chapter 9:

DISORDERS OF ACID–BASE BALANCE

OBJECTIVES

After studying this chapter you should be able to:

- describe how hydrogen ions are transported by the blood;
- outline the role and operations of the blood buffering systems;
- calculate the concentrations of ingredients used to prepare buffered solutions of defined pH and concentration;
- explain the role of kidney tubule cells in excreting hydrogen ions and regenerating plasma hydrogen carbonate;
- explain the causes of disorders of acid–base balance;
- describe the strategies for investigating disorders of acid–base balance;
- outline the management of disorders of acid–base balance.

9.1 INTRODUCTION

The concentration of hydrogen ions, H^+, in the blood is kept within a narrow reference range to give the blood a pH of approximately 7.4. The body possesses physiological and biochemical mechanisms that maintain this pH by removing excess H^+ and carbon dioxide produced during metabolism (*Figure 9.1*). These activities are vital for normal bodily functions and are performed by the renal and respiratory systems respectively. Failure to maintain the

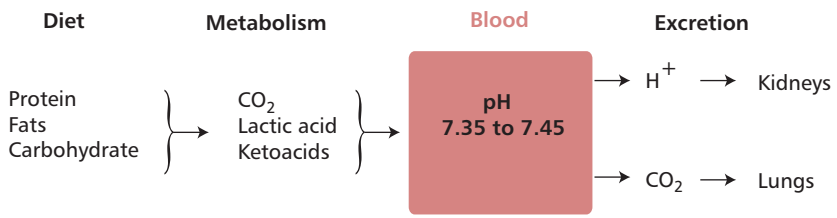

Figure 9.1 Overview of the production, transport and excretion of CO_2 and H^+.

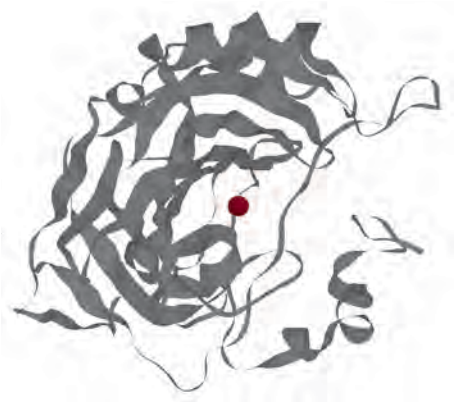

Figure 9.2 Molecular model of carbonic anhydrase. The red sphere represents a Zn^{2+} in the active site. PDB file 2CBD.

acid–base balance at an appropriate value will give rise either to an acidosis, with a blood pH below the reference range, or an alkalosis with the pH above it. Different types of acidoses and alkaloses produce specific characteristic clinical features. Once a specific acid–base disorder has been identified, a clinical strategy must be adopted to manage the symptoms and to treat the underlying cause(s).

9.2 THE PRODUCTION AND TRANSPORT OF CARBON DIOXIDE

Body tissues produce about 20 moles of CO_2 per day during oxidative metabolism. The CO_2 diffuses from the cells into the extracellular fluid (ECF), that is the blood and tissue fluid, and eventually enters the plasma in quantities with the potential to form enough carbonic acid to disturb its pH. However, in normal circumstances this does not occur because the CO_2 is transported to the lungs and excreted. During transport, a substantial proportion of the CO_2 enters the erythrocytes by diffusion. Within the erythrocytes, a small proportion of the CO_2 remains dissolved or combines with proteins, mainly hemoglobin, to form carbamino compounds:

$$\text{Protein-NH}_2 + \text{CO}_2 \rightleftharpoons \text{Protein-NH-COO}^- + \text{H}^+$$

The major portion, however, combines with water to produce carbonic acid in a reaction catalyzed by carbonic anhydrase (*Figure 9.2*):

$$\text{CO}_2 + \text{H}_2\text{O} \overset{\text{Carbonic anhydrase}}{\rightleftharpoons} \text{H}_2\text{CO}_3$$

Carbonic acid dissociates to H^+ and hydrogen carbonate (HCO_3^-, 'bicarbonate')

$$\text{H}_2\text{CO}_3 \rightleftharpoons \text{H}^+ + \text{HCO}_3^-$$

Figure 9.3 shows how H^+ are removed from solution when they react with oxyhemoglobin (HbO_8) and promote the release of its oxygen to the tissues and forms protonated hemoglobin ('H^+Hb'). The HCO_3^- formed diffuses down its electrochemical gradient out of the erythrocytes to the plasma in exchange for Cl^-, thus maintaining the electrochemical equilibrium of the erythrocyte. The exchange of HCO_3^- for Cl^- is normally called the **chloride shift**. Since both ions are charged, neither would pass freely across biological membranes, however, an anion exchanger protein facilitates their transport. This exchanger is a membrane protein that forms a pore through the membrane allowing the cotransport of the ions across the membrane. Given that the ions move in opposite directions, the anion exchanger or cotransporter is said to be an antiporter. The concentration of HCO_3^- in the plasma is normally kept between 21–28 mmol dm^{-3}.

In the lungs, the partial pressure of oxygen is high while that of carbon dioxide is low. Thus oxygen enters the erythrocytes forming oxyhemoglobin, releasing the bound H^+ and promoting the reverse of the events that occur in other body tissues (*Figure 9.3*). Thus, H^+ associates with HCO_3^- to produce carbonic acid which then breaks down to carbon dioxide and water. The water enters the large body pool of water while the CO_2 leaves the erythrocytes and is excreted on exhalation.

These events provide an interesting confirmation that enzymes catalyze reactions in either direction depending upon the position of equilibrium. Thus carbonic anhydrase promotes the formation of carbonic acid in most body tissues where the concentration of CO_2 is relatively high. However, in the lungs, where the concentration of CO_2 is reduced, the enzyme catalyzes the formation of CO_2 and H_2O from carbonic acid.

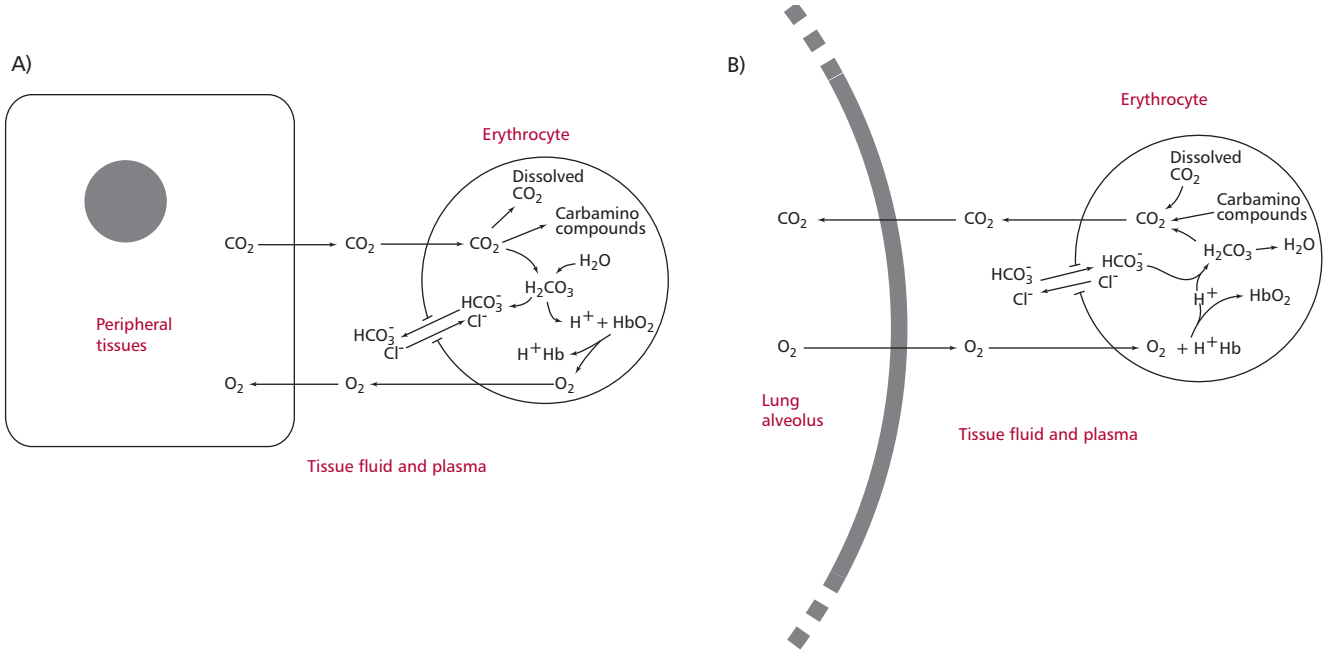

Figure 9.3 (A) Uptake by erythrocytes of CO_2 with the release of O_2. Note the Cl^- shift. See text for details. **(B) The excretion of CO_2 and uptake of O_2 at the lung epithelium.** See text for details.

9.3 BUFFERING AND THE EXCRETION OF H^+

About 60 mmol of H^+ are produced each day from the oxidation of sulfur-containing amino acid residues or from incomplete metabolic activities, such as anerobic glucose metabolism or ketone body formation (*Chapter 7*). If all the H^+ were released into the approximately 14 dm^3 of ECF, the concentration of H^+ would be 4 mmol dm^{-3} or about 100 000 times more acidic than normal. In reality, the concentration of H^+ is kept within the narrow limits of 40 ± 5 nmol dm^{-3} to maintain the appropriate body physiological pH of 7.4 ± 0.05. This pH is necessary for normal physiological functions and is maintained by temporary buffering systems that resist changes to the pH of the plasma until the excessive H^+ are excreted by the kidneys (*Chapter 8*).

When H^+ are released by cells, the ECF is buffered by the hydrogen carbonate–carbonic acid buffer system (*Box 9.1*):

$$H^+ + HCO_3^- \rightleftharpoons H_2CO_3 \rightleftharpoons CO_2 + H_2O$$

Other buffering systems, such as hemoglobin in the erythrocytes, also make significant contributions as described in *Section 9.2*. If the concentrations of H^+ and HCO_3^- reach equilibrium, buffering would become ineffective. However, in the case of the hydrogen carbonate–carbonic acid system this is usually prevented from occurring by the breakdown of carbonic acid to CO_2 and water. The formation of carbonic acid from H^+ and HCO_3^- is a rapid reaction. Its potentially slow breakdown to CO_2 and H_2O is accelerated by carbonic anhydrase in the erythrocytes and kidneys and the removal of carbon dioxide at the lungs prevents the system from reaching equilibrium.

Buffering by the hydrogen carbonate–carbonic acid system removes H^+ from the ECF but at the expense of HCO_3^-. The ECF contains relatively large amounts of HCO_3^-, for example, its concentration is usually about 24 mmol dm^{-3}. If, for any reason, the amount of H^+ produced increases, then the concentration of HCO_3^- will decrease as the hydrogen carbonate–carbonic acid buffering system operates. Any excess H^+ must be excreted from the body by the kidneys

BOX 9.1 Relationship between H^+, PCO_2 and HCO_3^-

The pH of a solution is defined as:

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

The pH scale (*Figure 9.4*) ranges from 0 to 14 and describes concentrations of H^+ of 10^0 (or 1) to 10^{-14} mol dm^{-3}. A pH of 7 is neutral; values below this are increasingly acidic and those above it increase in alkalinity.

A buffered solution is one that resists changes to its pH when relatively small amounts of acid or alkali are added to it. In organisms, the most significant buffers are protein molecules. However, buffered solutions can be prepared in the laboratory,

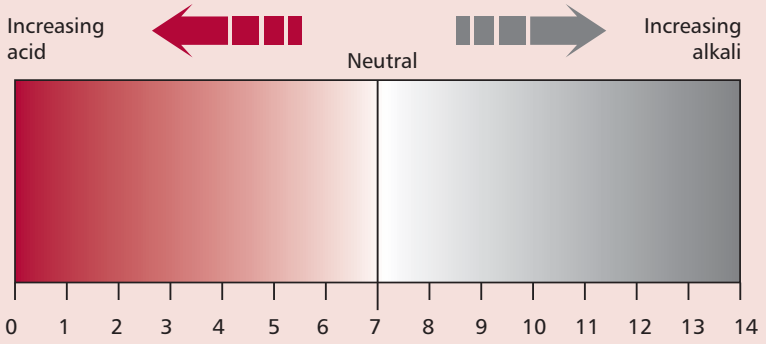

Figure 9.4 The pH scale.

(*Chapter 8*) to keep the ECF and tissues at an appropriate pH. In addition, the HCO_3^- used in buffering must be regenerated to return its concentration in the plasma to normal values, otherwise the body will become depleted of HCO_3^- and buffering capacity. Two separate mechanisms operate in the kidneys to recover the HCO_3^- initially removed from the blood by filtration at the glomerulus and to regenerate that used in buffering. The first mechanism is the HCO_3^- recovery system while the second regenerates the HCO_3^- (*Figures 9.5* and *9.6*).

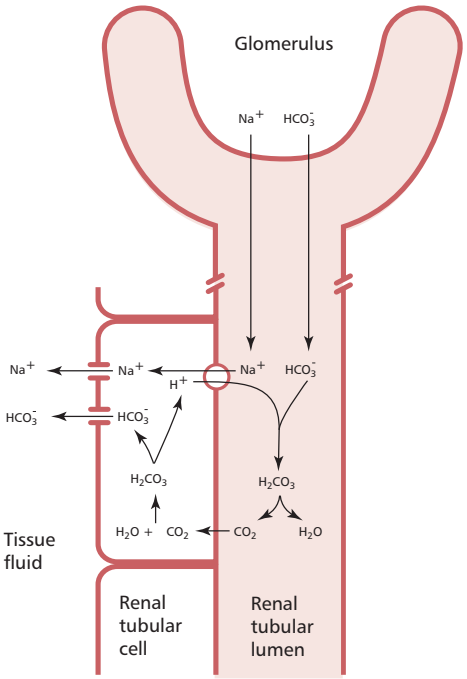

Figure 9.5 The indirect reabsorption of HCO_3^- by kidney tubule cells. See text for details.

In health, virtually all of the HCO_3^- is reabsorbed from the kidney tubule lumen. The operation of the system depends upon the tubule cells being polarized, that is, their luminal and basal surfaces differ in composition and permeability (*Figure 9.5*). In this manner, they resemble the enterocytes that line the absorptive surface of the gastroinstinal tract (*Chapter 11*). Direct reabsorption of HCO_3^- from the renal tubular fluid cannot occur because the luminal surfaces of renal tubular cells are impermeable to HCO_3^-. However, the concentration of CO_2 within the tubular cells is maintained at a relatively high value and so carbonic anhydrase catalyzes the formation of carbonic acid. The acid dissociates to HCO_3^- and H^+. The continuous formation of HCO_3^- and H^+ within the tubule cells is promoted by their removal. The HCO_3^- is transported across the basal membrane of the cell into the interstitial fluid and then into the capillaries. In contrast, H^+ is exchanged for Na^+ across the luminal membrane and enters the lumen of the kidney tubule. A membrane protein called the sodium bicarbonate cotransporter 1 (NBC 1) present in the luminal cell membrane facilitates the exchange of ions. Within the lumen, the H^+ combine with HCO_3^- to form carbonic acid. The acid breaks down spontaneously to CO_2 and H_2O in the proximal tubule, but carbonic anhydrase activity on the luminal surfaces of the cells speeds up the reaction in the distal tubule. The CO_2 can enter the tubule cell across its luminal membrane and so the HCO_3^- is recovered, indirectly, as CO_2. Approximately 80% of the filtered HCO_3^- in the proximal tubule is recovered by this mechanism. However, there

usually by combining a weak acid with the salt of that acid. The pH of these solutions can be calculated using the Henderson-Hasselbalch equation:

$$pH = pK_a + \log [base] / [acid]$$

It is important to note that buffering is only effective at pH values equal to the $pK_a \pm 1$.

The buffering systems of the body do not excrete excess H^+ but temporarily remove them from free solution preventing excessive changes in pH. The effect of any H^+ produced by the body is neutralized largely by the hydrogen carbonate–carbonic acid buffer system.

For the hydrogen carbonate–carbonic acid buffer system:

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

Therefore:

$$pH = pK_a + \log [HCO_3^-] / [H_2CO_3]$$

In plasma, H_2CO_3 breaks down to release carbon dioxide and water:

$$H_2CO_3 \rightleftharpoons CO_2 + H_2O$$

Since the concentration of H_2CO_3 is directly proportional to the partial pressure of CO_2 (PCO_2), it follows that:

$$[H_2CO_3^-] = PCO_2 \times 0.225$$

where 0.225 is the solubility constant of CO_2. Hence the Henderson-Hasselbalch equation can be rewritten as:

$$pH = pK_a + \log [HCO_3^-] / PCO_2 \times 0.225$$

It follows that the concentration of H^+ is directly proportional to the ratio, PCO_2 / $[HCO_3^-]$. Thus the concentration of H^+ in the blood varies as the concentration of HCO_3^- and the PCO_2 change: an increase in H^+ occurs when there is an increase in PCO_2 or a decline in HCO_3^-; while a decrease in H^+ will occur when the PCO_2 decreases or HCO_3^- increases.

has not been a net loss of H^+ and the HCO_3^- used in buffering has not been regenerated. The HCO_3^- is regenerated when carbonic acid is formed in the luminal cell as described above (*Figure 9.6*). Again, H^+ are exchanged for Na^+ and enter the lumen. Here the H^+ react with phosphate (HPO_4^{2-}) and ammonia (NH_3) to give $H_2PO_4^-$ and NH_4^+ respectively. Ammonia is a significant urinary buffer produced by the deamination of glutamine in the renal tubular cells in a reaction catalyzed by glutaminase (*Figure 9.7*). The ammonia formed can readily diffuse across cell membranes but NH_4^+ cannot enter the cells by passive reabsorption. Thus the NH_4^+, and the $H_2PO_4^-$, are excreted in the urine. For every H^+ excreted as NH_4^+ and $H_2PO_4^-$, a single HCO_3^- is formed in the tubule cell and secreted across the basal surface to the interstitial fluid and then into the blood. Hence the HCO_3^- concentration of the ECF is regenerated.

The synthesis of glutaminase is induced in states of chronic acidosis (*Section 9.4*) allowing an increase in the production of ammonia and an increased excretion of H^+ as NH_4^+.

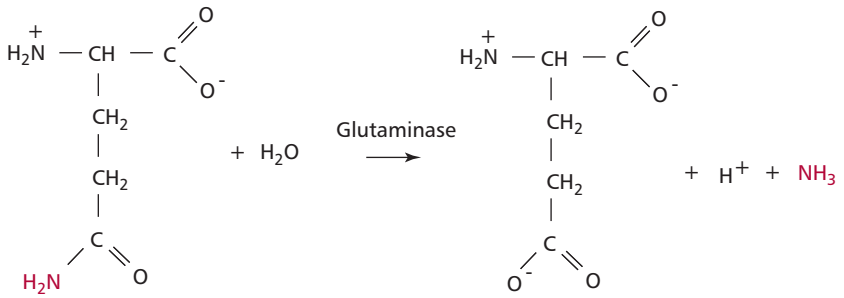

Figure 9.7 The formation of ammonia by the deamination of glutamine catalyzed by glutaminase

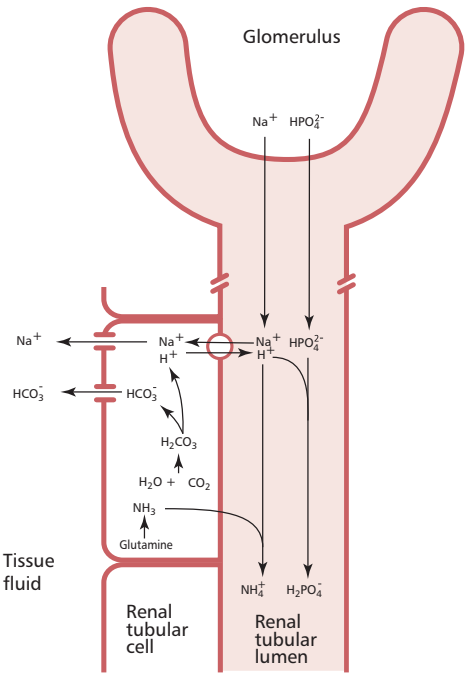

Figure 9.6 The regeneration of HCO_3^- by kidney tubule cells. See text for details.

9.4 TYPES OF ACID–BASE DISORDERS

Disorders of acid–base balance are either acidoses or alkaloses. In an acidosis, there is accumulation of H^+ in the blood and its pH falls below the reference range. In an alkalosis there is a depletion of H^+ and therefore the blood has a pH above its reference range. Acid–base disorders can be further divided into two groups depending on their causes. If the abnormal pH occurs because of a metabolic or renal dysfunction, it is referred to as a **metabolic** acid–base disorder. When the abnormal pH is due to lung dysfunction, then it is a **respiratory** acid–base disorder. Physiological mechanisms that attempt to return the pH back to values within the reference range are referred to as **compensation**. Metabolic disorders cause a change in the concentration of HCO_3^- in the blood but respiratory disorders cause a change in its PCO_2 (*Table 9.1*). In any acid–base disorder, the pH of the blood depends on the severity of the primary disturbance and the amount of compensation that has occurred.

Margin Note 9.1 Fistula

A **fistula** is an abnormal passage from a cavity or tube to another cavity or free surface.

Metabolic acidosis and alkalosis are the results of decreases and increases, respectively, in the concentration of HCO_3^-. These could be caused by the production of ketone bodies during diabetic ketoacidosis (*Chapter 7*) or from the loss of HCO_3^- from a duodenal fistula. Respiratory acidosis is associated with an increased PCO_2 whereas respiratory alkalosis occurs when the PCO_2 is decreased. For example, an impairment of respiratory function can increase the PCO_2 in the blood while hyperventilation would decrease it.

Compensation of acid–base disorders occurs by two major mechanisms: renal compensation and respiratory compensation. Renal compensation occurs when a respiratory disorder impairs lung function. The body attempts to adjust the pH of blood back to within its reference range by increasing the excretion of H^+ by the kidneys. Respiratory compensation is necessary when there is a metabolic acid–base disorder and involves changes in the ventilation of the lungs. Renal compensation is a relatively slow mechanism while respiratory compensation is much quicker to take effect. An acid–base disorder is said to be fully compensated if the compensatory mechanism returns the pH of the blood back to its reference range. However, compensation is usually partial and the pH remains outside the reference range.

METABOLIC ACID–BASE DISORDERS

Metabolic acid–base disorders lead to an accumulation or a loss of H^+ resulting in changes in the concentration of HCO_3^- in the blood. The direct loss or gain of HCO_3^- will also cause a metabolic acid–base disorder. Thus metabolic disorders are recognized by investigating the concentration of HCO_3^- in the blood. Respiratory compensation occurs quickly, often within hours, and patients will show some change in blood PCO_2 because of hypo- or hyperventilation.

Metabolic acidosis may arise from an increase in the amount of H^+ formed or a decrease in the concentration of HCO_3^-. Diabetic ketoacidosis (*Chapter 7*),

Primary disorder	Effect	Compensatory response
Respiratory acidosis	increased PCO_2	increased $[HCO_3^-]$
Respiratory alkalosis	decreased PCO_2	decreased $[HCO_3^-]$
Metabolic acidosis	decreased $[HCO_3^-]$	decreased PCO_2
Metabolic alkalosis	increased $[HCO_3^-]$	increased PCO_2

Table 9.1 Types of acid–base disorders and their compensatory mechanisms

lactic acidosis, poisoning with, for example, salicylate, methanol, ethylene glycol (*Chapter 12*) or the condition known as inherited organic acidosis all increase the production of H^+. In contrast, a decreased excretion of H^+ as in renal tubular acidosis, acute and chronic renal failure (*Chapter 8*), the use of inhibitors of carbonic anhydrase or a deficiency of mineralocorticoid, such as aldosterone (*Figure 9.8*) all increase blood H^+ content. Acid ingestion, as in acid poisoning, the excessive intake of amino acids by infusion, the direct loss of HCO_3^- by diarrhea or a pancreatic fistula can all reduce the concentration of HCO_3^- in the blood.

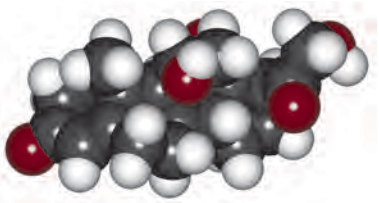

Figure 9.8 Computer generated model of aldosterone.

The clinical effects of metabolic acidosis include hyperventilation, where the increased H^+ concentration acts as a rapid and powerful stimulant of the respiratory center leading to a deep sighing breathing called **Kussmaul respiration**. The patients may also present with neuromuscular irritability that can cause cardiac arrhythmias. Cardiac arrest is more likely in the presence of hyperkalemia (*Chapters 8* and *14*). Eventually metabolic acidosis can depress the activities of the central nervous system and this can progress to coma and even death. Patients with metabolic acidosis are managed by treating the underlying cause and this usually resolves the acid–base disorder. In severe cases, the patients may be administered HCO_3^- intravenously to correct the acidosis.

Metabolic alkalosis may occur as a consequence of gastrointestinal loss of H^+ following vomiting and gastric aspiration or from excessive renal loss of H^+ in Conn's and Cushing's syndromes (*Chapter 7*). Some clinical treatments, such as the use of carbenoxolone, an anti-inflammatory drug used to treat ulcers, and thiazide diuretic drugs that reduce blood pressure by promoting the secretion of urine and by K^+ depletion, can also result in this condition. Finally, the administration of alkali, including alkali ingestion, and inappropriate treatment for acidosis can also cause metabolic alkalosis.

The clinical effects of metabolic alkalosis include hypoventilation that is a consequence of the low H^+ concentration. It is often accompanied by mental confusion and eventually coma. Patients may also suffer from paresthesia. Other effects of metabolic acidosis include tetany and muscle cramps that arise due to a decrease in the concentration of unbound Ca^{2+} in the plasma (*Chapter 8*) arising from the alkalosis. Metabolic alkalosis is usually managed by treating its underlying cause.

RESPIRATORY ACID–BASE DISORDERS

In respiratory acid–base disorders, the primary disturbance is caused by a change in the partial pressure of arterial CO_2. Respiratory disorders are related to a defect in the rate of ventilation of lungs or the exchange of gases across the alveolar membrane. The changes in PCO_2 (*Box 9.1*) alter the concentrations of carbonic acid in the blood, which, in turn, dissociates to HCO_3^- and H^+.

Some causes of respiratory acidosis are shown in *Table 9.2*. In general, obstruction of the airways by disease, or inhibition of the respiratory center in the brain by disease, trauma or drugs can cause respiratory acidosis.

Respiratory acidosis may be acute or chronic. Acute conditions occur within minutes or hours. It is usually the low PO_2 (**hypoxemia**) that is more dangerous than the high PCO_2 (**hypercapnia**). Further, renal compensation is slow, taking two or three days to become effective, so respiratory acidosis is usually uncompensated. Alveolar hypoventilation is usually the most common reason for acute respiratory acidosis. Hypoventilation increases the arterial PCO_2 and so the concentration of H^+ also rises quickly. The high PCO_2 and associated low PO_2 can cause coma and eventually death if untreated. Causes of acute respiratory acidosis include choking, bronchopneumonia and acute exacerbation of asthma.

Conditions giving rise to respiratory acidosis	Examples
Chronic obstructive airway diseases	bronchitis, emphysema
Obstruction of airways due to bronchospasms	asthma
Inhibition of respiratory center	anesthetics; sedatives
Cerebral damage	accidental trauma; stroke; tumors
Neuromuscular disease	poliomyelitis; tetanus; Guillain Barré syndrome
Pulmonary disease	fibrosis; pneumonia; respiratory distress syndrome
Sleep apnea	obesity

Table 9.2 Some conditions giving rise to respiratory acidosis

Chronic respiratory acidosis is, again, usually due to a decline in alveolar ventilation. However, this is normally a well established condition and subject to maximum renal compensation. Long-standing conditions responsible for chronic respiratory disorders include chronic bronchitis and emphysema.

The high PCO_2 is believed to be responsible for the clinical features of respiratory acidosis, such as peripheral vasodilatation and headaches. The acidosis can cause central nervous system depression leading to a coma. The treatment of respiratory acidosis is to improve alveolar ventilation, lowering the PCO_2 and increasing the PO_2. In chronic respiratory acidosis, it is usually not possible to treat the underlying cause and treatment is aimed at maximizing alveolar ventilation by using physiotherapy or bronchodilators.

Respiratory alkalosis is less common than respiratory acidosis. However, it is often an acute condition due to hyperventilation. Often renal compensation does not occur.

The clinical effects of respiratory alkalosis include confusion, headaches, dizziness and coma. Respiratory alkalosis may be caused by hypoxia, increased respiration or pulmonary disease. Hypoxia is associated with high altitudes, severe anemia and pulmonary disease. Increased respiration may result from the use of respiratory stimulants, such as salicylates, from primary hyperventilation syndrome, artificial hyperventilation, and pulmonary diseases, such as pulmonary edema and embolisms. The treatment of respiratory alkalosis is aimed at removing its underlying cause as this usually resolves the acid–base disturbance.

MIXED ACID–BASE DISORDERS

Sometimes patients may present with more than one acid–base disorder and this is known as a **mixed acid–base disorder**. These may present as (i) severe acidemia, that is a low blood pH, (ii) with a normal or near normal pH or (iii) with alkalemia, that is, a high blood pH. Whatever the underlying cause, all mixed acid–base disorders are associated with abnormal levels of blood PCO_2 and HCO_3^-.

For example, a patient with chronic bronchitis may also have renal failure. Both these disorders increase the concentration of H^+ in the blood. Chronic bronchitis leads to respiratory acidosis while the renal failure causes metabolic acidosis. This patient will therefore present with a mixed acid–base disorder with a high blood PCO_2 and H^+ concentration but a low concentration of HCO_3^-. In some cases, however, the two disorders in a mixed acid–base disorder can be antagonistic, that is, have opposing effects on the concentration of H^+ in blood. In this case the blood H^+ concentration may be near normal although

the PCO_2 and HCO_3^- concentration will both be abnormal. For example, a patient with salicylate poisoning may have a metabolic acidosis together with a respiratory alkalosis. Patients may also present with metabolic and respiratory alkaloses. This could occur in someone with congestive cardiac failure who is on diuretic therapy. The former will cause a respiratory alkalosis and the latter a metabolic alkalosis. Such individuals will usually have a high blood pH and increased HCO_3^- but the PCO_2 will be decreased.

9.5 INVESTIGATING ACID–BASE DISORDERS

An investigation of an acid–base disorder involves three stages. The first stage involves identifying whether the patient has an acidosis or an alkalosis. The second stage is to determine whether the acid–base disorder is metabolic or respiratory in nature while the third stage involves determining the degree of compensation.

Acid–base disorders are investigated as outlined in *Figure 9.9*. An arterial blood specimen is collected and its H^+ concentration (pH) and PCO_2 measured. The blood must be collected from an artery into a syringe containing an

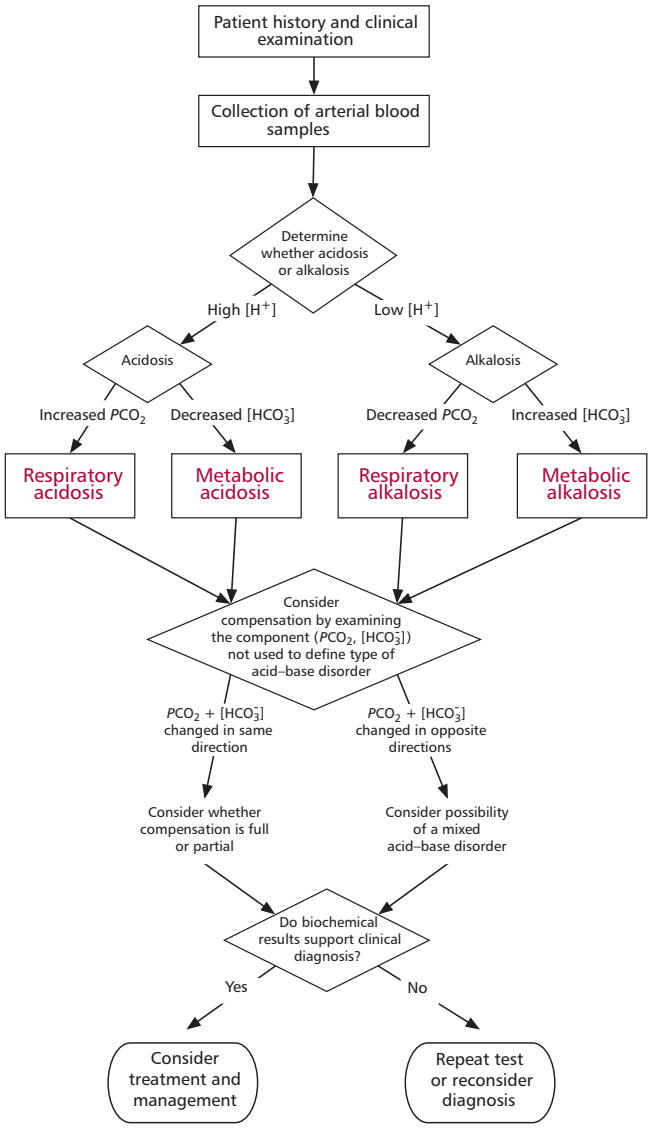

Figure 9.9 Outline of how disorders of acid–base balance are investigated. See text for details.

anticoagulant, such as heparin, and transported to the hospital laboratory at 4°C. Care must be taken that air does not enter any blood samples during collection. The concentration of H^+ and PCO_2 level are measured directly using an automated analyzer that is also programmed to calculate the corresponding concentration of HCO_3^- (*Figure 9.10*) according to the Henderson-Hasselbalch equation. An acidosis or alkalosis can be identified from the pH, that is the concentration of H^+, in the blood. An examination of the levels of PCO_2 and HCO_3^- shows whether the identified disorder is metabolic or respiratory in origin and indicates to what extent compensation is occurring.

A)

B)

PATIENT SAMPLE REPORT — 14 MAY 2004 11:50

SYSTEM 845-1008 — Analysis Date 02 MAR 2004

Analysis Time 18:53

Sequence no 17688 — Draw Date

Accession no 111 — Draw Time

Source — Operator ID 1

Patient ID — Sex

Birthdate — Physician ID

Age — Location

SYRINGE SAMPLE

ACID/BASE 37°C

		Units	Reference Range
pH	7.431		(7.360 - 7.440)
pC02	5.17	kPa	(4.53 - 6.00)
p02	14.58	kPa	(12.00 - 14.67)
HC03-act	25.2	mmol/L	
BEvt	0.9	mmol/L	

Figure 9.10 (A) An automated analyzer for determining blood pH and PCO_2 and programmed to calculate the corresponding concentration of HCO_3^-. (B) A sample of a read out from the automated analyzer. Courtesy of the Department of Clinical Biochemistry, Manchester Royal Infirmary, UK.

CASE STUDY 9.1

John is a young man with a history of dyspepsia (severe indigestion) and excessive alcohol intake. He was admitted into his local hospital following 24 hours of vomiting. An arterial blood specimen was taken and analyzed for a suspected acid–base disorder. The following results were obtained (reference ranges are indicated in parentheses).

$[H^+]$	28 nmol dm^{-3}	(35–45 nmol dm^{-3})
PCO_2	7.2 kPa	(4.4–5.6 kPa)
$[HCO_3^-]$	48 mmol dm^{-3}	(21–28 mmol dm^{-3})

Question

Does John have an acid–base disorder and, if so, what type of acid–base disorder is present?

CASE STUDY 9.2

Tom was admitted to hospital following an acute attack of asthma. A blood specimen was taken and analyzed giving the following results (reference ranges are shown in parentheses).

$[H^+]$	24 nmol dm^{-3}	(34–44 nmol dm^{-3})
PCO_2	2.5 kPa	(4.1–5.6 kPa)
$[HCO_3^-]$	22 mmol dm^{-3}	(21–28 mmol dm^{-3})

Question

Does Tom have an acid–base disorder and, if so, what type?

CASE STUDY 9.3

Terry, a 62 year factory worker has suffered with vomiting and diarrhea for the last two weeks. When examined by his doctor, he was dehydrated and his breathing was deep and noisy. An arterial blood specimen was taken and analyzed for blood gases (reference ranges are shown in parentheses).

$[H^+]$	65 nmol dm^{-3}	(34–44 nmol dm^{-3})
PCO_2	2.9 kPa	(4.1–5.6 kPa)
$[HCO_3^-]$	9 mmol dm^{-3}	(21–28 mmol dm^{-3})

Questions

(a) Does Terry have an acid–base disorder?

(b) Is there any compensation?

9.6 SUMMARY

The pH of the blood is maintained at 7.4 within normal limits by physiological mechanisms that remove the H^+ and CO_2 produced by metabolism. Excess CO_2 is transported by the blood to the lungs and excreted. In the blood, the dissolved CO_2 is converted to hydrogen carbonate in a reaction catalyzed by carbonic anhydrase. Buffering systems such as the hydrogen carbonate–carbonic acid system and hemoglobin serve to maintain the physiological pH in health. Acid–base disorders result in the blood pH being lower (acidosis) or higher (alkalosis) than normal. Such disorders may be metabolic or respiratory in nature and can be fatal if untreated, although there are physiological mechanisms for at least a partial compensation of the disorder. Treatment of most acid–base disorders involves treatment of the underlying causes.

QUESTIONS

1. Approximately how many molecules of CO_2 are produced daily by oxidative metabolism? Avogadro's number is 6.02×10^{23}.

   a) 12×10^{24}
   b) 1.2×10^{23}
   c) 1.2×10^{26}
   d) 1.2×10^{25}
   e) 1.2×10^{24}

2. (a) How much greater is the $[H^+]$ in a solution of pH 3 than one of pH 6?

   (b) What is the pH of a buffer prepared from 100 cm^3 of 0.1 mol dm^{-3} ethanoic acid ('acetic acid') solution (pK_a of ethanoic acid = 4.76) and 75 cm^3 of a 0.2 mol dm^{-3} sodium ethanoate solution?

3. A blood analysis of a patient gives values for PCO_2 of 5.0 kPa (4.4–5.6 kPa) and a pH of 7.56. The pK_a for the carbonic acid–hydrogen carbonate system is 6.10. (a) Calculate the corresponding $[HCO_3^-]$. (b) Is the patient in an acidosis or alkalosis? (c) If so, is this metabolic or respiratory in origin?

4. The following blood gas results were obtained for a patient (reference ranges are shown in parentheses):

$[H^+]$	50 nmol dm^{-3}	(35–45 nmol dm^{-3})
PCO_2	11.5 kPa	(4.4–5.6 kPa)
$[HCO_3^-]$	34 mmol dm^{-3}	(21–28 mmol dm^{-3})

   Which of the following conditions match most closely with these results?

   a) diabetic ketoacidosis;
   b) laboratory transcription error;
   c) chronic obstructive airways disease;
   d) pyloric stenosis;
   e) none of the above.

FURTHER READING

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