Clinical Chemistry Trainee Council
Pearls of Laboratory Medicine
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TITLE: Blood Gases

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Slide 1:
Hello, my name is Joe El-Khoury. I am a Clinical Chemistry Fellow at the Cleveland Clinic. Welcome to this Pearl of Laboratory Medicine on "Blood Gases."

Slide 2:
Blood gas testing traditionally referred to the determination of pH, pO_2, pCO_2, and sO_2, but with the introduction of modern blood gas analyzers, it now also includes other analytes such as lactate and glucose. Also, testing is no longer restricted to the central laboratory but can be performed at point-of-care or emergency departments, or even in helicopters transporting injured patients. This is because blood gas testing is urgent and provides vital information about the patient's acid/base regulation and oxygenation status.

Slide 3:
Some of the important blood gas terms that relate to acid/base regulation and their reference intervals are introduced on this slide. Please note that the reference intervals used in this presentation are based on values provided by the Contemporary Practice in Clinical Chemistry textbook. These intervals vary slightly between laboratories and methods which is why I recommend you refer to your own laboratory's intervals.

pH is an index of acidity or alkalinity of the blood, which in normal arterial blood is between 7.35 to 7.45. Patients with pH lower than 7.35 are in acidosis, while those with a pH higher than 7.45 are in alkalosis. pCO_2 is a measure of the partial pressure of carbon dioxide dissolved in blood; since its levels vary based on ventilation, it also represents the respiratory component of the acid/base balance. In arterial blood, the reference interval is between 35 to 45 mmHg. Lastly, bicarbonate (HCO_3^-), which some blood gas analyzers measure while others calculate, is an indicator of buffering capacity of the blood and is classified as the metabolic component of the acid/base balance. Its reference interval for arterial blood is between 21 to 28 mmol/L.

Slide 4:
Carbon dioxide and bicarbonate constitute the major buffering system in plasma, and together work to control the pH of blood in the narrow range between 7.35 and 7.45. However, it is important to recognize that proteins also play a role in buffering the plasma, and hemoglobin in particular acts as an acid transport between the tissue and the lungs by transporting H^+ from the acidic tissues to the lungs and exchanging it there for oxygen. Phosphate, on the other hand, acts as a major intracellular buffer.

Slide 5:
The two systems that control the levels of carbon dioxide and bicarbonate in the blood are the respiratory and metabolic systems, respectively. The respiratory system controls pCO_2 levels by changing the rate of ventilation by the lungs, with decreased ventilation rate causing build-up of CO_2 from cellular respiration, and increased ventilation rate causing more rapid elimination of CO_2. As a result, any abnormalities affecting the lungs' rate of respiration will directly affect the pH of the blood. In a similar way, the metabolic system controls bicarbonate levels by increasing or decreasing the rate of elimination of HCO_3^- by the kidneys. Under this mechanism, blood pH is maintained with the lungs controlling the level of acid remaining in the blood by controlling excretion of CO_2, which readily converts to carbonic acid in the blood, and the kidneys controlling the amount of base remaining, by controlling excretion of bicarbonate.

Slide 6:
Clinically, a decrease in blood pH due to an increased pCO_2 is termed respiratory acidosis. It is ventilatory failure that can be caused by diseases of the airways either by impairing gas exchange such as asthma, or by obstruction such as chronic obstructive lung disease, or diseases affecting the chest or the nerves and muscles that signal the lungs to inflate or deflate, or drugs that suppress breathing. Bicarbonate is usually normal or elevated depending on whether the condition is acute or chronic and if the body has had time to compensate. On the other hand, an increase in blood pH due to a decrease in pCO_2 is termed respiratory alkalosis. In this case, the patient is usually suffering from a condition that leads to hyperventilation, such as anxiety or fever. Typically, bicarbonate is usually either normal or low if the body has had time to compensate.

Slide 7:
Moreover, a decrease in blood pH due to a decreased HCO_3^- level is termed metabolic acidosis. This condition can be caused by a variety of factors that increase the rate of elimination of bicarbonate either in the kidneys or by the production or ingestion of acids. Common causes include loss of bicarbonate through diarrhea or impaired H/HCO_3^- exchange in renal tubules, a condition known as renal tubular acidosis. Typically, pCO_2 is either normal or also decreased as the body attempts to compensate.

On the other hand, an increase in blood pH due to an increased HCO_3^- level is termed metabolic alkalosis. This is more commonly due to impaired renal excretion of bicarbonate or loss of hydrogen ions such as in vomiting. Typically, pCO_2 is either normal or also increased as the body attempts to compensate.

Slide 8:
The body's attempt to restore pH to normal after an acid/base disorder is termed compensation. Compensation is usually accomplished by the unaffected system maintaining the acid-base balance. For example, if the problem is metabolic, the lungs will compensate by either hypo- or hyperventilating to increase or decrease pCO_2 and normalize the pH. Similarly, if the problem is respiratory, the kidneys will adjust the excretion rate of bicarbonate to lower or increase the amount of bicarbonate and normalize the pH. In the table shown on the slide, a summary of the changes seen during compensation for each acid-base disorder is provided. Note that the change due to compensation is always in the same direction as the effect of the primary disorder. For example, if pCO_2 is increased as the primary disorder, then the effect of compensation will be to increase HCO_3^-. Another important point to mention is that respiratory compensation occurs within minutes to hours for full compensation, while metabolic compensation is slower and requires days.

Slide 9:
Interpretation of blood gas results requires a systematic 3-step approach to correctly diagnose the patient with an acid-base disorder.

Step 1: always examine the pH first. If it is lower than 7.35 then the patient is in acidosis, if it is higher than 7.45 then the patient is alkalosis, and if it is in the reference interval, then the patient either has no acid-base disturbance or is fully compensated, which is why examining bicarbonate and pCO_2 is still required.

Step 2 can involve examining bicarbonate or carbon dioxide; it doesn't matter which one is examined first as long as both are examined eventually. The two golden rules are: 1) if the change in bicarbonate is in the same direction as pH, then it is the primary cause and the disturbance is metabolic, and 2) if the change in carbon dioxide is in the opposite direction as the pH, then it is the primary cause and the disturbance is respiratory. In fully compensated states with a normal pH, the same rules apply except the pH is considered low or high relative to 7.4, which is the average of the range.

Slide 10:
An interpretation chart is provided on this slide to help navigate through the process. I recommend printing it and using it as a tool to help with interpretation of blood gas results. The arrows in Step 1 between the normal pH range and the high and low pH, indicate that if the patient is fully compensated then compare the pH to 7.4 to determine if patient is in acidosis or alkalosis, then proceed through the chart accordingly. Patients who are fully compensated will have a normal pH but abnormal pCO_2 and HCO_3^-. Also, please note that if both conditions of Step 2 are met, meaning that bicarbonate and pCO_2 are changing in opposite directions, then this implies the patient has a mixed acid-base disorder which involves both the metabolic system and respiratory system being affected, which is beyond the scope of this chart.

Slide 11:
Some case examples are provided here to help us practice what we have learned so far. In the first case, the pH is 7.47, bicarbonate is 34 mmol/L and pCO_2 is 50 mmHg. Following the interpretation guide provided in earlier slides, the pH is examined first and is found to be greater than 7.45, which implies the patient is in alkalosis. Now to determine if the cause is metabolic or respiratory, we examine bicarbonate and notice it is greater than 24 mmol/L. So bicarbonate is abnormal and is changing in the same direction as pH, meaning that both are increasing, which implies that the cause is metabolic. So the primary disorder for this patient is a metabolic alkalosis.

The next question to answer is: Is the body attempting to compensate? By examining pCO_2 we notice that it is also increased, which means that yes, the body is compensating, but since the pH has not fully returned to normal, it is considered partial compensation. Similarly, for the second case presented here, for a normal pH of 7.37, the patient is either normal or in a fully compensated acidosis, since 7.37 is less than 7.4. In light of abnormal bicarbonate and pCO_2, we realize that the patient is in a fully compensated acidosis. But since both bicarbonate and pCO_2 are both elevated and therefore changed direction opposite to the pH, then the cause is respiratory. Remember, bicarbonate has to change in the same direction to be the cause. So, this patient is in a fully compensated respiratory acidosis.

Slide 12:
Once the primary disorder is established, it is important to determine the cause of this disorder and treat it. One useful metric to help determine the cause of a metabolic acidosis, which is often the most complicated to deal with, is anion gap. An anion gap is simply the difference between commonly measured cations and anions and has two known equations, one with potassium and one without, with their reference intervals shown on this slide. It is important to note that these reference intervals will vary depending on the lab's reference intervals for each analyte. If the anion gap is positive in the setting of a metabolic acidosis, then the mnemonic MUDPILES may be used to narrow down the possibilities and help determine the cause. M stands for methanol ingestion, U for uremia, D for diabetic ketoacidosis, P for paraldehyde, I for Isoniazid or iron poisoning, L for lactic acidosis, E for ethylene glycol ingestion, and S for salicylate poisoning. Similarly, if the anion gap is negative, the mnemonic HARD-UP may be used.

Slide 13:
Some of the important blood gas terms that relate to the patient's oxygenation status and their reference intervals are introduced on this slide. pO_2 stands for partial pressure of oxygen and relates to the ability of the lungs to oxygenate the blood. Its reference interval in arterial blood is between 83 and 108 mmHg. Percent O_2 saturation or sO_2 is another useful measure of percent of functional hemoglobin saturated with oxygen with its reference interval in arterial blood being between 96 and 100%. Functional hemoglobin includes oxyhemoglobin termed O_2Hb and deoxyhemoglobin termed HHb, while dysfunctional hemoglobin includes carbon monoxide bound hemoglobin termed carboxyhemoglobin or COHb and methemoglobin termed MetHb, in which the iron in the heme group cannot bind oxygen because it is in the ferric state and not the ferrous state.

Non-functional hemoglobin is usually present at low levels in the blood in normal individuals, about 1 to 6%, except in cases of carbon monoxide poisoning or in patients on nitric oxide therapy. In these cases, the third term, percent of total hemoglobin saturated with oxygen or $\%O_2Hb$, becomes important to detect increased amount of non-functional hemoglobin. The equations to calculate sO_2 and $\%O_2Hb$ are shown here to highlight the difference between the two terms.

Slide 14:

Evaluating blood gas results to determine a patient's arterial oxygenation status typically involves an examination of pO_2, especially in relation to the oxygen content of the air the patient is breathing termed FIO_2 or fraction of inspired oxygen, then sO_2 or $\%O_2Hb$ and hemoglobin concentration. Other factors that affect oxygen content in blood include temperature and pH, and should be taken into consideration when analyzing the data. Modern blood gas analyzers include temperature correction factors for the results reported if the patient is hypo- or hyper-thermic; however, this practice is controversial and the trend is away from temperature correction for most routine arterial blood gases. The ultimate goal is to determine if the patient is hypoxemic and requires O_2-enriched air or if the patient can survive breathing room air.

Slide 15:

Blood gas testing is highly affected by preanalytical variables, and appropriate specimen handling is essential. Anticoagulated whole blood specimen is the most commonly used type, and venous or arterial samples may be collected. The major differences between arterial or venous collections are simply pO_2 and pCO_2, and in fact, these are the only reasons an arterial collection should be made instead of a venous collection, which is easier to perform. Furthermore, it is important to perform these collections anaerobically; otherwise. air contamination will falsely increase pH and pO_2 while decreasing pCO_2. Another possible source of contamination is collection through catheters without appropriate flushing, which represents the most common source of non-physiologic results. Because cells are alive and readily consume oxygen and produce CO_2, samples should be analyzed as soon as possible and within 15 minutes when using plastic syringes because these absorb oxygen as well. Glass syringes may be analyzed within an hour, but these pose a greater risk of breaking during transport or analysis, which is why they are less frequently used. If delay in analysis is suspected, immerse syringe in ice bath, this will slow down cellular respiration and increase the stability of the sample. Most importantly, as is the case with all laboratory testing, it is essential to have the tube and tube type labeled appropriately, which poses a bigger challenge for blood gas testing because of the urgent nature of testing.

Slide 16:

The blood gas analyzer measures pH and pCO_2 potentiometrically by measuring the potential difference between two different electrodes. The only difference is that the pCO_2 electrode, known as the Severinghaus electrode, has an additional pCO_2 permeable membrane. On the other hand, pO_2 is determined amperometrically by measuring the current across two electrodes and is known as the Clarke electrode.

Slide 17:

Some take home messages are:

- Blood gas results are used to assess a patient's acid/base and oxygenation status
- Interpretation of pH, pCO_2, and $[HCO_3^-]$ results can help identify if the patient is in acidosis or alkalosis, if the problem is metabolic or respiratory, and if there is any compensation
- Interpretation of pO_2, sO_2, and [Hb] results can help identify if the patients are adequately oxygenating their blood or need O_2-enriched air
- Appropriate specimen handling and recognizing the various preanalytical sources of error is crucial to ensure high quality results and care are delivered

Slide 18: References

Slide 19: Disclosures

Slide 20: Thank You from www.TraineeCouncil.org

Thank you for joining me on this Pearl of Laboratory Medicine on "Blood Gases." I am Joe El-Khoury.