCO_3^- in the proximal tubule



Renal reabsorption of HCO_3^- in the late distal tubule and collecting duct

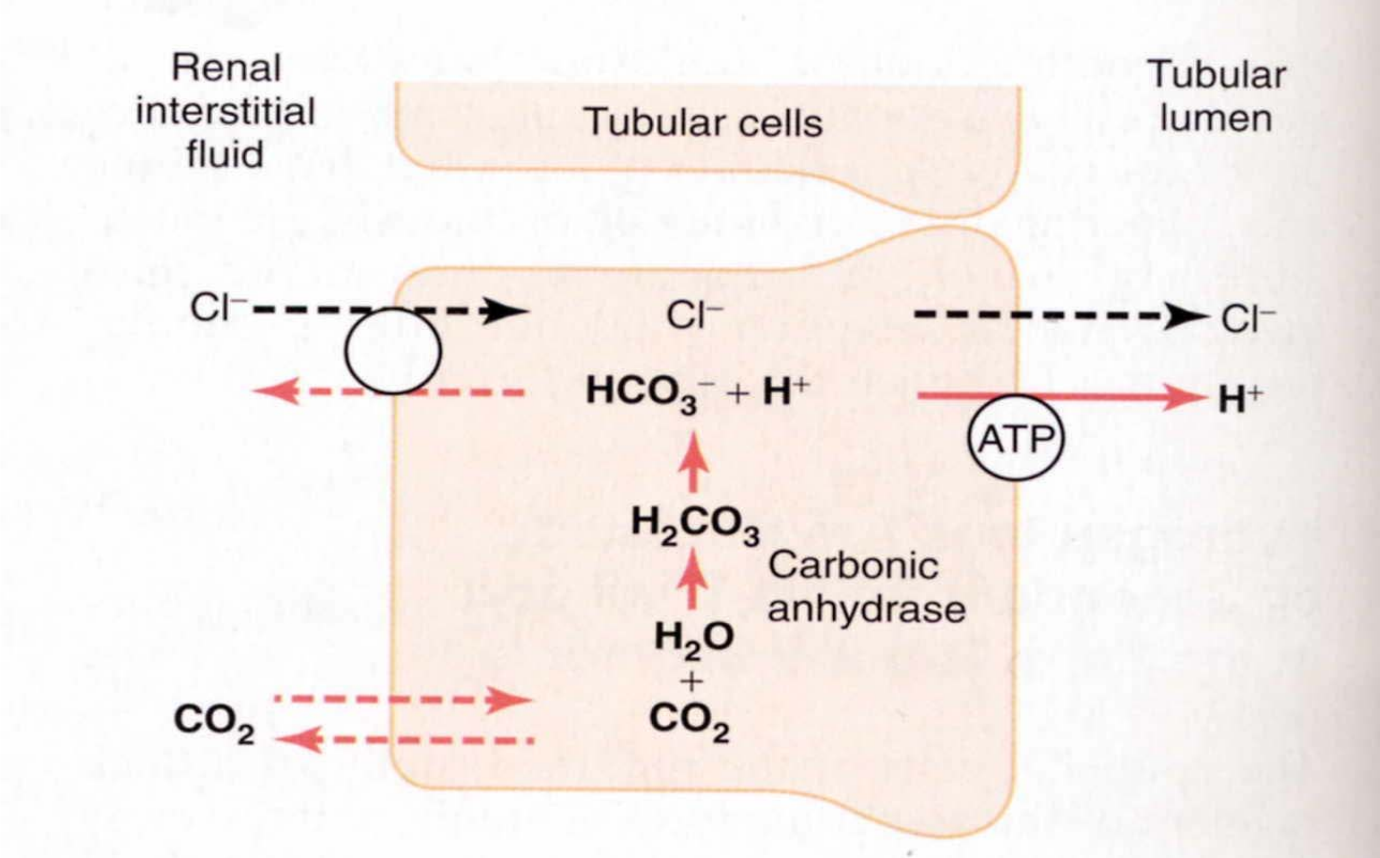


Figure 30–6

Primary active secretion of hydrogen ions through the luminal membrane of the intercalated epithelial cells of the late distal and collecting tubules. Note that one bicarbonate ion is absorbed for each hydrogen ion secreted, and a chloride ion is passively secreted along with the hydrogen ion.

Renal reabsorption of HCO_3^- in the distal tubule

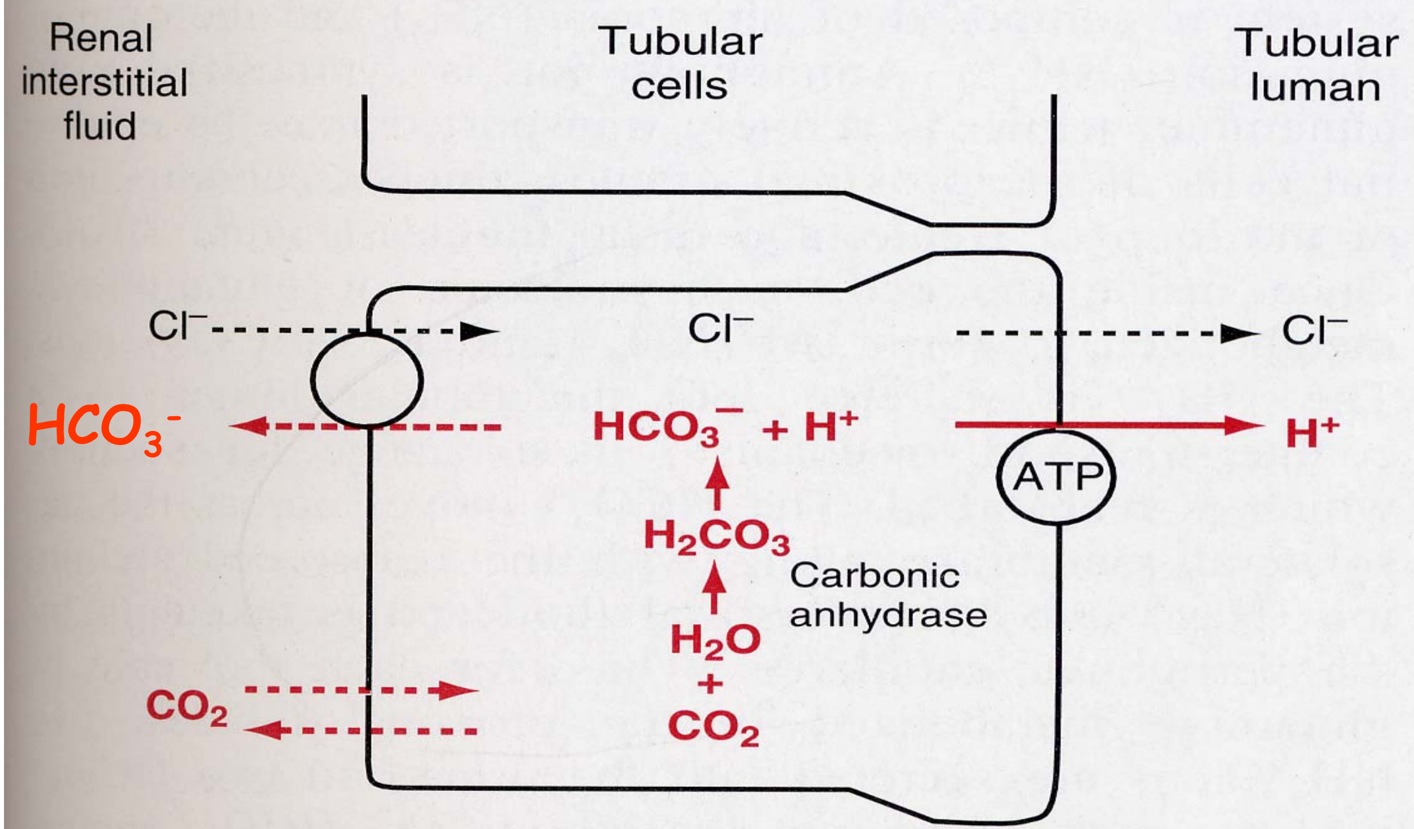


FIGURE 30 – 6

Primary active secretion of hydrogen ions through the luminal membrane of the epithelial cells of the distal and collecting tubules. Note that one bicarbonate ion is absorbed for each hydrogen ion secreted, and a chloride ion is passively secreted along with the hydrogen ion. This pattern of hydrogen ion secretion occurs in the intercalated cells of the late distal and collecting tubules.

Renal defense

1. Secretion of H^+ and reabsorption of HCO_3^-

2. Production of NH_4^+

3. HPO_4^{2-} / HPO_4^- buffer

Production of ammonium ion in the proximal tubule

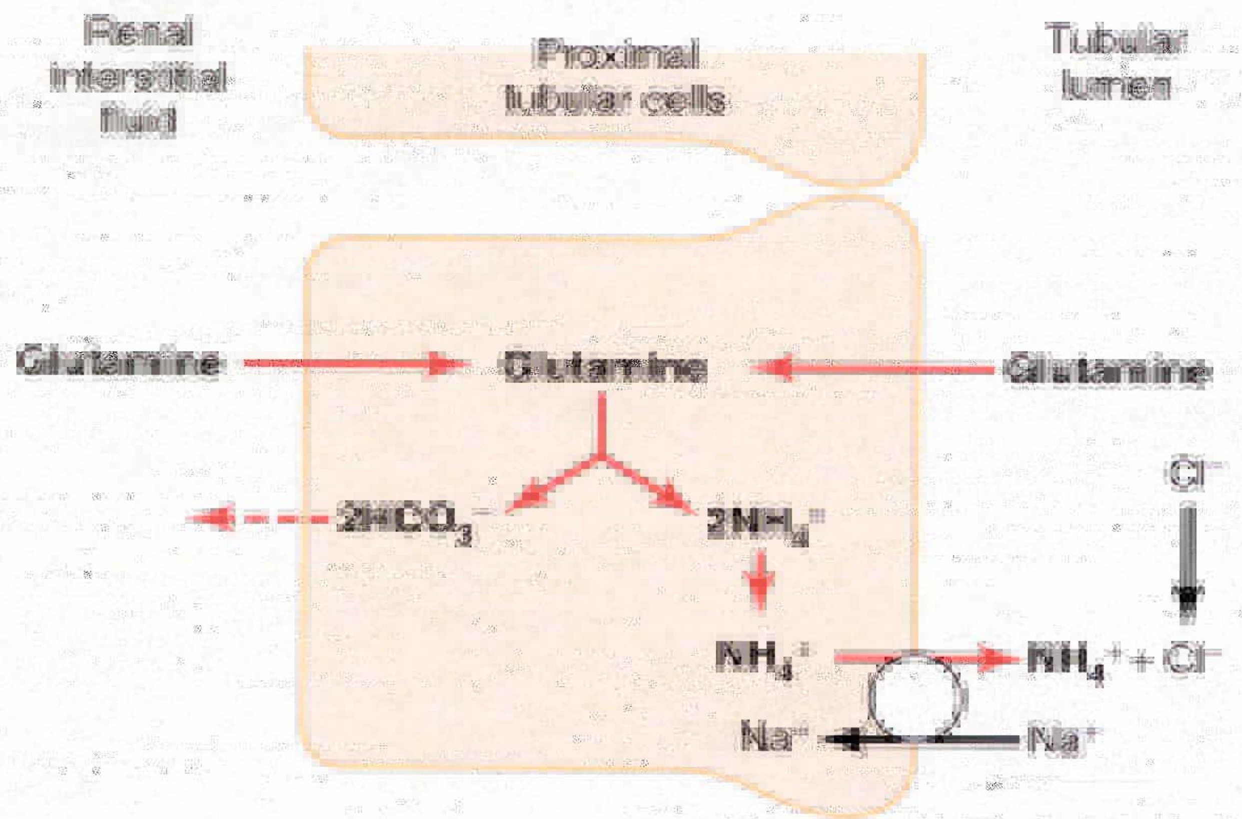


Figure 30–8

Production and secretion of ammonium ion (NH_4^+) by proximal tubular cells. Glutamine is metabolized in the cell, yielding NH_4^+ and bicarbonate. The NH_4^+ is secreted into the lumen by a sodium-NH_4^+ pump. For each glutamine molecule metabolized,

Production of ammonium in the collecting tubule

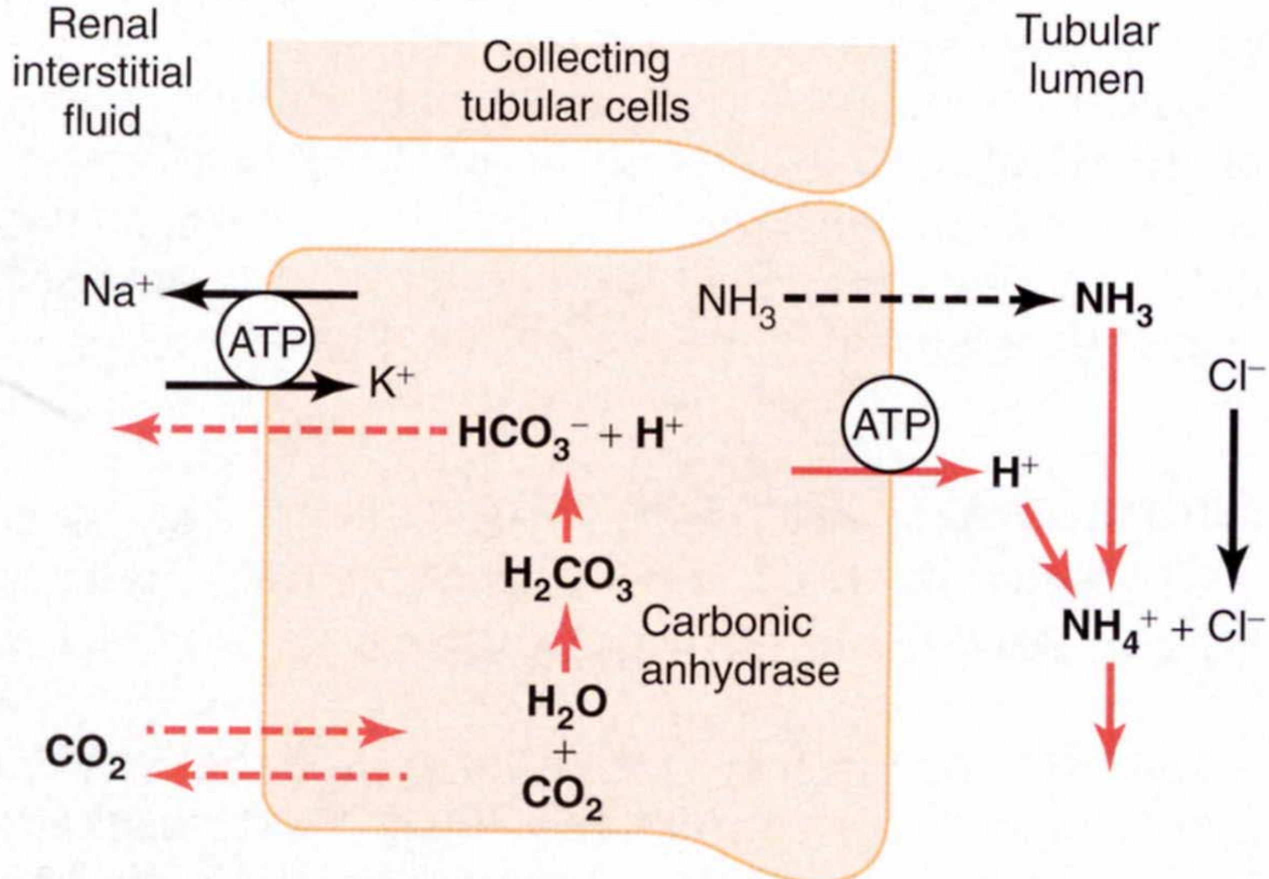


Figure 30–9

Buffering of hydrogen ion secretion by ammonia (NH_3) in the collecting tubules. Ammonia diffuses into the tubular lumen, where it reacts with secreted hydrogen ions to form NH_4^+, which is then excreted. For each NH_4^+ excreted, a new HCO_3^- is formed in the tubular cells and returned to the blood.

Production of glutamine $\propto$ Acidosis

Production of glutamine $\propto$ hyperkalaemia

Renal defense

1. Secretion of H^+ and reabsorption of HCO_3^-

2. Production of NH_4^+

3. HPO_4^{2-} / HPO_4^- buffer

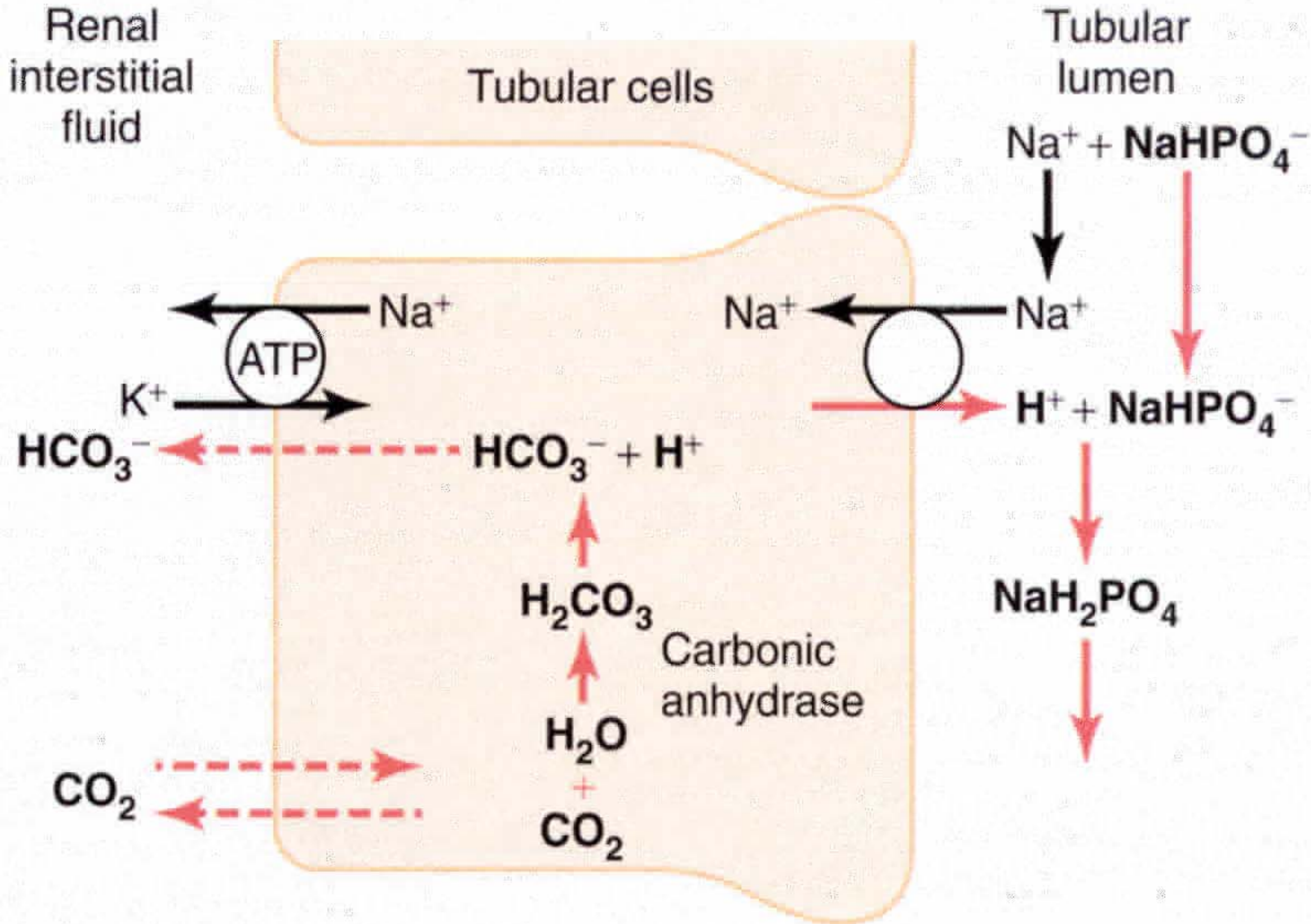


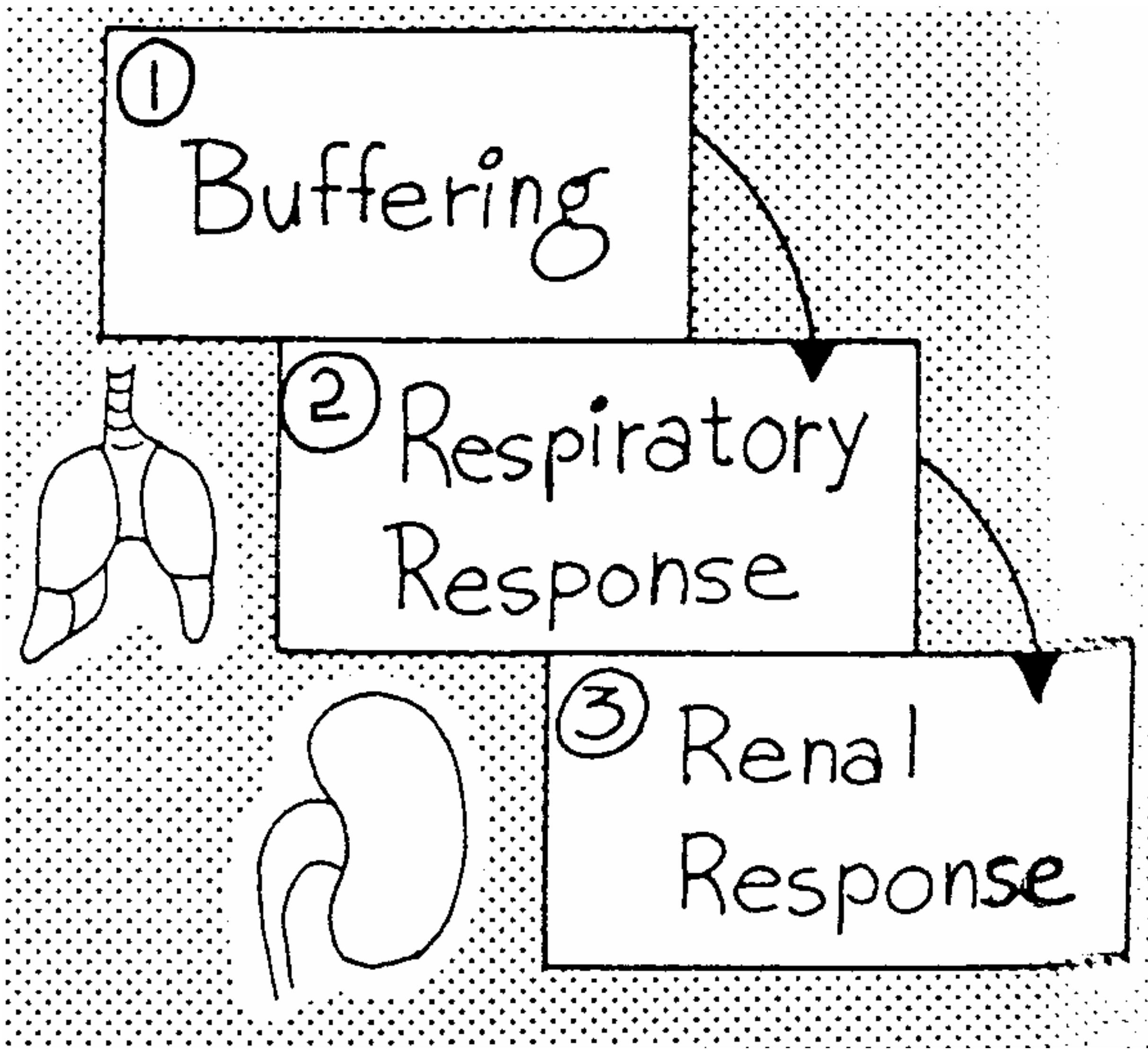
Figure 30–7

Buffering of secreted hydrogen ions by filtered phosphate ($NaHPO_4^-$). Note that a new bicarbonate ion is returned to the blood for each $NaHPO_4^-$ that reacts with a secreted hydrogen ion.

Renal defense

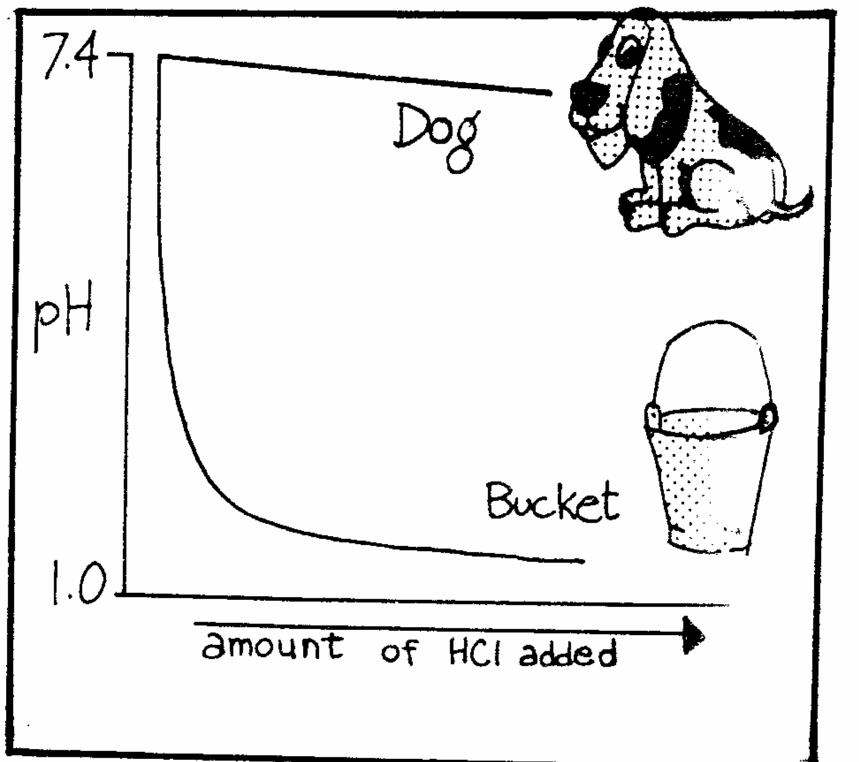
1. Takes days to complete

2. Able to restore the acid-base status provided the underlying cause is removed



1 Buffering
2 Respiratory Response
3 Renal Response

Buffering



After Pitts R.F. Harvey Lect. 48 172 (1952-53)

Buffer systems in our body

Buffer - a weak acid in equilibrium with its salt (base), such that it can either accept or donate H^+

e.g. $H_2CO_3 = H^+ + HCO_3^-$

(acid) (base)

Buffer systems in our body

ECF

$AlbuminH^+ = Albumin + H^+$

$H_2CO_3 = H^+ + HCO_3^-$

ICF

$ProtH^+ = Prot + H^+$

$HbH^+ = Hb + H^+$

$H_2PO4^- = H^+ + HPO4^{2-}$

Henderson-Hasselbach equation

$$pH = pK + \text{Log}\frac{\text{Base}}{\text{Acid}}$$

$$pH = 6.1 + \frac{[HCO_3^-]}{0.03\ PCO_2}$$

The Isohydrous Principle

Any condition that changes the balance of any one of the buffer systems also changes the balance of all the other

$$H = \frac{K_1 x HA1}{A1^-} = \frac{K_2 x HA2}{A2^-} = \frac{K_3 HA3}{A3^-}$$

The most important buffer in the body

$$H^+ + HCO_3^- = H_2CO_3$$

1. Most abundant - 12 times of phosphate buffer

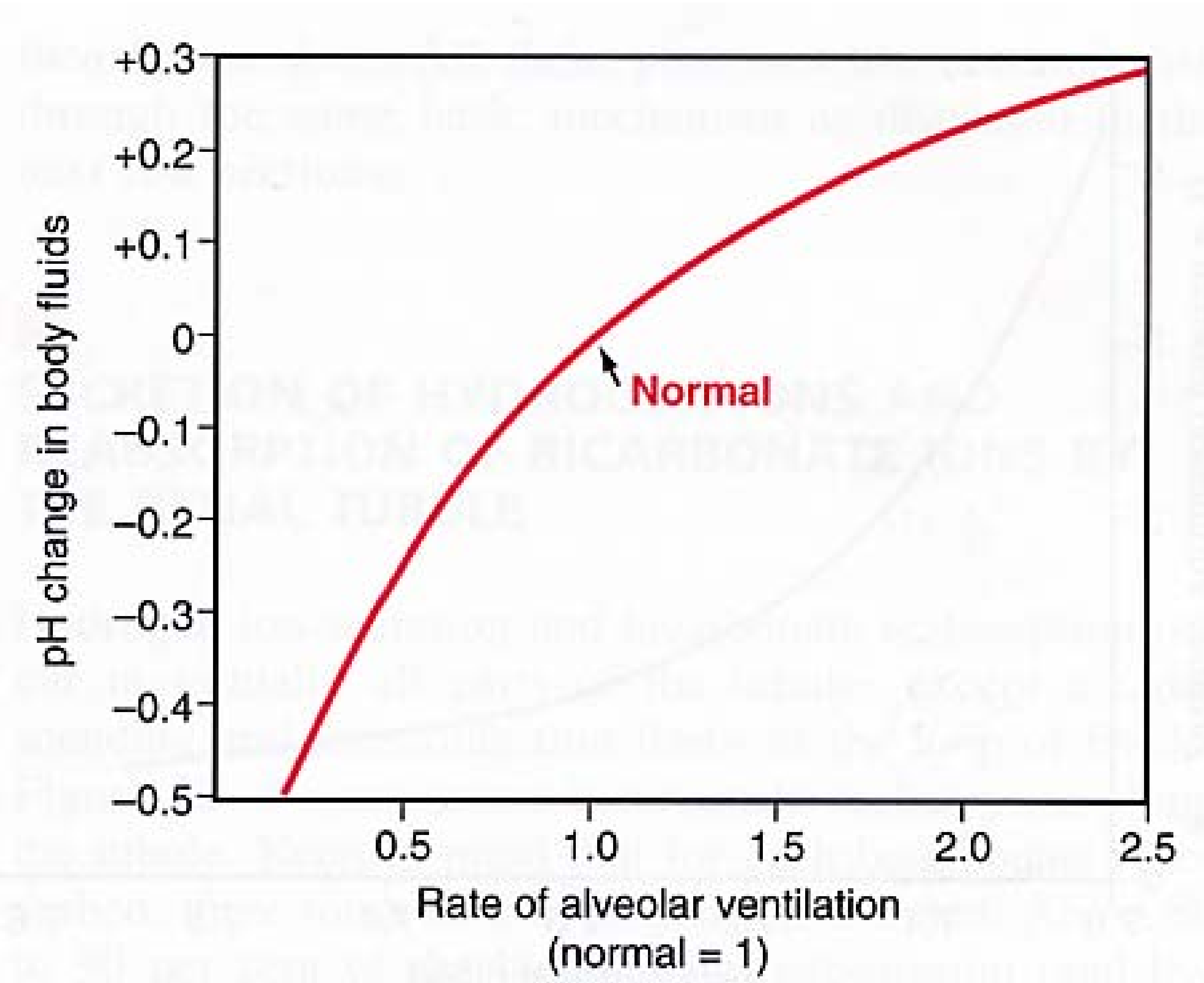
2. $H^+ + HCO_3^- = H_2CO_3 \longrightarrow H_2O + CO_2$

Kidney

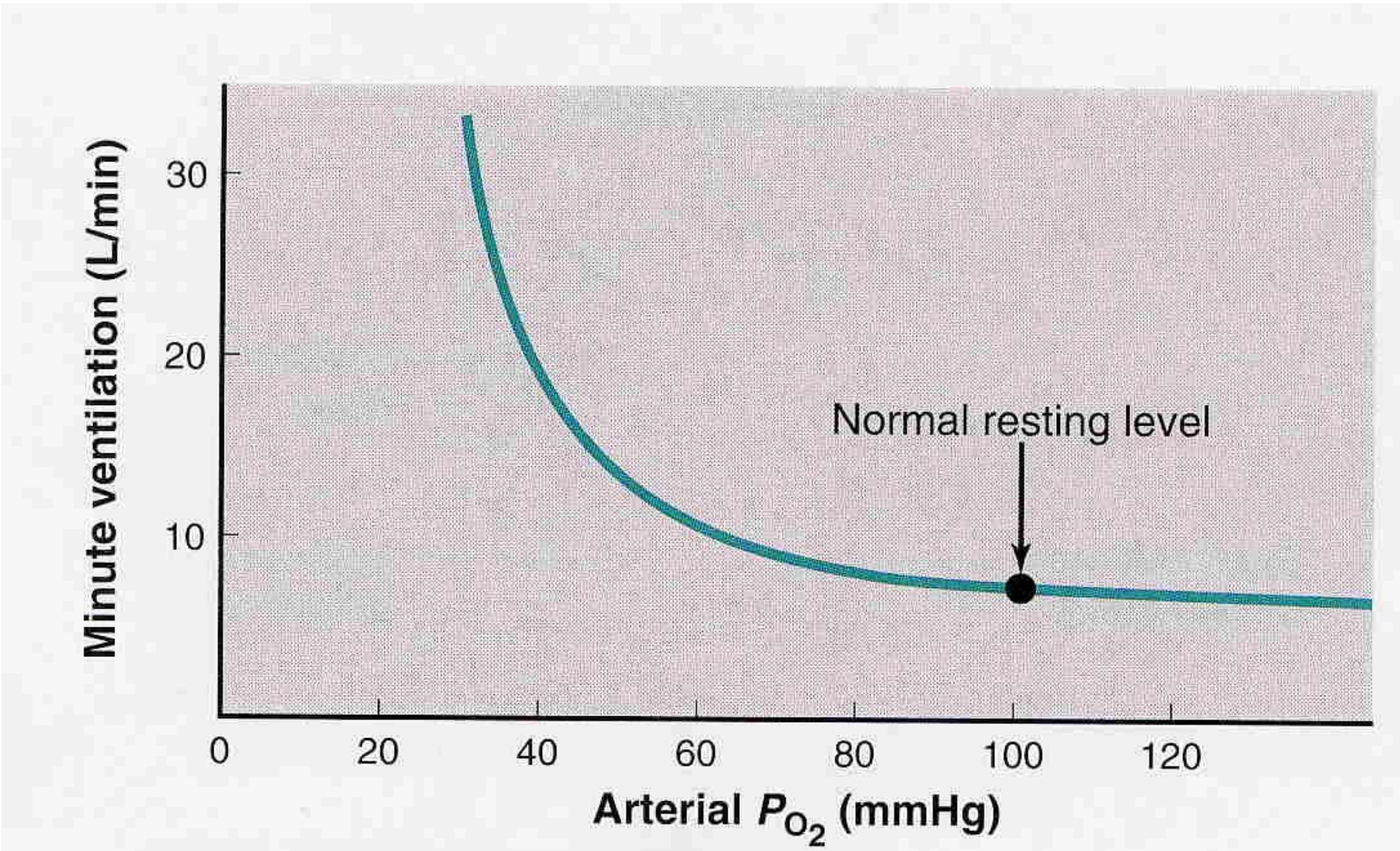
Lung

Respiratory defense

1. Change in ventilation causes changes in pH



Decease in ventilation is blocked by biphasic response to oxygen



Respiratory defense

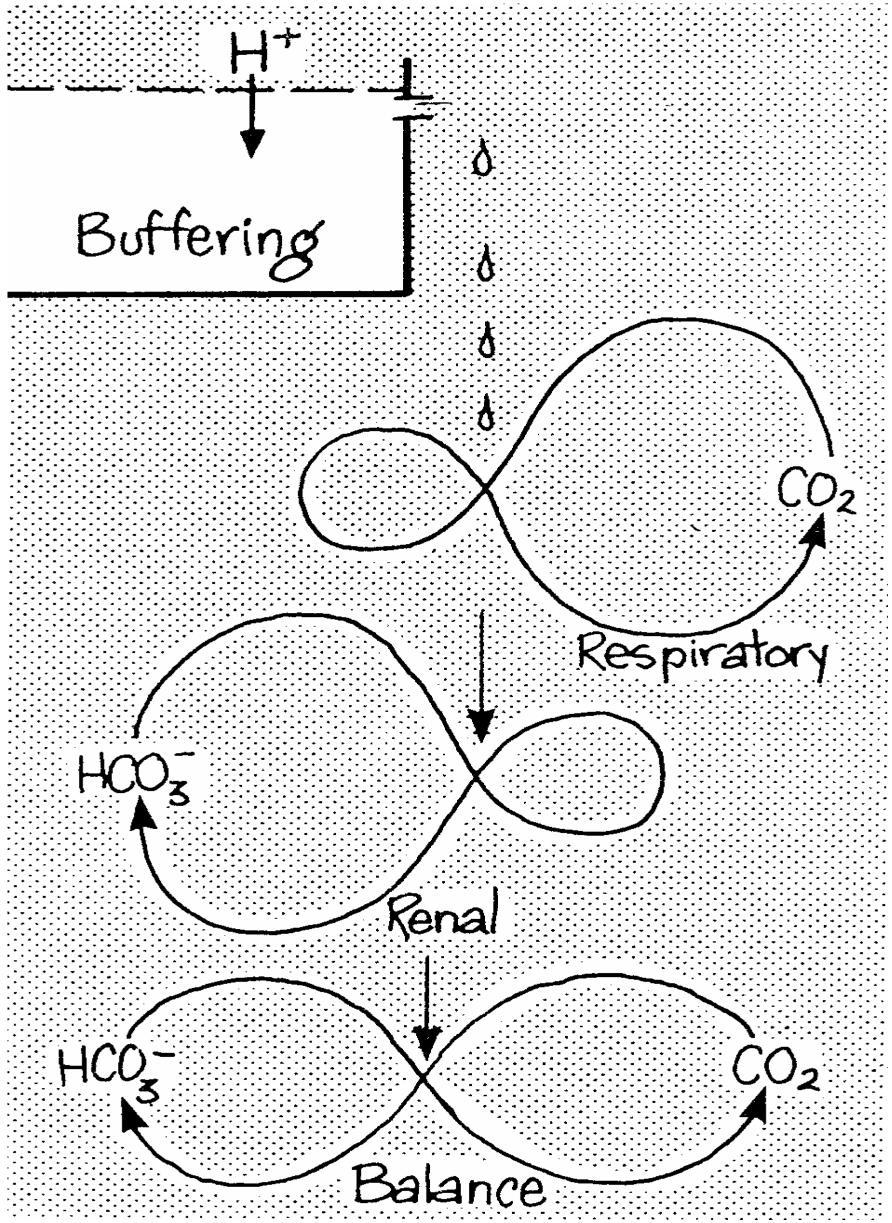
1. Takes several hours to complete

2. More powerful than buffering system, but unable to restore the acid-base status to normal

Renal defense

1. Takes days to complete

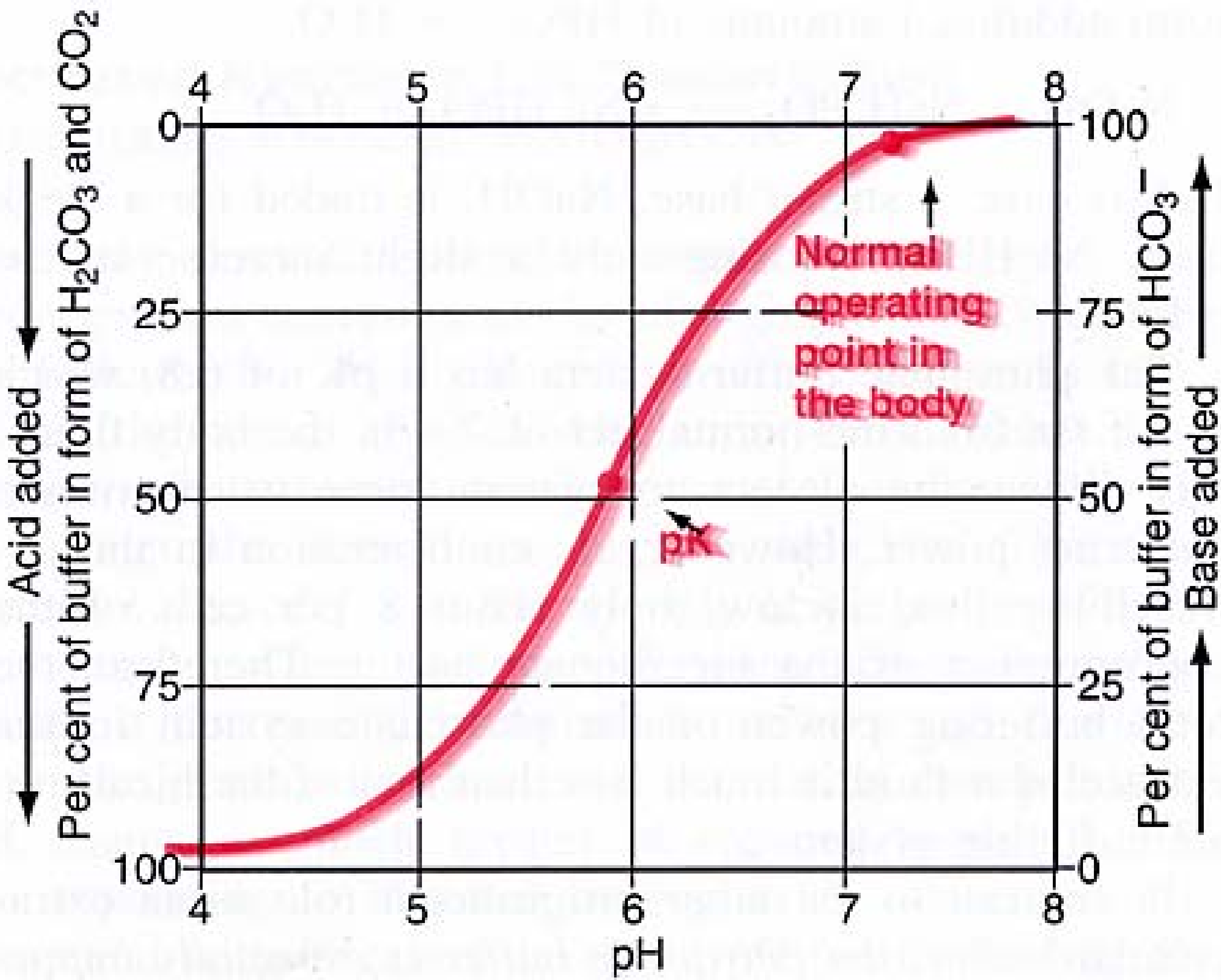
2. Able to restore the acid-base status provided the underlying cause is removed



H+
Buffering
CO2
Respiratory
HCO3−
Renal
HCO3−
CO2
Balance

H_2CO_3 not the most ideal buffer

pK = 6.1, not close to 7.4



Acid added
Per cent of buffer in form of H_2CO_3 and CO_2
0
25
50
75
100
4
5
6
7
8
pH
Normal operating point in the body
pK
100
75
50
25
0
Per cent of buffer in form of HCO_3^-
Base added

	Respiratory	Metabolic
Acidosis pH $\downarrow$	$\dfrac{[HCO_3^-] \uparrow}{P_{CO_2} \uparrow}$	$\dfrac{[HCO_3^-] \downarrow}{P_{CO_2} \downarrow}$
Alkalosis pH $\uparrow$	$\dfrac{[HCO_3^-] \downarrow}{P_{CO_2} \downarrow}$	$\dfrac{[HCO_3^-] \uparrow}{P_{CO_2} \uparrow}$

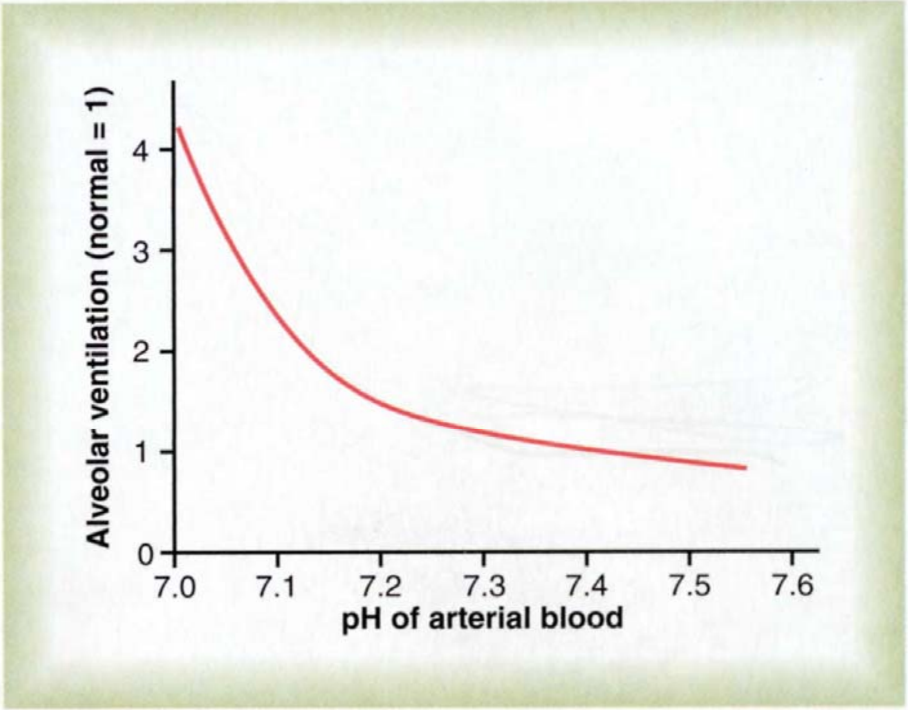


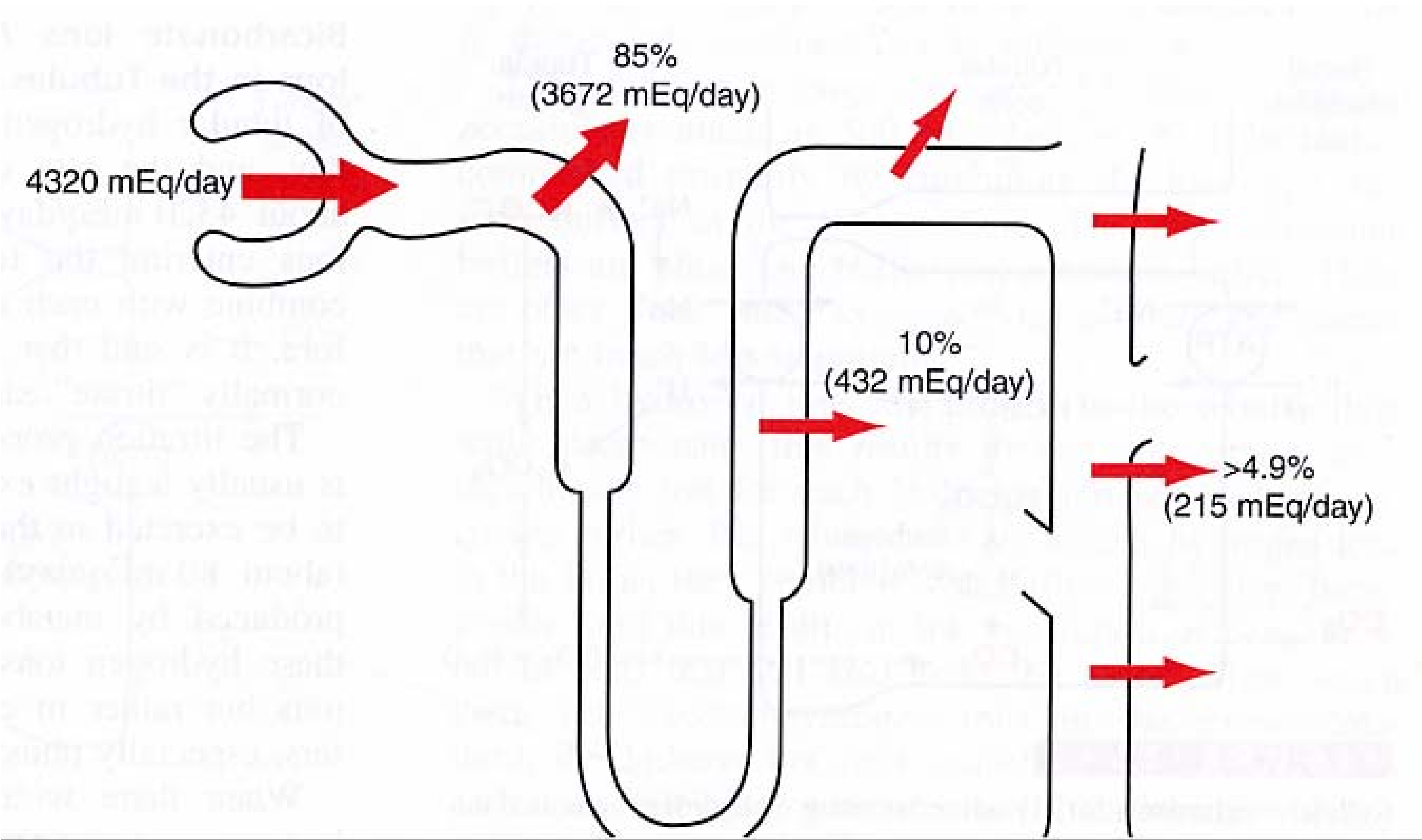
Figure 30–3

Effect of blood pH on the rate of alveolar ventilation.

Acidosis - pH $<$ 7.4

Alkalosis - pH $>$ 7.4

Renal reabsorption of HCO_3^-



Production of NH_4^+ in the proximal tubule

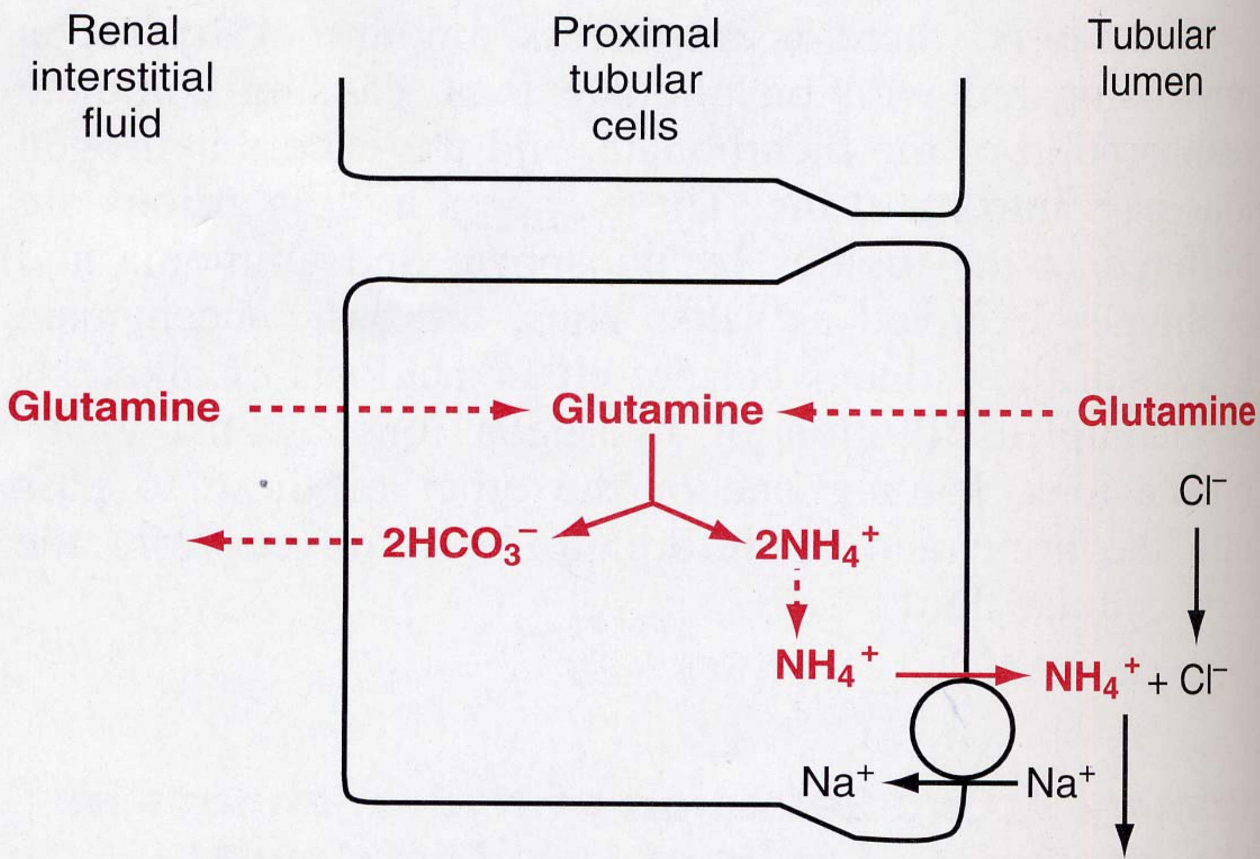
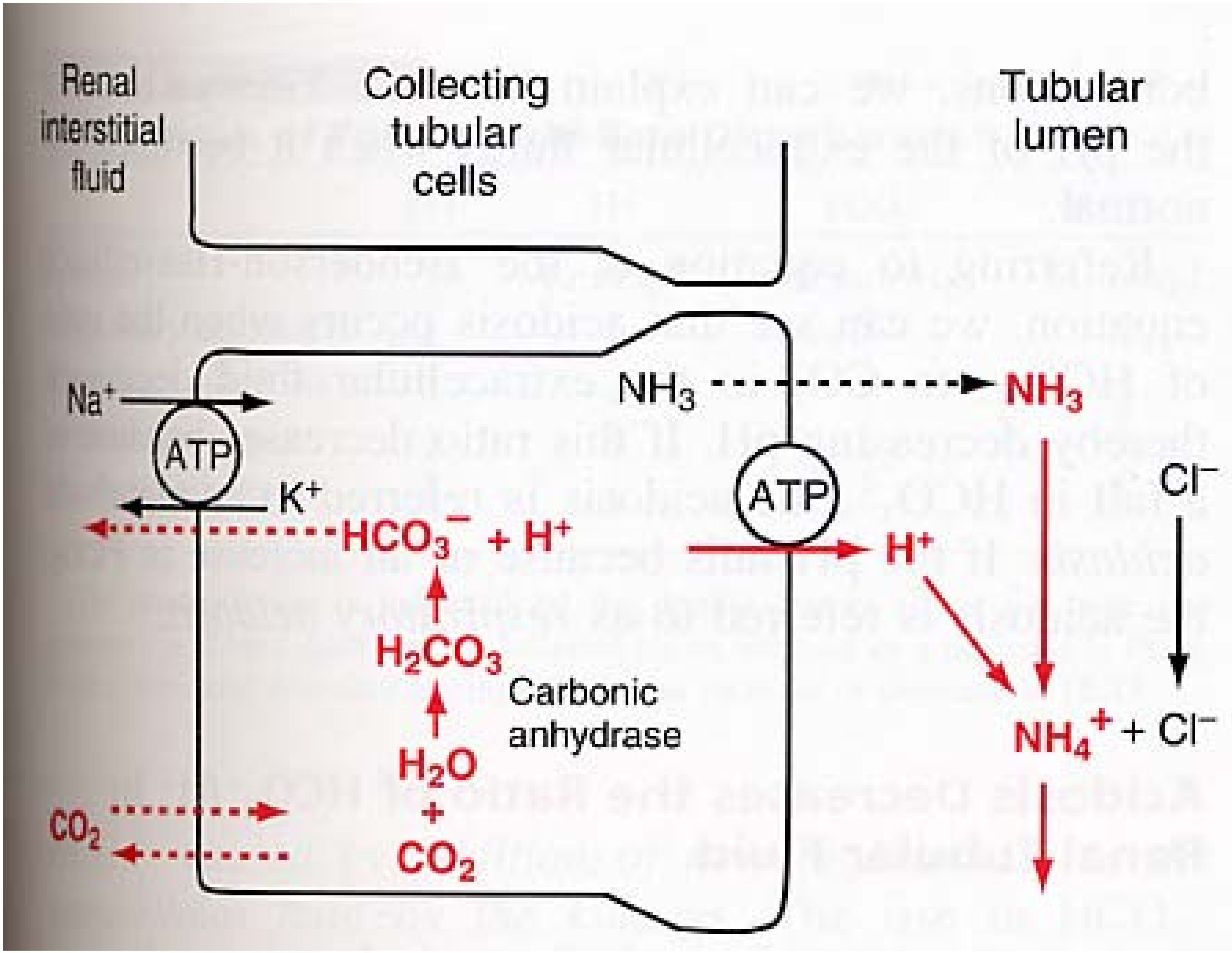


FIGURE 30–8

Production and secretion of ammonium ion (NH_4^+) by proximal tubular cells. Glutamine is metabolized in the cell, yielding NH_4^+ and bicarbonate. The ammonium ion (NH_4^+) is actively secreted into the

Production of NH_4^+ in the collecting duct



Formation of titratable acid