ER TRICKS & TIPS- GET THE MOST OUT OF YOUR ER BLOOD PANEL

David Liss, RVT, VTS (ECC, SAIM), CVPM | Los Angeles, CA

The Minimum database:

The minimum database is a collection of tests aimed at figuring out whether the patient is going to crash quickly. The database often includes: Blood glucose, BUN, Venous blood gas, electrolytes, lactate, PCV/TS.

- **Blood glucose**: If low, patient could crash. Are they a puppy? Are they diabetic?
  - If high, patient could be sick, but not likely to crash
- **BUN**: If very high, potentially renal failure or severe dehydration. Whether high or low, not likely to crash immediately
- **Venous blood gas**: if pH is low and patient is acidotic, could cause cardiac arrhythmias. Shock and toxins will cause metabolic acidosis.
- **Electrolytes**: Sodium: If Sodium is quite high or low patient could have neurologic issues: seizures. Chloride: Often follows sodium. Potassium: Very high or low potassium levels could cause death
- **Lactate:** Very high indicates shock. Low not really important
- **PCV/TS:** High PCV and high TS indicate dehydration. Low PCV indicates anemia. Low TS (<5.5g/dL) in trauma may indicate hemorrhage.

BUN

Chemistry results may reveal azotemia (hallmark of decreased GFR). Azotemia is characterized by an increase in nitrogenous waste products, namely BUN and Creatinine. Azotemia can be pre-renal, renal, or post-renal. A urine specific gravity will help differentiate between the two. The chart below helps break down the difference in azotemia.

Table 2. Classification of Azotemia

Types of Azotemia		
Type of azotemia	**USG results**	**Patient condition**
Pre-renal	Concentrated <1.030	Patient is dehydrated or hypovolemic. This results in a decline in GFR as the body preserves fluids for vascular volume.
Renal	Isosthenuric 1.007-1.012	If patient is dehydrated/hypovolemic: The kidneys are not doing their job and concentrating urine. The urine is the same USG as plasma, meaning it is being excreted without any water retention.
Post-renal	Varies: usually concentrated	Hard to simply diagnose post-renal azotemia from USG but if any evidence of osbtruction present this would result in a post-renal azotemia.

Blood Gases

INTRODUCTION

Blood gases are a very important part of the workup of a critical patient. They can provide a wealth of information and even point to specific disease processes. However, they are quite complex and can often be a puzzle to figure out. This presentation will serve to provide a solid foundation to the interpretation of blood gases. Basic physiology of acid-base regulation, step by step process for evaluating blood gases, and case examples will be reviewed.

PATHOPHYSIOLOGY

There are 3 parts to the blood gas. The ventilator component, the metabolic component, and the oxygenation index (if using an arterial sample). We will not be discussing the oxygenation portion if the blood gas for this lecture. Two organ systems are responsible for regulating acid-base balance in the body. The lungs retain and excrete CO2 and the kidneys retain and excrete HCO3. What is acidity? This refers to a net increase in the amount of protons (H+) in a solution. H+ ions result from all of the net metabolic processes in the body. Acids are produced in normal enzymatic reactions (such as lactic acid production in cellular respiration). The body must maintain homeostasis (pH 7.35-7.45) as best it can. pH is an inverse measurement of H^+ concentration. As pH decreases, H^+ ion concentration increases and vice versa. Only small decimal points can mean large changes in the concentration of H^+. Carbon dioxide is considered the "acid" portion of the acid-base profile. CO_2 readily combines with H_2O in the face of carbonic anhydrase to form carbonic acid. Thus, if there is an abundance of CO_2 available, H^+ ions will be made.

See the following equation:

$$\mathbf{CO_2 + H_2O \leftrightarrow H_2CO_3 \leftrightarrow H^+ + HCO_3^-}$$

If the body makes more acid, either inadervently or on purpose, the body must "buffer" the acid to ensure normal pH. The buffer the body uses is bicarbonate, or HCO_3^-. This is the chemical that can combine with H^+ to make water and CO_2, which the lungs can breathe off. It essentially "neutralizes" the pH or H^+ concentrations. Production of acids is called an acidosis, if talking about tissues, or academia, if talking about the bloodstreatm. Production of base is called an alkalosis, or alkalemia. So a rise in acid production (lactic, ketotic) or acid retention (pulmonary disease, hypoventilation) results in an academia. Retention of bicarbonate or hyperventilation will result in an alkalosis.

COMPENSATION

When acid levels rise, either from carbonic acid production, as a result of inefficient carbon dioxide excretion, or excess endogenous acids, chemoreceptors in the kidneys signal the retention of bicarbonate. Initially, the kidneys do not respond acutely. It takes 2-5 days for them to fully retain enough bicarbonate to cause buffering. Thus, chemoreceptors in the brain signal an increase in respiration rate (minute ventilation). By increasing rate, clearance of CO_2 will hopefully be enhanced. The pH drops and the body normalizes. So, acute responses to academia will be increasing minute ventilation. Chronic responses will be retention of bicarbonate.

The opposite is true with alkalemia. If either there is an increase in HCO_3^- concentration, or a decrease in CO_2, the body will respond appropriately. If CO_2 levels drop (remember CO_2 = acid), then the kidneys will begin to excrete bicarbonate, the buffer, because they do not need as much. If HCO_3^- is being retained for some reason, hypoventilation can ensue to increase the CO_2 (and thus acid) concentrations in the blood to counteract the amount of base present.

ANION GAP

The last concept of physiology is the Anion Gap. The idea is simple. All anions (negatively charged ions) must stay in balance in the body. If one increases, another must decrease to keep the same total number. The Anion Gap formula is as follows:

$$AG = (Na^+ + K^+) – (Cl^- + HCO_3^-)$$

There are obviously other ions in the body, but they are technically negligible. The total number of cations (positively charged ions) exceeds the number of anions. But this number needs to stay relatively constant. If, for example, the chloride levels decrease, the bicarbonate levels MUST increase for this to stay constant.You can see the level of bicarbonate decreased to compensate for the increase in chloride. Now in the real world the bicarbonate levels would match the chloride change. So if the chloride went up 13 points the bicarb would decrease by 13. So the AG = (144) – (125 + 5) = 14. The AG is considered normal in this situation.

What about a high anion gap? Well acids tend to be anionic, so if you add a bunch of acids (lactic, ketotic, uremic, glycolic) into the mix, it will drive the anion gap up, but they are not entirely figured into the calculation. So a normal AG is usually related to a loss of chloride causing the bicarbonate to increase causing a metabolic alkalosis. An increased AG is due to endogenous or exogenous acids and results in a metabolic acidosis.

STEPWISE APPROACH TO INTERPRETING A BLOOD GAS

- **Step 1**- What is the pH?
  Does the patient have an academia (low pH <7.35) or an alkalemia (high pH > 7.45)
- **Step 2**- What is the respiratory compenent?
  Do they have hypercarbia or hypocarbia?
- **Step 3**- What is the metabolic component?
  Do they have an increase or decrease in base?
- **Step 4 (optional)**- What is the anion gap?
  Is it normal or high? (It USUALLY isn't low, so don't worry about that)

NORMALS:

pH: 7.35-7.45
PCO_2: 35-45 mmHg
HCO_3: 18-24 meq/L
Anion Gap: 12-24 meq/L

EXAMPLE:

pH- 7.1 (Normal: 7.35-7.45)
HCO_3- 10 (Normal 18-24)
P_aCO_2- 30 (Normal 35-45)
Lets not worry about the anion gap for this one.

OK: Let's work through this blood gas using the step wise process:

Step 1- Is it acid or base?
Well the pH is lower than normal, and pH is an inverse of H+ concentration, so the H+ concentration is high. That means its acidic!
Step 2- Is the patient hypocarbic (low CO_2) or hypercarbic (high CO_2)?
Well the CO_2 is lower than normal, so the patient is hypocarbic
Step 3- Does the patient have an increase or decrease in base?
The base is below normal, so a decrease in base

So we have a patient that is acidic, with a low CO_2 and a low base level. How do we figure this out? Well, if you remember that CO_2 = acid, then because the CO_2 is low, it CANNOT be a respiratory acidosis. The HCO_3 is low, and that is by definition a metabolic acidosis. This is because somewhere in the body (lets say this patient's lactate was 11…) there is acid that is neutralizing base, and this is bringing the HCO_3 levels down. What the body does to compensate is increases respiratory rate (thereby decreasing CO_2 levels or ACID levels) to compensate! So we have a metabolic acidosis with respiratory compensation!

4 CLASSIC ACID-BASE PATTERNS

Metabolic Acidosis:
This presents with an acidic pH and a low bicarbonate. If the patient has had time to respond then the respiratory rate increases (or the patient takes deeper breaths) and the CO_2 begins to drop as well. It is associated with either an increase in Cl- (decrease in bicarbonate from the anion gap) which is rare, OR an increase in "endogenous" acids such as lactate, keto-acids, uremic acids, ethylene glycol metabolism, salicylate toxicitiy, The chloride-loss type will have a NORMAL anion gap, because the bicarbonate levels drop to compensate. The excess acid type will have an increased AG because those acids are usually negatively charged and thus contribute to a greater gap between cations and anions (bicarbonate levels drop without chloride compensating).

Metabolic alkalosis
This is defined as an eleveated bicarbonate (base) level and a high pH (alkaline)
This is somewhat rarer, but a common cause is upper GI vomiting and subsequent loss of H^+ and CL^- ions. These both contribute to an increase in HCO_3 levels and a subsequent metabolic alkalosis.

Respiratory acidosis
This is defined as an elevated CO_2 (acid) level and an acidic pH.

Common causes include any reason for hypoventilation (respiratory depression). Brain disease or head trauma, anesthetic depth, potentially opioid administration, pain with breathing (rib fractures), hypoxemia.

Respiratory alkalosis

This is defined as a decreased CO_2 level and an alkaline pH. This is usually caused by hyperventilation. This can certainly be from pain, fear, stress, anxiety, and also brain disease, hyperthermia, etc.

Table 1. Classic Acid-Base abnormalities

4 Classic Acid-Base Patterns					
Metabolic	**Type**	**pH?**	**CO_2?**	**HCO_3?**	**Compensation**
	Acidosis	↓	**↓-Acute**	↓	Bicarbonate levels decrease because of excess acid. Because the lungs can act quickly, they begin to increase minute volume either by increasing respiratory rate or tidal volume.
	Alkalosis	↑	**↑-Acute**	↑	Bicarbonate levels rise in a metabolic alkalosis. Thus the lungs will decrease minute volume in an attempt to increase CO2 retention (acid).
Respiratory	**Acidosis**	↓	↑	**↑-slow**	Initially a respiratory acidosis causes a decreased pH with an increased CO2 level. As the kidneys begin to reabsorb bicarbonate that level increases. However, it takes 3-5 days to fully compensate, so its not considered an acute event.
	Alkalosis	↑	↓	**↓-slow**	Here we have a respiratory alkalosis. Respiration has increased the amount of CO2 we have breathed off. Thus the pH trends upwards. The kidneys will begin to excrete bicarbonate but it takes time.

Glucose

Hyperglycemia is an observable pathology in critically ill patients. Studies have evaluated the detrimental effects of hyperglycemia and reveal that maintaining normoglycemia lowers morbidity and mortality.

Glucose is absorbed in the small intestine from carbohydrates ingested in the diet. It is then taken up by tissues. It is stored in large quantities in the liver as glycogen via glycogenolysis. Glucose can also be created in the liver from fat and amino acids in the liver via gluconeogenesis. It is transported into the cell via glucose uptake proteins stimulated by insulin. Inside the cell, glucose is either converted to glycogen or to pyruvate via glycolysis, where it can produce cellular energy in the form of ATP. Mild hyperglycemia is seen at levels of 130-150 mg/dL. Severe hyperglycemia is seen at levels > 180 mg/dL. Glucosuria will develop in states of hyperglycemia. Renal threshold of glucose is 180-220 mg/dL in dogs and 260-310 mg/dL in cats. Glucosuria will create an osmotic diuresis, contributing to volume depletion. Hyperglycemia in the critically ill can be the result of increased release of glucocorticoids, catecholamines, and insulin resistance. In hypovolemic and painful states, cortisol is released. Cortisol decreases the activity of a specific glucose transport protein, GLUT 4. Insulin is released in states of hyperglycemia, however, with decreased transport proteins, glucose cannot travel intracellularly. Some causes of hyperglycemia can be TPN administration, surgery, administration of steroids, vasopressors, and anesthetics. Ketamine/a_2's and opioids have been implicated in hyperglycemia. 30% of TPN patients were reported to be hyperglycemic. Hyperglycemia can also be found in early sepsis from a catabolic state and a need for glycogen.

Hyperglycemia induces and also has a detrimental effect on inflammation. Diabetics are known to be weaker at fighting infections. Inflammation is increased but the function is decreased (phagocytic cells function is reduced) and glucose inactivates immunoglobulins. There is also an increased production of pro-inflammatory cytokines like IL-1, IL-6. And TNF-α.

Hyperglyecemia also induces the coagulation system. Glucose activates the tissue factor pathway, increases the levels of circulating coagulation factors, and inhibits natural anticoagulants such as Protein C. It also stimulates activation of platelets and inhibits the fibrinolytic system.

Glucose also increases free fatty acid concentrations, which are toxic to the myocardium. Thus, cardiovascular effects, such as arrhythmias may ensue.

Finally, hyperglycemia is considered detrimental in traumatic brain injury. The brain needs glucose because it cannot store glycogen. However, during hypoxic states anaerobic metabolism produces lactate as a byproduct. Lactate is toxic to brain cells. Increased levels of free radicals, excitatory neurotransmitters (glutamate), cerebral edema, and vasoconstriction may occur.

In humans, there is evidence of decreased mortality with normoglycemia as well as decreased incidence of acute renal failure, ventilator requirements, transfusions, and infections.

Tight glycemic control is used routinely in humans to control blood glucose concentrations. Insulin is anti-inflammatory and decreases TNF-α concentrations. Insulin CRI's are not standards in veterinary medicine but are being investigated. Side effects of insulin therapy are hypoglycemia, hypokalemia, hypophosphatemia, and hypomagnesemia. Veterinary evidence does not point to morbidity or mortality but a recent study found that 63% of cats with hyperglycemia had a decreased length of hospitalization once normoglycemic.

Lactate

Lactate production is the result of anaerobic cellular metabolism. It is a bypdroduct of metabolizing pyruvate to produce ATP for cellular energy. Glycolysis produces pyruvate in the cytoplasm of cells. Under aerobic conditions pyruvate traverses into the mitochondria and produces lots of ATP iva the Kreb's cycle. Red blood cells do not have mitochondria, so lactate dehydrogenase converts pyruvate to lactate to produce ATP. The excess lactate diffuses out of the cell and back to the liver to assist in making glucose via gluconeogenesis. This is called the Cori cycle.

In states of cellular hypoxia, only glycolysis occurs, producing pyruvate. Because pyruvate cannot travel into the mitochondria, LDH converts pyruvate to lactate and produces a small amount of ATP. As more and more lactate accumulates, it cross into the intravascular space and travels around the body. If global hypoxia is present, other tissues will be unable to utilize lactate to make glucose and it accumulates in the intravascular space. Lactate is dissociated with a Hydrogen ion at physiologic pH. Thus the excess hydrogen lower blood pH. Lactate is metabolized by the liver, and excreted by the kidneys.

There are two types of Lactic Acidosis. Type A, where tissue hypoxia is present with normal mitochondrial function and Type B, where oxygen delivery is adequate, but carbohydrate metabolism/mitochondrial dysfunction are present.

Type A lactic acidosis indicates decreased DO_2 (oxygen delivery to tissues) through either, a decreased cardiac output, hypovolemia, or decreased oxygen content (as in anemia) or a decreased ability to extract O_2 (edematous states).

Type B lactic acidosis has 3 subtypes. Type B-1 comes from decreased clearance of lactate. This may occur with liver failure, diabetes (from abnormal carbohydrate metabolism), renal failure, or in neoplasia. Type B-2 lactic acidosis occurs with drugs/toxins that affect a portion of glycolysis called oxidative phosphorylation. These include ethylene glycol, carbon monoxide, salicylates and acetaminophen. Type B-3 lactic acidosis occurs with mitochondrial diseases.

There is some evidence that lactate can serve as a prognostic indicator. Measurement of lactate may help determine the severity of the disease. In GDV patients, a study revealed that 74% of patients with a lactate >6.0 mmol/L had gastric necrosis. The chances increased to 80%, 92%, and 100% of patients having gastric necrosis at lactate levels of 7 mmol/L, 8 mmol/L, and 10mmol/L, respectively.

Evaluation of lactate in abdominal fluid may reveal a septic effusion. It should always be evaluated with glucose measurements,. A blood:fluid glucose difference of >20 mg/dL is 100% sensitive and specific for septic peritonitis. A blood:fluid lactate difference of >2 mmol/L is highly suggestive of a septic effusion.