spontaneous effort is assisted with an increase in inspiratory pressure to a predetermined level that increases tidal volume and reduces the work of breathing. Inspiration is terminated when the inspiratory flow rate drops significantly below the peak inspiratory flow rate (usually to 25% of peak flow). Pressure support is used with SIMV, during weaning and as a full support mode when respiratory drive is normal and work of breathing is not excessive.

Ventilator-associated lung injury - laboratory studies and recent clinical trials have demonstrated that exposing already injured lungs to excessive tidal volume and pressure results in an insidious and progressive worsening of the underlying lung injury. Overdistension (volutrauma) and tidal lung recruitment-derecruitment (atelectrauma) appear to be the important mechanisms. Barotrauma describes extrapulmonary air (pneumothorax, subcutaneous emphysema or mediastinal emphysema) and appears to be more a consequence of exposing injured lungs to positive-pressure ventilation rather than excessive airway pressure.

Initiating mechanical ventilation - regardless of the mode, tidal volume should be 8-10 ml/kg ideal body weight in normal lungs and no more than 6-8 ml/kg in acute lung injury. The end-inspiratory plateau pressure (P_{plat}) reflects alveolar distension and should usually be limited to a maximum of 30 cm H_2O. P_{plat} depends on the delivered tidal volume and not the mode of ventilation. Depending on the ventilator, the inspiratory phase is set by adjusting the inspiratory:expiratory ratio (I:E), inspiratory flow rate or inspiratory time. A short inspiratory time may be appropriate to limit auto-PEEP in airway obstruction, while longer times may be used to improve oxygenation in acute lung injury. The respiratory rate depends on the required minute ventilation which should be set according to the pH rather than the $PaCO_2$.

Oxygen and positive end-expiratory pressure (PEEP) - the PaO_2 is maintained above 8 kPa by adjusting the inspired oxygen tension and level of PEEP. Prolonged exposure to high inspired oxygen should be avoided to reduce the risk of pulmonary oxygen toxicity. Excessive PEEP increases the risk of barotrauma and may reduce cardiac output and oxygen delivery. PEEP can be set according to the lower inflection point of the static pressure-volume curve or from the value that results in the greatest improvement in compliance. However, empirical titration of PEEP and fractional concentration of inspired oxygen (FiO_2) to the target PaO_2 appears to be a pragmatic and effective method (Figure 2).

Complications - tension pneumothorax, though rare, should be considered if hypotension, poor gas exchange and increased airway pressures (in volume modes) occur after the initiation of mechanical ventilation. Treatment requires emergency needle thoracocentesis. More commonly, hypotension is due to hypovolaemia compounded by the effects of raised intrathoracic pressure impairing venous return. In airway obstruction (asthma, COPD) excessive auto-PEEP may occur if there is inadequate time for expiration and profound hypotension may occur. Rapid improvement following disconnection from the ventilator is confirmatory and prevention includes increasing expiratory time and treating the underlying bronchoconstriction. ◆

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Acid-base and blood gas analysis

Sheena M A Hubble

The concentration of hydrogen ions in blood plasma is very tightly regulated and in contrast to most other ions, is maintained in the nanomolar (36-43 nmol/litre) rather than the millimolar range. This is because the high charge density and large electrical field surrounding the hydrogen ion influences nearly all biochemical processes, including protein structure and function, ionic dissociation and movement, and chemical or drug reactions.

The pH is the negative $\log_{10}$ of the hydrogen ion (H^+) concentration with a normal value at 37°C of 7.34-7.42, which is equivalent to a $[H^+]$ of 37-46 nmol/litre. Acid load comes primarily from cellular respiration as carbon dioxide via carbonic acid (15,000-20,000 mmol H^+/day) and to a lesser extent from the metabolism of fats and proteins (50 mmol/day).

Defence of normal body pH is traditionally thought to be achieved through the three following basic mechanisms.

- Respiratory control of the partial pressure of carbon dioxide in arterial blood ($PaCO_2$) by the respiratory centre, which regulates alveolar ventilation. The higher the concentration of $[H^+]$ the more CO_2 (volatile acid) is expired from the lungs, which is a rapid and powerful compensatory system.
- Renal bicarbonate control and excretion of metabolic (non-volatile) acids, which is a relatively slow system (hours to days).
- Buffering by bicarbonate, sulphate and haemoglobin, which minimizes acute changes.

Traditional approach to altering pH

The traditional approach to acid-base control centres round the Henderson-Hasselbalch equation, which describes the carbonic acid buffer system, fundamental to respiratory and renal control of pH. The reaction of carbon dioxide with water forms carbonic acid, which dissociates to form bicarbonate and H^+ ions:

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

If by the law of mass action:
$[H^+][HCO_3^-]/[H_2CO_3] = k$ (constant).

Sheena M A Hubble *is Consultant in Intensive Care Medicine and Anaesthesia at the Royal Devon and Exeter Hospital, UK. She qualified from Bristol University in 1991 and trained in medicine, anaesthesia and intensive care in the South-West. Her research interests include lactate, the microcirculation and intensive care patient follow up.*

Then by rearranging and taking logs of both sides:
pH = pKa + log ([HCO_3^-]/ [0.03 × pCO_2 mm Hg]) where the pKa value at 37°C is 6.1.

From this equation, pH can be defined as the ratio of bicarbonate to carbon dioxide. Therefore, alterations in acid–base result from either changes in CO_2 (respiratory) or changes in HCO_3^- (metabolic) and compensatory mechanisms exist to maintain this ratio (normally 20:1).

The Henderson–Hasselbalch equation does not quantify metabolic derangement as clearly as respiratory derangement because HCO_3^- is dependent on pCO_2 *in vivo*. The concepts of standard bicarbonate and standard base excess or deficit were introduced to assist with quantifying the metabolic derangement. Standard bicarbonate is the calculated bicarbonate value that would be present if the blood sample was adjusted to a pCO_2 of 40 mm Hg (5.3 kPa) and therefore removes the respiratory component of the acid–base abnormality to reveal any metabolic derangement. Standard base excess or deficit quantifies the amount of acid in mmol/litre that must be added or subtracted from the same blood sample to regain a normal pH at a pCO_2 of 40 mm Hg. Figure 1 summarizes the expected changes in HCO_3^-, pCO_2 and standard base excess in the range of primary acid–base disorders.

Blood gas analysers directly measure pH, pCO_2 and pO_2. Bicarbonate is calculated from a modified Henderson–Hasselbalch equation, while standardized HCO_3^- and base excess are derived from computerized nomograms.

Respiratory acidosis (primary change ↑pCO_2 and compensatory change ↑HCO_3^-): elevation of pCO_2 above the normal range indicates inadequate alveolar ventilation as a result of respiratory muscle failure, CNS pathology or drug intoxication. Other causes include excess CO_2 production in hypercatabolic states, inadequate ventilator minute volume or administration of exogenous CO_2 (e.g. peritoneal insufflation during laparoscopy). Renal compensation by increased H^+ excretion and bicarbonate retention takes some days to be complete. Once this has occurred, sudden correction to a normal pCO_2 reveals the associated metabolic alkalosis.

Respiratory alkalosis (primary change ↓pCO_2 and compensatory change ↓HCO_3^-): the primary cause is usually alveolar hyperventilation causing a fall in $PaCO_2$. It is important to examine the PaO_2 and determine whether hyperventilation is compensating for arterial hypoxia and underlying lung pathology. Central causes include pain, anxiety and CNS disease. Iatrogenic overventilation is a common cause in critical-care patients. Renal compensation causes a fall in measured bicarbonate and potassium if the process is chronic.

Metabolic acidosis (primary change ↓HCO_3^- and compensatory change ↓pCO_2) results from a primary metabolic abnormality (i.e. fall in HCO_3^- or gain of acid). Alveolar hyperventilation occurs in an attempt to lower CO_2 and attenuate the fall in pH. This respiratory compensation is often rapid and profound in spontaneously breathing patients. When instituting mechanical ventilation in a patient with severe metabolic acidosis, targeting a normal $PaCO_2$ worsens the acidosis because the respiratory compensation is inadequate.

Assessing the cause of metabolic acidosis is aided by calculation of the anion gap. Blood contains anions and cations and the laws of electrical neutrality dictate that:

- the sum of cations = the sum of anions
- $Na^+ + K^+$ + unmeasured cations = $Cl^- + HCO_3^-$ + unmeasured anions
- anion gap = $(Na^+ + K^+) - (Cl^- + HCO_3^-)$ = 10–12 mmol/litre.

High anion gap acidosis is caused by unmeasured anions such as lactate, ketoacids, exogenous acids (e.g. salicylates) or ethanol. Inadequate tissue oxygen delivery because of either low PaO_2 or poor perfusion is a common cause of lactic acidosis in critically ill patients. Renal failure increases the anion gap due to accumulation of organic acids.

Normal anion gap acidosis is often due to hyperchloraemia and loss of bicarbonate or retention of H^+. Causes include renal tubular acidosis, gastrointestinal losses, ureteric fistulae, acetazolamide therapy or the administration of large volumes of intravenous normal saline.

The accuracy of the anion gap is questionable in critically ill patients who are often acidotic and hypoalbuminaemic. The normal range of anion gap can be adjusted according to the patient's albumin and phosphate concentration:

Normal anion gap = 0.2 × albumin g/litre + 1.5 × phosphate mmol/litre.

Metabolic alkalosis (primary change ↑HCO_3^- and compensatory change ↑pCO_2) is commonly iatrogenic, related to the administration of diuretics (especially furosemide), hypokalaemia or chronic hypovolaemia when renal tubular sodium reabsorption occurs in

Expected changes in primary acid–base abnormalities

Disorder	pH	HCO_3^-	pCO_2	Standard base excess (SBE) (mmol/litre)
Metabolic acidosis	↓	↓↓	↓	↓↓↓
Metabolic alkalosis	↑	↑↑	↑	↑↑↑
Acute respiratory acidosis	↓	↑	↑↑	N
Chronic respiratory acidosis	N or ↓	↑↑	↑↑	↑↑
Acute respiratory alkalosis	↑	↓	↓↓	N
Chronic respiratory alkalosis	N or ↑	↓↓	↓↓	↓↓

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exchange for H^+ excretion. Loss of acid from the upper gastrointestinal tract, administration of HCO_3^- or its precursors (e.g. citrate in blood, lactate or acetate in fluids) are other causes. Persistent metabolic alkalosis is often associated with renal impairment because the kidney normally compensates well to alkalotic states.

Stewart's physicochemical approach

Stewart's physicochemical approach is an alternative mathematical approach to acid–base analysis that is gaining popularity. While there is agreement that pCO_2 is an independent variable that determines pH, the assessment of the metabolic component differs and challenges the concept that metabolic changes in pH are caused by alteration in bicarbonate concentration. In the Stewart hypothesis, bicarbonate merely reflects acid–base state, but as a dependent variable cannot affect pH on its own.

Biochemistry of aqueous solutions

A virtually inexhaustible supply of H^+ is provided from the dissociation of water, which is governed by the laws of electroneutrality and conservation of mass. Even in a solution as complex as plasma, the source of $[H^+]$ is still water and the determinants of $[H^+]$ can be mathematically reduced to three independent variables: the strong ion difference (SID), pCO_2 and the total weak acid concentration (A_{TOT}) (Figure 2).

The SID is the net charge balance of all strong ions present, where a strong ion is one that is completely or nearly completely dissociated in aqueous solution. SID has a powerful electrochemical effect on water dissociation and hence on H^+ concentration. As SID becomes more positive, the concentration of H^+ decreases, in order to maintain electrical neutrality. Practically, SID is calculated as follows:

$$(Na^+ + K^+ + Ca^{2+} + Mg^{2+}) - (Cl^- + \text{lactate}) = \text{Apparent SID (SIDa)}$$

In healthy humans this value is positive and equals 40–42 mEq/litre. It represents the total anionic contribution of bicarbonate, phosphate and albumin needed to maintain electrical neutrality (Figure 3). Their actual milli-equivalent concentrations, termed the effective strong ion difference (SIDe) are more difficult to calculate than SIDa because of variable dissociation, but the two values should be equal. If not, then there must be other unmeasured ions present (strong ion gap (SIG)). Unlike traditional anion gap measurements, SIG is not affected by changes in pH or albumin concentrations.

The pCO_2 is another independent variable, assuming ventilation is present. Finally, the conjugates of weak acids (A^-), which are mainly proteins and phosphates, contribute to the remaining charges to satisfy neutrality. However, A^- is not an independent variable because it changes with alteration in SID and pCO_2. A_{TOT} ($AH + A^-$) is the third independent variable because its value is not determined by any other.

The essence of the Stewart approach is the understanding that neither H^+ nor HCO_3^- can change unless one of these three variables change. Electroneutrality cannot be satisfied by the creation or destruction of strong ions but by changes in water dissociation to produce or consume H^+ (Figure 3).

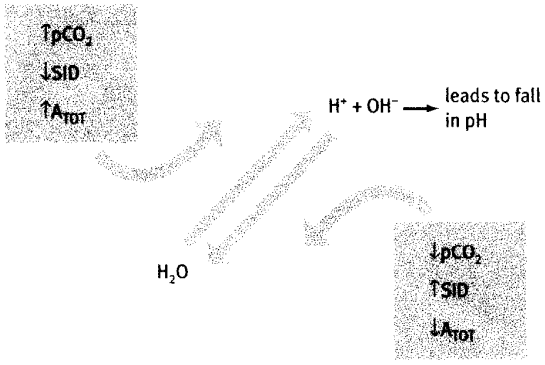
Clinical applications

The new approach does not change the measurement or classification of acid–base disorders. In fact, the standard base excess can be used to quantify the amount of change in SID that has occurred from baseline, or the amount of strong anion that must be removed or strong cation added to restore the pH to 7.4, given a pCO_2 of 40 mm Hg. For example, in order to change the standard base excess from −20 to −10 mEq/litre by adding $NaHCO_3$, the serum Na^+ concentration would need to be increased by 10 mEq/litre.

Chloride

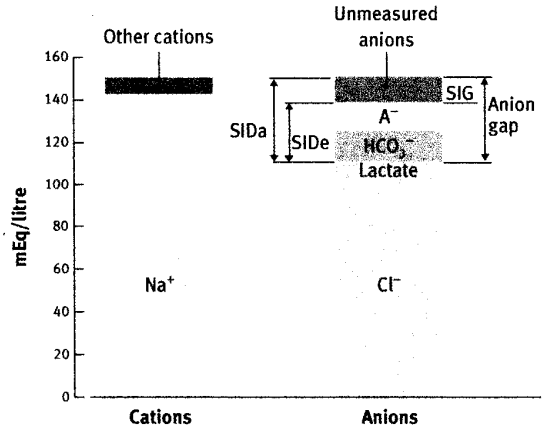
One of the most important implications of the Stewart analysis is

Factors affecting the dissociation of water



pCO_2 partial pressure of carbon dioxide, SID strong ion difference, A_{TOT} total weak acid concentration.

Charge balance in blood plasma



Other cations include Ca^{2+}, Mg^{2+} and K^+. The strong ion difference (SID) is always positive (in plasma) and SID–SIDe (effective) should equal zero. Any difference between SIDe and apparent SID (SIDa) is the strong ion gap (SIG) and presents unmeasured anions. A^- represents dissociated weak acids (mainly albumin and phosphates)

Acid–base interpretation

- Take a comprehensive history and examination
- Request a simultaneous blood gas and biochemical profile
- Assess the accuracy of the data
- Identify the primary disturbance
  pH < 7.36 acidaemia
    Respiratory acidosis: $PaCO_2$ > 44 mm Hg (5.9 kPa)
    Metabolic acidosis: HCO_3^- < 22 mmol/litre
    Combined?
  pH > 7.44 alkalaemia
    Respiratory alkalosis $PaCO_3$ < 36 mm Hg (4.8 kPa)
    Metabolic alkalosis HCO_3^- > 26 mmol/litre
    Combined?
- After identifying the primary or major abnormality (pCO_2 for respiratory and HCO_3^- for metabolic), estimate the expected compensation of the other component. If the compensation is not in the correct direction a mixed abnormality is present
- Assess any metabolic component from standard base excess or deficit
- In a metabolic acidosis calculate the anion gap including K^+ (normal 15 mmol/litre) and adjust for hypoalbuminaemic patients

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the role of chloride in acid–base homeostasis. The primary determinants influencing SID clinically are the Na^+ and Cl^- concentrations. An increase in Cl^- relative to Na^+ decreases the SID and hence the pH. The pH increases when the concentration of these ions moves apart. Since Na^+ control is more tightly regulated to control tonicity, Cl^- is increasingly recognized as an important determinant of pH. For example, persistent vomiting often result in alkalosis. The traditional view is that this is due to H^+ loss as HCl. In the Stewart hypothesis, plasma SID is increased because chloride (a strong ion) is lost without a corresponding strong cation. Increased SID forces a decrease in water dissociation and thus a decrease in plasma H^+ concentration. The treatment of this disorder is chloride replacement with normal saline. The hyperchloraemic acidosis that arises following large volume saline infusions can be explained by the excess administration of chloride relative to sodium. Normal saline contains 150 mmol/litre of sodium and chloride compared with the normal plasma concentrations of 135 and 100 mmol/litre, respectively. The result is that SID is reduced, free water dissociation increases and pH falls.

Practical acid–base interpretation

A practical method of determining acid–base status is given in Figure 4. ◆

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Pneumonia in the ICU

David Sinclair

Community-acquired and nosocomial (hospital-acquired) pneumonia are common conditions. Community-acquired pneumonia has an estimated incidence of 2–12 cases/1000 population/year. Most of these cases are managed outside hospital with about 20% requiring hospital admission. Of this group, about 10% develop severe pneumonia requiring treatment in an ICU. Nosocomial pneumonia is the second most common hospital-acquired infection and the most commonly acquired infection in the ICU. Nosocomial pneumonia usually affects mechanically ventilated patients and is described as ventilator-associated pneumonia. Death rates are increased in critically ill patients developing ventilator-associated pneumonia, with an estimated attributable mortality of 10–50%.

Community-acquired pneumonia in hospital has been defined as symptoms and signs consistent with an acute lower respiratory tract infection associated with new shadowing on the chest radiograph for which there is no other explanation (e.g. not pulmonary oedema or infarction). The illness is the primary reason for hospital admission.

Nosocomial pneumonia is defined as pneumonia acquired after hospital admission. It is divided into:

- early onset (< 5 days after hospital admission or intubation)
- late onset (≥ 5 days after hospital admission or intubation).

Community-acquired pneumonia

Severe community-acquired pneumonia is almost always a multisystem disease and at presentation patients will have, or will be rapidly developing, multiple organ failure. The importance of recognizing this aspect of the disease cannot be over-emphasized. Apparent stability on high-flow oxygen can rapidly change to respiratory, circulatory and renal failure. Progressive loss of tissue oxygenation needs to be anticipated, recognized and acted on to prevent progression to established organ failure.

Assessing the severity of the disease in patients with community-acquired pneumonia is therefore an integral part of hospital management in terms of initial presentation and monitoring response to treatment (Figure 1). Patients who have two or more core adverse prognostic features are at high risk of death and should be managed as having severe pneumonia. Patients who have one core adverse feature are at an increased risk of death. The presence of pre-existing and/or additional adverse prognostic features can assist in deciding whether to treat such patients as having severe pneumonia. Patients who fulfil the criteria for severe community-acquired

David Sinclair *is Consultant Physician at South Devon Healthcare Trust. He qualified from Birmingham University and has trained in respiratory and intensive care medicine.*

