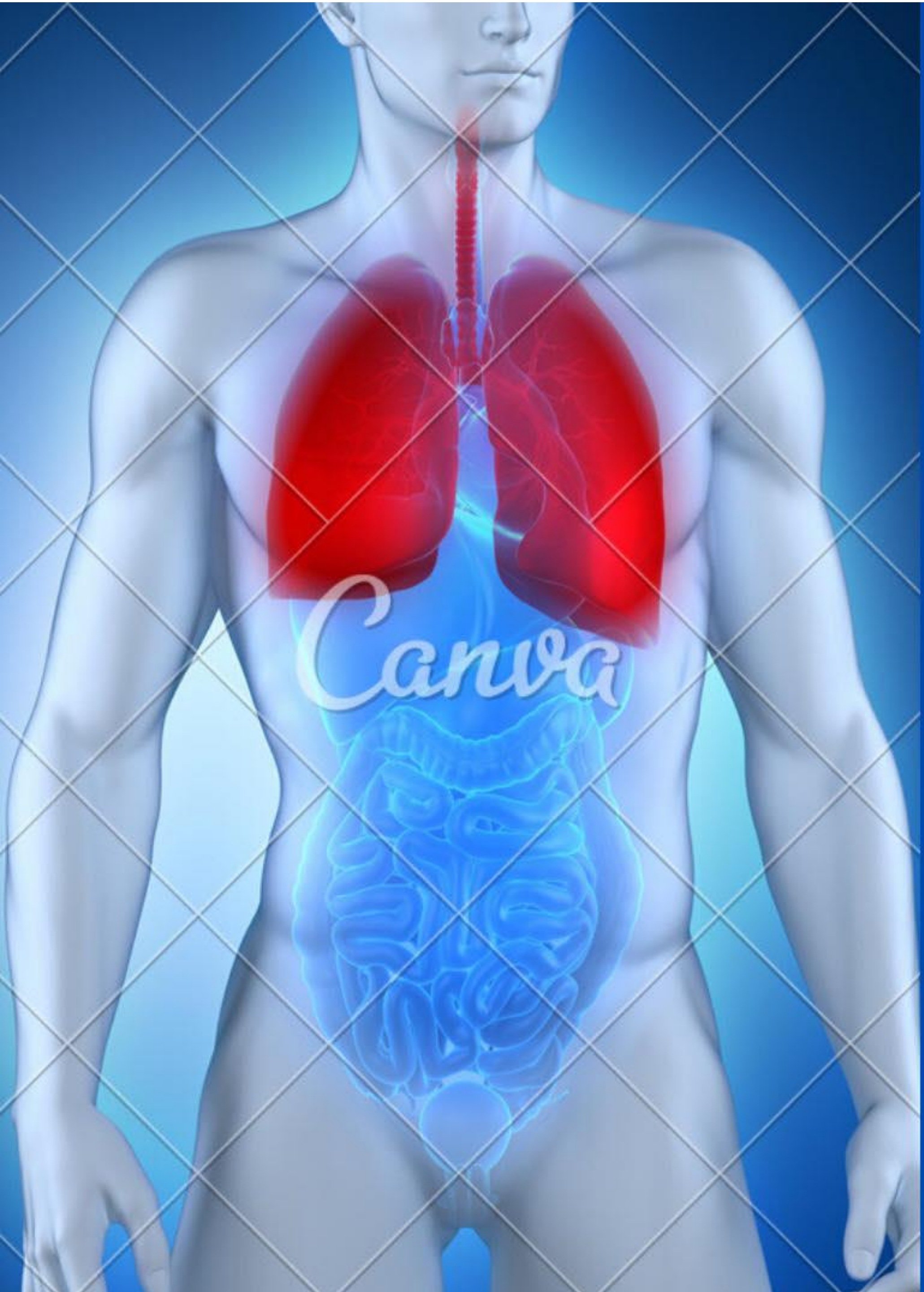


PASSION ACADEMIC TEAM **YU - MEDICINE**

Sheet#

Lec. Date : Acid-base balance 2

Lec. Title : 16-2-2020

Written By :

If you come by any mistake , please kindly report it to shaghafbatch@gmail.com

RESPIRATORY SYSTEM

Acid-Base Balance

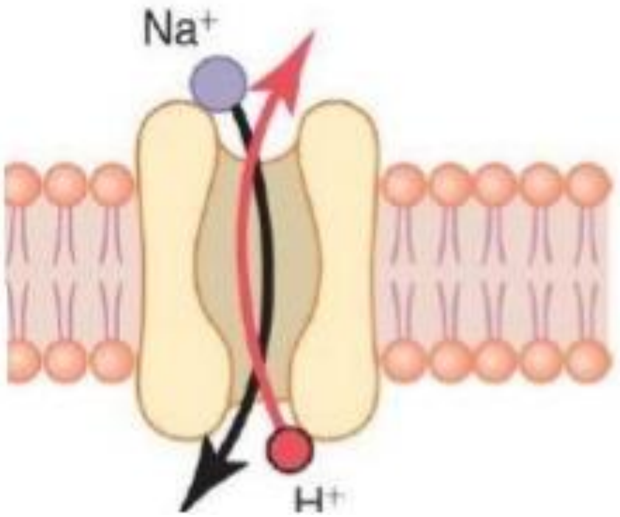
Dr. Mazhar Al Zo'ubi| RS-Biochemistry

Source: Textbook of Biochemistry for Medical students, Chapter 29: P 390-406

- We mentioned before that we have 3 lines of acid-base balance:
- 1- the blood buffers.
- 2- the respiratory system.(not prolonged one)
- 3- the renal system , which is working to control our PH all of the time (it is working in normal conditions)
- The renal system control our PH as a course adjustment , while in the blood it is fine adjustment.
- We want to know that urine PH is very high and kindly it more acidic than blood, due to the excretion of the hydrogen ions all of the time ,in the other hand while we are releasing cations (H+)we are reabsorbing the filtrated Na.

- ايش الحجب الي انحكا فوق عن الصوديوم والهيدروجين ☹
- Don’t be depressed ☹
- القصة وما فيها انه الصوديوم بيروح ع نفس الناقل الي هو باتجاه متعاكس (اذا ما فهمت ايش يعني ب اتجاه متعاكس انزل ع الترجمة تحت بتفهمها ب الانجليزي) , المهم انه بهاد الناقل المتعاكس نحنا بنطلع ايونات
- الهيدروجين (بنصرفه للخارج) , وبيتم امتصاص ايونات الصوديوم ثم باتجاه الدم
- القصة نفسها بس ب الانجل

- Na ions go to t (which H ions go) , this transporte we excrete H ions and reabsorb I



وصلت ؟! اذا لسا شوف

RENAL REGULATION OF pH

- Urine is acidic compared to plasma
- However, it has a wide range pH (4.5 to 9.8)

The major renal mechanisms for regulation of pH are:

A. Excretion of H+ (Fig. 29.2), is combined with generation of bicarbonate.
(while you are releasing H+ , you are making new bicarbonate)

B. Reabsorption of bicarbonate (recovery of bicarbonate) (Fig. 29.3), just for reabsorbing of bicarbonate that are filtrated bu glumerular system.

C. Excretion of titratable acid (net acid excretion) (Fig. 29.4), other acids that are used for buffer the urine.

D. Excretion of NH4+ (ammonium ions) (Fig. 29.5).

A. Excretion of H ions Generation of Bicarbonate

- **Net excretion of hydrogen ions, and net generation of bicarbonate**
- Totally we are maintaining the bicarbonate at high concentrations in the plasma due to:
- 1-as it was filtered it should be recovered
- 2- we are always producing acids that why we need other thing to adjust the PH value.

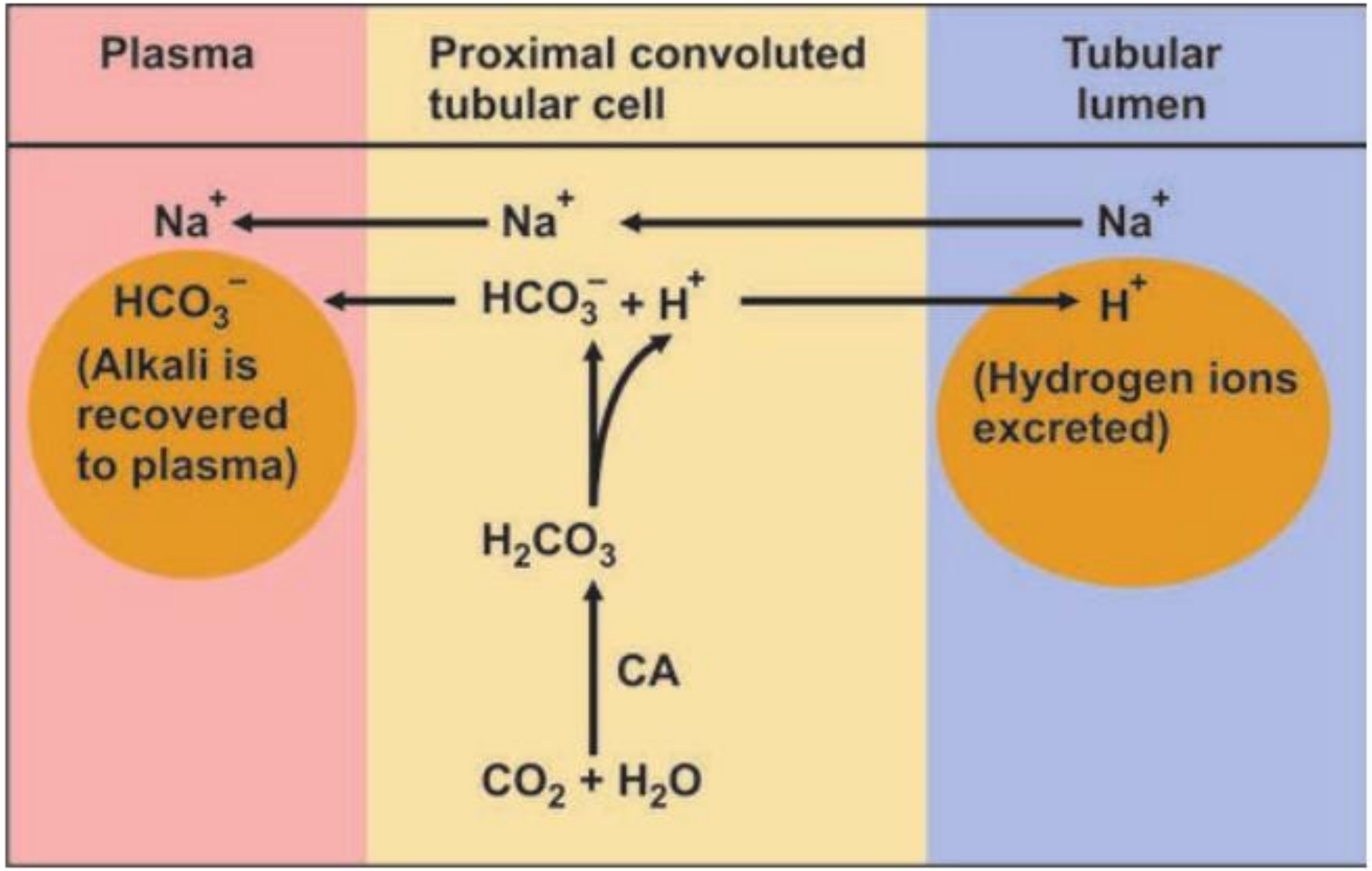


Fig. 29.2. Excretion of hydrogen ions in the proximal tubules; CA = Carbonic anhydrase

- Means that you are transport the H+ from the tubular system into the lumen through the generation of carbonic acid → bicarbonate.
- The tubular cells itself do that ,, generate the carbonic acid then it will be separated into bicarbonate and hydrogen ions, then the bicarbonate will be reabsorbed to the blood and the H+ will be excreted to the tubular lumen.

Just note that : the water is available all the time

B. Reabsorption of Bicarbonate

- **No net excretion of H^+**
- **Bicarbonate free urine**
- **No net generation of new bicarbonate**
- The aim is reabsorption of filtrated bicarbonate rather than formation of it.

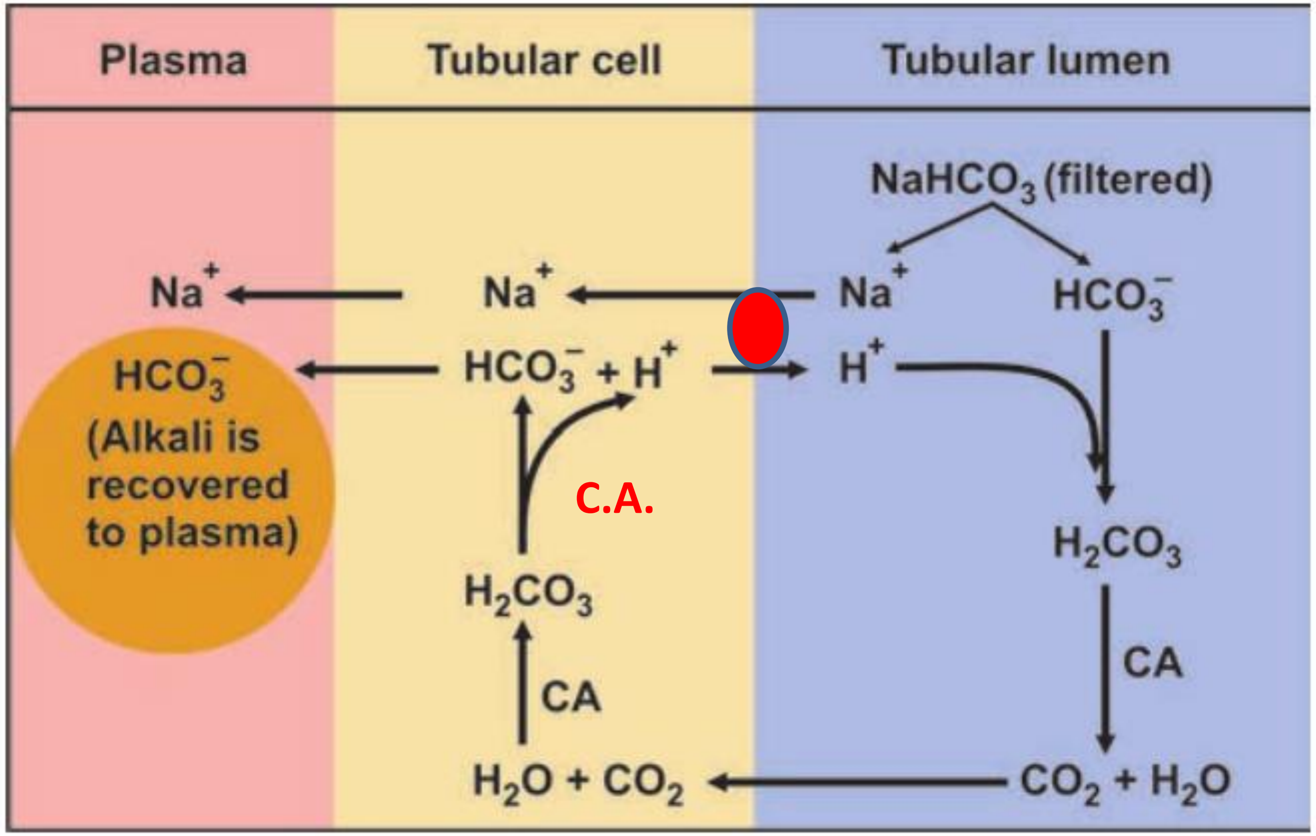


Fig. 29.3. Reabsorption of bicarbonate from the tubular fluid; CA = Carbonic anhydrase

C. Excretion of H^+ as Titratable Acid

- **H^+** are secreted by the distal tubules and collecting ducts by **H^+-ATPase located in the apical cell** membrane.
- Sodium acid phosphate is the major titratable acid.
- The acid and basic phosphate pair is considered as the **urinary buffer.**

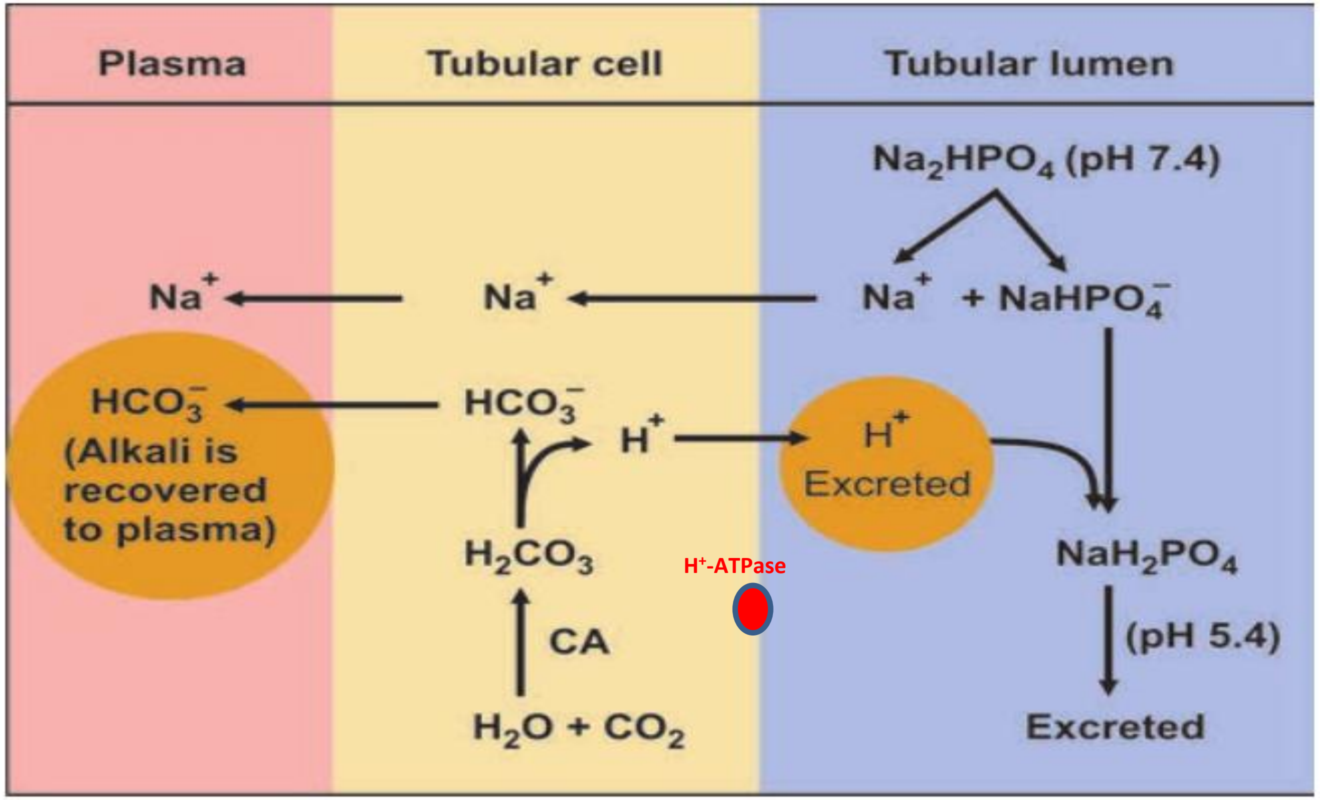


Fig. 29.4. Phosphate mechanism in tubules

After reabsorption of Na2PO4 it will be Decomposed so we will have HPO4 which will combined with the H+ that produced previously , so it will be more acidic.

D. Excretion of Ammonium Ions

- Predominantly occurs at the **distal convoluted tubules.**
- Helps to trap hydrogen ions in the urine.
- ***The glutaminase activity is increased in acidosis***
- **Normally**, about 70 mEq/L of acid is excreted daily; but in condition of acidosis, this can rise to 400 Eq/day.

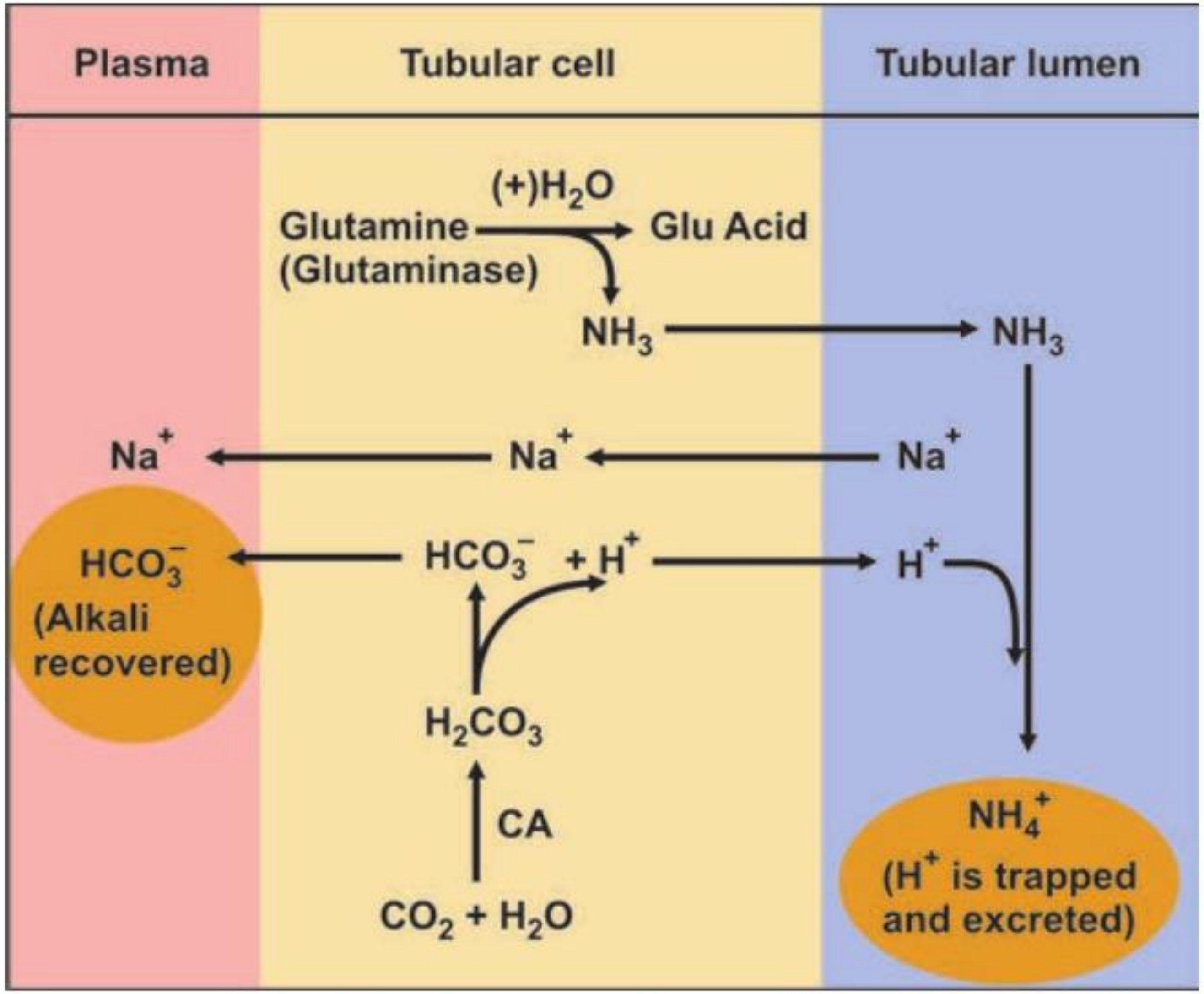


Fig. 29.5. Ammonia mechanism

- We need more acids to control the PH, which is in this case the ammonium (formed from the excretion of ammonia and then conjugated with the hydrogen ions).
- But the ammonia is a toxic molecule, so we don't preferring transporting it freely and blood.
- We have 2 mechanisms to transport ammonia in blood.

1- Making Urea, which is less toxic (CO_2 and 2 NH_3), These 2 is available in the liver, so liver is responsible for the formation of urea.

2- Conjugation with glutamate to form glutamine and we have glutaminase in tubular system that is responsible to break down and releasing free ammonia

Buffering against Acid Load

Stages	Features	Buffer components
Normal	Normal ratio = 20:1 Normal pH = 7.4	$\frac{HCO_3^-\ (N)}{H_2CO_3\ (N)}$
First line of defense Plasma buffer system	Acidosis; H^+ enters blood, bicarbonate is used up	HCO_3^- (↓↓)
Second line defense Respiratory compensation	Hyperventilation $H_2CO_3 \rightarrow H_2O^+$ $CO_2\uparrow$	H_2CO_3 (↓)
Partially compen—sated acidosis	Bicarbonate ↓; pH ↓	$\frac{HCO_3^-\ (\downarrow\downarrow)}{H_2CO_3\ (\downarrow\downarrow)}$
Third line of defense kidney mechanism	Excretion of H^+; Reabsorption of bicarbonate; Ratio and pH tend to restore	$\frac{HCO_3^-\ (\downarrow\downarrow)}{H_2CO_3\ (\downarrow\downarrow)}$

بالسلايد ال بعده شوية حكي عن كل صف (كل صف حكيه ب لونه)

*The PH is depend on the site we take blood (usually :artery) because the venous blood more acidic as it comes from the tissues.

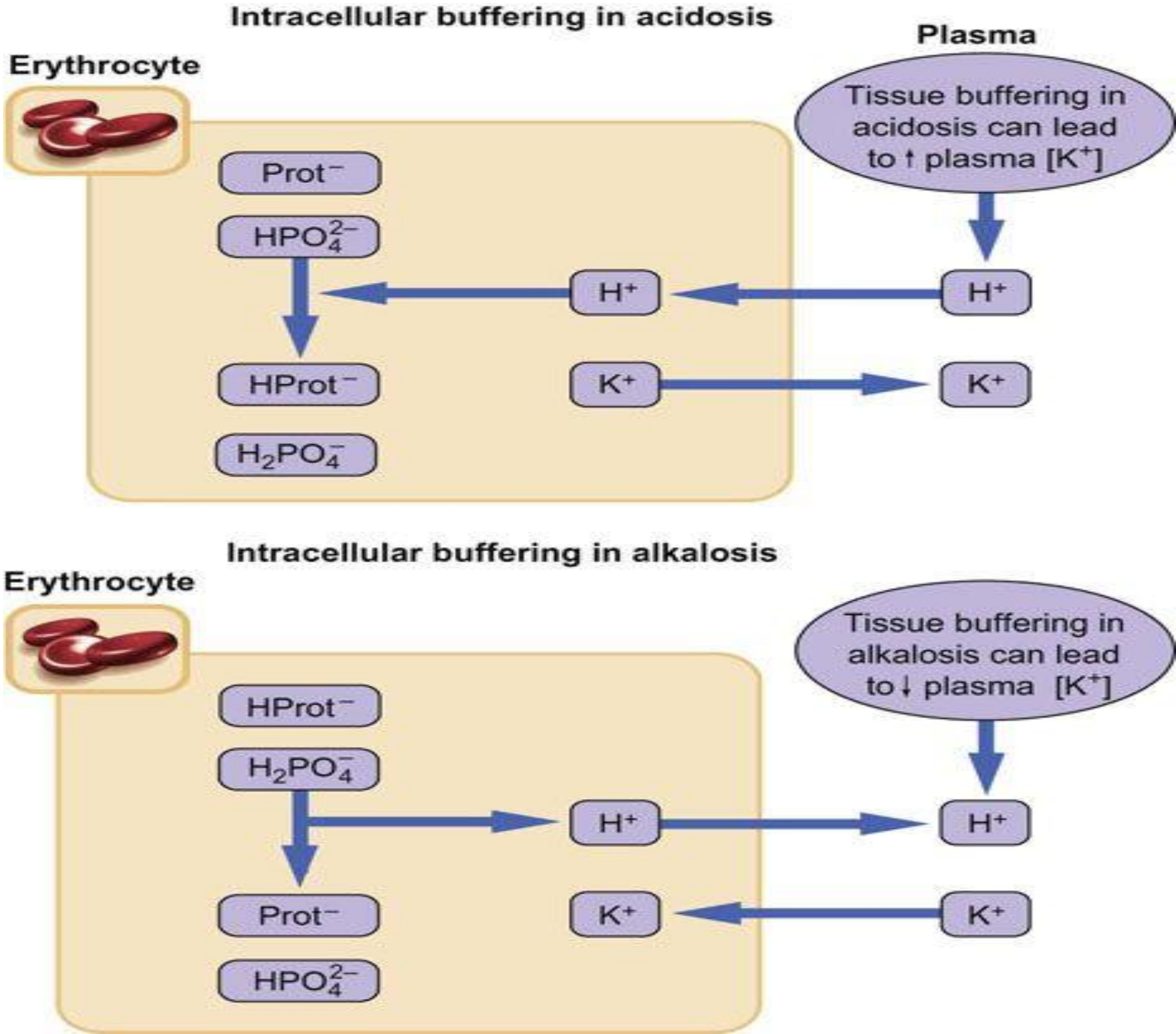
*Here we have acidosis and in the same time the CO_2 is decreasing so you are doing partial compensation through the res. System.
You are producing bicarbonate, so it's means that you are reducing the ratio (less than 20:1)→acidosis →you have to triggered to the seconds mechanism, (which is respiratory)→hyper ventilation → ↓CO_2, So you have reduction in both.(compensation)
If the hyperventilation continue, that's mean more reduction in CO_2 and you already excreted the H^+ and absorbed bicarbonate so you will have alkalosis.

*We have reduction in both in order to maintain constant ratio.

Relationship of pH with K^+ Ion Balance

- Metabolic **acidosis is associated with hyperkalemia and metabolic alkalosis** with hypokalemia.

- In renal tubular acidosis, due to failure to excrete hydrogen ions, potassium is lost in urine; then **hypokalemia results**



- We have to be attention to other ions when we talk about acidosis and alkalosis.
- One of the vital ions is potassium, the normal range of potassium is 4 to 5 (narrow range, any change can be lethal).
- Renal functional tests, 4 parameters:
- (urea, creatinine, Na+, K+).

- These have to be monitored in acidosis or alkalis cases.
- If you have alkalosis, you will excrete the hydrogen ions → potassium ions will go to RBCs. And so hypokalemia.
- If you have acidosis, you will absorbe the hydrogen ion → potassium ions will go to plasma and so hyperkalemia . (because we calculate it and plasma).

Factors Affecting Renal Acid Excretion

- **1. Increased filtered load of bicarbonate**
- **2. Decrease in ECF volume**
- **3. Decrease in plasma pH**
- **4. Increase in pCO** of blood
- **5. Hypokalemia**
- **6. Aldosterone secretion (Diuretics).**
- *all of these parameters is going to affect compensation mechanism.

Box 29.6. Acid-base Disturbances

pCO_2	> 45 mm Hg	=	Respiratory acidosis
pCO_2	< 35 mm Hg	=	Respiratory alkalosis
HCO_3	> 33 mmol/L	=	Metabolic alkalosis
HCO_3	< 22 mmol/L	=	Metabolic acidosis
H^+	> 42 nmol/L	=	Acidosis
H^+	< 38 nmol/L	=	Alkalosis

↓PH
The ratio will be less than 20
↓H2CO3

Table 29.3. Types of acid-base disturbances

Disturbance	pH	Primary change	Ratio	Secondary change
Metabolic Acidosis	Decreased	Deficit of bicarbonate	<20	Decrease in $PaCO_2$
Metabolic alkalosis	Increased	Excess of bicarbonate	>20	Increase in $PaCO_2$
Respiratory acidosis	Decreased	Excess of carbonic acid	<20	Increase in bicarbonate
Respiratory alkalosis	Increased	Deficit of carbonic acid	>20	Decrease in bicarbonate

Take home

Table 29.4. Stages of compensation

Stage	pH	HCO_3	$PaCO_2$	Ratio
Metabolic acidosis	**Low**	**Low**	**N**	**<20**
Uncompensated	Low	Low	N	<20
Partially compensated	Low	Low	Low	<20
Fully compensated	N	Low	Low	20
Metabolic alkalosis	**High**	**High**	**N**	**>20**
Uncompensated	High	High	N	>20
Partially compensated	High	High	High	>20
Fully compensated	N	High	High	20
Respiratory acidosis	**Low**	**N**	**High**	**<20**
Uncompensated	Low	N	High	<20
Partially compensated	Low	High	High	<20
Fully compensated	N	High	High	20
Respiratory alkalosis	**High**	**N**	**Low**	**>20**
Uncompensated	High	N	Low	>20
Partially compensated	High	Low	Low	>20
Fully compensated	N	Low	Low	20

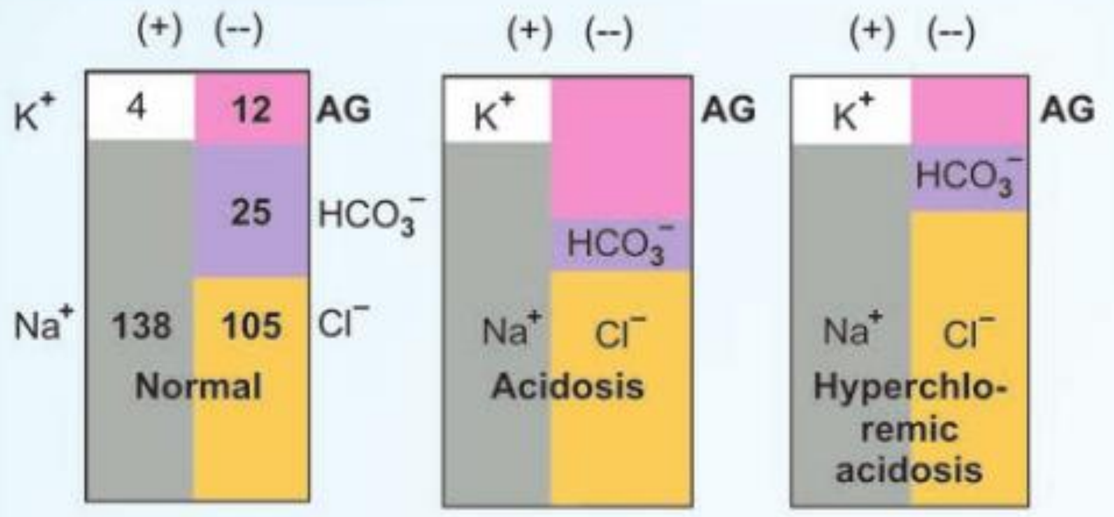
Anion Gap

- **unmeasured anions constitute the anion gap.**
  - **Protein** anions, sulphate, phosphate and organic acids

- Normally this is about **12 mmol/liter**

$(Na^+ + K^+)$ and $(HCO_3^- + Cl^-)$

- **Urine anion gap (UAG) is useful to estimate** the ammonium excretion. It is calculated as
  - UAG = UNa + UK – UCl
  - The normal value is –20 to –50 mmol/L.



The figures are the concentration in mEq/l or mmol/L. The red shaded area denotes **AG (anion gap)**. In acidosis, the bicarbonate is reduced causing an increase in the anion gap. In hyperchloremic acidosis, there is no change in the anion gap, but as a compensation, chloride ions are increased.

Fig. 29.7. Gamblegram showing cations on the left and anions on the right side. Such bar diagrams were first depicted by Gamble, hence these are called Gamble grams

Why we have high anion gap (we have another anion that are measured)?
we have a reduction in bicarbonate

*reduction in bicarbonate and no anions that's mean we have recovering of chloride. (reabsorption)

The anion gap, represented as A^- in the following equations, is the difference between the total concentration of measured cations (Na^+ and K^+) and measured anions (Cl^- and HCO_3^-); it is normally about 15–20 mEq/L. Therefore:

$$\begin{array}{llllll} [Na^+] & + [K^+] & = [HCO_3^-] & + [Cl^-] & + [A^-] & \\ 140 & + 4 & = 25 & + 100 & + 19 & \text{mEq/L} \end{array} \quad (4.13)$$

High anion gap acidosis

A useful mnemonic to help remember some of the causes of a high anion gap metabolic acidosis is DR MAPLES: D = **d**iabetic ketoacidosis, R = **r**enal, M = **m**ethanol, A = **a**lcoholic ketoacidosis, P = **p**aracetamol, L = **l**actic acidosis, E = **e**thylene glycol, S = **s**alicylates.

Increase the anion gap due to toxication

Table 29.5. High anion gap metabolic acidosis (HAGMA) (Organic acidosis)

Cause	Remarks
Renal failure	Sulfuric, phosphoric, organic anions. Decreased ammonium ion formation. Na^+/H^+ exchange results in decreased acid excretion.
Ketosis	Acetoacetate; beta hydroxy butyrate anions. Seen in diabetes mellitus or starvation.
Lactic acidosis	Lactate anion accumulates when the rate of production exceeds the rate of consumption.
Salicylate	Aspirin poisoning
Amino acidurias	Acidic metabolic intermediates. Accumulation due to block in the normal metabolic pathway.
Organic acidurias	Organic acids (methyl malonic acid, propionic acid, etc.) excreted.
Methanol	Formate, glycolate, oxalate ions. Acids formed leads to increase in AG. Increase in plasma osmolality. Osmolal gap is also seen.
Drugs	Corticosteroids, Dimercaprol, Ethacrynic acid, Furosemide, Nitrates, Salicylates, Thiazides

Gift for you

Table 29.6. Normal anion gap metabolic acidosis (NAGMA) (Inorganic acidosis)

Cause	Remarks
Diarrhea, intestinal fistula	Loss of bicarbonate and cations. Sodium or Potassium or both.
RTA Type I	Defective acidification of urine. I or distal RTA, urine pH is >5.5 with hypokalemia. Due to inability to reabsorb bicarbonate. Compensatory increase in chloride (hyperchloremic acidosis).
Type II	II or proximal RTA, urine pH is <5.5, K normal. Due to inability to excrete hydrogen ions.
Type IV	Resistance to aldosterone, urine pH <5.5, hyperkalemia.
Carbonic anhydrase inhibitors	Loss of bicarbonate, Na and K. Similar to proximal RTA.
Uretero-sigmoidostomy	Loss of bicarbonate and reabsorption of chloride. Hyperchloremic acidosis.
Drugs	Antacids containing magnesium, Chlorpropamide, Iodide (absorbed from dressings), Lithium, Polymixin B

Lactic Acidosis

Box 29.8. Types of Lactic Acidosis

Type A : Impaired lactic acid production with hypoxia. Type A is seen in
tissue hypoxia (anaerobic metabolism);
Shock (anaphylactic, septic, cardiac);
Lung hypoxia,
Carbon monoxide poisoning, seizures

Type B: Impaired lactic acid metabolism without hypoxia.
Type B is seen in liver dysfunctions (toxins, alcohol, inborn errors);
Mitochondrial disorders (less oxidative phosphorylation and more anaerobic glycolysis)
Thiamine deficiency (defective pyruvate dehydrogenase)

Decreased Anion Gap is Seen in

- Hypoalbuminemia. (we have a protein that can't be measured, if it ↓ the gap ↓.
- Multiple myeloma (paraproteinemia)
- Bromide intoxication
- Hypercalcemia

Osmolal Gap

(not very common)

- This is the difference between the measured plasma osmolality and the calculated osmolality

- The normal osmolal g $2 \times [Na] + [glucose] + [urea]$
- A high osmolal gap (> 25) implies the presence of unmeasured osmoles such as alcohol, methanol, ethylene glycol, **Acute poisoning**.

Compensated Metabolic Acidosis

- **Hyperventilation**—Kussmaul respiration to eliminate carbon dioxide leading to hypocapnia (Hypocarbia)
- **Renal compensation: Increased excretion** of acid and conservation of base occurs. Na-H exchange, NH_4^+ excretion and bicarbonate reabsorption are increased (2-4 days).
- Acidosis is Associated **hyperkalemia (**correcting acidosis which may lead to sudden **hypokalemia.)**

Treatment of Metabolic Acidosis

- Oxygen is given in patient with lactic acidosis

- **Bicarbonate Requirement**

Metabolic alkalosis

Type	Causes	Changes
Chloride Responsive Alkalosis Contraction Alkalosis	Prolonged vomiting, Nasogastric suction, Upper GI obstruction	Urine Chloride <10 mmol/L Hypovolemia, increased loss of Cl, K, H ions. Increased reabsorption of Na with bicarbonate Loss of H^+ and K^+ Hypokalemia leads to alkalosis due to H^+-K^+ exchange. Cl is reabsorbed along with Na Hence urine chloride is low Alkalosis responds to administration of NaCl.
Loop diuretics	Blocks reabsorption of Na, K and Cl	Aldosterone secretion occurs causing Na retention and wastage of K^+ and H^+
Chloride resistant metabolic alkalosis	Mineralocorticoid excess, Primary and secondary hyperaldosteronism, Glucocorticoid excess, Bartter's syndrome, Cushing's, Adrenal tumor.	Urine chloride > 20 mmol/L Defective renal Cl^- reabsorption Associated with an underlying cause where excess mineralocorticoid activity results in increased sodium retention with wastage of H and K ions at the renal tubules
Exogenous base	Intravenous bicarbonate, Massive blood transfusion, Anatacids, Milk alkali syndrome Sodium citrate overload	Excess base enters the body or potential generation of bicarbonate from metabolism of organic acids like lactate, keto acids, citrate and salicylate

H^+ loss

- There are two main ways by which H ions can be lost from the body:

  1. Through the kidneys or some of the intestine.
  2. Mainly the stomach.

  This mechanism is coupled with the generation of HCO^-_3

- In the kidney this is the method by which secretion of excess H^+ ensures regeneration of buffering capacity

Clinical Features of Metabolic Alkalosis

- **Hypoventilation**

Respiratory Acidosis

Table 29.8. Lab findings in respiratory acidosis

	pH	pCO_2	HCO_3^-
Acute respiratory acidosis	↓↓	↑↑	*N or* ↑
Chronic respiratory acidosis (partially compensated)	↓	↑	↑↑

N = normal; ↓ = decreased; ↑ = increased

Box 29.11. Causes of Acid-Base Disturbances

Acidosis	Alkalosis
A. Respiratory Acidosis Pneumonia Bronchitis, Asthma COPD, pneumothorax Narcotics, Sedatives Paralysis of respiratory muscles CNS trauma, tumor Ascites, Peritonitis Sleep apnea	**A. Respiratory Alkalosis** High altitude Hyperventilation Hysteria Febrile conditions Septicemia Meningitis Congestive cardiac failure
B. Metabolic Acidosis **i. High anion gap** Diabetic ketosis Lactic acidosis Renal failure **ii. Normal anion gap** Renal tubular acidosis (hyperchloremic) CA inhibitors Diarrhea Addison's disease	**B. Metabolic Alkalosis** Severe vomiting Cushing syndrome Milk alkali syndrome Diuretic therapy (potassium loss)

Box 29.12. Normal Serum Electrolyte and Arterial Blood Gas Values

pH	=	7.4	
Bicarbonate	=	22-26	mmol/L
Chloride	=	96-106	mmol/L
Potassium	=	3.5-5	mmol/L
Sodium	=	136-145	mmol/L
pO_2	=	95 (85-100)	mm Hg
pCO_2	=	40 (35-45)	mm Hg

Table 29.9. Acid-base abnormalities

No.	pH	pCO_2 mmHg	HCO_3^- mmol/L	Interpretation
1.	7.14	15	5	Overcompensated metabolic acidosis
2.	7.21	70	27	Uncompensated respiratory acidosis
3.	7.4	60	36	Fully compensated metabolic alkalosis
4.	7.32	30	15	Partially compensated metabolic acidosis
5.	7.50	46	35	Partially compensated metabolic alkalosis
6.	7.57	25	22	Uncompensated respiratory alkalosis
7.	7.59	45	42	Partially compensated metabolic alkalosis

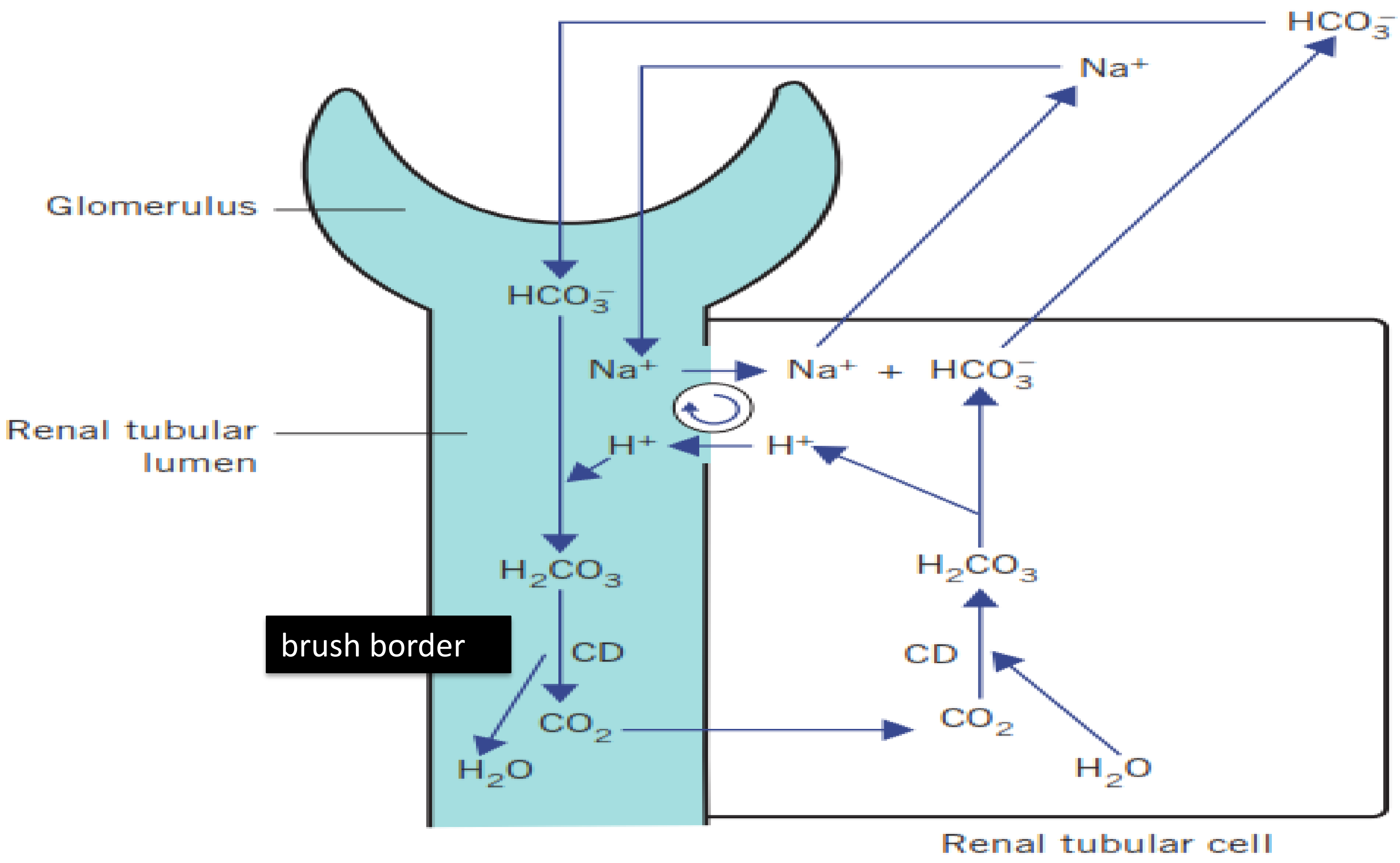


Figure 4.2 Normal reabsorption of filtered bicarbonate from the renal tubules. CD, carbonate dehydratase.

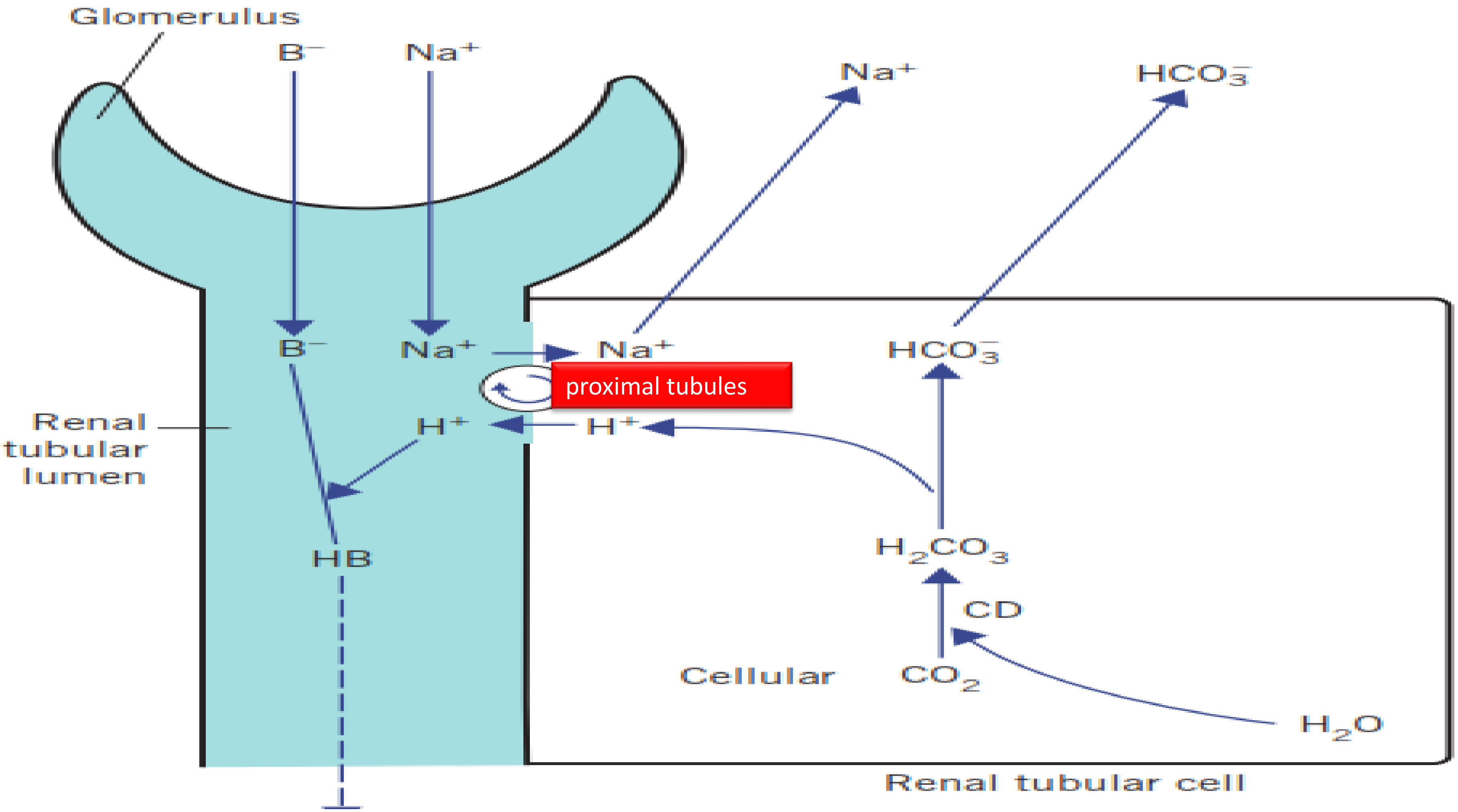


Figure 4.3 Net generation of bicarbonate by renal tubular cells with excretion of hydrogen ions. B^-, non-bicarbonate base; CD, carbonate dehydratase.

Urinary Buffers

- Phosphate buffer
- Ammonia

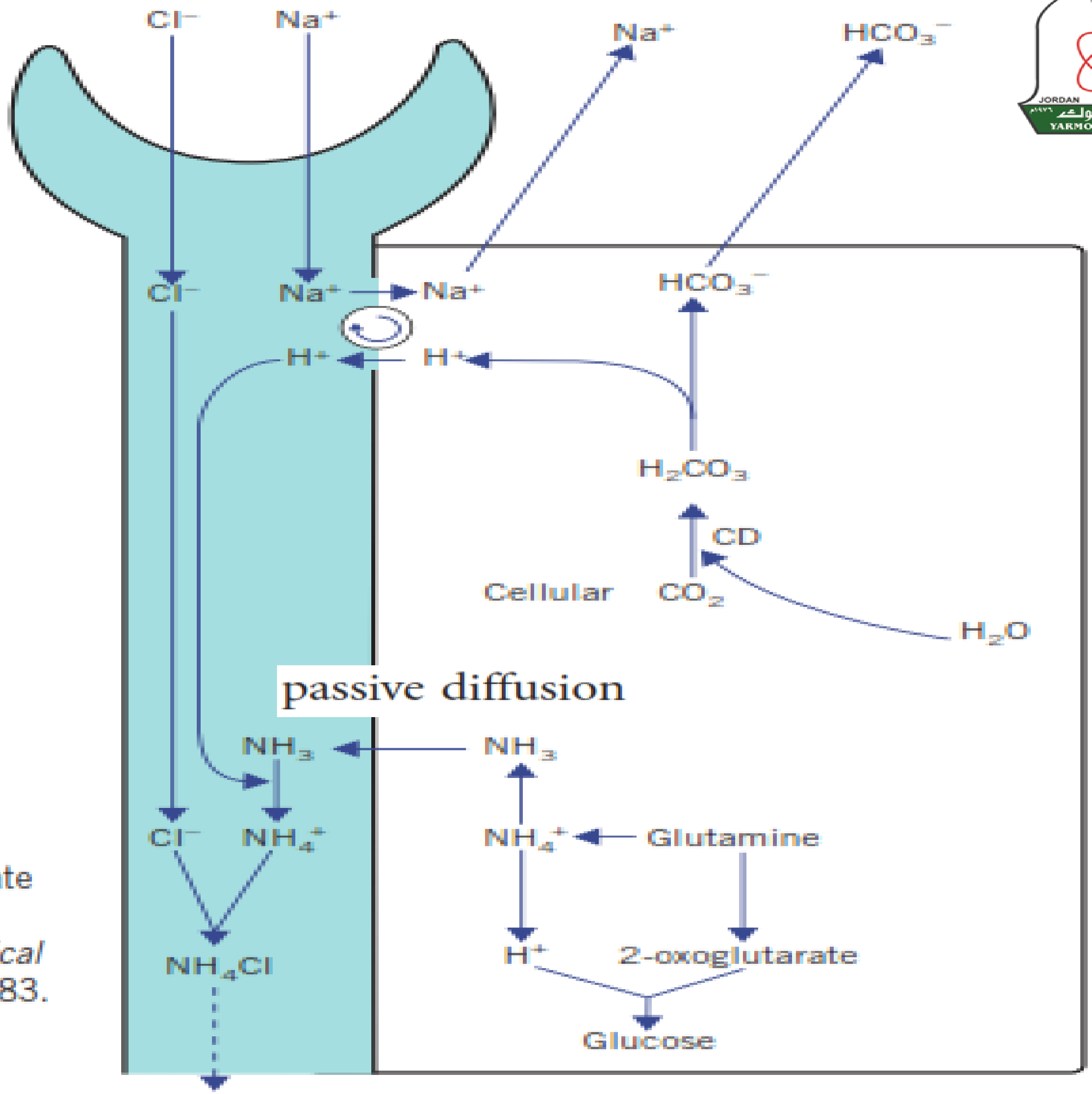
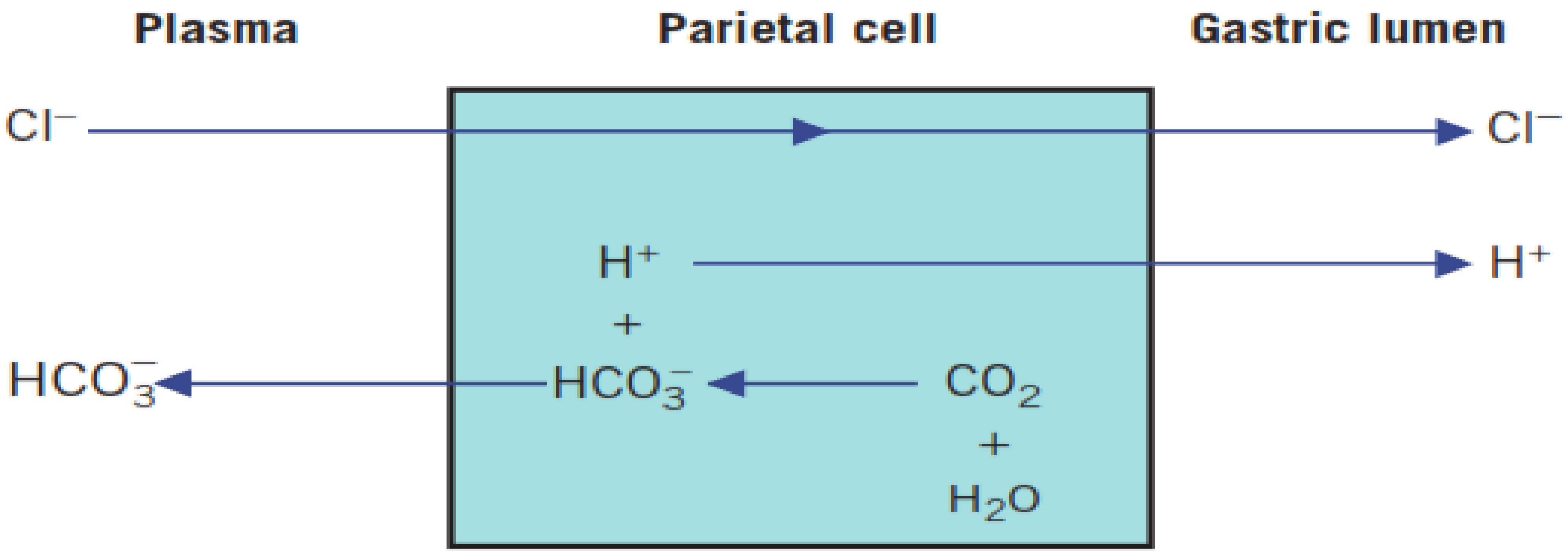


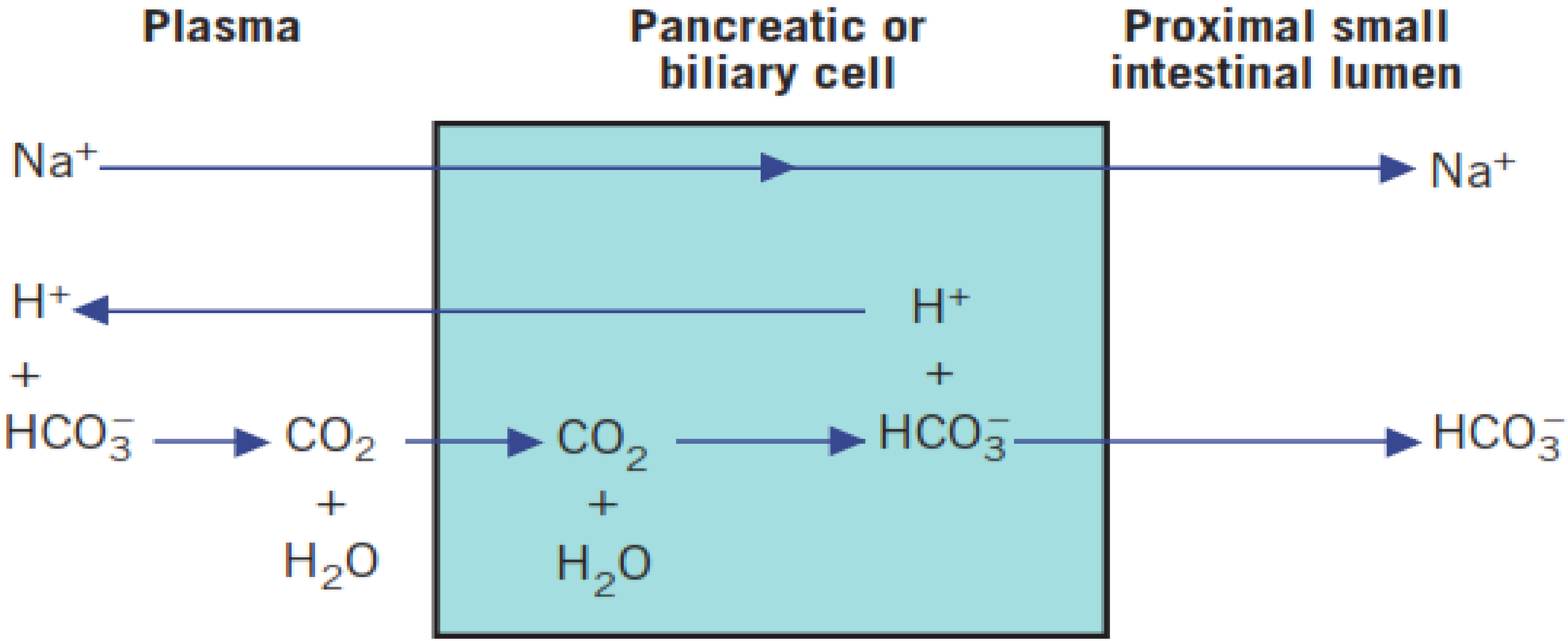
Figure 4.4 The role of ammonia in the generation of bicarbonate by renal tubular cells. CD, carbonate dehydratase. Modified with kind permission from Williams DL, Marks V (eds), *Biochemistry in Clinical Practice*. London: Heinemann Medical Books, 1983. © Elsevier.

Acid secretion by the stomach



Net effect on plasma – gain of bicarbonate and loss of chloride

Sodium bicarbonate secretion by pancreatic and biliary cells



Net effect on plasma – loss of sodium bicarbonate

Figure 4.5 Acid–base balance in intestinal cells.

Bicarbonate secretion and chloride reabsorption by intestinal cells

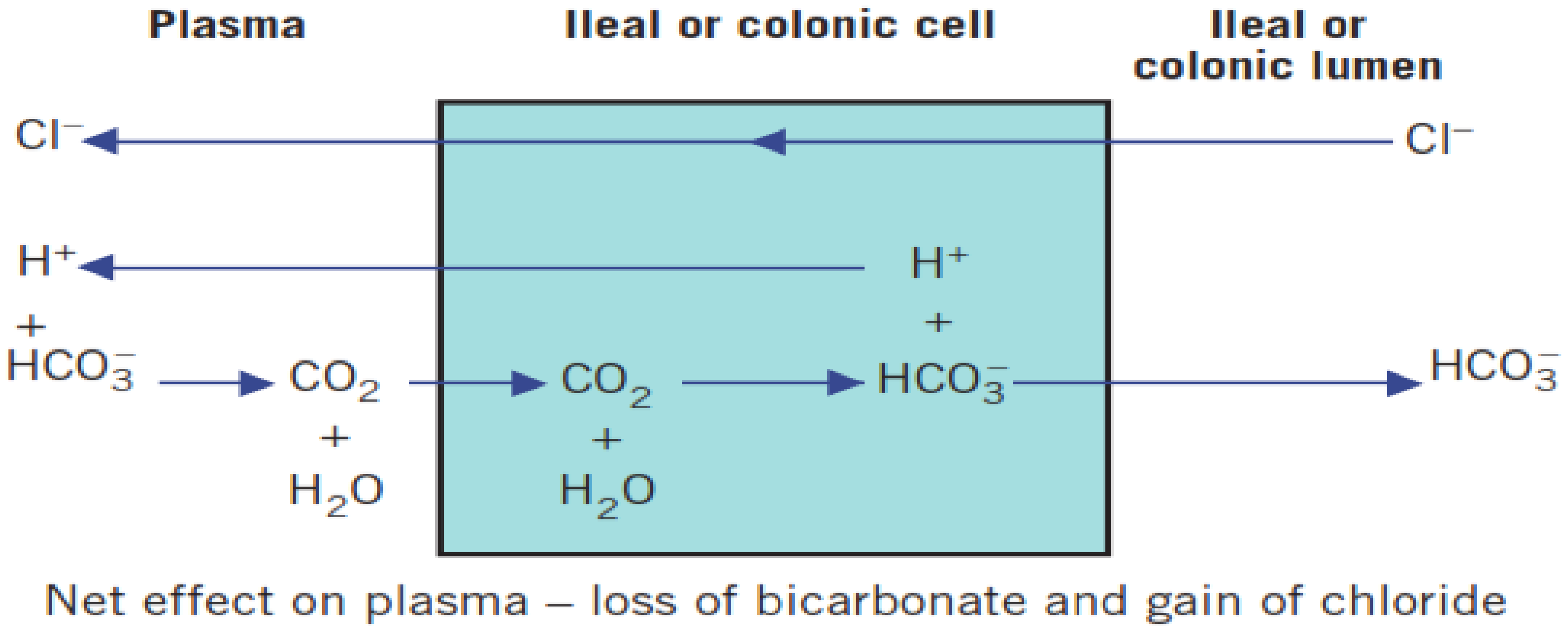
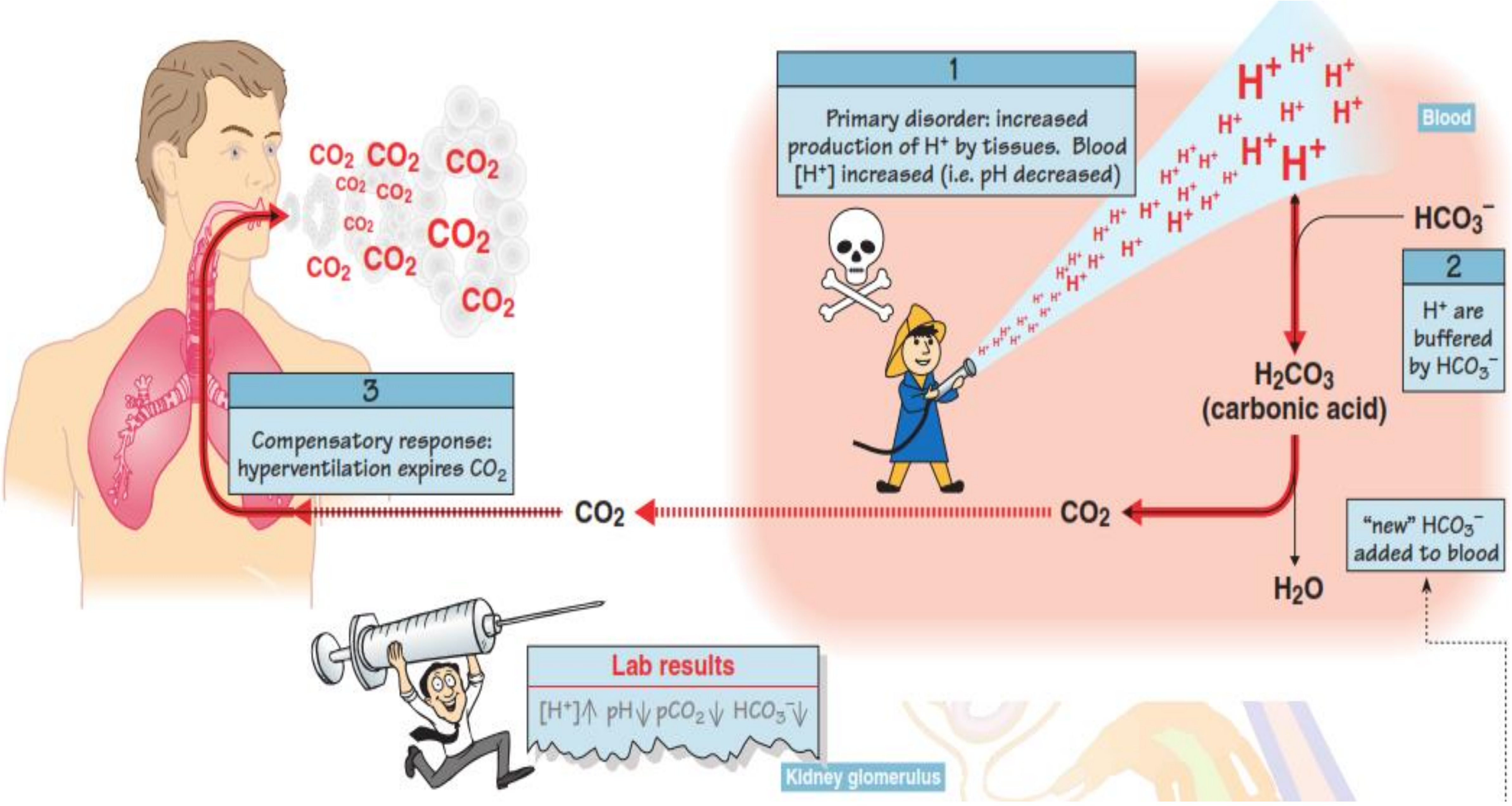


Figure 4.5 Acid–base balance in intestinal cells.

metabolic acidosis



Metabolic acidosis

1. **Primary disorder:** massive production of H^+ (protons) occurs in extreme metabolic conditions such as **diabetic ketoacidosis (DKA)** (Chapters 28, 33) and **lactic acidosis** (Chapter 17). The resulting low blood pH can be life-threatening
2. **Buffer response:** the bicarbonate buffering system is the first line of defence. HCO_3^- combines with the protons to form **(carbonic acid)** H_2CO_3 which dissociates to form CO_2 and H_2O
3. **Compensation:** the low pH stimulates the respiratory centre in the brain causing hyperventilation. This expires CO_2 in an attempt to lower the pCO_2. This dramatic hyperventilation has been described as "air hunger" or "Kussmaul respiration"
4. **Correction (i) removal of protons:** glutamine from muscle and liver is deaminated by **glutaminase** to form **glutamate** which is deaminated by **glutamate dehydrogenase** to form α-ketoglutarate. The NH_3 (ammonia) formed diffuses into the tubular urine where it accepts a proton forming NH_4^+ which is excreted in the urine. The kidney has a prodigious ability to excrete H^+ as ammonium ions. In response to metabolic acidosis, NH_4^+ excretion can increase by 10 times the basal level
5. **Correction (ii) regeneration of the** HCO_3^-**:** renal production of new blood HCO_3^- to replace that lost in 2 above is linked to ammonium excretion

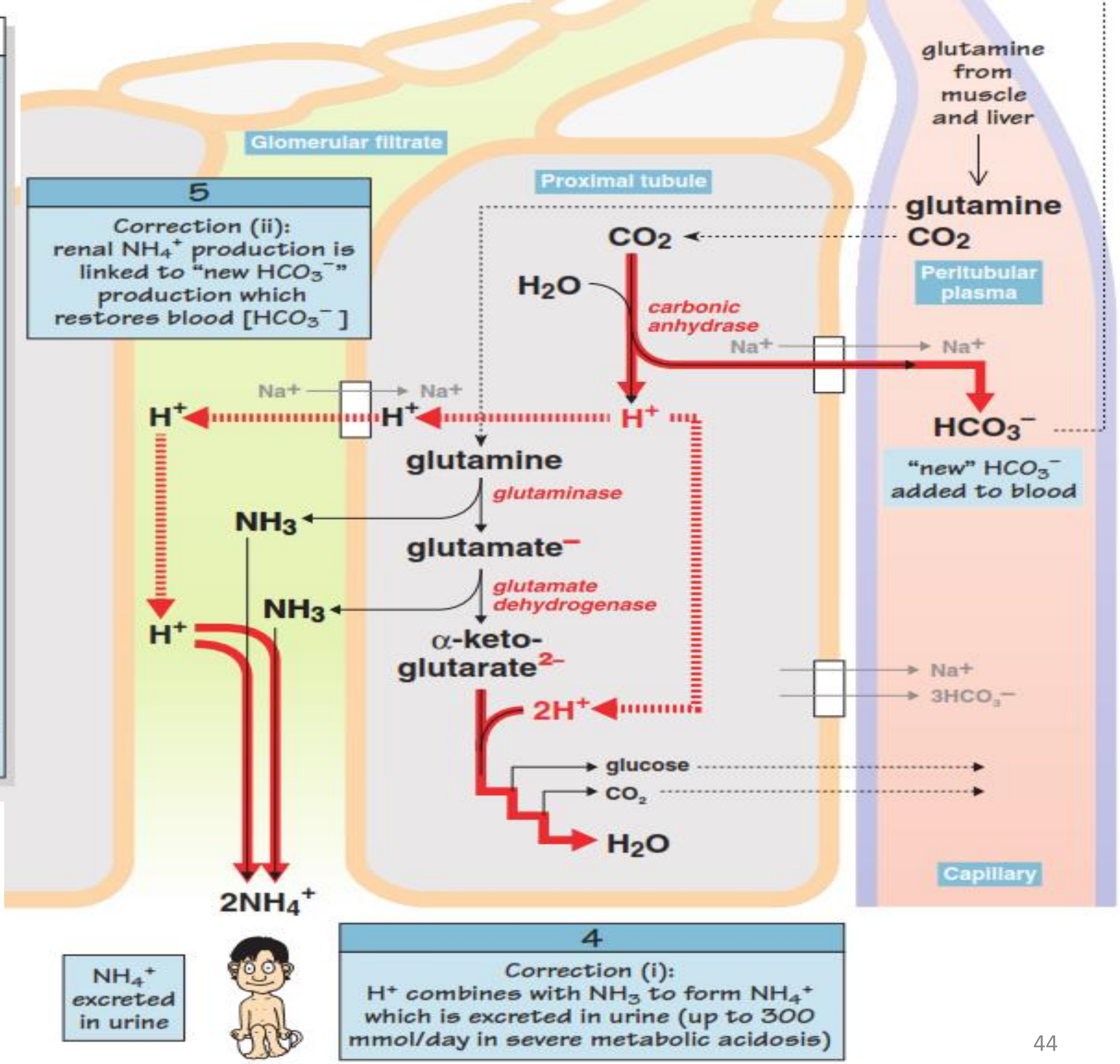


Figure 4.2 Metabolic acidosis.

Metabolic alkalosis

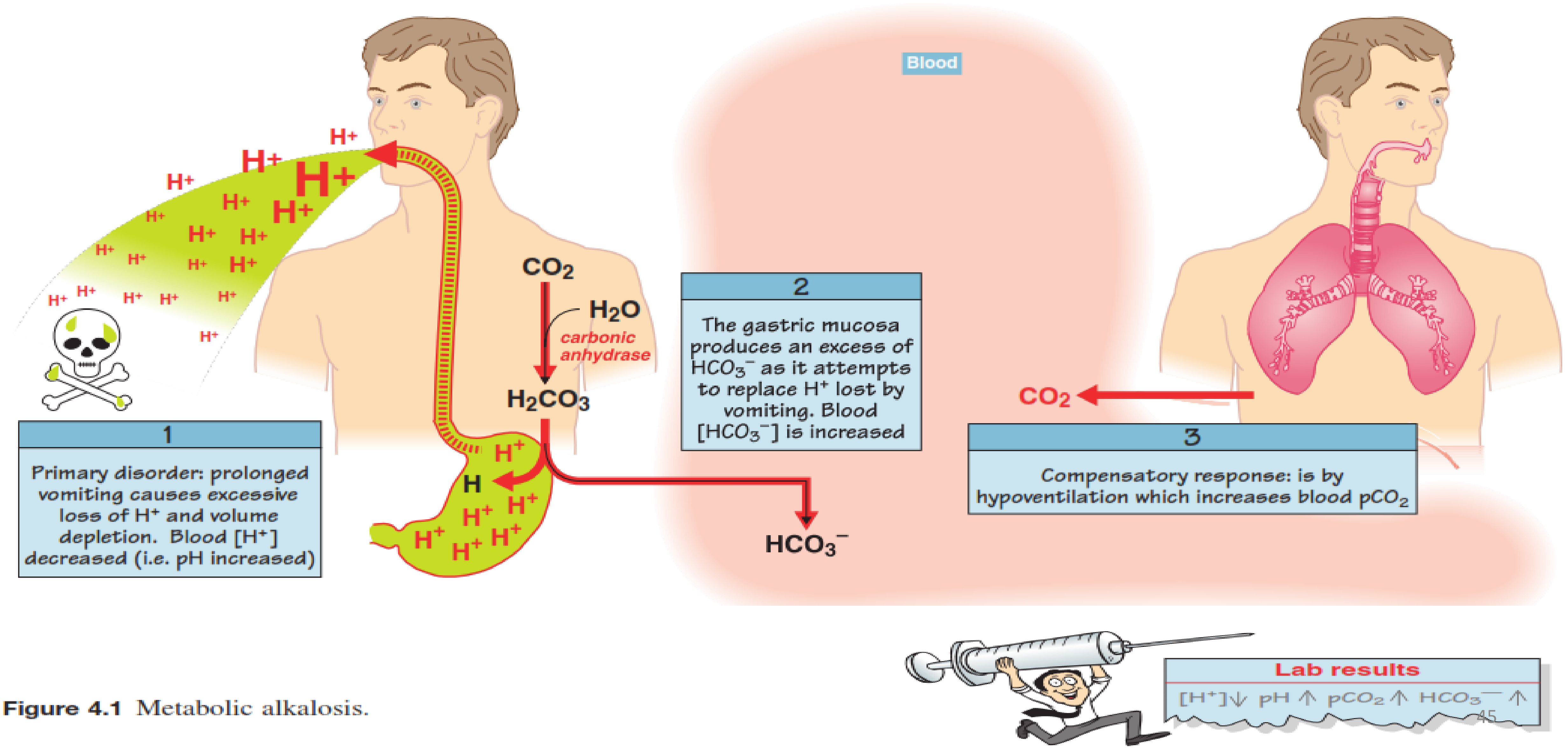


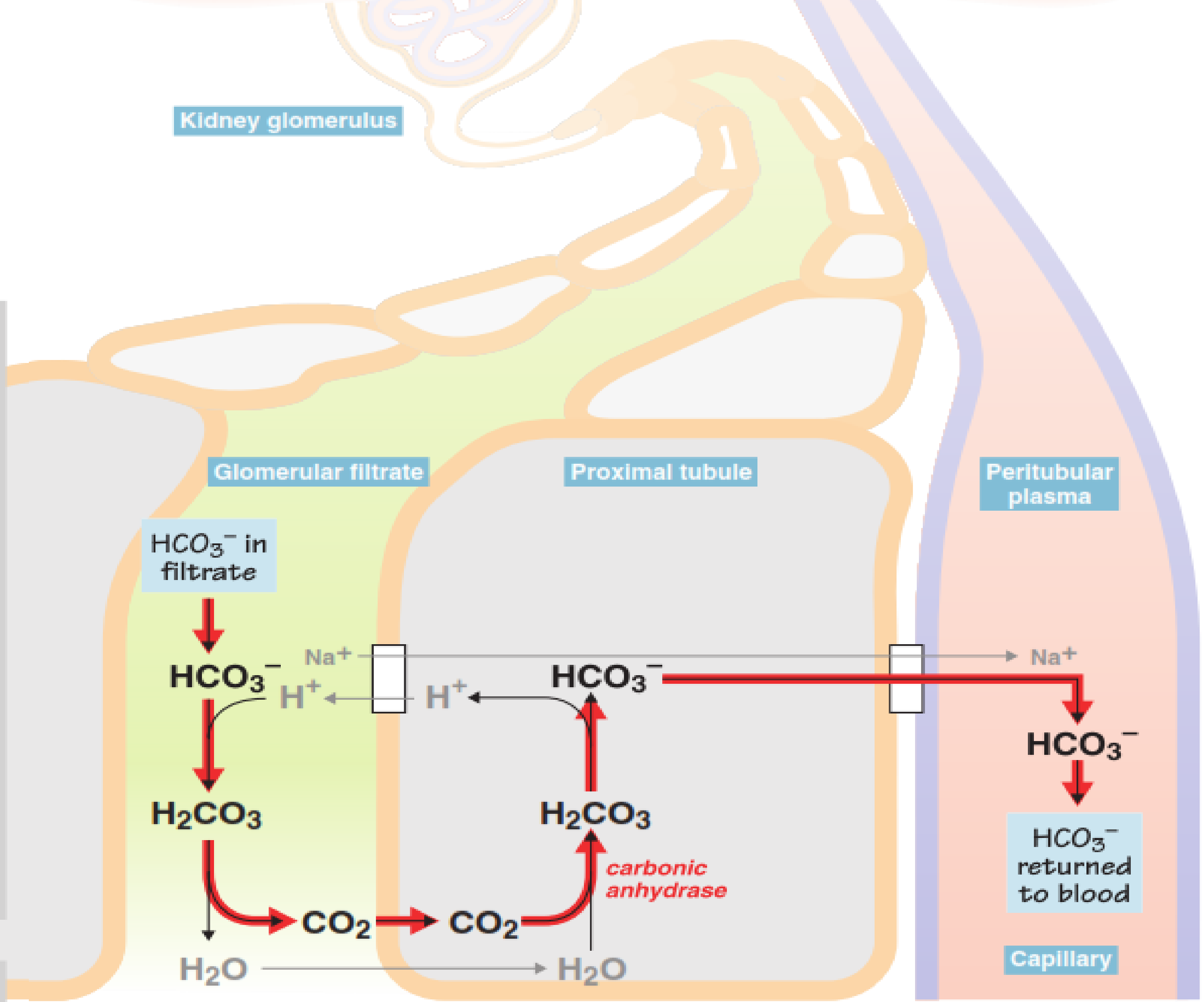
Figure 4.1 Metabolic alkalosis.

Metabolic alkalosis

1. **Primary disorder:** one cause is prolonged vomiting which causes excessive loss of H^+ (protons) from the stomach
2. The gastric mucosa attempts to replace the lost H^+ by the carbonic anhydrase reaction but the result is formation of HCO_3^- which accumulates in the blood increasing the pH
3. **Compensation:** the lungs compensate by hypoventilating which retains CO_2 and thereby increases arterial pCO_2
4. **Inappropriate HCO_3^- production by the kidney:** normally, if the blood concentration of HCO_3^- rises above the upper limit of normal (approximately 33 mmol/l) it exceeds its renal threshold and is excreted in the urine. However, in metabolic alkalosis caused by vomiting, the threshold can be increased to an inappropriately high level by (i) volume depletion, (ii) aldosterone, and (iii) hypokalaemia. This unfortunate response stimulates reabsorption of HCO_3^- from the tubular urine and maintains the blood HCO_3^- concentration at a raised level

Other causes of metabolic alkalosis

- Thiazide diuretics
- Administration of HCO_3^-
- Hyperaldosteronism



4

NB blood [HCO_3^-] is maintained at an abnormally high level because the renal threshold for HCO_3^- (normally 23–33 mmol/l) is inappropriately increased in response to volume depletion

respiratory acidosis

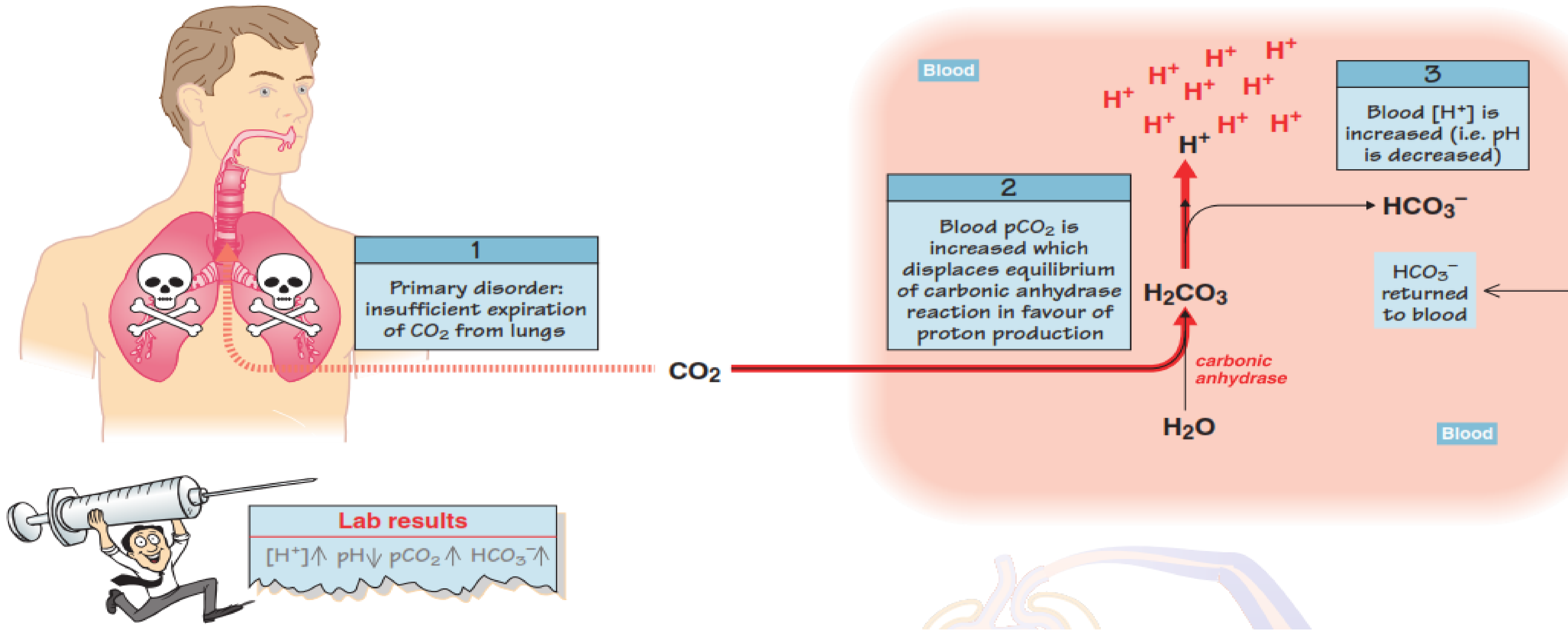


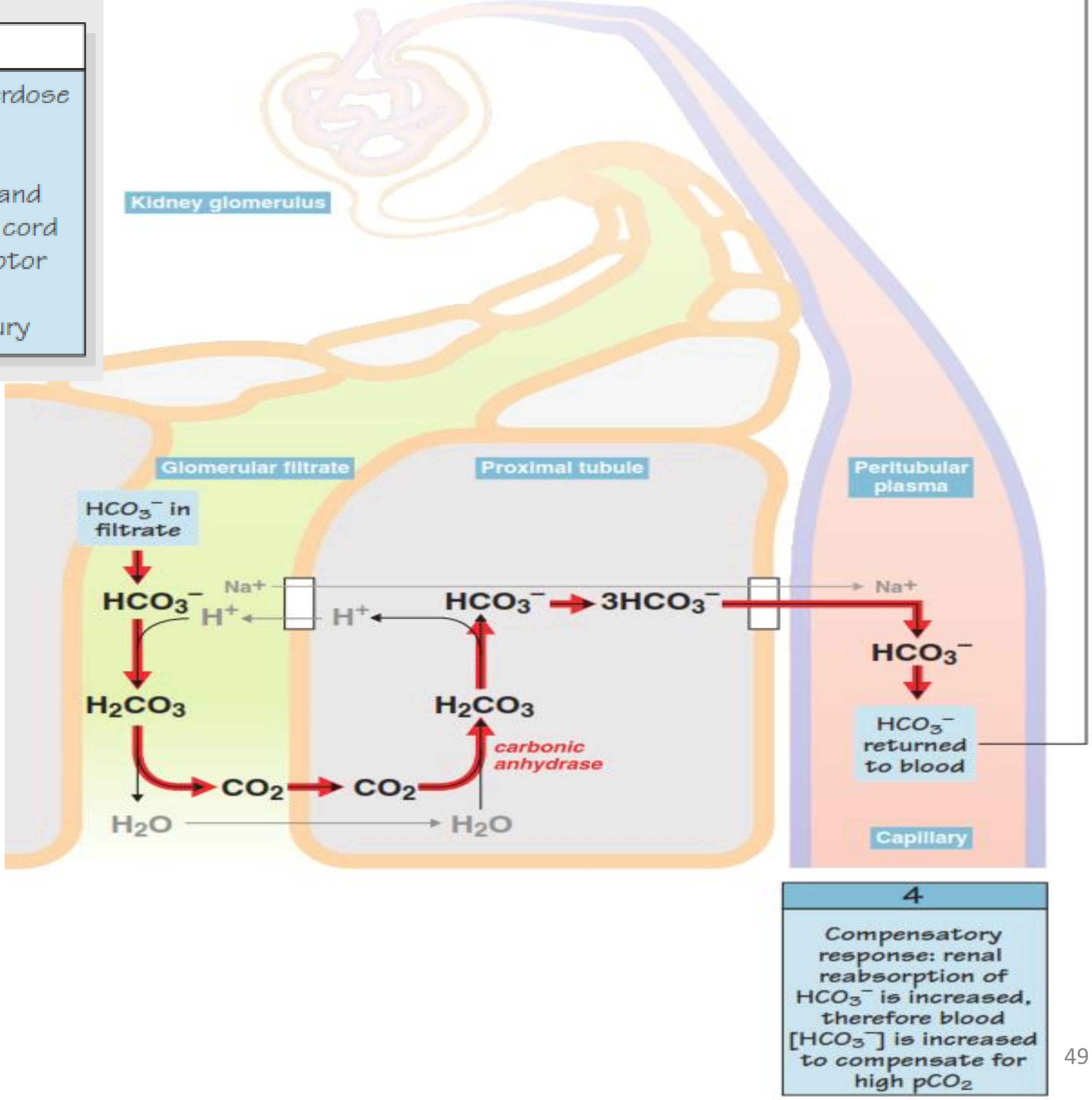
Figure 5.2 Respiratory acidosis.

Respiratory acidosis

1. **Primary disorder:** lung disease causes impaired ventilation or gas diffusion resulting in hypercapnia (increased arterial pCO_2). Alternatively, non-pulmonary hypercapnia is caused by failure of the CNS respiratory centre to stimulate the respiratory muscles, see below
2. The high pCO_2 displaces the equilibrium of the carbonic anhydrase reaction in favour of proton (H^+) production
3. As a result of 2 above the **blood $[H^+]$ increases**, i.e. the **pH decreases**
4. **Compensation:** the kidney increases the amount of HCO_3^- reabsorbed from the tubular urine into the blood in an attempt to increase the pH to normal by increasing the ratio $\frac{HCO_3^-}{pCO_2}$

Other causes of respiratory acidosis

- CNS trauma damage, stroke or CNS suppression by overdose of drugs such as opiates and anaesthetics reduces stimulation of the respiratory muscles
- Damage to nerves between the CNS respiratory centre and the respiratory muscles causes hypercapnia, e.g. spinal cord damage, Guillain–Barré syndrome, multiple sclerosis, motor neurone disease, poliomyelitis
- Lung ventilation disorders, e.g. pneumothorax, chest injury



Respiratory alkalosis

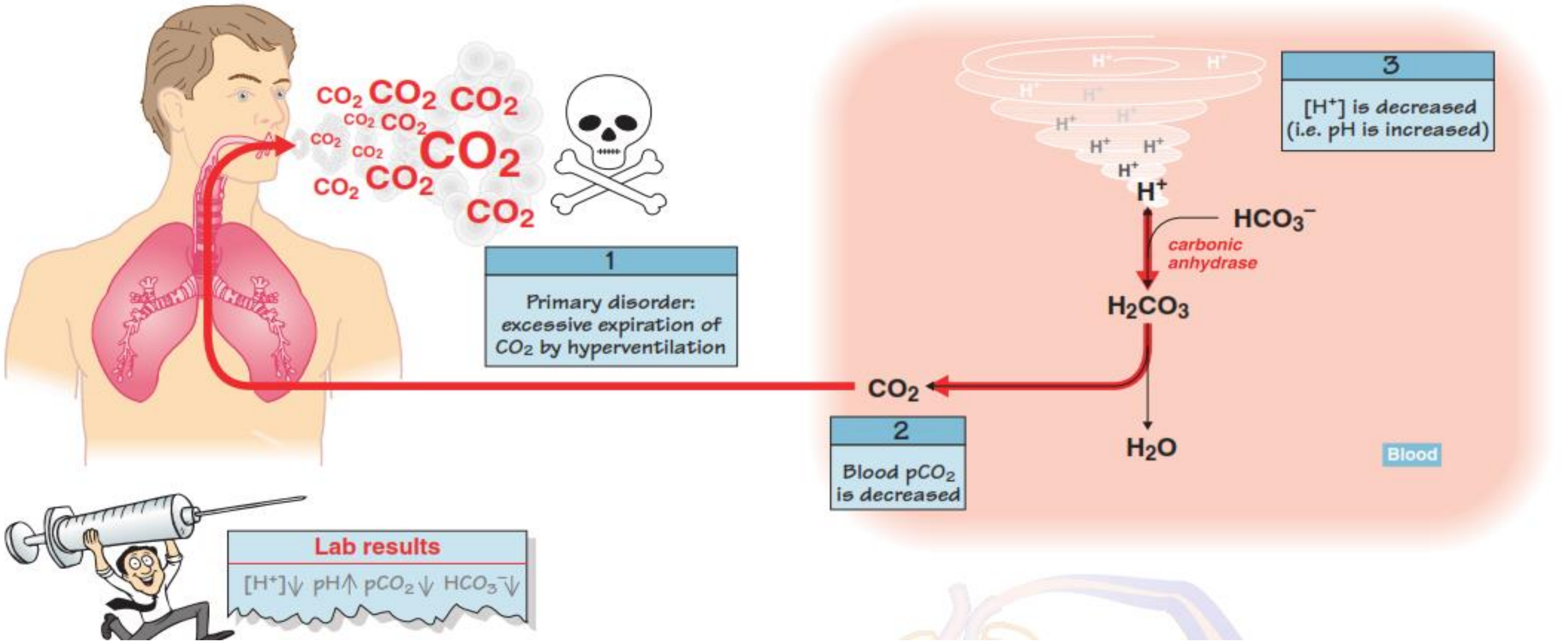


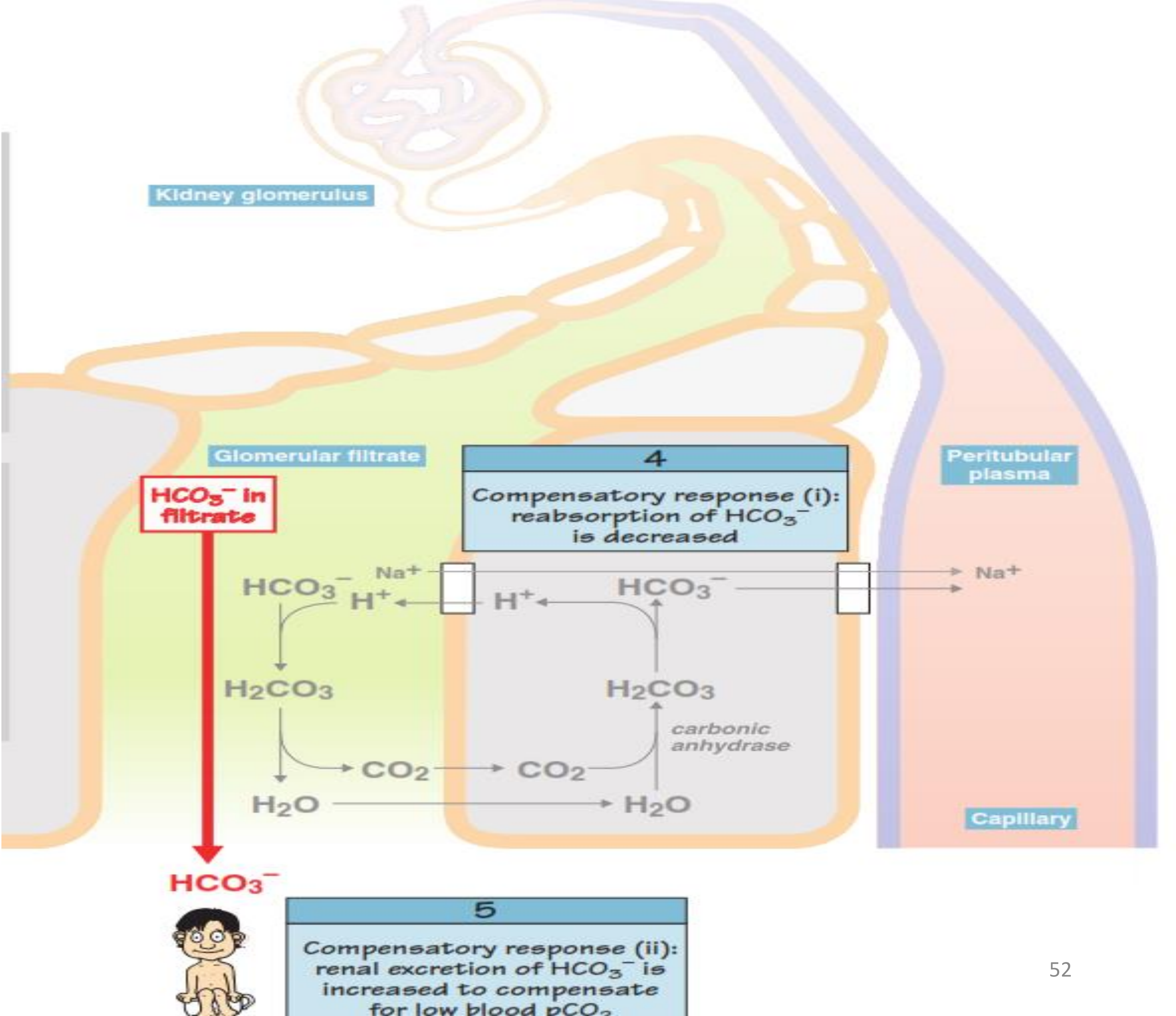
Figure 5.1 Respiratory alkalosis

Respiratory alkalosis

1. **Primary disorder:** hyperventilation
2. Hyperventilation results in hypocapnia (low arterial pCO_2)
3. The low pCO_2 displaces the equilibrium of the carbonic anhydrase reaction towards the formation of CO_2. This process consumes protons, i.e. it lowers the H^+ concentration which increases the pH
4. **Compensation:** patients with normal renal function compensate by reducing reabsorption of HCO_3^- from the tubular urine. This lowers the blood concentration of HCO_3^- thereby reducing the ratio $\frac{HCO_3^-}{pCO_2}$ which lowers the pH

Other causes of respiratory alkalosis

Respiratory alkalosis is associated with many illnesses. Hyperventilation has several causes. The CNS respiratory centre is stimulated by many factors including anxiety, psychosis, pain and fever. Overdosage of salicylates can initially stimulate ventilation causing respiratory alkalosis which may be followed by metabolic acidosis. Stimulation of the chest receptors by conditions such as pneumothorax, pulmonary embolism and pulmonary oedema can cause hyperventilation and hypocapnia. Other causes include mechanical ventilation, hepatic failure and sepsis


Kidney glomerulus
Glomerular filtrate
4
Compensatory response (i): reabsorption of HCO3⁻ is decreased
Peritubular plasma
HCO3⁻ in filtrate
Na+
HCO3⁻
H+
H+
HCO3⁻
Na+
H2CO3
H2CO3
carbonic anhydrase
CO2
CO2
H2O
H2O
Capillary
HCO3⁻
5
Compensatory response (ii): renal excretion of HCO3⁻ is increased to compensate for low blood pCO2