\( \dot{V}O_2 \) is identical to tissue \( \dot{V}O_2 \). This is extremely difficult to achieve clinically, particularly in mechanically ventilated subjects. Also determination of \( \dot{V}O_2 \) becomes progressively less accurate as \( F_O_2 \) increases.

Various alternative means of measuring \( \dot{V}O_2 \) which overcome some of these difficulties are available and may be more appropriate for clinical use. For example, a pneumotachograph can be used to measure inspired and expired volumes continuously, as described previously. This can be combined with continuous determination of \( F_O_2 \) and \( F_O_2 \) to obtain \( \dot{V}O_2 \). \( \dot{V}CO_2 \) can also be determined if \( F_CO_2 \) is measured (\( F_CO_2 \) can be assumed to be zero). This allows calculation of the respiratory quotient (RQ).

A suitable device for use in critically ill patients is the *Deltatrac* (Datex/Instrumentarium, Helsinki, Finland). This system measures the difference between \( F_O_2 \) and \( F_O_2 \) using a fast-response, paramagnetic differential oxygen sensor; \( F_CO_2 \) is measured with an infrared carbon dioxide analyser. Expired air is collected through an inbuilt mixing chamber and flow is measured by gas dilution. Spontaneously breathing patients can be studied using a canopy system (Takala *et al.*, 1989).

### BLOOD GAS ANALYSIS AND ACID–BASE DISTURBANCES

In the early days of intensive care, blood gas analysis was performed using the equilibration technique. This method, developed over 40 years ago by Professor Astrup, was a relatively time-consuming procedure and required a degree of technical expertise. Combined with the reluctance of clinicians to puncture arteries, this meant that blood gas analysis was performed only rarely.

The original Astrup trolleys consisted of a pH electrode and a microtonometer, but some of the later versions also included a direct-reading Clark electrode for the determination of blood oxygen tension. Subsequently, the equilibration technique was superseded by the commercial development of the direct-reading \( PCO_2 \) electrode and all three were then sufficiently miniaturized to be incorporated in a single cuvette, allowing measurements to be performed on one blood sample. Following the introduction of the microprocessor, automation of most of the processes involved became feasible and modern automated blood gas analysers were soon available commercially. At the same time, there was an increasing acceptance of the ease and relative safety of arterial puncture and cannulation. Consequently, arterial blood gas analysis is now one of the most commonly performed objective tests of respiratory function.

As well as direct measurements of \( H^+ \) activity (expressed as \( pH \) or \([H^+]\)), \( PO_2 \) and \( PCO_2 \), other values relevant to the assessment of the patient’s oxygenation and acid–base status are measured or calculated. Most analysers include the option to incorporate ion-sensitive electrodes for measurement of \( Na^+ \), \( K^+ \), \( Cl^- \), and \( Ca^{2+} \), as well as lactate. Some also include an oximeter for measurement of haemoglobin concentration and oxygen saturation.

More recently the traditional electrodes have been miniaturized and reformed into electrochemical sensors that can be imprinted on a card and combined with a disposable cartridge containing a supply of calibrating reagents, allowing analysis to be performed at the bedside (point-of-care analysers). There is, however, some concern about the reliability and accuracy of these devices, especially in relation to the measurement of haemoglobin and oxygen saturation.

#### ACCURACY OF BLOOD GAS ANALYSIS

Automation of measurement, calculation and display can give a false impression of reliability and accuracy. This may lead to an uncritical acceptance of the results obtained. The clinician must therefore be aware of the potential sources of error when performing blood gas analysis and of the ways in which these can be minimized.

#### Sampling

In the past, it was recommended that glass syringes should be used to obtain the arterial sample. These were said to have two advantages:

- the plunger moves freely, allowing arterial blood to flow into the syringe under its own pressure;
- glass is an efficient barrier to diffusion of gases out of the sample.

In fact, most clinicians find an ordinary plastic syringe, with a continuous negative pressure applied to the plunger, quite satisfactory, and in practice diffusion of gases into the wall of the syringe is not a problem. Purpose-designed, pre-heparinized plastic syringes are also available, but are expensive.

*Continuing metabolism of white blood cells*, and to a lesser extent reticulocytes, can cause significant reductions in \( PO_2 \) and \( pH \), combined with increases in \( PCO_2 \), particularly when the initial gas tension is high. If the sample cannot be analysed immediately (within a few minutes), metabolism can be slowed by immersing the syringe in iced water, having first sealed the end with a plastic cap (Biswas *et al.*, 1982).

To prevent clot formation within the analyser, the sample must be adequately anticoagulated. On the other hand, *excessive dilution of the blood with heparin*, which is acidic, will significantly reduce its \( PCO_2 \), although dilution probably has little effect on \( pH \) or \( PO_2 \) (Bradley, 1972). Therefore, heparin should be used in a concentration of 1000 u/mL, and the volume limited to that contained within the dead space of the syringe (i.e., approximately 0.1 mL). Although this will adequately anticoagulate a 2-mL sample, it is not sufficient for the unnecessarily large volumes of blood sometimes presented for analysis.

Even with the most careful technique, air almost inevitably enters the sample. The gas tensions within these *air bubbles* will equilibrate with those in the blood, thereby lowering the \( PCO_2 \) and usually raising the \( PO_2 \) of the sample.
Measurement errors

**pH ELECTRODES**

Although the traditional pH notation is still used extensively, many now refer to the hydrogen ion concentration ([H\(^+\)]) in nmol/L. The measurement of H\(^+\)/pH is prone to error, the commonest cause of erroneous readings being contamination of the electrode with blood proteins.

**PCO\(_2\) ELECTRODES**

PCO\(_2\) measurements are generally very accurate. When errors do arise they are usually associated with the development of holes in the electrode membrane or, less often, loss of the silver chloride coating on the reference electrode. The membrane can be replaced relatively easily, but in the latter instance a new electrode is required. Since holes in the membrane occur fairly frequently, there is usually no time for protein contamination to become a problem.

**PO\(_2\) ELECTRODES**

The current output of the oxygen electrode is less for blood than for a gas with an identical PO\(_2\). This discrepancy is called the blood gas factor and is peculiar to oxygen electrodes. It is thought to be due to consumption of oxygen by the electrode from blood immediately adjacent to the tip of the cathode. This generates a gradient of oxygen tension across the sample and causes the electrode to under-read. The blood gas factor has a proportionately greater effect on the absolute value of PO\(_2\) at higher oxygen tensions. Furthermore, loss of oxygen into the plastic walls of the cuvette and tubing increases as PO\(_2\) rises; therefore, considerable care is necessary to obtain accurate measurements of oxygen tension when PO\(_2\) is high. As with the other electrodes, protein contamination may also cause problems.

**Quality control and maintenance**

It is essential that on-site equipment that is used extensively out of hours by both medical and nursing staff is subject to strict quality control procedures and regular maintenance. Although automated blood gas analysers are self-calibrating, they should be checked regularly with quality control material, preferably daily. Ampoules containing buffered liquid of known pH and blood gas tensions are available for this purpose. The discrepancy between the measured and the known standard values can then be recorded. Any deviation of these figures outside the predetermined limits indicates a significant fault in the relevant electrode. This can then be remedied (e.g. by replacing the membrane). In practice, however, it is more usual to avoid problems by changing the membranes according to the manufacturer’s instructions or when prompted by the analyser. Although buffered liquids can detect the majority of errors associated with the O\(_2\) and CO\(_2\) electrodes, they may fail to demonstrate protein contamination of the pH electrode. The latter can be avoided by cleaning the electrode at regular intervals.

**INTERPRETATION OF BLOOD GASES AND ACID–BASE STATUS**

The range of normal values obtained when blood gas analysis is performed are shown in Table 6.2.

**Total or actual bicarbonate concentration**

Total or actual bicarbonate concentration is influenced by alterations in the amount of carbon dioxide, and by metabolic changes in the amounts of acid and alkali in the blood. It is calculated from the Henderson–Hasselbalch equation (see later).

**Standard bicarbonate**

The standard bicarbonate concentration can be derived to assess the contribution of metabolic factors, disregarding changes due to alterations in PCO\(_2\). The standard bicarbonate is the amount of bicarbonate that would be present in the sample if the PCO\(_2\) was 5.3 kPa (40 mmHg), the temperature was 37°C and the blood was fully oxygenated at sea level.

**Base deficit**

Base deficit is simply a convenient number for calculating the amount of sodium bicarbonate required to correct a metabolic acidosis. It is calculated as the amount of base that needs to be added to or subtracted from each litre of extracellular fluid to return the pH to a value of 7.4 at a PCO\(_2\) of 5.3 kPa (40 mmHg) at 37°C. Most often, the clinician is given the base excess, which is negative if there is a base deficit (i.e. a metabolic acidosis) and positive if there is a metabolic alkalosis.

**Saturation of haemoglobin with oxygen**

Automated blood gas analysers can also calculate the saturation of haemoglobin with oxygen using one of the mathe-
matical formulae describing the oxyhaemoglobin dissociation curve. This calculation is usually performed assuming that the curve is normally positioned, although in some shifts caused by pH changes are taken into account. Percentage saturation is closely related to the oxygen content of the blood, which, as discussed in Chapter 3, can be of more clinical relevance than the PO₂. Some analysers will also calculate oxygen content, either assuming a value for the haemoglobin concentration or by using a value entered by the operator. Others measure haemoglobin concentration optically. The calculation also assumes that all the haemoglobin is available to bind oxygen, (i.e. there is no met- or carboxyhaemoglobin present). Increasingly, modern automated blood gas analysis measures the haemoglobin concentration and the saturation of haemoglobin with oxygen, as well as carboxy – and met – haemoglobin directly using an oximeter.

The interpretation of these results can be considered in two separate parts: disturbances of carbon dioxide homeostasis and acid–base balance, and alterations in oxygenation. In all cases, the following information is essential for correct interpretation:
- the history;
- the age of the patient;
- the PO₂;
- any other relevant treatment (e.g. the administration of sodium bicarbonate and the ventilator settings for those on mechanical ventilation).

**DISTURBANCES OF ACID–BASE BALANCE**

All enzymatically driven biological reactions have optimum values for pH at which the reaction proceeds most rapidly. Alterations in pH can, therefore, lead to a state of ‘metabolic chaos’ in which some reactions proceed faster than they should, while others slow down. The pH also affects the degree of ionization of various molecules (e.g. an alkalosis causes ionized calcium to bind to protein and may precipitate tetany), as well as altering hydrogen bonding and protein structure. The distribution of ions across cell membranes is also influenced by the quantity of H⁺ ions in the body. Severe metabolic acidosis can cause cerebral and myocardial depression, while the respiratory centre is stimulated initially, but is subsequently depressed as the acidoses becomes more severe. A marked metabolic alkalosis may combine with an associated hypokalaemia to depress cardiac function. As discussed in Chapter 3, changes in both pH and PCO₂ cause shifts of the oxyhaemoglobin dissociation curve.

The body therefore resists changes in pH using a variety of buffer systems, as well as by regulating the renal excretion of non-volatile acids and bases and adjusting minute ventilation to control the arterial carbon dioxide tension.

**Buffer systems**

A buffer is a mixture of a weak acid (which, in contrast to a strong acid, is only partially dissociated in water) and its conjugate base. In the body, the main buffer systems are carbonic acid/bicarbonate, phosphates and proteins.

For the phosphate system: \( \text{H}_2\text{PO}_4^- \rightleftharpoons \text{H}^+ + \text{HPO}_4^{2-} \)

For the carbonic acid/bicarbonate system: \( \text{H}_2\text{CO}_3 \rightleftharpoons \text{H}^+ + \text{HCO}_3^- \)

At equilibrium the law of mass action applies and states that the product of the concentrations of \( \text{H}^+ \) and \( \text{HCO}_3^- \) divided by the concentration of \( \text{H}_2\text{CO}_3 \) will remain constant. That is:

\[
K = [\text{H}^+] \left[ \text{HCO}_3^- \right]/[\text{H}_2\text{CO}_3]
\]

Henderson rearranged this equation to allow calculation of the \( [\text{H}^+] \):

\[
[\text{H}^+] = K[H_2\text{CO}_3]/[\text{HCO}_3^-]
\]

Later Hasselbalch modified this equation using the pH nomenclature:

\[
\text{pH} = \text{pK} + \log[\text{HCO}_3^-]/[\text{H}_2\text{CO}_3]
\]

Buffer systems are most effective when they are maximally dissociated, that is, when the pH is close to their dissociation constant (pK). Protein is an effective intracellular buffer because its pK is similar to the intracellular pH (7.0), while the pK of haemoglobin is 7.4. The pK of the phosphate system is 6.8, but that of the bicarbonate system is only 6.1. Nevertheless, the latter is of particular interest to clinicians because it is present in large amounts, its components can be measured and it is influenced by renal and respiratory compensatory mechanisms.

\[
\begin{align*}
\text{H}^+ + & \text{HCO}_3^- \rightleftharpoons \text{H}_2\text{CO}_3 \quad & \text{Ionic dissociation} \\
& \text{Carbonic anhydrase} & \text{Kidneys} \\
\text{CO}_2 + & \text{H}_2\text{O} \downarrow \quad & \text{Lungs} \\
\text{CO}_2(\text{gas}) & \downarrow & \text{phase}
\end{align*}
\]

Alterations in minute ventilation can rapidly compensate for metabolic abnormalities by adjusting \( P_{\text{CO}_2} \), while renal mechanisms operate over a longer time course and can also compensate for respiratory disturbances. Renal regulation of H⁺ balance is achieved by reabsorption or excretion of filtered HCO₃⁻, excretion of ammonia or excretion of titratable acidity. Electrical neutrality is usually maintained by reabsorption of Na⁺.

The haemoglobin within circulating red blood cells also acts as a buffering system. Carbon dioxide in plasma diffuses into red cells down a concentration gradient. Within erythrocytes CO₂ is converted to HCO₃⁻, which diffuses back into the plasma, in a reaction catalysed by carbonic anhydrase. The H⁺ generated in this reaction is buffered by combination with haemoglobin. Electrical neutrality is maintained by the movement of Cl⁻ ions from plasma into the cells (chloride shift).

Since \( [\text{H}_2\text{CO}_3] \) is proportional to the \( P_{\text{CO}_2} \), the Henderson–Hasselbalch equation can be rewritten as:

\[
[H^+] \propto P_{\text{CO}_2}/[\text{HCO}_3^-]
\]

\( P_{\text{CO}_2} \) can therefore be plotted against \( [H^+] \) (or pH) and the various acid–base disturbances described in relation to this diagram (Fig. 6.8). Both acidosis and alkalosis can occur, and
either may be metabolic (i.e. primarily affecting the bicarbonate component of the system) or respiratory (i.e. primarily affecting $P_{CO_2}$). Compensatory changes may also appear. In clinical practice, arterial [H+] values outside the range 18–126 nmol/L (pH 6.9–7.7) are very rarely encountered. There is no scientific justification for routinely temperature-correcting blood gas measurements when body temperature is altered, although some recommend correction during hypothermic cardiopulmonary bypass.

**Respiratory acidosis**

Respiratory acidosis is caused by retention of carbon dioxide; the $P_{CO_2}$ and [H+] rise (see Fig. 6.8). Sometimes there is a small increase in $HCO_3^-$. A chronically raised $P_{CO_2}$ is compensated by renal retention of bicarbonate and [H+] returns towards normal. A constant arterial bicarbonate concentration is then usually established within 2–5 days. This represents a primary respiratory acidosis with a compensatory metabolic acidosis. It is worth recognizing that because treatment such as the administration of diuretics can exacerbate hypochloraemia and produce further retention of bicarbonate, [H+] may be on the low side of normal, even when carbon dioxide retention is the primary abnormality.

Common causes of respiratory acidosis include ventilatory failure and chronic obstructive pulmonary disease (COPD, type II respiratory failure; see Chapter 8).

**Respiratory alkalosis**

In respiratory alkalosis the reverse occurs, with a fall in $P_{CO_2}$ and [H+] (see Fig. 6.8), often with a small reduction in bicarbonate concentration. If hypocarbia persists some degree of renal compensation may occur, producing a metabolic acidosis, although in practice this is unusual. A respiratory alkalosis is often produced intentionally or un-
**Type A lactic acidosis.** This is more common and is due to inadequate tissue perfusion, cellular hypoxia and anaerobic glycolysis. The ability of the liver to remove the excess lactic acid is often impaired by underperfusion, as well as by severe acidosis, and in extreme cases the liver may actually produce, rather than consume, lactate. The clinical picture is usually dominated by the underlying cause and treatment is directed at reversing tissue hypoxia (see Chapter 5).

**Type B lactic acidosis.** This occurs in the absence of tissue hypoxia. In the past, the most common cause was the administration of phenformin to patients with impaired renal or hepatic function. Other causes include diabetic ketoacidosis (see Chapter 17), severe liver disease (see Chapter 14), intravenous infusion of sorbitol or fructose, ethanol ingestion, methanol poisoning (see Chapter 19), acute infections and rare hereditary disorders (e.g. glucose-6-phosphate dehydrogenase deficiency). Renal failure is commonly present, but is probably not a cause in itself. The patient usually presents with marked hyperventilation, which may progress to drowsiness, vomiting and eventually coma. Blood pressure is normal, there is no cyanosis and the patient is well perfused.

Treatment of severe type B lactic acidosis involves removal of the precipitating cause and the intravenous administration of sodium bicarbonate; it may prove to be extremely difficult to reverse the acidosis and very large amounts of bicarbonate may be required (e.g. 1000 mmol). Therefore, some recommend that the first 2–3 litres are given as an isotonic (1.4%) solution, followed by 8.4% sodium bicarbonate. The large volumes of fluid required may precipitate volume overload and pulmonary oedema. Haemofiltration has been advocated for resistant cases.

**Metabolic alkalosis**

Metabolic alkalosis can be caused by loss of acid (e.g. from the stomach with nasogastric suction or in high intestinal obstruction) or by excessive administration of absorbable alkali. Overzealous treatment with intravenous sodium bicarbonate is sometimes implicated. In such causes of metabolic alkalosis the urinary chloride concentration is usually low. Some less common causes of metabolic alkalosis in which urinary chloride is high include hyperaldosteronism, Cushing’s syndrome, ingestion of liquorice and severe potassium deficiency. Depletion of the extracellular fluid volume and a reduction in total body potassium are both important precipitating factors in the development of metabolic alkalosis. Contraction of the extracellular compartment causes increased sodium reabsorption in exchange for hydrogen ions. The latter are lost in the urine and bicarbonate reabsorption is increased. Similarly, potassium depletion stimulates the kidneys to retain potassium in exchange for hydrogen ions. Diuretics are frequently implicated in both extracellular fluid volume depletion and hypokalaemia.

Respiratory compensation for a metabolic alkalosis is often slight and it is rare to encounter a $P_{\text{CO}_2} > 6.5$ kPa (50 mmHg), even with severe alkalosis.

Treatment consists of correcting the underlying cause; specific treatment is rarely required. If severe alkalosis persists, despite restoring the extracellular fluid volume and correction of potassium depletion, the carbonic anhydrase inhibitor acetazolamide or, very occasionally, intravenous hydrochloric acid may be indicated. There is evidence that a single intravenous dose of acetazolamide 500 mg is as effective as 250 mg every 6 hours for a total of four doses, and reverses metabolic alkalosis for a prolonged period (Mazur *et al.*, 1999).

**Interpreting the acid–base status**

Proced as follows (Table 6.2):

- Look at the pH to see whether the patient is acidic or alkalotic.
- Look at the $P_{\text{CO}_2}$ to determine whether there is a respiratory component. If the $P_{\text{CO}_2}$ is high, there is a respiratory acidosis; if it is low, there is a respiratory alkalosis.
- Look at the standard bicarbonate and the base excess. If the standard bicarbonate is low and the base excess is negative (i.e. there is a base deficit), there is a metabolic acidosis. If the standard bicarbonate is high and the base excess is positive, there is a metabolic alkalosis.
- Although the primary abnormality is often indicated by the direction of the pH change, this is not always the case. The nature of the primary abnormality can then only be determined by considering the clinical context in which it has arisen.

It should be noted that, during cardiac arrest and in severe circulatory failure, carbon dioxide tension may be considerably higher and pH markedly lower in venous blood than in arterial blood. This discrepancy is particularly marked when $P_{\text{CO}_2}$ is controlled by mechanical ventilation and may be exacerbated by the administration of sodium bicarbonate (Adrogüe *et al*., 1989). Therefore, it has been suggested that a widened arteriovenous $P_{\text{CO}_2}$ difference may be a useful indicator of circulatory failure and that analysis of venous blood may provide a better guide to tissue acid–base status.

**AN ALTERNATIVE APPROACH TO UNDERSTANDING ACID–BASE PHYSIOLOGY** (*Sirker et al.*, 2002)

Because the Henderson–Hasselbalch approach to analysing acid–base disorders is relatively easy to understand and apply, this method is still by far the most widely used in clinical practice. There are, however, some problems with interpretation. These include the supposition that $\text{HCO}_3^-$ and $P_{\text{CO}_2}$ are independently adjusted variables that ultimately determine pH and the assumption that the dissociation equilibrium for carbonic acid is used as the control system for setting pH (*Sirker et al.*, 2002). Another limitation of the traditional approach is that the various possible causes of a metabolic acidosis can only be distinguished by calculating the anion gap (see above).
Stewart (1983) therefore proposed an alternative approach which used fundamental principles of physical chemistry to identify factors that must determine the pH of biological solutions. The principles employed were those of electrical neutrality and the conservation of mass, combined with the requirement that the dissociation equilibria of all incompletely dissociated substances must be satisfied at all times. These principles were then applied to the various components which constitute fluids in the human body (i.e. water, strong ion solutions in water, weak acid or buffer solutions in water and solutions containing carbon dioxide). Stewart was able to show that three independent variables determine pH in plasma by altering the degree of dissociation of water into H\(^+\) ions. These three directly measurable, independent variables were:

1. The strong ion difference (SID). (A strong ion is defined as an ion which is effectively fully dissociated in biological solutions.) The SID is the net charge difference between the sum of the measured strong plasma cations (Na\(^+\), K\(^+\), Ca\(^{2+}\) and Mg\(^{2+}\)) and strong plasma anions (Cl\(^-\), lactate\(^-\)). In a patient with a normal acid–base status the SID is usually 38–42 mEq/L. This charge difference is called the effective SID;

2. Total weak acid ([A\(_{TOT}\)]) (mainly albumin and inorganic phosphate);

3. Carbon dioxide in solution (PCO\(_2\)).

This approach postulates that both HCO\(_3^-\) and H\(^+\) are dependent variables and that HCO\(_3^-\) cannot be independently adjusted to regulate pH.

Using the Stewart approach the direct contribution of unmeasured anions to a metabolic acidosis can be accurately quantified, thus defining the cause, and acid–base disorders can be classified on the basis of alterations in the independent variables. Thus, as with the traditional approach, respiratory disorders are those primarily attributable to changes in carbon dioxide, whilst changes in SID represent the compensatory response. A metabolic alkalosis will occur if there is an increase in plasma SID or a fall in [A\(_{TOT}\)], whereas an increase in [A\(_{TOT}\)] or a decrease in plasma SID will cause a metabolic acidosis.

The kidneys are the most important regulators of SID for acid–base purposes; because [Na\(^+\)] and [K\(^+\)] must be tightly controlled for other functions (e.g. maintenance of intravascular volume and neuromuscular function respectively), the kidneys use Cl\(^-\) to regulate acid–base status without interfering with other important homeostatic mechanisms. Thus, for example, compensation for a respiratory acidosis involves urinary excretion of Cl\(^-\) (together with ammonium cations) which increases the SID, whereas correction of an alkalosis is achieved by renal tubular resorption of Cl\(^-\), with a consequent reduction in SID. Similarly, the chloride shift in red cells described above can raise plasma SID and help to compensate for increased plasma carbon dioxide concentration. This approach emphasizes the importance of chloride in acid–base disturbances and can explain the metabolic acidosis commonly observed in patients who have received large volumes of normal saline, which, unlike plasma, contains equal amounts of sodium and chloride. The resulting hyperchloremia reduces plasma SID and causes an increase in [H\(^+\)]. Similarly, the loss of large amounts of Cl\(^-\) in gastric fluid will increase plasma SID and cause a metabolic alkalosis. Because there are no known mechanisms that control ([A\(_{TOT}\)]) for the purpose of acid–base regulation, some authorities do not classify alterations in pH caused by changes in [A\(_{TOT}\)] as acid–base disorders.

The strong ion difference gap (SIG) is calculated as the difference between the SID and the effective SID. The normal range for the SIG is zero, implying that there are very few strong ions other than Na\(^+\), K\(^+\), Ca\(^{2+}\), Mg\(^{2+}\) and Cl\(^-\) in the plasma of healthy individuals. The ions which may increase the SIG are the same as those which can cause an elevated anion gap or normochloremic metabolic acidosis (see above), as well as a number of other unidentified strong anions which can be detected in critically ill patients. In critical illness the relationship between the SIG and the anion gap can be improved by correcting the latter for the charge contribution from protein and phosphate.

Although Stewart’s approach provides useful insights into the mechanisms by which the body regulates pH and the causes of acid–base disturbances (particularly the relevance of Cl\(^-\) ion homeostasis), the cumbersome mathematical equations required have so far limited the introduction of this method into routine clinical practice, although a simplified approach suitable for use in clinical practice has recently been described (Story et al., 2004).

**ALTERATIONS IN OXYGENATION**

Having interpreted the acid–base state, the adequacy of oxygenation can be evaluated. When interpreting the PO\(_2\) it is important to remember that it is often the oxygen content of the arterial blood (C\(_O_2\)) that is most relevant clinically; this is determined by the percentage saturation of haemoglobin with oxygen. The latter is related to the PO\(_2\) by the oxyhaemoglobin dissociation curve. The clinical significance of the dissociation curve is discussed in Chapter 3, but it is most important to consider the PO\(_2\) in conjunction with the percentage saturation of haemoglobin with oxygen; in general, if the latter is greater than 95%, oxygenation can be considered to be adequate. Remember that P\(_O_2\) is influenced by factors other than pulmonary function, including alterations in the mixed venous oxygen tension (P\(_{vO_2}\)) caused by changing metabolic rate and/or cardiac output, and shifts in the position of the dissociation curve (see Chapter 3). Also the normal range for P\(_O_2\) decreases with age, although in subjects more than 74 years old there is a tendency for this trend to reverse. In the age group 40–74 years, P\(_O_2\) is influenced by age, body mass index (BMI) and P\(_{CO_2}\) such that:

\[
P_{O_2} (\text{mmHg}) = 143.6 - (0.39 \times \text{age}) - (0.56 \times \text{BMI}) - (0.57 \times P_{CO_2})
\]

(Cerveri et al., 1995).


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