

## Interpretation of acid-base abnormalities

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The following notes set out to provide essential information for use in the interpretation of blood gas printouts as encountered in the clinical environment. Basic concepts and definitions are emphasised, all of which are essential in the accurate interpretation of blood gasses.

### The definition of pH

pH is defined as the concentration of hydrogen ions expressed as the negative log to base 10.

$$pH = -\log_{10}[H^+]$$

As an abnormality of pH indicates an abnormality of hydrogen ion concentration, interpretation of this variable alone, can only indicate either acidaemia or alkalaemia.

### The blood gas analyser

From a pure blood gas perspective, a blood gas analyser only measures three variables – pH, pO<sub>2</sub> and pCO<sub>2</sub>. For the purposes of the following discussion, only pH and pCO<sub>2</sub> are relevant.

All of the remaining variables are calculated – primarily through manipulation of the Henderson-Hasselbalch equation.

### Important concepts for interpreting blood gasses

#### The Henderson-Hasselbalch equation

This equation expresses the relationship between pH, pK<sub>a</sub> and [acid] and [base].

$$pH = pK_a + \log \frac{\text{base}}{\text{acid}}$$

For blood gas interpretation purposes this equation can be expressed as:

$$pH = pK_a + \log \frac{[HCO_3^-]}{[H_2CO_3]}$$

Or more simply:

$$pH = 6.1 + \log \frac{[HCO_3^-]}{0.03 pCO_2}$$

Here 0.03 is the solubility coefficient of CO<sub>2</sub> when expressed in mmHg. [0.225 is the solubility coefficient expressed in kPa]. 6.1 is the pK<sub>a</sub> of the bicarbonate buffer system.

#### Bicarbonate

As the blood gas analyser measures pH and pCO<sub>2</sub>, the HCO<sub>3</sub> is a calculated variable.

Bicarbonate can only be used to assess metabolic disturbance in a patient with no respiratory abnormality!

As a calculated variable, bicarbonate is affected by both respiratory and metabolic disturbances. It cannot, therefore, be an ideal measure of either. Moreover, the relationship between metabolic acidosis and bicarbonate is neither consistent nor linear. And, finally, in acid-base determinations the concentration (in mEq/L) of the bicarbonate ion ( $\text{HCO}_3^-$ ) is not measured, it is calculated from the  $\text{pCO}_2$  and pH.

Bicarbonate is therefore not a particularly useful variable – it is merely the product of calculation!

## Standard bicarbonate

While bicarbonate itself is a poor measurement of either the respiratory or metabolic regulator, **standard bicarbonate** is a better measurement of the metabolic component.

It was introduced in 1957 by Jorgensen and Astrup. It was defined as the bicarbonate concentration under standard conditions:  $\text{pCO}_2=40$  mmHg (5.3kPa), temperature of  $37^\circ\text{C}$ , and haemoglobin being fully saturated with oxygen.

As the standard bicarbonate includes correction for any respiratory abnormality, it is useful in the identification of metabolic disturbance.

## Base excess

The year after introducing Standard Bicarbonate, Astrup and Siggard-Andersen in 1958 introduced Base Excess as a better method of measuring the metabolic component. In essence the method calculated the quantity of Acid or Alkali required to return the plasma **in-vitro** to a normal pH under standard conditions (these being  $\text{pCO}_2$  and temperature).

## Standard Base excess

Standard Base Excess is the Base Excess value calculated for anemic blood ( $\text{Hb} = 5$  g/dl) on the principle that this closely represents the behavior of the whole human being. The rationale for this is that in the whole body, hemoglobin effectively buffers the plasma and the much larger extracellular fluid, i.e., the behavior is that of anemic blood. The method predicts the quantity of Acid or Alkali required to return the plasma **in-vivo** to a normal pH under standard conditions.

In the clinical arena, if standard base excess is available, it represents the **best** measure of the metabolic disturbance.

## Assessing metabolic disturbance

From above it is appreciated that base excess and standard base excess can be used to identify metabolic disturbance. Remember that respiratory abnormalities are excluded in these calculations.

Nevertheless, neither of the above can explain the mechanism of any metabolic disturbance. Metabolic disturbance can only be explained through the calculation of anion gap, or better through the appreciation of strong ion difference and total ionized protein.

## The Anion gap

This is calculated as:

$$\text{Anion gap} = [\text{Na}^+ + \text{K}^+] - [\text{Cl}^- + \text{HCO}_3^-]$$

The anion gap is only useful in the description of metabolic acidosis, where it is classified as either being increased, or decreased.

The causes of a raised anion gap acidosis are:

- lactic acidosis
- ketoacidosis
- chronic renal failure (accumulation of sulfates, phosphates, uric acid)

- intoxication or drug overdose, e.g., ethanol, methanol, ethylene glycol, formaldehyde, paraldehyde, salicylates, INH, toluene, sulfates, metformin.
- rhabdomyolysis

The causes of a normal anion gap acidosis (mostly associated with a  $\text{Cl}^-$  abnormality) are:

- Longstanding diarrhoea (bicarbonate loss)
- Uretero-sigmoidostomy
- Pancreatic fistula
- Renal Tubular Acidosis
- Intoxication, e.g., ammonium chloride, acetazolamide, bile acid sequestrants

### Strong ion difference

The Strong Ion Difference is the difference between the sums of concentrations of the strong cations and strong anions:

$$[\text{SID}] = [\text{Na}^+] + [\text{K}^+] + [\text{Ca}^{2+}] + [\text{Mg}^{2+}] - [\text{Cl}^-] - [\text{Other Strong Anions}]$$

Lactate is a strong anion and should be considered in the above equation.

Strong ions are always completely dissociated in solution. Note that bicarbonate is not a strong ion at all!

The normal strong ion difference is about 35. Any departure from this number is roughly equivalent to the SBE.

### Weak non-volatile acids - $[\text{A}_{\text{TOT}}^-]$

$[\text{A}_{\text{TOT}}^-]$  is the total plasma concentration of the weak non-volatile acids, inorganic phosphate, serum proteins, and albumin.

$$[\text{A}_{\text{TOT}}^-] = [\text{P}_{\text{iTOT}}] + [\text{Pr}_{\text{TOT}}] + \text{albumin.}$$

Proteins provide a significant source of ionisable substrate that is useful in the buffering of acid-base disturbances. A low albumin plays an alkalinizing role from an acid-base perspective.

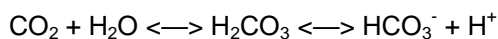
The use of the strong ion difference and abnormalities of  $\text{A}_{\text{TOT}}^-$  can provide additional insight into the appreciation of the cause of an acid-base disturbance.

### Clinical considerations

Changes in acid-base status are either respiratory or non-respiratory, i.e., metabolic:

#### Respiratory:

The effects of changes of  $\text{pCO}_2$  are well understood and produce the expected alterations in  $[\text{H}^+]$ :



#### Metabolic (Non-Respiratory):

Metabolic disturbances cannot be viewed as a consequence of bicarbonate concentration because bicarbonate is merely a dependent variable. The two possible sources of metabolic, i.e. non-respiratory, disturbances are either  $[\text{SID}]$  or  $[\text{A}_{\text{TOT}}^-]$ , or both.

With normal protein levels,  $[\text{SID}]$  is about 40mEq/L. Any departure from this normal value is roughly equivalent to the standard base excess (SBE), i.e., if the measured  $[\text{SID}]$  were 45 mEq/L, the BE would be about 5 mEq/L, and a measured  $[\text{SID}]$  of 32 mEq/L would approximate to a BE = -8 mEq/L. Because  $[\text{SID}]$  does not allow for haemoglobin, there is often a small discrepancy.

### Changing [SID]:

[SID] can be changed by two principal methods:

#### 1) Concentration:

Dehydration or over-hydration alters the concentration of the strong ions and therefore increases, or decreases, any difference. The body's normal state is on the alkaline side of neutral. Therefore, dehydration concentrates the alkalinity (contraction alkalosis) and increases [SID]; whereas, over-hydration dilutes this alkaline state towards neutral (dilutional acidosis) and decreases [SID].

#### 2) Strong Ion Changes:

If the sodium concentration is normal, alterations in the concentration of other strong ions will affect [SID]:

##### a. Inorganic Acids:

The only strong ion capable of sufficient change is chloride, (potassium, calcium and magnesium do not change significantly). An increased  $\text{Cl}^-$  concentration causes an acidosis and a decreased [SID] – hyperchloraemic acidosis. Because the chloride ions are measured, the anion gap will be normal.

##### b. Organic Acids:

By contrast, if the body accumulates one of the organic acids, e.g., lactate, formate, keto-acids, then the metabolic acidosis is characterized by a normal chloride concentration and an abnormal anion gap because of the presence of the "unmeasured" organic acid.

### Changing $[\text{A}_{\text{TOT}}]$ :

The non-volatile weak acids comprise inorganic phosphate, albumin and other plasma proteins. Making the greatest contribution to acid-base balance are the proteins, particularly albumin, which behave collectively as a weak acid.

Hypoproteinemia, therefore, causes a base excess and vice versa.

Phosphate levels are normally so low that a significant fall is impossible. However, in renal failure, high phosphate levels contribute to the acidaemia.

### **Interpreting acid-base derangement**

The initial inspection of pH,  $\text{pCO}_2$  and SBE are likely to be most helpful.

Simple respiratory acidosis is easy to identify, most commonly resulting from a depression of minute ventilation, for a variety of reasons. The SBE is normal.

Respiratory alkalosis is relatively rare. Hyperventilation is an unusual physiologic disturbance that may be secondary to hypoxia (with no depression of minute ventilation), high altitude or unusual drive of the respiratory center. Once again the SBE is normal.

Interpreting metabolic disturbance is best done through the inspection of SBE, thus discounting any respiratory component of the disturbance to pH.

For metabolic acidosis further insight is gained through the use of anion gap, or SID and  $[\text{A}_{\text{TOT}}]$ .

Primary metabolic alkalosis may occur for a variety of reasons:

- Loss of acid via: urine, stools, or vomiting
- Transfer of hydrogen ions into the cells
- Excessive bicarbonate administration, e.g. alkali given to patients with renal failure.
- Contraction of the extracellular space due to excessive diuretic treatment

## Simple mathematics!

As a rule of thumb the following holds true:

pCO <sub>2</sub>	pH	HCO <sub>3</sub> <sup>-</sup>
12 mmHg	0.1	6 mEq/l
1.6 kPa		

The equation means that a change of 0.1 in the pH can be caused by either:

1. A respiratory change (PCO<sub>2</sub> change) of 12mmHg, or
2. A metabolic change (Base Excess change) of 6 mEq/L.
3. A mixture of the two.

This relationship allows the components to be "added" and "subtracted". For example, a pH of 7.2 (0.2 more "Acid") can be caused by:

1. a PCO<sub>2</sub> of 64 with a BE = 0 mEq/L
2. a PCO<sub>2</sub> of 52 with a BE = -6 mEq/L
3. a PCO<sub>2</sub> of 40 with a BE = -12 mEq/L
4. a PCO<sub>2</sub> of 32 with a BE = -18 mEq/L

Although this relationship is an approximation, it provides acceptable clinical results in most circumstances; its real value is in granting insight and understanding.

## Identifying compensation

Compensation for acid-base disturbances is never complete from a mathematical perspective. In other words the pH can never be brought back to 7.4 by physiologic means. Compensation may be complete in that physiology has done all it can to offset the disturbance. At best complete physiologic compensation will lie roughly halfway between full mathematical compensation, and no compensation.

## Conclusion

Acid-base interpretation is easy!

- Identify an acidaemia or alkalaemia
  - If the pH falls within the normal range in the face of significant respiratory and metabolic disturbance consider that there may be added complexity! Remember that compensation is never mathematically complete.
- Then look at pCO<sub>2</sub> and SBE.
  - Start to identify either respiratory or metabolic causes of the disturbance
- For metabolic acidosis
  - Consider both the anion gap and SID for insight
- Consider SID and [A<sub>TOT</sub><sup>-</sup>] for all metabolic disturbances
- Use the rule of thumb relationship to help predict necessary compensation.
- For the last time – remember that Compensation is never mathematically complete – usually only half compensation is possible.

