11.5: The Great Trans-Atlantic Acid-Base Debate

The approach to evaluation of acid-base disorders used in this on-line text is known as the Boston approach. The researchers promoting this approach are from Boston. An alternative method of evaluation promoted by Astrup and Siggaard-Anderson from Copenhagen uses the Base Excess approach. At times the differences between the two groups has stirred controversy (called the ‘Great Trans-Atlantic Acid-Base Debate’ by Bunker in 1965). Many of the differences between the two groups persist and it is important to have some understanding of the issues involved. The controversy has recently been stirred again by Severinghaus (1993) who favours the Copenhagen approach.

The basic idea is that we need a way to quantify the various acid-base disorders. This tells us the severity of the acid-base disturbance and this is important clinical information. We also need to determine whether the body’s compensation for the acid-base disorder is appropriate. If not, this indicates the presence of a second acid-base disorder.

9.5.1: Background to Copenhagen Approach

Acid-base disorders are classified as being of respiratory origin (primary change in pCO₂) or of metabolic origin (primary change in fixed acids). Some basic questions to be answered by any approach are:

- How can the magnitude of a respiratory disorder be determined?
- How can the magnitude of a metabolic disorder be determined?

Respiratory disorders are quantified by the amount of change in pCO₂ in the arterial blood. If the pCO₂ is further away from its normal value, then a larger disorder is present. This seems simple enough as CO₂ is the respiratory acid and can be easily measured.

Metabolic disorders are quantified by the amount of excess fixed acids (the metabolic acids) present in the blood. If
more fixed acids are present, then a disorder of larger magnitude is present. This is clear enough but in a particular metabolic disorder, we may not know what are the particular fixed acids that are causing the acidosis. Indeed there may be more than one type involved.

Is it feasible to measure every possible fixed acid?

No. BUT we can estimate the total amount of excess fixed acid present indirectly.

The argument goes like this:
1. Buffering of fixed acids in the extracellular fluid is predominantly by bicarbonate.
2. One bicarbonate molecule will react with one $H^+$ molecule produced by one molecule of fixed acid.
3. So $[\text{HCO}_3^-]$ will decrease by one molecule for every molecule of fixed acid present.
4. The total amount of excess fixed acids should therefore be equal to the amount by which the bicarbonate concentration drops from its usual value.

Conclusion: The magnitude of the metabolic disorder (in the ECF) can be quantified indirectly by the amount of change in the $[\text{HCO}_3^-]$. This seems an improvement because now there is only one quantity to measure and also it is easy to 'measure' (Bicarbonate is not actually measured in a blood-gas machine but instead is calculated, using the Henderson-Hasselbalch equation, by substituting into this equation the measured values of pH & pCO$_2$).

But there are other problems:

- The implicit assumption so far that pCO$_2$ and HCO$_3^-$ are independent of one another is not correct. (What this means is that changes in pCO$_2$ also will change the bicarbonate level because these 2 compounds are in chemical equilibrium. This interferes with the usefulness of changes in bicarbonate as a way to quantify the metabolic component of an acid-base disorder because respiratory disorders also alter the baseline HCO$_3^-$)
- The buffering by the HCO$_3^-$ in the blood sample is not representative of the buffering by the ECF as a whole. (What this means is that because blood is a better buffer than ECF as a whole then doing your measurements in a blood-gas machine on blood will not give you results representative of the whole ECF. Blood is a better buffer then the whole ECF because of its content of the buffer haemoglobin.)
- The assumption that all buffering of metabolic acids is by HCO$_3^-$ and not other unmeasured ECF buffers is not totally correct.
- Buffering by intracellular buffers is ignored
- The system assesses compensation as another primary disorder

The Copenhagen approach has developed several 'work-arounds' to cope with some of these problems.

As stated above, the pCO$_2$ and the [HCO$_3^-$] are not independent of one another as the argument so far has tacitly assumed. An increase in pCO$_2$ will cause an increase in [HCO$_3^-$]. This occurs because of the Law of Mass Action in the following equation:
This is a problem because a change in respiratory acid is changing the baseline used for assessment of the metabolic disorder. What we need is some way of assessing the metabolic disorder that corrects or allows for this interaction between CO$_2$ and HCO$_3^-$.

Several **pCO$_2$-independent indices** have been proposed as being suitable for this purpose:

- Standard bicarbonate
- Buffer Base
- Base Excess

**Standard bicarbonate** is the bicarbonate concentration of a sample when the pCO$_2$ has been adjusted (or standardised) to 40 mmHg at a temperature of 37°C. This would remove the influence of changes in pCO$_2$ by seeing what the [HCO$_3^-$] would be if the respiratory component was made the same for all measurements. The term was introduced by Jorgensen & Astrup in 1957 but is conceptually the same as the idea of a 'standard pH' (at pCO$_2$ of 40mmHg & temperature of 37°C) introduced by Henderson much earlier.

**Buffer base** is a measure of the concentration of all the buffers present in either plasma or blood.

**Base Excess (BE)** is a measure of how far Buffer Base has changed from its normal value & was introduced by Astrup and Siggaard-Andersen in 1958. BE in whole blood is independent of pCO$_2$ in the sample when measured in the blood gas machine. BE is proposed as a measure of the magnitude of the metabolic disorder because it assesses all the extracellular buffers (in the blood sample) and is independent of pCO$_2$ (in vitro). Unfortunately, there are several problems with the use of BE in this way. For example:

- It is not independent of pCO$_2$ *in vivo* (This is because blood -which contains haemoglobin - is a better buffer than the total ECF
- It does not distinguish compensation for a respiratory disorder from the presence of a primary metabolic disorder

If BE is calculated for a haemoglobin concentration of 30 or 50 g/l instead of the actual haemoglobin, the differences between in vitro and in vivo behaviour can be mostly eliminated (See Severinghaus, 1976). This lower [Hb] is considered to be the effective [Hb] of the whole ECF (ie what the [Hb] would be if the haemoglobin was distributed throughout the whole ECF rather than just the intravascular compartment). This attempts to eliminate the error introduced by the incorrect assumption that the buffering of blood is the same as the buffering by the whole ECF.

The **Radiometer** range of blood gas machines are made in Copenhagen and are very successfully used worldwide. These machines provides a printout with the full family of 'derived' (or 'contrived', depending on your perspective) Copenhagen-type blood gas variables for those who are interested. Other brands of machine have usually followed this practice so they can survive in the competitive marketplace. This assists in the survival of the Copenhagen approach.

### 9.5.2: Background to Boston Approach

The alternative method of quantifying acid-base disorders has been developed by investigators from Boston (eg
Schwartz & Relman). This Boston approach is the method used so far in this book and the six bedside rules have been outlined in section 9.3

This approach is based on actual experimental work in humans (eg whole body titrations) rather than on blood samples in a machine.

The aim has been to determine the magnitude of the compensation that occurs to graded degrees of acid-base disturbance.

These results are based on buffering and compensatory processes that affect the whole body rather than just the blood. Additionally, appropriate compensation for both acute and chronic disorders can be determined and corrected for when interpreting the blood gas results. The results are presented in a couple of different ways: as graphs with 90% confidence intervals, or as a set of calculation rules. This book uses the rules method because these can be easily committed to memory and can be easily used at the bedside when assessing patients with acid-base disorders.

This does not require the introduction of new terms like Base Excess and Buffer Base. The assessment of the magnitude of metabolic disturbances is based on a comparison of the actual (ie measured) and the expected values of \([\text{HCO}_3^-]\). The determination of the expected value (using clinical knowledge and the rules of section 9.3) incorporates the corrections necessary to adjust for the interaction between \(p\text{CO}_2\) and \(\text{HCO}_3^-\).

9.5.3: What Approach is 'The Best'?

Conclusion: Boston approach is better the Copenhagen approach

Within the traditional approach to acid-base analysis, the Boston 'bicarbonate method' is preferable to the Copenhagen 'base excess method' because:

- it is simpler to understand and to teach
- it is based on whole body experiments rather than on test tube results on a blood sample
- it emphasises the need for clinical assessment and interpretation rather than being driven by laboratory based derived quantities

Quote from the original critique of Schwartz and Relman in 1963

"The traditional measurements of pH, \(p\text{CO}_2\) and plasma bicarbonate concentration continue to be the most reliable biochemical guides in the analysis of acid-base disturbances. These measurements, when considered in the light of the appropriate clinical information and a knowledge of the expected response of the intact patient to primary respiratory or metabolic disturbance, allow rational evaluation of even the most complicated acid-base disorders."
BUT is the Stewart Approach the best of all?

Despite the above, it should be noted that the quantitative approach pioneered by Stewart may be a better approach. It has great strength in aiding understanding about what is going on but unfortunately it is difficult to use clinically. It is very limited in usefulness for routine clinical application and interpretation of blood-gas results. An introduction to this alternative approach is presented in Chapter 10.