



Blood Gas Analysis

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pH is the conventional way of describing the concentration of hydrogen ions. It is a logarithmic scale that allows representation of a wide range of hydrogen ion concentrations in a simplified way. Because it's a logarithmic scale, a small change in pH represents a significant change in hydrogen ion concentration. The pH considered compatible with life in a mammalian system ranges from 6.8 to 8, with normal for most mammalian species being around 7.4 and kept within a very tight range because of how important pH is for the chemical reactions that support life. The adverse effects of abnormal pH are worrying when we get down to about 7.2

Acidaemia is a blood pH lower than normal, alkalaemia is a blood pH higher than normal. This is important to distinguish from the terms acidosis and alkalosis, which refer to processes that tend to decrease or increase pH. When analysing acid-base, sample collection is particularly important because the pCO₂ of the sample will rapidly decrease as it equilibrates with air. The main factors that will result in erroneous results are time delays, exposure to air (including bubbles within the sample) and over-dilution of the sample with anticoagulant such as heparin.

Acid-base disturbances are common in critically ill and emergency patients, and it can help determine the severity of their condition and sometimes provide the answer. Tracking changes in blood gas parameters can provide information about the patient's response to your interventions. The acid base will generally point us to acid-base disturbances- the oxygenation and ventilation parameters will help to point us toward primary respiratory acidosis/alkalosis.

By definition:

Acidaemia: A decrease in blood pH (or an increase in blood H⁺ concentration). This differs from acidosis-a pathophysiologic process causing accumulation of an acid (containing protons) or loss of a base (both will increase H⁺), which lowers the pH.



This may or may not result in an acidaemia. An acidosis can be respiratory or metabolic in origin, i.e. primary respiratory or metabolic acidosis.

Alkalaemia: An increase in blood pH (or a decrease in blood H^+ concentration). Again, this differs from alkalosis- a pathophysiologic process causing accumulation of a base or loss of an acid (both will decrease H^+), which increases the pH. This may or may not result in an alkalaemia. An alkalosis can be respiratory or metabolic in origin, i.e. primary respiratory or metabolic alkalosis.

When we talk about primary acid-base disturbance, we are talking about a major abnormality that will drive the direction of pH changes. For example, a primary metabolic acidosis will decrease the pH. Secondary or compensatory acid-base disturbance is a compensatory response by the body in an attempt to correct or normalise alterations in pH (specifically, H^+) caused by the primary disturbance. The pH can sometimes return to normal within this compensation, but it often overshoots and goes the other way. Simple (uncomplicated) disturbance indicates that there is a single primary acid-base disturbance. This may or may not be accompanied by the expected compensatory response. A mixed disturbance indicates that there is more than one primary disturbance (two or three), e.g. a primary respiratory acidosis and primary metabolic acidosis. You will never find a mixed respiratory disturbance (i.e. alkalosis and acidosis).

An acid is a hydrogen ion (or proton) donor, a base is a hydrogen ion acceptor. We've already said the body keeps very tight control over pH to optimise biochemical processes. However, a small change in pH represents a large change in hydrogen ion concentration, so actually we can see that the body doesn't keep that tight a control over the hydrogen ion concentration – a 4 times difference is acceptable. If we think about other ions in the body that are tightly controlled, things like potassium, sodium and calcium, the body would never tolerate a 4 times fluctuation in those. The reason the body can tolerate more fluctuation in hydrogen ion concentration is because it has several buffer systems in place that either accept or donate hydrogen ions in order to keep the pH under control.

The traditional approach to acid-base analysis is based on the Henderson-Hasselbalch equation. From this equation, it is clear that it that pH is directly related to bicarbonate (that is, as bicarbonate increases, pH increases) and inversely related to pCO_2 (so as pCO_2 goes up, pH goes down). We can also see from the equation that



pH is a consequence of the ratio of pCO₂ and bicarbonate. When an abnormality in one side of the system occurs, the other side of the system attempts to return the ratio of bicarbonate and pCO₂ back to normal, in order to restore a normal pH, this is called compensation.

The body has 3 major processes to maintain acid-base balance: regulation of pCO₂ by ventilation, buffering of acids with buffer systems (both bicarbonate and non-bicarbonate), and altering renal excretion of hydrogen ions or bicarbonate. The respiratory component of the system is represented by pCO₂, whereas bicarbonate and base excess represent the metabolic component, which is influenced by both buffering systems and renal excretion.

Carbon dioxide acts as an acid because of its ability to react with water and produce carbonic acid, as the equation shows. As the pCO₂ increases, the equation is driven to the right and the hydrogen ion concentration will increase. As we've said, pCO₂ represents the respiratory side of the system.

Bicarbonate and base excess are both ways of quantifying the effect of the metabolic side of the system. Bicarbonate concentration is an easier concept to understand: bicarbonate is basic (as opposed to acidic) so more bicarbonate means more base, which is an alkalotic process. Less bicarbonate means less base, which is an acidotic process. Bicarbonate is a calculated parameter rather than one that our EPOC and iStat machines measure directly, but that's not the main problem with bicarbonate. The main problems with it is that it is not independent of pCO₂, and therefore although we're using it as a measure of the metabolic side of the system, it's not independent of the respiratory side. We've said that as pCO₂ increases, the carbonic acid equation at the top gets driven towards the right, meaning more acidic hydrogen ions are produced, but this also means that more bicarbonate is produced. This is why Base Excess can be a more useful way of representing the metabolic side of the system.

Base excess is a more complicated concept: it is the amount of acid that would need to be added to a sample of oxygenated whole blood to restore the pH to 7.4 assuming a pCO₂ of 40mmHg and a temperature of 37C. Theoretically, a normal individual should not have an excess or deficit of acid or base, so the base excess should be zero. Of course, this concept was developed in human medicine and our patients aren't humans, so the normal base excess is slightly different for them with



cats having a lower base excess than dogs. The major advantage of base excess over bicarbonate is that it is independent of the respiratory side of the system because it is not influenced by $p\text{CO}_2$. If there are minimal changes in $p\text{CO}_2$, base excess and bicarbonate should correlate well, but if there are significant changes in PCO_2 the base excess will be the more reliable measure.

So to tie in with base excess and its effect on acid base, it is useful to remember that there are two columns with cations and anions, and how the primary and secondary profiles can point us towards acid-base disorders. In this diagram, there are the cations on the left (sodium and potassium) as well as the urine pH (part of the secondary profile alongside the potassium), and on the right in the column for the anions and what we call the primary profile. This column contains the Anion Gap which is made up of predominately albumin, but also things such as phosphates and are the 'unmeasured' anions (hence the name) that help to maintain electroneutrality against the measured cations. The other two 'blocks' in this column include the TCO_2 , which includes bicarbonate, and Chloride; remember the chloride will always aim to keep a 1:1 ratio to Sodium. The way to measure if the chloride is maintaining that ratio, is to look at both the sodium and chloride ranges and assess how far the result for both from the bottom reference range- if the difference between the two changes is greater than 3 then this is not proportional. So, for example, if the chloride was 80 mmol/L and the range is 105-118 mEq/L and the sodium was 140 mmol/L and the range is 142-150 mEq/L, this means that the chloride is -25 versus sodium which is -3 so this is clearly a disproportional gap and above a difference of 3 mmol/L. The idea with this column is that it will always maintain the same 'size/amount' as the left-hand column. So, you will never have all three in the right column rise at the same time, they will always counterbalance the other- and this is how we can assess what simple metabolic acid-base disorders are occurring.

The secondary profile consists of the potassium and the urine pH. These will often change in retaliation to the changes in the right column. For example, the potassium will rise in acidosis; so, you see a decrease in metabolic alkalosis. A frequently cited mechanism for this is that acidosis causes potassium to move from cells to extracellular fluid (plasma) in exchange for hydrogen ions, and alkalosis causes the reverse movement of potassium and hydrogen ions (seen in the diagram in the previous slides). With this change you will also find what is called a paradoxical aciduria (so think of them as opposites attract), as we talked about earlier the renal



system will compensate by excreting excess sodium bicarbonate found in metabolic alkalosis, causing the urine to become acidic.

When it comes to alkalotic processes, hypokalaemia itself is an important cause of the initial generation and ongoing maintenance of a metabolic alkalosis due to the same mechanism we discussed before: a relatively low concentration of potassium outside the cell causes diffusion of potassium from inside to outside along its concentration gradient. To maintain electroneutrality, the hydrogen ions enter the cell, which reduces the acidity of the extracellular fluid, resulting in an alkalosis. Moreover, hypokalaemia promotes renal acid loss, which is also an alkalotic process. The kidneys can only do their job effectively and get rid of bicarbonate in order to resolve the alkalosis if they have the right conditions to do so: reduced circulating volume will limit their effectiveness, as will electrolyte abnormalities, particularly hypochloraemia and hypokalaemia. Therefore, we need to choose our fluid therapy carefully to support the circulating volume and correct the electrolyte abnormalities. This is one scenario where normal saline might be a better choice, possibly spiked with potassium.

Metabolic acidosis is due to increases in non-volatile (non-carbonic) acids, which can contain chloride as their anion (e.g. ammonium chloride) or another anion (e.g. lactate). Body buffers in plasma (bicarbonate particularly, but also proteins) and intracellularly (haemoglobin in RBCs in particular) or in bone immediately start to offset any increase in H^+ from a non-volatile acidosis. The lungs also blow off carbon dioxide, which is respiratory compensation. If needed, the kidney will kick in and increase ammoniogenesis (regenerating new bicarbonate and excreting ammonium chloride) and excreting H^+ directly via H -ATPases (in all tubules, but primarily collecting tubules; chloride follows) as correction for the acidosis (as long as the kidney is not dysfunctional and causing the acidosis in the first place).

In titrational acidosis, the decreased tCO_2 will be accompanied by an increase in the anion gap- this means that there will be increased acids in the circulation- using up the tCO_2 ; this is called a 'titration' process. With the secondary profile you may see an increase with potassium (thinking of the buffer systems) and a possible decrease in urine pH. More often than not titrational acidosis will be part of a mixed base disorder as both the Cl^- and TCO_2 will decrease with an increase in AG, when there is a mixed metabolic alkalosis or respiratory acidosis too.



The third simple pattern we can gain from these profiles is secretional acidosis. Since this is a metabolic acidosis the $t\text{CO}_2$ will once again decrease, but this time the Chloride will increase (vs sodium). This is called a secretional acidosis because the decrease in $t\text{CO}_2$ is due to loss from the body, or a secretional process. The chloride increases (or is retained) in these processes, to maintain the total anion pool and electroneutrality. With the secondary profile you may see an increase with potassium (thinking of the buffer systems) and a possible decrease in urine pH.

Respiratory rate alone cannot be used to try to establish if an animal is hypo or hyperventilating. Ventilation is a function of respiratory rate and tidal volume. So, you can have a dog that is panting but doesn't have a respiratory alkalosis because they're not actually hyperventilating – normal panting is dead-space ventilation so does not change the $p\text{CO}_2$. Equally, you can have a slow respiratory rate but with a large tidal volume that does cause hyperventilation. So, we mustn't assume ventilation status from the respiratory rate, we need to measure the $p\text{CO}_2$.

Respiratory acidosis occurs due to increases in the volatile (it can be blown off) or so-called "respiratory" acid, carbonic acid (hypercapnia), which comes from increases in carbon dioxide due to inadequate ventilation (hypoventilation). Carbon dioxide is freely diffusible and moves rapidly into cells (haemoglobin in RBCs in particular) which starts to offset any increase in H^+ from a volatile acidosis. The kidney will kick in and increase ammoniogenesis (regenerating new bicarbonate and excreting ammonium chloride) and excreting H^+ directly via H-ATPases (chloride follows) as compensation for the volatile acidosis (this is very effective and, in some species, can correct pH given time). Carbonic acid, which generates bicarbonate when combined with water, cannot (obviously) be buffered by bicarbonate. Conditions which cause acidosis are usually those that interfere with oxygen delivery and carbon dioxide exchange; for example pulmonary thromboembolism (PTE), pulmonary oedema, pulmonary fibrosis (also known as westie lung), alveolar pneumonia, lung shunts and atelectasis. Other disease processes such as pyrexia and hyperthyroidism can also be responsible. Treatment is aimed at the underlying cause, but it is worthwhile performing an arterial sample on these patients to assess the PaO_2 , as these patients may require mechanical ventilation or some form of oxygen supplementation.

Respiratory alkalosis is the least likely of the 4 acid-base disturbances and is due to hypocapnia secondary to hyperventilation (increased tidal volume). Hydrogen is liberated off intracellular buffers (haemoglobin in RBCs in particular), which moves



extracellularly offsetting the decrease in H^+ in plasma. The kidney will kick in and decrease H^+ excretion (chloride is retained). This is very effective and, in some species, can correct pH given time (usually 3-4 days). Severe alkalaemia only occurs in acute hypocapnia which is difficult to measure on conscious animals- under GA we will see drops in blood pressure and drops in $ETCO_2$; correction in these acute cases can occur within 15 minutes. Ultimately treatment of respiratory alkalosis is by correction of the underlying cause, but anxiolytics and increased oxygen supplementation will benefit the patient.

To confirm whether there is acute lung injury (ALI) or acute respiratory distress syndrome (ARDS), arterial blood gases should be taken to assess the ventilation, therefore oxygenation, of the patient and the acid base status. To assess for ventilation, the PaO_2 can be assessed for any hypoxemia and the alveolar-arterial equation (A-a) gradient can be calculated from this. Calculating the Alveolar-arterial gradient helps to identify the cause of hypoxemia, and in particular will evaluate the presence of significant venous admixture (V/Q mismatch) which is a common cause of hypoxemia. Normal values for these are 0-10, 10-20 means there is some impairment, 20-30 value means severe impairment and >30 will require mechanical ventilation and likely means ARDS. Using the "120 rule" the A-a gradient equation can be simplified (the patient must be on room air- FiO_2 21%), to $A-a = 150 - 1.1 (PaCO_2) - PaO_2$. Finally, the PaO_2 / FiO_2 ratio can assess the severity of hypoxemia and the presence of ALI/ARDS, a normal ratio should lie at 500, with values less than 300 being associated with ALI and values lower than 200 consistent with ARDS.

Compensation involves responses by the respiratory tract and kidney to primary metabolic and respiratory acid-base disturbances, respectively. Compensation opposes the primary disturbance, although the laboratory changes in the compensatory response parallel those in the primary response.

Respiratory compensation for a primary metabolic disturbance: Alterations in alveolar ventilation occurs in response to primary metabolic acid-base disturbances. This begins within minutes to hours of an acute primary metabolic disturbance. Note that complete compensation via this mechanism may take up to 24 hours. Renal compensation for a primary respiratory disturbance: Here, the kidney alters excretion of acid (which influences bases as well) in response to primary respiratory disturbances. This begins within hours of an acute respiratory disturbance but takes several days (3-5 days) to take full effect.



As you can see from the table in the webinar, there are values associated with what is considered a 'normal' response to these acid-base changes. Anything above these values is likely to be a mixed base disorder. So, for example if your PCO₂ is higher than 0.7 mmHg per 1 mEq/L rise in HCO₃⁻, then it is likely that you have a concurrent respiratory acidosis as well as a metabolic alkalosis. This is where it is useful to look at the primary profiles we were speaking about earlier, to see the changes in the anion gap, tCO₂ and Cl⁻.

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