POW ICU

Guide to Acid/Base Analysis

1. Introduction

Metabolic processes in the body result in the production of relatively large amounts of carbonic, sulfuric, phosphoric, and other acids. A person weighing 70 kg disposes daily of about 13 moles of carbon dioxide through the lungs and about 70 to 100 mmol of titratable, nonvolatile acids, mainly sulfuric and phosphoric acids, through the kidneys.

Acid/base balance is generally explained in terms of the carbonic acid-bicarbonate system. This is the most important buffer system and describes the relationship between the respiratory and metabolic components of acid/base balance, the partial pressure of carbon dioxide (pCO_2) and bicarbonate (HCO_3^-), respectively. This relationship is defined by the Henderson and Henderson-Hasselbach equations.

The relationship between bicarbonate (HCO_3^-), CO_2, and pH is described by the

Henderson-Hasselbalch Equation

Like all acids Carbonic acid (H_2CO_3) dissociates to some degree when in solution. The degree of dissociation refers to the relative concentrations of carbonic acid and the three ions that make it up (H^+, HCO_3^- and CO_3^{2-}). The degree of dissociation is described by a dissociation constant (K') such that;

$$K' = \frac{[H^+]X\,[HCO_3^-]}{[H_2CO_3]}$$

The concentration of carbonic acid is not able to measured. Carbonic acid also dissociates to CO_2 and H_2O.

$$H^+ + HCO_3^- \leftrightarrow H_2CO_3 \leftrightarrow CO_2 + H_2O$$ (in the presence of carbonic anhydrase)

The CO_2 can be measured. Allowances for the difference in concentration of H_2CO_3 and CO_2 give rise to a new dissociation constant K such that

$$K = \frac{[H^+]\,X\,[HCO_3^-]}{[CO_2]}$$

When this is expressed as $\log_{(10)}$,and rearranged, it becomes the Henderson-Hasselbalch Equation

$$pH = 6.1 + \log \frac{[HCO_3^-]}{[CO_2]}$$ (6.1 is the pK)

From this equation it can be seen that;

- an increase in **HCO_3^-** is associated with a rise in **pH**
- a decrease in **HCO_3^-** is associated with a fall in **pH**
- an increase in dissolved **CO_2** is associated with a fall in **pH**
- a decrease in dissolved **CO_2** is associated with a rise in **pH**

The fact that HCO_3^- is not an independent variable and varies with changing pCO_2 has meant that empirically derived correction formulas need to be used to adjust the HCO_3^- for both acute and chronic changes in pCO_2. A parameter termed "standard bicarbonate of blood" was defined as the plasma HCO_3^- in blood that has been equilibrated with a pCO_2 of 40 mmHg at 37^oC, and used as a reference value to assess the change of HCO_3^- .

The base excess (BE) was introduced in the late 1950's as a more pure measure of metabolic disturbance. The BE is calculated as the amount of acid or base that must be added to a litre of blood to achieve a normal pH (the hydrogen ion concentration expressed as it's negative log) after correcting the pCO_2 to 40 mmHg at normal body temperature. This was called actual BE (ABE) by Radiometer or invitro BE by Corning. This definition caused problems in practice, as the pH fall with increasing pCO_2 was greater in the intact individual than for blood invitro due to haemoglobin's buffering of CO_2. This led to a fall in BE (a metabolic acidosis) being apparently caused by an acute increase in an individual's pCO_2, which was not the intent of the original definition.

This led to the concept of extracellular Base Excess or invivo Base Excess (Corning) or Standard Base Excess (SBE, Radiometer) assuming the haemoglobin to be spread throughout the extracellular fluid giving an effective haemoglobin concentration of 6 g/100mL. SBE does not change with acute changes in pCO_2. If, after theoretical equilibration with a pCO_2 of 40 mmHg, the blood sample is acidic compared to normal pH, then alkali must be added to titrate pH back to normal, i.e. it has a negative SBE or a base deficit (BD). On the other hand, if after theoretical equilibration with a pCO_2 of 40 mmHg, the sample has an alkaline pH compared to normal, acid must be added to titrate the pH back to a normal i.e. it has a positive SBE or simply SBE.

Although these measures may be used to establish if a metabolic abnormality is present or not they do not give insight into the cause or mechanism underlying the abnormality. The anion gap (AG) has been used to establish, in the case of a metabolic acidosis, whether the acidosis is associated with an increase in unmeasured anion (eg. lactate) if the AG is raised or, if normal, a hyperchloraemic acidosis. However, AG in critically ill patients has been shown to be unreliable, probably because of the generally low albumin levels seen in this patient group.

Stewart (1986) proposed an alternative approach to acid/base physiology using physiochemical principles. He analysed the reactions of the components of plasma with respect to dissociation equilibria, electroneutrality and conservation of mass. Stewart developed six equations based upon the dissociation equilibrium reactions of the strong ions, weak ions, CO_2 and the requirement for electroneutrality. Strong ions are those that ionise (dissociate) completely when in solution. Strong ions are spectator ions because their concentrations do not change in solution, as they remain completely dissociated. The dissociation of weak ions on the other hand varies depending upon factors such as changes in pH and temperature within the normal physiological range. Stewart used an older definition of acids and bases in that an acid was a substance that produced an increase in $[H^+]$ as against the more "modern" definition of an acid as a proton (or H^+) donor.

2. The Stewart Approach - Acid/Base Physiology

2.1 *The pH of water*

The starting point for Stewart's analysis was the ionic nature of water. Pure water (H_2O) ionises slightly at body temperature to form minute quantities of hydrogen ion (H^+) and hydroxyl ions (OH^-). This dissociation occurs so that at equilibrium the compound (i.e. H_2O) and the dissociation products occur in concentrations such that;

$$\frac{[H^+] \times [OH^-]}{[H_2O]} = \text{dissociation constant } (K_{H20})$$

As a result of the requirement of electroneutrality the $[H^+]$ is the same as the $[OH^-]$. The pH of neutrality is 7.0 at room temperature and 6.8 at 37^0C. The important point here is that pure water contains hydrogen ions, albeit in very small quantities, as a result of dissociation and there is a very large potential pool of hydrogen ions in water if conditions result in a change in dissociation. A solution does not become acidic until there are more H^+ than OH^-.

2.2 *The Effect of Strong Ions on the pH of Water - The Strong Ion Difference (SID)*

Compounds that ionise (dissociate) strongly when in solution are called strong ions. Conversely compounds that ionise (dissociate) weakly when in solution are called weak ions.

The addition of strong ions to water changes the pH of the resulting solution. That is, the strong ions change the rate of dissociation of water molecules. Stewart determined that the pH of the resulting solution is dependent on the difference in concentration of strong cations relative to strong anions. Ions such as sodium (Na^+), potassium (K^+), magnesium (Mg^+), and calcium (Ca^+) are strong cations whilst chloride (Cl^-) and sulphate (SO_4^{2-}) are strong anions. The difference between the concentrations of strong cations and strong anions in a solution is termed the strong ion difference or SID. It follows that in solutions of strong ions a change of pH indicates that there has been a change of the relative concentration of strong cations and strong anions i.e. the SID has changed.

Stewart made the point that it was incorrect to maintain that $[H^+]$ of a solution could be changed by moving H^+ into or out of a solution. This is not possible simply because pH is the result of the reactions caused by the SID.

2.3 *The pH of Blood Plasma explained by Stewart*

Blood plasma is a complex solution containing not only strong ions such as the cations Na^+, K^+, Mg^+, Ca^+, and the anions Cl^-, SO_4^{2-}, but also weak ions such as inorganic phosphate (HPO_4^{3-}, $H_2PO_4^-$ etc) and proteins, and is made up with a great deal of water. Blood plasma also contains CO_2 as a result of cellular respiration. The dissolution of CO_2 results in the formation of dissolved CO_2, bicarbonate ion (HCO_3^-), carbonic acid (H_2CO_3), and carbonate

ion (CO_3^{2-}).The Stewart approach established hydrogen ion concentration ($[H^+]$) and HCO_3^- concentration $[HCO_3^-]$ as dependent on the difference between the concentration of strong cations and strong anions (the strong ion difference or SID), the pCO_2, and the total concentration of ionised and non ionised weak acids ($[A_{TOT}]$) where $[A_{TOT}] = [HA] + [A^-]$. With the aid of a computer program Stewart was able to solve the resulting polynomial equation for the dependent variables, [H+] and $[HCO_3^-]$ for differing values of the independent variables, SID, A_{TOT}, and pCO_2.

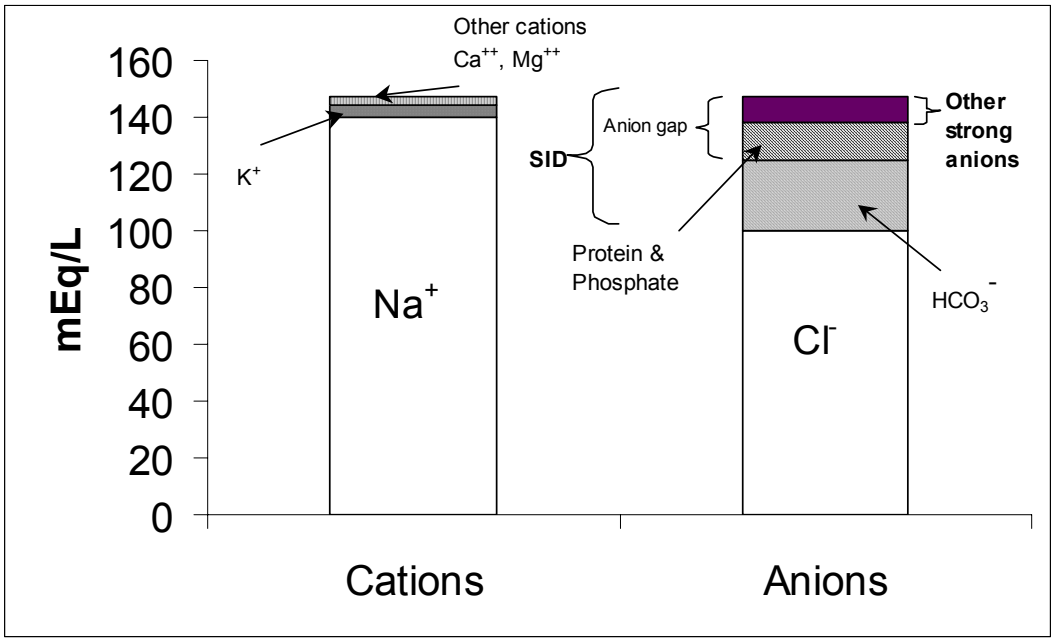
In summary Stewart determined that hydrogen ion concentration was dependent upon the SID, A_{TOT}, and pCO_2. A change in pH and $[HCO_3^-]$ therefore indicates that there must be a change in one of these independent variables. Or conversely, the change in the independent variables has caused a change in the pH and $[HCO_3^-]$.

This is very different from the relationship of pH to pCO_2 and $[HCO_3^-]$ in the Henserson-Hasselbach equation, which is one of association, not cause.

2.4 *A Closer Look at SID*

Figure 1 displays the relative value of anions and cations in plasma. The area marked "anion gap" represents the anions that are not usually measured.

Figure 1. Balance of Cations and Anions in Plasma



The requirement for electroneutrality means that the sum of positive charges equals the sum of the negative charges i.e. plasma cation charges = plasma anion charges. This can be approximated for the plasma by;

$[Na^+] = [HCO_3^-] + [Cl^-] + [\text{unmeasured anions}]$

The unmeasured anions represent the AG. The unmeasured anions are normally made up of phosphates, sulphates, creatinates, and proteins. The Stewart approach defines another gap that has been termed the strong ion gap. The strong ion gap is made up of strong ions not normally present or not present in large amounts such as lactate, keto-acids, or ureamic acids. Unmeasured strong ions can be produced endogenously as in the production of lactate in anaerobic glycolysis, keto-acids as in diabetic ketoacidosis, or uraemic acids in renal failure, or they can be from an exogenous source as in the infusion of lactate containing fluids or as a result of ingesting poisons such as ethylene glycol and methanol, which are metabolised to oxalic and formic acids.

As described earlier the relative balance of strong ions is termed the strong ion difference or SID.

The SID is the difference between the concentration of the strong cations, sodium (Na^+), potassium (K^+), calcium (Ca^{2+}), and magnesium (Mg^{2+}), and the strong anions, chloride (Cl^-), lactate, and unmeasured anions. The contribution of Ca^{2+} and Mg^{2+} are usually ignored, as the respective values are small and don't vary much. SID is then calculated as;

SID = [Na+] + [K+] - ([Cl^-] + [lactate] + [unmeasured strong anions]).

Stewart determined that for plasma "the SID is nearly always positive, and typically has a value of about 40 meq/L. As the SID increases, [H^+] falls (i.e. pH rises). Conversely, as SID decreases, [H^+] rises." (ie. pH falls).

This fact can be used to determine if unmeasured strong anions are contributing to the acid/base state if the use of [Na^+], [K^+], [Cl^-] and lactate in the calculation of SID does not explain the pH of a blood sample. Therefore other strong ions (a strong ion gap) must be present. This is expanded upon in a later section *Analysis of acid/base status using the Stewart approach*.

2.5 *Effect of pCO_2 on [H^+] and pH*

If the SID were held constant an increase in pCO_2 results in an increase in [H^+] and thus a decrease in pH. Conversely a decrease in pCO_2 results in a decrease in [H^+] and an increase in pH.

2.6 *The Effect of [A_{TOT}] on [H^+]*

As discussed earlier [A_{TOT}] represents the total concentration of non-volatile weak acids (protein and phosphate). The contribution of A_{TOT} to acid/base balance has been described in a number of laboratory as well as clinical studies. Plasma proteins are the major contributors of weak acid anions and albumin has been found to be the major component of the protein contribution. Hypoalbuminaemia has been shown to be a common cause of metabolic alkalosis in the critically ill. The other contributor to A_{TOT} is the concentration of inorganic

phosphate (Pi). The blood levels of Pi are generally low so it only effects acid/base balance when Pi levels are raised, as in renal failure.

$[A_{TOT}]$ along with SID and pCO_2 is an independent determinant of $[H^+]$ or pH such that an increase in $[A_{TOT}]$, as a result of raised plasma albumin results, in a fall in plasma pH whilst a decrease in $[A_{TOT}]$, as a result of lowered plasma albumin, results in a rise in plasma pH. For instance chronic hypoproteinaemia (and thus low albumin) as a result of liver cirrhosis, nephrotic syndrome, and malnutrition can be associated with a metabolic alkalosis.

3. Regulation of pH using the Stewart Approach

In addition to the respiratory system and renal system Stewart included the gastrointestinal tract as key elements in the regulation of acid-base balance. The following is a summary of how Stewart explains pH regulation in respect of the respiratory, renal, and gastrointestinal systems.

3.1 *Respiratory Regulation*

If there is a change in $[H^+]$ the respiratory centre is stimulated to alter alveolar ventilation. Acidosis results in an increase in ventilation whilst alkalosis results in a decrease in ventilation. Blood levels of carbon dioxide are thus decreased or increased which results in a decrease and increase in $[H^+]$ respectively. This respiratory compensation occurs rapidly but is unable to compensate completely because as the pH approaches normal the drive from the respiratory centre also diminishes.

The respiratory centre responds to changes in pH and $PaCO_2$ to alter the minute ventilation. An increased minute ventilation lowers $PaCO_2$ and thus results in an increase in pH whilst decreased minute ventilation results in increased $PaCO_2$ and thus a decrease in pH.

3.2 *Renal Regulation*

Stewart suggests the kidneys contribute to the regulation of acid/base balance by controlling the SID by Na^+, K^+, and Cl^- excretion / reabsorption. The kidneys also act to adjust SID by the relative reabsorption of Na^+ and Cl^- in order to restore the SID. Every Cl^- filtered but not reabsorbed results in an increase in plasma SID, whilst every Na^+ and K^+ not reabsorbed results in a decrease in plasma SID. NH_4^+ production from NH_3^+ split from glutamine and glutamic acid allows the kidneys to increase the Cl^- loss in urine relative to Na^+ and K^+ and still maintain electroneutrality in urine.

> "If the circulating plasma arriving at the kidneys has an above normal $[H^+]$ (low pH), the kidneys will react by reabsorbing less Cl^-, thereby slowly raising plasma [SID], increasing Cl^- excretion, and lowering urine [SID]. Conversely, if plasma $[H^+]$ is below normal (raised pH), Cl^- reabsorption will be increased, plasma [SID] decreased, and urine [SID] increased. Because of the primary role of plasma $[Na^+]$ in ECF volume regulation,

manipulation of Cl^- reabsorption is the only mechanism the kidney has for affecting plasma [SID] and thereby plasma [SID]"

The relatively small urine volume per hour compared to the plasma flow through the kidneys means that changes in strong ion excretion can only change plasma levels of strong ions by a small amount per unit time. Therefore renal compensation is slower than the respiratory compensation but has the ability to produce a complete correction.

3.3 *GI Regulation*

The GI tract deals directly with strong ions and therefore has a strong bearing on acid/base balance. Chloride is secreted into the gastric lumen as gastric acid. This results in a slight increase in plasma SID and thus an increase in pH. Under normal circumstances the Cl^- is returned to plasma by reabsorption in the duodenum and the normal plasma SID is maintained. If there is loss of gastric contents from vomiting or nasogastric drainage this reabsorption does not take place and Cl^- is lost i.e. this results in an increase in the SID and thus a metabolic alkalosis.

The alkaline pancreatic juices excreted into the duodenum contain large amounts of Na^+ to achieve an increased SID. The Na^+ is reabsorbed in the small intestine. In the large intestine water absorption takes place along with Na^+ and K^+ exchanges. In diarrhoea water, Na^+, and K^+ are unable to be reabsorbed resulting in a loss of strong cation, a decrease in SID, and metabolic acidosis.

4. Acid- Base Disorders

In this discussion acidaemia and alkalaemia refer to a deviation in the pH of blood from normal whilst acidosis and alkalosis refer to the underlying metabolic or respiratory disturbance.

Acid/base disorders are usually classified as, respiratory acidosis, respiratory alkalosis, metabolic acidosis, metabolic alkalosis or a combination of these. It is important to recognise that a normal pH does not mean that a patient has no acid-base disturbance.

Using this approach acid/base disturbances can result from changes to the SID, pCO_2, or A_{TOT}. The SID can change as a result of excess or deficit of plasma water as seen by abnormal $[Na^+]$, an increase or decrease in $[Cl^-]$ relative to $[Na^+]$, or the addition of unidentified strong anions such as occurs in lactic acidosis, keto acidosis, renal failure, and some poisoning.

4.1 *Respiratory Acidosis and Alkalosis*

Respiratory acidosis results from inadequate ventilation and the retention of CO_2 whilst respiratory alkalosis results from hyperventilation or excessive ventilation and a reduction in pCO_2. (see section 6 for a discussion of compensatory changes)

4.2 *Metabolic Acidosis and Alkalosis*

Metabolic acidosis can result from a reduction in the SID or from an increase in A_{TOT} as in hyperphosphataemia resulting from renal failure.
A reduction in SID can result from an increase in strong anion concentration relative to strong cation concentration for instance;

- Loss of Na^+ relative to Cl^- associated with diarrhoea.
- Administration of a solution with zero SID or low SID as with the administration of large quantities of normal saline (SID = 0). This results in an increase in Cl^- relative to Na^+, a reduction in plasma SID and metabolic acidosis.
- Production of excess amounts of "other strong anions" as in lactic acidosis where the raised plasma lactate level causes a reduction in SID i.e. SID = $[Na^+]$ + $[K^+]$ - $[Cl^-]$ + lactate.
- Administration of haemofiltration fluid containing lactate in the setting of reduced ability to metabolise lactate, for example in liver failure, or when the administration of lactate exceeds the ability to metabolise lactate, as in high volume haemofiltration. In the circumstance where lactate metabolism is adequate, the exogenous lactate is metabolised with no net change to plasma SID. However, if the exogenous lactate is unable to be metabolised the plasma lactate level rises resulting in a reduced SID and metabolic acidosis.
- Renal failure and the accumulation of ureamic products.
- Ingestion of poisons that result in an increase in "unmeasured strong anions" such as methanol poisoning and ethylene glycol poisoning

Metabolic Alkalosis can result from;

- An increase in the SID as a result of decreases in strong anions relative to strong cations, for example, as a result of Cl^- loss from vomiting or nasogastric aspiration, or the loss of Cl^- in the urine as a result of diuretic therapy.
- An increase in strong cation relative to strong anion, for example, as a result of sodium bicarbonate administration. In the case of the administration of sodium bicarbonate for the correction of a metabolic acidosis the administration of the strong cation Na^+ and the increase in plasma SID is the mechanism underlying it's effect. The bicarbonate is an accompanying weak anion that is quickly metabolised and thus does not effect SID. A similar effect results from the administration of sodium acetate and sodium citrate.
- A decrease in $[A_{TOT}]$ as a result of a lowered plasma albumin level as a result of liver cirrhosis, nephrotic syndrome, malnutrition, critical illness and haemodilution.

5. Analysis of Acid/Base Status Using the Strong Ion Approach

Although the Stewart approach provides a comprehensive quantitative analysis of acid/base balance it's utility at the bedside is limited by the need to solve complicated equations. A simple bedside approach using the principles outlined by Stewart has been presented by Gilfix et. al. These authors used the fact the SBE could also be seen as a measure of strong ion excess and strong ion deficit. The SBE could then be used as a reference value for the net base excess or strong ion effects of changes SID and A_{TOT}. The individual effects of changes in free water, changes in $[Cl^-]$, changes in protein concentration, and changes in concentration of unmeasured cations or anions could be expressed as strong ion equivalents or SBE effects. The method described by Gilfix et. al. still requires the calculation of equations. Whilst these are simpler than Stewart's complicated polynomial equation, they still require the assistance of a programmable calculator or computer.

5.1 *Calculation of Strong Ion Effects*

Strong ion effects can be calculated as described by Gilfix et. al. The equations are presented in Table 1.

The effect of the change of $[Na^+]$ from normal is calculated to determine the free water effect. The hospital's laboratory mean normal value is used as the reference value. The measured $[Cl^-]$ is corrected ($[Cl^-]_{corrected}$) for the change in measured $[Na^+]$ from normal $[Na^+]$ and the $Cl^-_{corrected}$ effect calculated. The ionisation of Albumin (Alb^-) is calculated using the equation derived by Figge et.al (12).

Although Gilfix et al included lactate as an unmeasured anion, we consider it a measured strong ion and calculate the lactate strong ion effect. Unmeasured anions or cations are termed "Other Species" and calculated as the difference between measured SBE and the sum of the free water, Cl^-, and Alb^- effects. The effect of the change in SI is termed Delta SI and calculated as the sum of the free water, Cl^-, and lactate effects.

Table 1. Calculations of Strong Ion Effects

Parameter (mEq/L)	Calculation
Alb^-	Albumin (g/L) X (0.123 X pH - 0.631) (12)
Pi^-	Pi (mmol/L) X (0.309 X pH - 0.469) (15)
Pi^- effect	2.09 - Pi^-
Free water effect	0.3(measured Na^+ -141) (16)
$Cl^-_{corrected}$	$Cl^-_{measured}$ X (141 /$Na^+_{measured}$) (16)
Cl^- effect	102 - $Cl^-_{corrected}$ (16)
Alb^- effect	(0.123 * pH - 0.631) X (41 - Albumin (g/L)
Lactate effect	-1 X lactate
Delta SI effect	Free water effect + Cl^- effect + lactate effect

The effect of Pi is also calculated as the difference between the concentration of Pi ions (mono-hydrogen and di-hydrogen forms) and the normal concentration of Pi ions at pH 7.4. The hospital's laboratory normal value for Pi is 1.15 mmol/L which, using the equation in Table 1 for the ionisation of Pi, equals a concentration of 2.09 mEq/L.

Note.
These calculations and a graph of the results can be obtained from the SID calculator on the ward PC workstation.

5.2 *The POW Way (Estimation of Strong Ion Effects)*

5.2.1 **How to determine if a metabolic acidosis or alkalosis is present**

The pH is looked at first to determine if there is an acidaemia or alkalaemia. If the pH is within the normal range a respiratory or metabolic acidosis or alkalosis can still be present. The respiratory and metabolic components must be looked at to determine if there is a corresponding acidosis or alkalosis.

The respiratory component of course is the pCO_2. The pCO_2 indicates whether a respiratory acidosis or alkalosis is present. If the pCO_2 is < 35mmHg a respiratory alkalosis is present and if the pCO_2 is > 45mmHg a respiratory acidosis is present.

Next, it needs to be determined if the change in pCO_2 explains the pH. The SBE is used to determine if more than an alteration in pCO_2 is present.

5.2.2 **The meaning of Base Excess**

The BE asks the question – is the cause of any acid/base change the result of a change in pCO_2? The change in pH as a result of a change in pCO_2 is “removed” by adjusting the pCO_2 to 40 mmHg. The question then becomes; “*is there a remaining acid/base change?” (i.e. a metabolic acidosis/alkalosis).*

The SBE is actually a measure of the net strong ion (and/or $[A_{TOT}]$) effect or the strong ion (and/or $[A_{TOT}]$) excess or deficit as the case may be. A base deficit (or negative SBE) corresponds to a positive difference between normal SID and the actual SID whilst a SBE corresponds to negative difference between normal SID and actual SID.

If there is a metabolic component the next question is "is it explained by alterations in the strong ions that have been used in the calculation of [SID]?" Or is it explained by the addition of “unmeasured” strong anions i.e. is there a strong ion gap? Also the effects of changes in albumin and phosphate must be considered.

5.2.3 **Analysing the metabolic component – estimating Strong Ion effects**

An estimate of the SID is made using $[Na^+]+ [K^+] - [Cl^-]$ - Lactate. The reference value of SID of 42 mEq/L is used to estimate the change of SID from normal. This is termed the estimated Delta SID and is equal to estimated SID minus normal SID (42 mEq/L). This is arranged in this way so that a negative estimated Delta SID corresponded to a negative SBE or SBD.

A negative value for estimated Delta SID corresponds to strong anion excess or a strong cation deficit, e.g. a raised $[Cl^-]$ relative to $[Na^+]$ or low $[Na^+]$ relative to $[Cl^-]$. A positive value for estimated Delta SID corresponds to strong cation excess or a strong anion deficit, e.g. a low $[Cl^-]$ relative to $[Na^+]$ or a raised $[Na^+]$ relative to $[Cl^-]$. An estimate of the Alb^- effect (estimated Alb^- effect) is made by calculating 0.25 of the difference between the normal or reference albumin and the measured value. 0.25 is used to allow mental calculation. The use of 0.25 of the difference in measured albumin and normal albumin to estimate Alb^- is reasonable as the ionisation is 0.26 at a pH of 7.2, 0.28 at a pH of 7.4 and 0.29 at pH of 7.5. The use of 0.25, assuming a change of albumin from normal of 20g/L, would result in an error of less than 1 mEq/L for this pH range.

The SBE based upon the estimated Delta SI effect and the estimated Alb^- effect is termed the predicted SBE. The effect of Other Species is then calculated as the difference between SBE and the predicted SBE. The equations used to calculate the estimated SI effects are presented in Table 2.

Table 2. Calculation of Estimated Strong Ion Effects

Parameter (mEq/L)	Calculation
SID	$[Na^+] + [K^+] - [Cl^-]$ - Lactate - unmeasured anions
estimated SID	$[Na^+]+ [K^+] - [Cl^-]$ - Lactate
estimated Delta SI effect	estimated SID - 42
estimated Alb^- effect	0.25 X (40 - measured Albumin (g/L))
predicted SBE	estimated SID - 42 + estimated Alb^- effect
estimate Other Species effect	SBE - predicted SBE

The use of negative and positive numbers for SBE where a negative SBE is really a SBD has the potential to lead to some confusion when discussing SBE of SI effects. However, the SBE is a measure of the net result of the various acidifying and alkalising effects of changes in the determinants of $[H^+]$. This fact is illustrated in Figure 2. It is obvious from this analysis that two equal and opposite effects could coexist, producing a normal SBE. Or alternatively, metabolic acid/base abnormalities can exist when SBE is normal. For example, a hyperchloraemia may develop, by renal resorption of Cl^-, to produce a change in SID to compensate for the alkalising effect of low albumin that often develops in the critically ill. This of course would not be considered a clinically treatable acid/base abnormality. However, it is interesting to note that if a patient in this situation were given albumin to correct the hypoalbuminaemia this would "unmask " the SI effect resulting from the hyperchloraemia, and this acidifying effect would be seen by a change in the SBE.

5.2.4 **An Example**

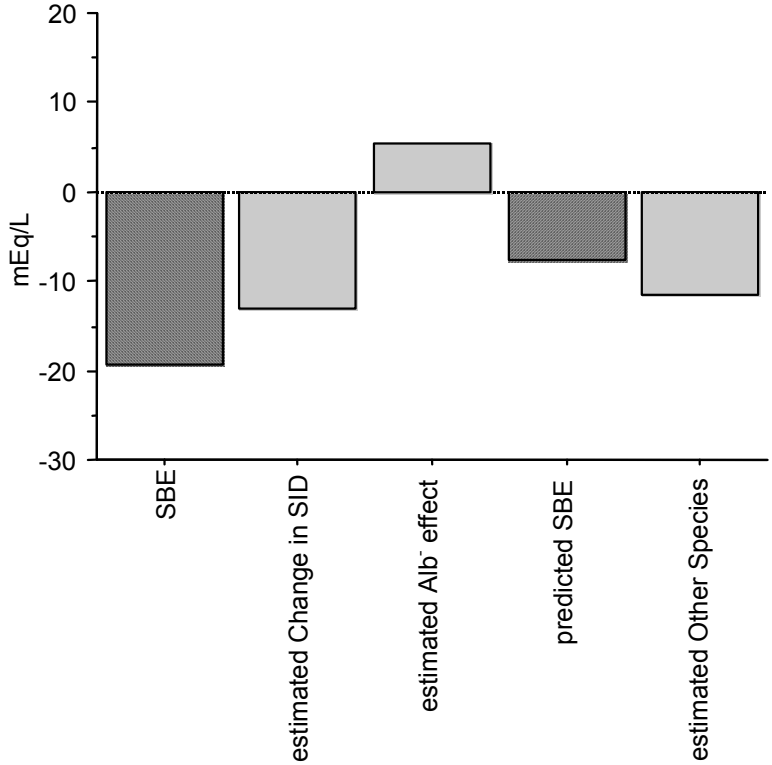
The technique of estimating SI effects using SBE as a reference lends itself to a comprehensive and simple bedside analysis of acid/base balance.

The results for a patient suffering from rhabdomyolysis and renal failure:

pH	7.07
SBE (mEq/L)	-19.3
pCO_2 (mmHg)	31.4
Na^+ (mEq/L)	147
K^+ (mEq/L)	3.9
Cl^- (mEq/L)	120
lactate (mEq/L)	1.8
Albumin (g/L)	31
Phosphate (Pi) mmol/L	1.5
ionised phosphate (Pi-) mEq/L	2.7

The estimate of the SID, taking into account [Na^+], [K^+], [Cl^-] and lactate, is 28.8 mEq/L. The difference between this and the reference value of 42 is -13.2. That is, if there were no other acid/base abnormality other than a change in SID, resulting from changes in the concentrations of the strong ions used in the calculation, the SBE would be -13.2. The change of albumin from normal must also be taken into account. The albumin is 18g/L, which is a change from the normal value of 40g/L of 22g/L. We can estimate the charge contribution of the ionisation of albumin as 0.25 of the difference in measured albumin and normal albumin i.e Alb^- (mEq/L) = 0.25 x 22 (g/L) = 5.5. Therefore the low albumin will have an SBE effect or alkalising effect of 5.5 and the delta SID an SBE effect or acidifying effect of -13.2. The predicted SBE is then -7.7 (-13.2 + 5.5). However the reported SBE is -19.3. The slightly raised phosphate does not explain this difference. There then must be "Other Species" or unmeasured strong ions contributing to the metabolic acidosis. The "Other Species" effect is equal to the reported SBE minus the predicted SBE (-19.3 + 7.7) ie. -11.6 mEq/L. The patient was suffering from acute renal failure as a result of rhabdomyolysis and shock, and, had a diabetic keto acidosis indicated by hyperglycaemia and the presence of ketones in the urine. Renal failure and diabetic keto acidosis both result in the accumulation of strong ions, acetoacetate and β-hydroxybutyrate in the case of DKA, and sulphate, phosphate and other ureamic acids in renal failure. Whereas, if this patient had been unconscious in the emergency department, and was not diabetic, it would indicate that a check for other strong anions such as formate, oxalate, and salicylate would be indicated. The strong ion effects for this patient are displayed graphically in Figure 2.

Figure 2. Estimated Strong Ion Effects.



Where it is established that a change in the strong ions are contributing to the acid/base disturbance it may be useful to calculate the free water effect and $[Cl^-]_{corrected}$ effect, although an examination of the blood results together with the clinical history, in our experience, is generally sufficient to establish if $[Cl^-]$ is high or low with respect to $[Na^+]$.

Unmeasured anions other than lactate have been shown to be increased in patients with sepsis and liver disease and the presence of unmeasured cations have been suggested

To establish the presence of small concentrations of unmeasured ions the determination of the strong ion gap or SIG can be used. The SIG is the difference between the apparent SID and the effective SID. The apparent SID is calculated as the difference between the strong cations (Na, K, Mg, Ca) and the strong anions (Cl^-, lactate). The effective SID is the sum of the charge contribution of CO_2, albumin and phosphate.

Note.
These calculations and a graph of the results can be obtained from the SID calculator on the ward PC workstation.

6. Compensatory changes to pCO2 and SBE for acute and chronic conditions.

The following extract is from an article;

Schlichtig R, Grogono AW, Severinghaus JW. Human PaCO2 and the standard base excess compensation for acid-base imbalance. Crit care Med 1998;26(7):1173-1179

OBJECTIVES: Renal and respiratory acid-base regulation systems interact with each other, one compensating (partially) for a primary defect of the other. Most investigators striving to typify compensations for abnormal acid-base balance have reported their findings in terms of arterial pH, PaCO2, and/or HCO3-. However, pH and HCO3- are both altered by both respiratory and metabolic changes. We sought to simplify these relations by expressing them in terms of standard base excess (SBE in mM), which quantifies the metabolic balance and is independent of PaCO2.
DESIGN: Meta-analysis.
SETTING: Historical synthesis developed via the Internet.
PATIENTS: Arterial pH, PaCO2, and/or HCO3- data sets were obtained from 21 published reports of patients considered to have purely acute or chronic metabolic or respiratory acid-base problems.
INTERVENTIONS: We used the same data to compute the typical compensatory responses to imbalances of SBE and PaCO2. Relations were expressed as difference (delta) from normal values for PaCO2 (40 torr [5.3 kPa]) and SBE (0 mM).
MEASUREMENTS AND MAIN RESULTS: The data of patient compensatory changes conformed to the following equations, as well as to the traditional PaCO2 vs. HCO3- or H+ vs. PaCO2 equations:

	Acute	**Chronic**
Metabolic change responding to change in PaCO2	$\Delta SBE = 0 \times \Delta PaCO_2$, hence: SBE = 0	$\Delta SBE = 0.4 \times \Delta PaCO_2$

	Acidosis	**Alkalosis**
Respiratory change responding to change in SBE	$\Delta PaCO2 = 1.0 \times \Delta SBE$	$\Delta PaCO2 = 0.6 \times \Delta SBE$

CONCLUSION: Data reported by many investigators over the past 35 yrs on typical, expected, or "normal" human compensation for acid-base imbalance may be expressed in terms of the independent variables: PaCO2 (respiratory) and SBE (metabolic).

Note.

The Siggaard-Anderson Acid-Base Chart can also be used to determine the expected change in SBE and pCO2 to acid-base abnormalities

7. References & Further Reading

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