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# Pathophysiology of acid base balance: The theory practice relationship

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## KEYWORDS

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**Summary** There are many disorders/diseases that lead to changes in acid base balance. These conditions are not rare or uncommon in clinical practice, but everyday occurrences on the ward or in critical care. Conditions such as asthma, chronic obstructive pulmonary disease (bronchitis or emphysema), diabetic ketoacidosis, renal disease or failure, any type of shock (sepsis, anaphylaxis, neurogenic, cardiogenic, hypovolaemia), stress or anxiety which can lead to hyperventilation, and some drugs (sedatives, opioids) leading to reduced ventilation. In addition, some symptoms of disease can cause vomiting and diarrhoea, which effects acid base balance. It is imperative that critical care nurses are aware of changes that occur in relation to altered physiology, leading to an understanding of the changes in patients' condition that are observed, and why the administration of some immediate therapies such as oxygen is imperative.

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## Introduction

The implications for practice with regards to acid base physiology are separated into respiratory acidosis and alkalosis, metabolic acidosis and alkalosis, observed in patients with differing aetiologies. By understanding normal physiological principles and how they relate to clinical situations can enhance patient care. A good understanding of

the essential concepts of acid base physiology is necessary so that quick and correct diagnosis can be determined and appropriate treatment implemented.

The homeostatic imbalances of acid base are examined as the body attempts to maintain pH balance within normal parameters.

## General principles of acid base balance

The primary function of the respiratory system is to supply an adequate amount of oxygen (O<sub>2</sub>) to tissues and remove carbon dioxide (CO<sub>2</sub>). The kidneys

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**Table 1** The major body buffer systems

Site	Buffer system	Description
Interstitial fluid (ISF)	Bicarbonate Phosphate and protein	For metabolic acids Not important because concentration is too low
Blood	Bicarbonate Haemoglobin Plasma proteins Phosphate	Important for metabolic acids Important for buffering CO <sub>2</sub> and H <sup>+</sup> Minor buffer Concentration too low
Intracellular fluid	Proteins Phosphates	Important buffer of extracellular H <sup>+</sup> Important buffer
Urine	Phosphate Ammonia	Responsible for most of titratable acidity Important—formation of NH <sub>4</sub> <sup>+</sup> and hence excretion of H <sup>+</sup>
Bone	Calcium carbonate	In prolonged metabolic acidosis

will excrete any excess acids or alkali. The respiratory and renal organs together with the buffering effects of blood maintain hydrogen ion (H<sup>+</sup>) concentration. H<sup>+</sup> concentration is one of the most important aspects of acid base homeostasis. When there is an increase or decrease in acid production, blood bicarbonate (HCO<sub>3</sub><sup>-</sup>), proteins, and phosphate buffer body fluids (Table 1). However, there comes a point in the disease process when these buffers can no longer maintain appropriate concentrations of H<sup>+</sup>. Patients admitted to hospital can have life threatening situations such as diabetic ketoacidosis, asthma, severe vomiting, which alter pH balance and exacerbate their problems.

To maintain homeostasis during stress/strenuous exercise and/or illness/diseased states there is generally an increase in depth and rate of breathing due to stimulation of the sympathetic nervous system (Richardson, 2003). High alveolar ventilation brings more O<sub>2</sub> into the alveoli, increasing O<sub>2</sub>, and rapidly eliminating CO<sub>2</sub> from the lungs (for chemical abbreviations see Table 2).

**Table 2** Chemical abbreviations

Abbreviation	Interpretation
O <sub>2</sub>	Oxygen
CO <sub>2</sub>	Carbon dioxide
kPa	Kilo pascals
PO <sub>2</sub>	Partial pressure of oxygen
PCO <sub>2</sub>	Partial pressure of carbon dioxide
H <sup>+</sup>	Hydrogen ions
HCO <sub>3</sub> <sup>-</sup>	Bicarbonate ions
H <sub>2</sub> CO <sub>3</sub>	Carbonic acid
Na <sup>+</sup>	Sodium
K <sup>+</sup>	Potassium
Cl <sup>-</sup>	Chloride
NH <sub>4</sub> <sup>+</sup>	Ammonium

### Partial pressure of gases

Dalton's law explains the partial pressure of a gas, which is the pressure exerted by a gas within a mixture of gases independent of each gas in the mixture (Marieb, 2004). The partial pressure of each gas is directly proportional to its percentage in the total mixture and in air is determined by atmospheric pressure. Atmospheric pressure is 101 kPa (760 mmHg), 21% of this air is oxygen, and the partial pressure of oxygen (PO<sub>2</sub>) in atmospheric air is:

$$\frac{21}{100} \times 101 = 21.2 \text{ kPa}$$

Within the alveoli the PO<sub>2</sub> is different to air because of enrichment in the air passages (dead space) with CO<sub>2</sub> and water vapour. Alveolar air contains much more CO<sub>2</sub> and water vapour and much less O<sub>2</sub> and so makes a greater contribution to the near-atmospheric pressure in the lungs, then they do in air. This is due to:

- gas exchanges occurring in the lungs,
- humidification of air by the conducting passages,
- mixing of gases in the dead space (contains air not involved in gaseous exchange) between the nose and alveoli.

In alveoli, PO<sub>2</sub> averages only 13.2 kPa (100 mmHg). Continuous consumption of O<sub>2</sub> and production of CO<sub>2</sub> in the cells means that there is a partial pressure gradient both in the lungs and at the tissue level ensuring diffusion of oxygen into the blood and CO<sub>2</sub> from it (Waterhouse and Campbell, 2002).

Changes in partial pressures of carbon dioxide (PCO<sub>2</sub>) and H<sup>+</sup> are sensed directly by the respiratory centre central chemoreceptors in the medulla (Guyton and Hall, 2000). In contrast, a reduction

in PO<sub>2</sub> is monitored by the peripheral chemoreceptors located in the carotid and aortic bodies which transmit nervous signals to the respiratory centre in the medulla for control of respiration (Schlichtig et al., 1998; Williams, 1998). However, it is the CO<sub>2</sub> 'drive' for breathing that dominates in health, although the O<sub>2</sub> 'drive' can be significant in some disordered states as an adaptation to chronic elevations of PCO<sub>2</sub> for example in chronic obstruction lung conditions.

### Metabolic generation of acids and alkali

Each day the body produces acids through normal metabolism, and acid or alkali is ingested in diet (Koeppen, 1998). The lungs release or strengthen the bond to acids as necessary and the kidneys also effectively eliminate or reabsorb acids, so there is no impact on whole body acid base status. If there is an increase in production of acids, the body has a number of buffers outlined in Table 1. If there is a reduction in acids or loss of acids the excess bicarbonate (HCO<sub>3</sub><sup>-</sup>) is buffered by H<sup>+</sup> to minimise any change in pH.

### Normal pH and hydrogen ion concentration of body fluids

The pH is related to actual H<sup>+</sup> concentration (Guyton and Hall, 2000). A low pH corresponds to a high H<sup>+</sup> concentration and is evidence of an acidosis, and conversely a high pH corresponds to a low H<sup>+</sup> concentration known as an alkalosis. The interrelationships between O<sub>2</sub>, H<sup>+</sup>, CO<sub>2</sub> and HCO<sub>3</sub><sup>-</sup> are central to the understanding of acid base balance and reflect the physiological importance of the CO<sub>2</sub>/HCO<sub>3</sub><sup>-</sup> buffer system (Fig. 1). The CO<sub>2</sub>/HCO<sub>3</sub><sup>-</sup> buffer system largely takes up the majority of the excess H<sup>+</sup>. The H<sup>+</sup> + HCO<sub>3</sub><sup>-</sup> converts into H<sub>2</sub>CO<sub>3</sub> in the presence of carbonic anhydrase (present in red

blood cells) and breaks down into CO<sub>2</sub> and water (H<sub>2</sub>O) (Fig. 1). The CO<sub>2</sub>/HCO<sub>3</sub><sup>-</sup> interaction is slow in plasma, but quicker in red blood cells due to the presence of carbonic anhydrase.

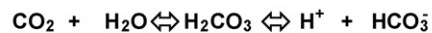
### Respiratory disorders

Acid base disorders resulting from primary alterations in the PCO<sub>2</sub> are termed respiratory disorders. Any increase in concentration or retention of CO<sub>2</sub> (considered a volatile source of acid which evaporates rapidly in body fluids) i.e. production > excretion will produce an increase in H<sup>+</sup> through the generation of carbonic acid (H<sub>2</sub>CO<sub>3</sub>) (Fig. 1). This lowers the pH and thus promotes the development of a respiratory acidosis observed in conditions where CO<sub>2</sub> excretion is impaired such as chronic obstructive pulmonary disease (COPD) (Koeppen, 1998).

Decreases in PCO<sub>2</sub> concentration i.e. if excretion is greater than production, will result in a decrease in H<sup>+</sup>. The pH will rise and a respiratory alkalosis results from a decreased concentration of free H<sup>+</sup>. This is seen in conditions such as hyperventilation where CO<sub>2</sub> excretion is excessive. The lungs therefore play a major role in ensuring maintenance of H<sup>+</sup> ion concentration (Guyton and Hall, 2000).

### Metabolic disorders

Disorders of acid base physiology of non-respiratory origin are metabolic disorders and result from abnormal metabolism (Holmes, 1993). Metabolic disorders may be due to excessive intake of acid or alkali or due to failure of renal function. If non-respiratory acid production exceeds the excretion of acid from the body HCO<sub>3</sub><sup>-</sup> decreases, and H<sup>+</sup> concentration increases as in a metabolic acidosis (Koeppen, 1998). The CO<sub>2</sub> yielded in a metabolic acidosis is lost via the lungs. This is achieved, as an



CO<sub>2</sub> = carbon dioxide, HCO<sub>3</sub><sup>-</sup> = bicarbonate, H<sub>2</sub>CO<sub>3</sub> = carbonic acid, H<sup>+</sup> = hydrogen ions, H<sub>2</sub>O = water

The CO<sub>2</sub>/HCO<sub>3</sub><sup>-</sup> buffer system is important in acid base balance but the H<sup>+</sup> concentration of body fluids is influenced by both PCO<sub>2</sub> and HCO<sub>3</sub><sup>-</sup> concentration. The figure demonstrates that the lungs and the kidneys largely determine acid base balance. The lungs maintain acid base balance through control of PCO<sub>2</sub> and the kidneys through the excretion or re-absorption of HCO<sub>3</sub><sup>-</sup>. It should also be noted that this equation is completely reversible. Therefore, increases in CO<sub>2</sub> can be converted into H<sup>+</sup>, and H<sup>+</sup> can be converted to CO<sub>2</sub> for excretion – depending upon the presence of the enzyme carbonic anhydrase.

(Modified from Marieb 2004)

**Figure 1** The interrelationship between H<sup>+</sup>, CO<sub>2</sub> and HCO<sub>3</sub><sup>-</sup> in acid base balance.

increase in  $H^+$  will reduce pH, immediately stimulating central chemoreceptors increasing rate and depth of respiration. This can be observed in conditions such as diabetic ketoacidosis (due to elevated  $H^+$  production) and renal failure (due to inadequate  $H^+$  excretion), and is referred to as 'respiratory compensation'.

If acid production is less than the excretion of acid from the body, then  $HCO_3^-$  concentration increases and  $H^+$  concentration decreases and a metabolic alkalosis result. A decrease in  $H^+$  will increase pH depressing central chemoreceptor response, reducing rate and depth of breathing.  $CO_2$  is retained which generates  $H^+$  and so reduces blood pH close to normal limits. This response is observed with severe vomiting when gastric acid loss depletes body fluid of  $H^+$  (Taylor, 1990a). This is another example of respiratory compensation. The rapidity of respiratory compensation is evident in these conditions, but it is also limited.

### Renal compensation

The ultimate acid base regulatory organs are the kidneys, which act slowly to compensate for acid base balance situations. The most important renal mechanisms for regulating acid base balance of the blood involve:

- excreting  $HCO_3^-$  and conserving (reabsorbing)  $H^+$  in an alkalosis,
- excreting  $H^+$  and reclaiming  $HCO_3^-$ , conserving (reabsorbing) bicarbonate ions, as in an acidosis (the dominant process in the nephrons).

This response to acid base disturbances requires several days to be marginally effective.

### Arterial blood gas analysis

Blood can be taken from an artery and analysed to determine  $PO_2$  and  $PCO_2$  to interpret a patient's acid base balance (Coombs, 2001; Fletcher and Dhrampal, 2003). Arterial blood gas analysis is part of the medical and nursing care of a patient who may have a related physiological disorder (Woodrow, 2004). Blood gas machines measure pH,  $PCO_2$ ,  $PO_2$ , base excess (BE) and  $HCO_3^-$  (Table 3). A BE is the change from normal of the concentration of bicarbonate (Schlichtig et al., 1998). With excess alkali in the blood there is a positive BE (excess bicarbonate), whereas with excess non-respiratory acid there is a base deficit, or negative base excess (reduced bicarbonate). By measuring partial pressure and these other values in arterial blood a

respiratory or metabolic acid base disorder can be determined and whether the respiratory system or kidneys are compensating.

When attempting to analyse a person's acid base balance, scrutinise blood values in the following order (Table 4). Notice that  $PCO_2$  levels vary inversely with blood pH, ( $PCO_2$  rises as blood pH falls);  $HCO_3^-$  levels vary directly with blood pH (increased  $HCO_3^-$  results in increased pH). If any changes occur in the partial pressures of  $O_2$  or  $CO_2$  e.g. due to respiratory disease (asthma, COPD, adult respiratory distress syndrome—ARDS), metabolic disease (diabetes, renal failure), or because of symptoms of disease (vomiting and diarrhoea), then the changes will be reflected in these measures (Williams, 1998).

### An increase in acids ( $H^+$ ) in the body (acidosis)

There are generally two categories of acid accumulation in the body a respiratory acidosis and a metabolic acidosis, determined if the primary change is either metabolic or respiratory (Table 5).

#### Respiratory acidosis ( $\downarrow$ pH $\uparrow$ PCO<sub>2</sub>)

Respiratory acidosis occurs when the respiratory system is unable to eliminate  $CO_2$  produced from cellular metabolism, quickly enough (Holmes, 1993). An increase in  $CO_2$  increases  $H^+$  ion concentration and the body's pH starts falling below 7.40. However, normally the body is able to particularly maintain acid base homeostasis, since the increase in  $PCO_2$  stimulates central chemoreceptors to increase respiratory rate. When  $PCO_2$  can no longer be maintained e.g. in COPD, the body can still help to maintain pH by the elimination of excess acid in urine. Although this is of a slow onset and will not be so effective in say acute airway obstruction. An individual can live for many years with conditions such as COPD, partly because of the efficiency of renal compensation.

**Table 3** The measures obtained from arterial blood gas analysis and normal values

Measure	Normal range
pH	7.35–7.45
$PCO_2$	4.6–5.6 kPa (35–42 mmHg)
$PO_2$	12–14.6 kPa (90–110 mmHg)
$HCO_3^-$	22–26 mmol/L
BE (base excess)	0
$O_2$ saturation	94–98%

To convert from mmHg to kPa divide by 7.5.

**Table 4** Measure of arterial blood gases

Measure	Normal limits	Interpretation
pH	7.35–7.45	This indicates whether the person is in acidosis (pH < 7.35) or alkalosis (pH > 7.45), but it does not indicate the cause.
PCO <sub>2</sub>	4.6–5.6 kPa (35–42 mmHg)	Check the PCO <sub>2</sub> to see if this is the cause of the acid base balance. The respiratory system acts fast, and an excessively high or low PCO <sub>2</sub> may indicate either the condition is respiratory or if the patient is compensating for a metabolic disturbance. <ul style="list-style-type: none"> <li>• The PCO<sub>2</sub> is over 5.7 kPa (40 mmHg), the respiratory system is the cause of the problem and the condition is a respiratory acidosis;</li> <li>• The PCO<sub>2</sub> is below normal limits 5.2 kPa (35 mmHg), the respiratory system is not the cause but is compensating.</li> </ul>
PO <sub>2</sub>	12–14.6 kPa (90–110 mmHg)	This does not reveal how much oxygen is in the blood but only the partial pressure exerted by dissolved O <sub>2</sub> molecules against the measuring electrode.
HCO <sub>3</sub> <sup>-</sup>	22–26 mmol/l	Abnormal values of the HCO <sub>3</sub> <sup>-</sup> are only due to the metabolic component of an acid base disturbance: <ul style="list-style-type: none"> <li>• A raised HCO<sub>3</sub><sup>-</sup> concentration indicates a metabolic alkalosis (values over 26 mmol/L)</li> <li>• A low value indicates a metabolic acidosis (values below 22 mmol/L).</li> </ul>
BE	-2 ± 2 mmol/l	Is the amount of acid required to restore 1 L of blood to its normal pH, at a PCO <sub>2</sub> of 5.3 kPa (40 mmHg). The BE reflects only the metabolic component of any disturbance of acid base balance: <ul style="list-style-type: none"> <li>• If there was a metabolic alkalosis then acid would have to be added to return the blood pH to normal, the BE will be positive</li> <li>• If there is a metabolic acidosis, acid would need to be subtracted to return blood pH to normal, the BE is negative.</li> </ul>

### The accumulation of carbon dioxide in respiratory acidosis

It is well known that haemoglobin (Hb) can carry O<sub>2</sub> and CO<sub>2</sub> at the same time, but the presence of one reduces the bonding power of the other, known as the Haldane effect (Carpenter, 1991). The Haldane effect is when CO<sub>2</sub> transported in blood is affected by the partial pressure of O<sub>2</sub> in the blood (Marieb, 2004). The PO<sub>2</sub> in the alveoli normally gives a sufficient pressure (partial pressure) to facilitate CO<sub>2</sub> release from Hb in the alveoli and CO<sub>2</sub> binding in the tissues. The amount of CO<sub>2</sub> transported by Hb in blood is influenced by PO<sub>2</sub>. When PO<sub>2</sub> decreases in conditions such as COPD, the CO<sub>2</sub> is less likely to be released from the Hb, consequently CO<sub>2</sub> levels increase.

In a worsening respiratory acidosis through airway obstruction PO<sub>2</sub> decreases in the alveoli and as such cannot sufficiently facilitate the release of CO<sub>2</sub> from Hb. A greater proportion of CO<sub>2</sub> remains attached and will eventually lower pH. The deoxygenated Hb carrying an excess of CO<sub>2</sub> is less likely to bind to O<sub>2</sub>, thus exacerbating the

problem of poor O<sub>2</sub> uptake. In some conditions administration of oxygen will improve PO<sub>2</sub> and facilitate the removal of the accumulated CO<sub>2</sub> from Hb.

### Improved release of oxygen in respiratory acidosis

When there is an increase in CO<sub>2</sub> and H<sup>+</sup>, as observed in a respiratory acidosis e.g. COPD, the blood pH will drop. In an acid environment less oxygen can be carried by haemoglobin leading to a reduction of oxygen delivery to cells (Marieb, 2004). Conversely, an acid environment in tissues causes haemoglobin (Hb) to release O<sub>2</sub> more readily to cells and facilitates unloading of O<sub>2</sub>. This effect is known as the Bohr effect and is important adaptation to increased acidity in metabolically active tissues. The increased H<sup>+</sup> bind to Hb in red blood cells and alters the structure of the molecules temporarily causing it to release O<sub>2</sub>. The Hb molecule therefore gives up its O<sub>2</sub> to tissues under conditions of increased H<sup>+</sup> ion concentration.

**Table 5** Acid base categories and related conditions

Acid base is separated into four categories:	The conditions/diseases that lead to acid base abnormalities
Respiratory acidosis—any disorder that interferes with ventilation ( $\text{PCO}_2 > 5.7 \text{ kPa}$ ; $\text{pH} < 7.35$ )	<ul style="list-style-type: none"> <li>• Any condition that impairs gas exchange or lung ventilation (chronic bronchitis, cystic fibrosis, emphysema, pulmonary oedema)</li> <li>• Rapid, shallow breathing, hypoventilation</li> <li>• Narcotic or barbiturate overdose or injury to brain stem</li> <li>• Airway obstruction</li> <li>• Chest or head injury</li> </ul>
Metabolic acidosis ( $\text{HCO}_3^- < 22 \text{ mmol/L}$ ; $\text{pH} < 7.35$ )	<ul style="list-style-type: none"> <li>• Severe diarrhoea causing loss of bicarbonate from the intestine</li> <li>• Circulatory failure/hypovolaemia</li> <li>• Renal disease/failure</li> <li>• Untreated diabetes mellitus</li> <li>• Starvation</li> <li>• Excess alcohol ingestion</li> <li>• High ECF potassium concentrations</li> <li>• Lactic acid production</li> </ul>
Respiratory alkalosis ( $\text{PCO}_2 < 5.7 \text{ kPa}$ ; $\text{pH} < 7.45$ )	<ul style="list-style-type: none"> <li>• Direct cause is always hyperventilation (e.g. too much mechanical ventilation, pulmonary lesions)</li> <li>• Brain tumour or injury</li> <li>• Acute anxiety</li> <li>• Early stages of congestive obstruction airway disease</li> <li>• Asthma</li> </ul>
Metabolic alkalosis ( $\text{HCO}_3^- > 26 \text{ mmol/L}$ ; $\text{pH} > 7.40$ ) is the result of excess base bicarbonate ion ( $\text{HCO}_3^-$ ) or decreased hydrogen ion ( $\text{H}^+$ ) concentration, caused by an excessive loss of non-volatile or fixed acids	<ul style="list-style-type: none"> <li>• Vomiting or gastric suctioning of hydrogen chloride-containing gastric contents</li> <li>• Selected diuretics</li> <li>• Ingestion of excessive amount of sodium bicarbonate</li> <li>• Constipation</li> <li>• Excess aldosterone (e.g. tumours)</li> <li>• Loss of gastric-intestinal hydrochloric acid and potassium (e.g. severe vomiting or gastric suctioning)</li> <li>• Over-use of potassium wasting diuretics</li> </ul>

### Metabolic acidosis ( $\downarrow \text{pH}$ $\downarrow \text{HCO}_3^-$ )

Metabolic acidosis occurs when there is excess acid or reduced  $\text{HCO}_3^-$  in the body (Holmes, 1993). Over production or excess  $\text{H}^+$  will lead to decreased pH of less than 7.40. This is followed by a reduction in  $\text{HCO}_3^-$  (used to buffer excess  $\text{H}^+$ ) in an effort to return pH to within the normal range of 7.35–7.45. Body enzymes can only function in a pH range of between 6.80 and 7.80 with reducing pH there is 50% mortality rate at a  $\text{pH} \leq 6.80$  (Holmes, 1993).

### Compensatory mechanisms for respiratory and metabolic acidosis

When  $\text{H}^+$  accumulate in the body chemical buffers in cells and extracellular fluid (ECF) bind with

the excess  $\text{H}^+$ . As  $\text{H}^+$  reaches excessive proportions, buffers cannot bind with them and blood pH decreases. The compensation for an accumulation of respiratory or metabolic acids occurs in the lungs and kidneys.

### The role of the lungs in compensation

In a respiratory acidosis there is a low/normal  $\text{PO}_2$  and a high  $\text{PCO}_2$  concentration and a low pH. An increase in  $\text{CO}_2$  is observed in all tissues and fluids, including cerebral spinal fluid (CSF) and in the medulla oblongata. The  $\text{CO}_2$  reacts with  $\text{H}_2\text{O}$  to form  $\text{H}_2\text{CO}_3$  (quicker in the presence of carbonic anhydrase in red blood cells) that dissociates to  $\text{H}^+$  and  $\text{HCO}_3^-$  (Fig. 1). When both  $\text{CO}_2$  and  $\text{H}^+$  are increased in CSF and tissues they have a strong stimulatory effect on central chemoreceptors act-

ing on inspiratory and expiratory muscles leading to an increase in the respiratory rate and depth of breathing (Edwards, 2001a).

A reduced  $PO_2$  will also contribute to an increase in ventilation since  $O_2$  saturation will decrease. The role of a reduced  $O_2$  in lung ailments such as pneumonia, asthma, emphysema, plays a major role in increasing respiration via peripheral chemoreceptors and can increase alveolar ventilation as much as five–seven fold (Guyton and Hall, 2000). If the compensation of a deeper and faster respiratory rate is efficient e.g. in asthma, it may significantly reduce  $PCO_2$  to maintain  $O_2$  levels (Woodrow, 2004). However, the increase in alveoli ventilation may lead to overcompensation and a patient suffering an asthmatic attack may present with a detrimental respiratory alkalosis ( $\uparrow pH$   $\downarrow PCO_2$ ) (Figs. 2 and 3).

In a metabolic acidosis removal of a proportion of the excess  $H^+$  can occur as  $CO_2$ , as the equation presented in Fig. 1 is completely reversible. This allows more  $H^+$  to bind with  $HCO_3^-$  to form  $H_2CO_3$  that dissociates to  $CO_2$  and  $H_2O$  (Fig. 1). Respiration is stimulated due to reduction in pH in CSF stimulating central chemoreceptors, leading to hyperventilation.  $CO_2$  excreted from the body and the arterial  $PCO_2$  therefore reduces.

This explains why patients with a metabolic acidosis have a fast respiratory rate, which further increases as acids continue to rise, and can lead to a reduction in  $PCO_2$  to less than is normal in health (Fletcher and Dharampal, 2003). A complete compensatory respiratory alkalosis through a reduction in  $CO_2$  is unlikely to completely restore normality because, if it were to do so, the compensatory mechanisms would be eradicated (Holmes, 1993). Therefore, in a metabolic acidosis, respiratory compensation is not sufficient alone.

If  $PCO_2$  cannot be reduced and compensation becomes inefficient, in conditions such as a chest infection or asthma  $PCO_2$  may eventually start to rise. This may be an indication to instigate additional interventions such as non-invasive intermittent positive pressure ventilation (NIPPV) (Butler, 2005) or invasive intubation.

### The role of the kidneys in compensation

As blood acidity increases, renal compensatory mechanisms act slowly in maintaining pH (Yucha, 2004). In respiratory acidosis excess  $CO_2$  can be converted through the equation in Fig. 1. The retained  $CO_2$  combines with  $H_2O$  to form large amounts of  $H_2CO_3$ . In the kidneys  $H_2CO_3$  dissociates to release free  $H^+$  and  $HCO_3^-$ , and stimulates the

kidneys to retain  $HCO_3^-$  and sodium ions ( $Na^+$ ), and excrete  $H^+$ . The  $HCO_3^-$  retained is re-circulated and helps to buffer further free  $H^+$ .

Similar effects occur in a metabolic acidosis. After about 30 min the kidneys start to compensate for the acidosis by secreting excess  $H^+$  secreted in the renal tubule and excreted in the urine as weak acids (Yucha, 2004). For every  $H^+$  secreted into the renal tubule, a sodium and bicarbonate ion is re-absorbed and returned to the blood. The pH is unlikely to be completely restored, as this would reduce the efficiency of compensatory mechanisms. The  $CO_2$  and  $HCO_3^-$  will be far from their normal values, as a consequence of altered buffering capacity and respiratory compensation.

It takes around 3 days for a patient to have established a steady state of compensation e.g. a respiratory hyperventilation (Guyton and Hall, 2000). The kidney can only retain so much  $HCO_3^-$  with the consequence that the blood contains a higher concentration of  $HCO_3^-$  than produced by the  $CO_2$  retention alone (Fig. 2), hence an improved base excess (BE).

### $H^+$ buffer by intracellular proteins in exchange for $K^+$

If the concentration in  $H^+$  in extracellular fluid rises to a level beyond the compensatory mechanism  $H^+$  move into cells by simple diffusion to be buffered by intracellular proteins, in exchange for potassium ions ( $K^+$ ) (Holmes, 1993). As cells need to maintain a balanced membrane charge cells release  $K^+$  into blood in exchange for  $H^+$ , this may lead to a high blood  $K^+$  (hyperkalaemia) and characteristic changes in the electrocardiogram (ECG) (peaked T waves and abnormal QRS complexes) may be observed (Richards and Edwards, 2003). However, with normal renal functions the majority of excess ECF  $K^+$  will be excreted in urine. If normal ventilation is restored or the acidosis is treated for example in diabetic ketoacidosis is treated with insulin and glucose, the  $K^+$  will return into the intracellular fluid (ICF) in exchange for  $H^+$  and the patient may then develop a hypokalaemia (as demonstrated in Model Case 1).

### A decrease or loss of acids ( $H^+$ ) in the body (alkalosis)

There are generally two categories of reduced acids in the body, a respiratory alkalosis and a metabolic alkalosis (Table 5). These two conditions stimulate compensatory mechanisms that serve to maintain acid base homeostasis.

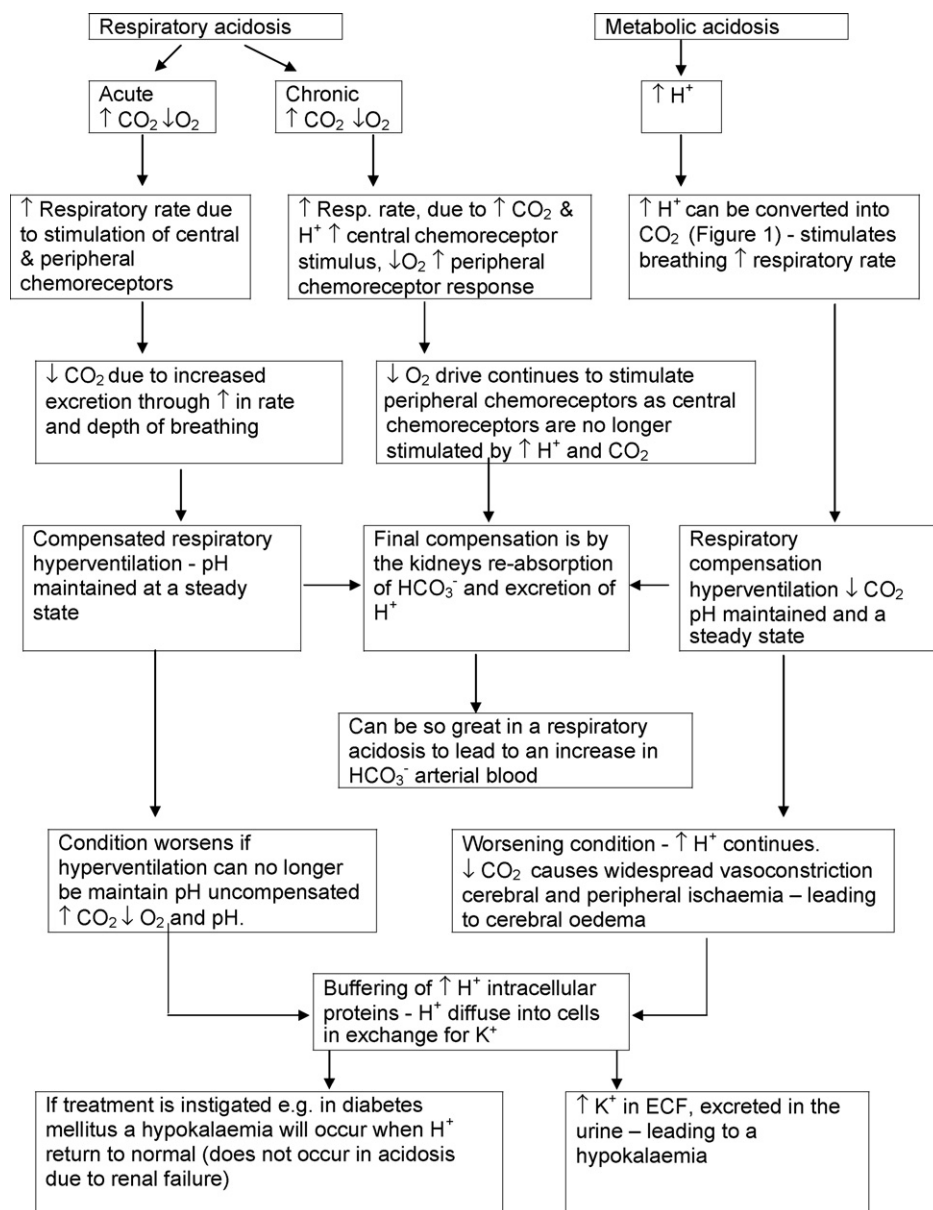


Figure 2 Processes involved in respiratory and metabolic acidosis.

### Respiratory alkalosis ( $\uparrow$ pH $\downarrow$ PCO<sub>2</sub>)

Respiratory alkalosis occurs when the respiratory system eliminates too much CO<sub>2</sub>. This reduction of PCO<sub>2</sub> below the range of 4.5–5.6 kPa (30–35 mmHg) causes a reduction in H<sup>+</sup> generation (Taylor, 1990b). The decreasing H<sup>+</sup> concentration raises the blood pH above the normal range of 7.45. Any condition that causes hyperventilation can cause a respiratory alkalosis.

#### The processes of carbon dioxide excretion

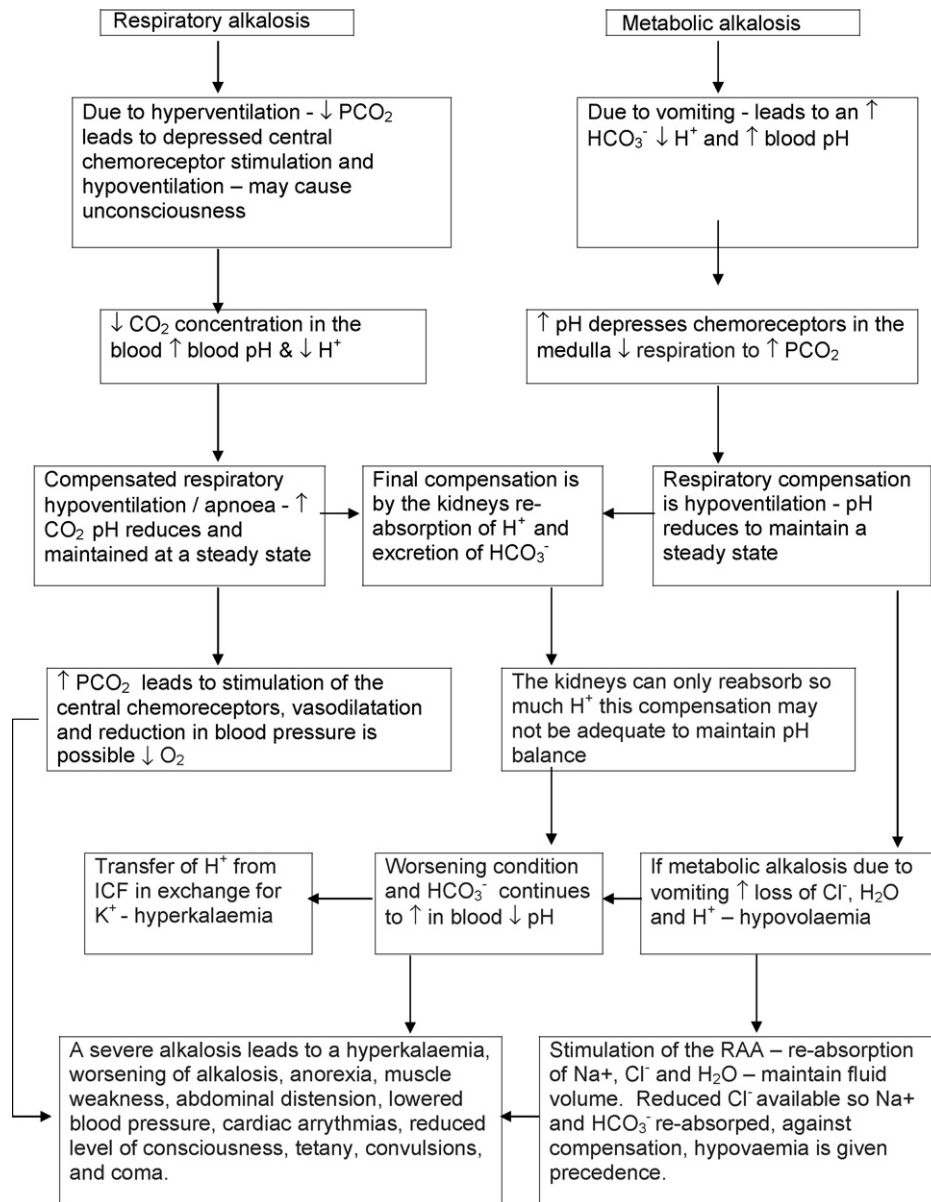
When ventilation is increased above the normal rate, excessive amounts of CO<sub>2</sub> are excreted in

expired air. In this situation CO<sub>2</sub> is washed out of the body leading to a hypocapnia the pH rises. A rise in pH is sensed by central chemoreceptors in the medulla and CSF (Taylor, 1990b). Both CO<sub>2</sub> and H<sup>+</sup> concentration are reduced resulting in a decrease in ventilation. Thus reducing the elimination of CO<sub>2</sub> and reducing pH to within the normal range (Guyton and Hall, 2000). Arterial blood gas analysis will show a lowered PCO<sub>2</sub> (Coombs, 2001) and respiratory rate may be decreased in both depth and rate.

#### The binding of Hb and O<sub>2</sub> in alkaline states

When there is a decrease in CO<sub>2</sub> and H<sup>+</sup>, the pH will rise and consequently more oxygen remains





**Figure 3** Processes involved in respiratory and metabolic alkalosis. RAA = renin–angiotensin–aldosterone system.

bound to Hb in the tissues (Marieb, 2004).  $O_2$  delivery to cells is therefore reduced as the Hb/ $O_2$  bond is strengthened (The Bohr effect). This will maintain  $O_2$  saturation, but not cellular oxygen delivery. Therefore, the apparent normality of  $O_2$  saturation can be misleading in an alkalosis.

### Metabolic alkalosis ( $\uparrow pH$ $\uparrow HCO_3^-$ )

Metabolic alkalosis ( $HCO_3^- > 26$  mmol/L;  $pH > 7.40$ ) is the result of excess  $HCO_3^-$  or decreased  $H^+$  concentration, caused by an excessive loss of non-volatile or fixed acids (Fletcher and Dharpal, 2003). Metabolic alkalosis over excites central and peripheral nervous systems.

### Compensatory mechanisms for respiratory and metabolic alkalosis

When the body  $HCO_3^-$  increases in ECF, it binds with  $H^+$ . As the bicarbonate reaches excessive proportions  $H^+$  cannot bind with them sufficiently to buffer the consequences of pH and blood pH increases. The compensation for a respiratory or metabolic alkalosis occurs in the lungs, kidneys and by the release of  $H^+$  from cells.

#### The role of the lungs in compensation

In alkaline environments blood  $H^+$  has been lost or there is an excess base  $HCO_3^-$ . The unbound excess  $HCO_3^-$  elevates blood pH. The arterial blood

will show a pH above 7.45, a  $\text{PCO}_2$  below 4.5 kPa (35 mmHg) and  $\text{HCO}_3^-$  above 26 mmol/l. In an alkalosis blood and tissues give up more  $\text{H}^+$  as a compensatory response (Janusek, 1990). So as  $\text{HCO}_3^-$  starts to accumulate in the body  $\text{H}^+$  combine with it to form  $\text{H}_2\text{CO}_3$ , this chemical reaction buffers excess  $\text{HCO}_3^-$ .

An increase in blood pH is sensed in the CSF and depresses respiratory centre central chemoreceptors in the medulla. This reduces respiration,  $\text{CO}_2$  is retained in an attempt to increase blood  $\text{PCO}_2$  and decrease pH. However, this is limited since as the reduction in respiratory rate and depth lowers  $\text{O}_2$  levels. The reduced  $\text{CO}_2$  and  $\text{H}^+$  observed in a metabolic alkalosis combine to form two powerful respiratory inhibitory effects on the peripheral chemoreceptors opposing the excitatory effects of a diminished oxygen concentration (Guyton and Hall, 2000). A blood sample taken now will show decreasing  $\text{HCO}_3^-$  and pH as the body attempts to compensate (Woodrow, 2004).

#### The role of the kidneys in compensation

After approximately 6 h the kidneys start to increase excretion of  $\text{HCO}_3^-$  and reduce the excretion of  $\text{H}^+$ . This renal compensation returns the plasma  $\text{H}^+$  concentration towards normal (Holmes, 1993) and urine will be very alkaline with a high pH. To maintain electrochemical balance, excess sodium ions ( $\text{Na}^+$ ) and chloride ions ( $\text{Cl}^-$ ) are excreted along with  $\text{HCO}_3^-$ . This can lead to a hyponatraemia.

The decreasing pH may in turn cause the respiratory centre chemoreceptors to increase respiratory rate and consequently a compensatory hyperventilation may ensue. If the  $\text{PCO}_2$  becomes too low, due to the hyperventilation, this imposes a respiratory alkalosis on top of the metabolic alkalosis and hence metabolic compensation may not be adequate (Yucha, 2004). At this stage the patient could have bradypnea or Cheyne Stokes respiration.

A prolonged alkaline environment leads to vasoconstriction, which increases cerebral and peripheral hypoxia (Fig. 3). As alkalosis becomes more severe, calcium ions increasingly bind to proteins and so hypocalcaemia develops. This increases nerve excitability and muscle contractions (Koeppen, 1998). If left untreated an alkalosis can put excess strain on the heart and central nervous system.

#### Alkalosis in severe vomiting

An alkalosis can be seriously exacerbated if there is a severe drop in circulating volume e.g. in vomiting. In persistent vomiting of gastric contents, electrolytes are no longer available to the body from

the alimentary canal to replace those lost in the vomit and in urine ( $\text{Na}^+$ ,  $\text{Cl}^-$ ,  $\text{HCO}_3^-$ ). The principle electrolytes in addition to water lost as a result of vomiting gastric contents are:

- hydrochloric acid (hydrogen and chloride ions),
- sodium chloride (sodium and chloride ions).

The single electrolyte lost in greatest amounts is  $\text{Cl}^-$ , as a result the plasma  $\text{Cl}^-$  concentration falls. A loss of fluid and plasma volume due to vomiting can lead to a hypovolaemic state, which can affect acid base balance.

Compensation for a hypovolaemia will impose powerful compensatory mechanisms stimulating the kidney to release renin from the juxtaglomerular apparatus stimulating the adrenal gland to release aldosterone (Edwards, 2001b). The effect of aldosterone promotes sodium ( $\text{Na}^+$ ) and chloride ( $\text{Cl}^-$ ) reabsorption (and hence water) in the renal tubules to maintain circulating volume in exchange for  $\text{K}^+$  and  $\text{H}^+$  (Holmes, 1993).

The low concentration of chloride in the plasma results in a relatively small filtered load of  $\text{Cl}^-$  by comparison with  $\text{Na}^+$ . There are less chloride ions to balance the re-absorption of sodium. The body cannot respond by reducing  $\text{Na}^+$  re-absorption, which is required to restore circulating volume. The only mechanism available to the kidney is to increase the re-absorption of  $\text{Na}^+$  and  $\text{HCO}_3^-$  and consequently increase the excretion of  $\text{K}^+$  and  $\text{H}^+$ . Vomiting therefore leads to processes of  $\text{Na}^+$  and  $\text{HCO}_3^-$  re-absorption,  $\text{K}^+$  and  $\text{H}^+$  loss due to excess  $\text{Cl}^-$  depletion because of vomiting. This triggers mechanisms that are inappropriate in an existing alkalosis (Fig. 3). The retention of electrolytes and fluid during a hypovolaemia takes precedence over acid base homeostasis (Holmes, 1993).

A cautious intravenous infusion of isotonic sodium chloride solution at this stage may improve the patients' hypovolaemia (Janusek, 1990). The replacement of the principal ECF electrolytes necessary, e.g.  $\text{Na}^+$  and  $\text{Cl}^-$ , will return fluid volume towards normal. It switches the drive from retention of  $\text{Na}^+$  and  $\text{HCO}_3^-$  and excretion of  $\text{K}^+$  and  $\text{H}^+$ , to those of correction of metabolic alkalosis e.g. the retention of  $\text{H}^+$ ,  $\text{Na}^+$  and  $\text{Cl}^-$  and excretion of  $\text{K}^+$  and  $\text{HCO}_3^-$ , putting the acid base problem in order.

#### $\text{H}^+$ release from cells in exchange for ECF $\text{K}^+$

A decreased  $\text{H}^+$  level in ECF causes  $\text{H}^+$  to diffuse passively out of cells to buffer excess  $\text{HCO}_3^-$ . To maintain balance of charge across the cell membrane, ECF  $\text{K}^+$  moves into cells (Holmes, 1993). When  $\text{K}^+$  cannot be replaced by absorption in the alimentary tract there is a severe

depletion of the body's total ECF  $K^+$  content (hypokalaemia), which can ultimately lead to confusion and arrhythmias (Richards and Edwards, 2003).

## Conclusion

The primary function of the respiratory system is to supply an adequate amount of oxygen to tissues and remove carbon dioxide. The kidneys will excrete any excess acids or alkali. The respiratory and renal organs together with the blood maintain hydrogen ion concentration. Hydrogen ion concentration is one of the most important aspects of acid base homeostasis. When there is an increase or decrease in acid production by body tissues, the blood bicarbonate, proteins, and phosphate buffer body fluids or both. There comes a point in the disease process when these buffers can no longer maintain adequate concentrations of hydrogen ions. Patients admitted to hospital can have life threatening situations, which alter pH balance.

This article has attempted to provide the reader with a grounding in acid base physiology and its importance to the clinical practice of nursing. It is also hoped that the reader will be able to apply this knowledge in the interpretation of conditions that commonly occur in the real unpredictable environment of clinical practice.

## Appendix A. Short quiz to accompany acid base balance article

### A.1. Short answer questions

1. What are central and peripheral chemoreceptors, how do they relate to the maintenance of homeostasis in acid base conditions?
2. What are the normal arterial blood partial pressures concentrations of oxygen ( $O_2$ ), carbon dioxide ( $CO_2$ ) and bicarbonate ( $HCO_3^-$ )?
3. What do you know about any of the conditions that lead to an increase in acids and alkaline in the body?
4. What are the Haldane and Bohr effects in relation to exchange of gases in the lungs and tissues?
5. In model case one a diabetic patient is presented. What do you think happens to pH,  $PCO_2$ ,  $PO_2$ ,  $HCO_3^-$ , BE in this type of patient and why? Why is the effect of interventions so dramatic?

### Appendix A.1 (Continued)

6. Indicate which acid base imbalance, e.g. respiratory/metabolic acidosis or respiratory/metabolic alkalosis, is most likely to occur in the following conditions:
  - Hypoventilation
  - Excessive intake of antacids
  - Asthma attack
  - Prolonged vomiting
  - Hyperventilation
  - Pulmonary oedema
  - Prolonged diarrhoea resulting in excessive loss of bicarbonate
  - Cardiac arrest

### A.2. Multiple choice questions

1. When hydrogen chloride, a strong acid, is added to water, the pH of the resulting solution:
  - (a) goes up
  - (b) stays the same
  - (c) goes down
  - (d) cannot be determined
2. Hydrochloric acid:
  - (a) is an enzyme
  - (b) creates the acid condition within the stomach
  - (c) is found in the intestinal tract
  - (d) all of these
3. What is the barometric pressure at sea level in kPa?
  - (a) 99 kPa
  - (b) 100 kPa
  - (c) 101 kPa
  - (d) 108 kPa
4. What is the percentage of oxygen in inspired air?
  - (a) 15%
  - (b) 21%
  - (c) 26%
  - (d) 31%
5. What is the percentage of oxygen in alveolar air?
  - (a) 12%
  - (b) 14%
  - (c) 16%
  - (d) 21%
6. What is the percentage of carbon dioxide in inspired air?
  - (a) 4%
  - (b) 0.4%
  - (c) 0.04%
  - (d) 0.004%

## Appendix A.2 (Continued)

7. What is the percentage of carbon dioxide in alveolar air?  
(a) 3.2%  
(b) 4.5%  
(c) 5.5%  
(d) 6.2%
8. The normal pH of the blood is approximately:  
(a) 7.2  
(b) 7.4  
(c) 7.6  
(d) 7.8
9. A pH of 7.4 is equivalent to base excess (BE) of:  
(a) -2  
(b) -1  
(c) 0  
(d) +2
10. pH:  
(a) increases with acidity  
(b) is measured on a scale of 0–10  
(c) is a measure of the hydrogen ion concentration  
(d) reflects sodium content of body fluid
11. Chemicals that function to minimise changes in the pH of body fluids are called:  
(a) buffers  
(b) inhibitors  
(c) accelerators  
(d) activators
12. If hydrogen ion concentration in the blood increases, bicarbonate ions act as buffers by:  
(a) removing excess hydrogen ions from the plasma  
(b) releasing hydrogen ions into the plasma  
(c) dissociating into hydrogen and bicarbonate  
(d) combining with chloride ions
13. Which of the following is not a buffer system of the body?  
(a) bicarbonate buffer system  
(b) phosphate buffer system  
(c) protein buffer system  
(d) sodium chloride buffer system
14. Which of the following can play a role in buffering the pH of urine?  
(a) ammonia  
(b) bicarbonate ions  
(c) phosphate ions  
(d) all of the above
15. As a result of hyperventilation  
(a) the body pH decreases  
(b) the plasma partial pressure of carbon dioxide decreases  
(c) the kidney will increase the rate of hydrogen ion excretion

## Appendix A.2 (Continued)

- (d) more bicarbonate ions are added to the plasma
16. Once alkalosis has occurred, which of the following would you expect to happen?  
(a) increased respiratory rate  
(b) a plasma pH less than 7.4  
(c) retention of hydrogen ions by the kidney  
(d) increased renal reabsorption of bicarbonate ions
17. When normal buffer mechanisms are overwhelmed by excessive numbers of hydrogen ions, which of the following will result:  
(a) acidosis  
(b) alkalosis  
(c) all of the above  
(d) none of the above
18. A falling blood pH and a rising concentration of carbon dioxide due to emphysema, indicate:  
(a) metabolic acidosis  
(b) metabolic alkalosis  
(c) respiratory acidosis  
(d) respiratory alkalosis
19. Respiratory alkalosis can occur as a result of:  
(a) asphyxia  
(b) asthma  
(c) severe emphysema  
(d) hyperventilation
20. Prolonged vomiting of stomach contents will result in:  
(a) metabolic acidosis  
(b) metabolic alkalosis  
(c) respiratory acidosis  
(d) respiratory alkalosis
21. During exercise, ventilation initially increases due to:  
(a) increased blood carbon dioxide levels stimulating baroreceptors  
(b) decreased blood oxygen levels stimulating chemoreceptors  
(c) decreased blood pH levels stimulating baroreceptors  
(d) limb movements that stimulate the respiratory centre
22. An increase in blood CO<sub>2</sub> levels is followed by a(n) \_\_\_ in H<sup>+</sup> ions and a(n) \_\_\_ in blood pH:  
(a) decrease, decrease  
(b) decrease, increase  
(c) increase, increase  
(d) increase, decrease
23. Mr. Smith's plasma pH is 7.2. Which of the following indicates that the body is attempting to compensate and return the body pH to normal?

## Appendix A.2 (Continued)

- (a) an increase in respiration rate  
 (b) a decrease in respiration rate  
 (c) no change in respiration rate.
24. In renal compensation of acidosis:  
 (a) H<sup>+</sup> secretion decreases; bicarbonate excretion increases  
 (b) H<sup>+</sup> secretion decreases; bicarbonate reabsorption increases  
 (c) H<sup>+</sup> secretion increases; bicarbonate reabsorption increases  
 (d) H<sup>+</sup> secretion increases; bicarbonate excretion increases

## A.3. Model case 1

An 18-year-old man is seen in A&E. He has a history of recent weight loss (7 kg), blurred vision, general malaise, excessive thirst and frequency of micturition. On examination his skin and buccal mucosa appear dry. His breath smells of 'pear drops' and his breathing is deep and rapid (30 rpm).

A blood and urine sample is obtained. The results are as follows:

Plasma concentration  
 Sodium (Na<sup>+</sup>) = 135 mmol/L  
 Potassium (K<sup>+</sup>) = 6.5 mmol/L  
 Glucose = 55 mmol/L  
 Urinalysis  
 Glucose (++++)  
 Ketones (+++)  
 Other parameters NAD

Therapy is started at 1400 h. The patient is rehydrated using normal saline and a sliding scale of intravenous insulin is prescribed. The following parameters are monitored over the next few hours.

Time	Serum K <sup>+</sup> (mmol/L)	Serum glucose (mmol/L)
1400	6.5	55
1500	5.5	28
1600	4.5	18
1700	4.5	11
1800	3.5	5

Note: Return to normality of serum glucose but lower than normal K<sup>+</sup>, see text for details.

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