

A Primer on Arterial Blood Gas Analysis

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Arterial blood gases play an important role in the work-up and management of critically ill patients and patients with a variety of pulmonary complaints and disorders. For example, they are used to guide the adjustment of ventilator parameters on mechanically ventilated patients and are also a standard part of the work-up of patients who present with unexplained hypoxemia or dyspnea. It is, therefore, important that students and physicians be able to interpret the results of arterial blood gas sampling, determine the patient's acid-base status and assess the adequacy of oxygenation.

This primer describes a clinical approach to interpreting arterial blood gases. It will outline a step-wise approach to interpreting the acid-base status and generating differential diagnoses for the observed problems. It will then address the proper means for assessing the adequacy of oxygenation and determining the etiology of any observed abnormalities.

The physiologic principles underlying acid-base physiology are beyond the scope of this review and will not be considered here, but information about this topic can be obtained from the following additional resources:

- **HuBio 541 Course Syllabus:**

- <http://courses.washington.edu/hubio541/secure/syllabus/06AcidBase.pdf>

- **Murray and Nadel's Textbook of Respiratory Medicine:**

- http://www.mdconsult.com/das/book/body/121296754-2/0/1288/55.html?tocnode=51470230&fromURL=55.html#4-u1.0-B0-7216-0327-0..50010-0_294

Acid-Base Status

Terms and Normal Values

Before reviewing the assessment of acid-base status, it is helpful to review the normal values for the main acid-base parameters and some basic terminology.

The normal values for acid-base parameters are as follows:

- pH: 7.38 - 7.42
- P_aCO₂: 36 - 44 mmHg
- Bicarbonate: 22 – 26 mmol/L

Be aware that the normal ranges for these parameters will vary slightly from laboratory to laboratory.

The following terminology is applied to acid-base interpretation:

- **Acidemia:** refers to a low blood pH (< 7.38). Patients with a low pH, are said to be “acidemic.”
- **Alkalemia:** refers to a high blood pH (> 7.42). Patients with a high pH are said to be “alkalemic.”
- **Acidosis:** refers to any process that, if left unchecked, will lead to acidemia. This can occur through one of two mechanisms.
 - A respiratory acidosis is present when the PCO_2 is high (> 44)
 - A metabolic acidosis is present when the HCO_3^- is low (< 22)
- **Alkalosis:** refers to any process that if left unchecked will lead to alkalemia. This can occur through one of two mechanisms.
 - A respiratory alkalosis is present when the PCO_2 is low (< 36)
 - A metabolic alkalosis is present when the HCO_3^- is high (> 26)

It is important to keep these terms straight in your mind and in your communications with others. It is common for people to refer to the patient with a low pH, for example, and say they are “acidotic.” Similarly, they often refer to the patient with a high pH as “alkalotic.” This is incorrect terminology. When you are referring to the patient and their pH, the correct terminology is as follows:

- The patient with a low pH has “acidemia” or is “acidemic.”
- The patient with a high pH has “alkalemia” or is “alkalemic”

How the Data Are Presented

While the laboratory will always label each value in the arterial blood gas results, it is not uncommon for residents, fellows and attending physicians to either write or state the results without labeling each value. For example, rather than stating: “the pH is 7.40, the PCO_2 is 40, the PO_2 is 85 and the HCO_3^- is 24” they may simply state or write: “7.4/40/85/24.”

If ABG results are presented in this manner, by convention, they will be written or spoken in the following order: $pH \rightarrow PCO_2 \rightarrow PO_2 \rightarrow HCO_3^-$

Before you get started.... Make Sure the Numbers Are Consistent

Before you do your acid-base interpretation, it is important to do a little troubleshooting and make sure there are no measurement errors with your blood gas results.

There are two things you should do. First, make sure it is an arterial sample and not a venous sample. The best way to do this is to observe how the blood comes back into the blood gas syringe as the sample is drawn. Pulsatile flow is seen with an arterial sample but would be lacking with a venous sample. Similarly, arterial samples usually fill the syringe quickly, while venous samples move much more slowly into the syringe. You cannot always rely on the color of the blood to tell you it is arterial because a very hypoxemic patient will have dark, "venous-appearing" blood. If you did not see the sample as it was drawn into the syringe, you can use the PO₂ as a guide. If the patient was not very hypoxemic when the blood gas was drawn but you get a very low PO₂ with the results (30s-40s), it is likely that you have a venous sample. This tactic is a bit harder to use when the patient is very hypoxemic when the sample is drawn.

Second, you should make sure there are no measurement errors. A simple way to do this is to compare the bicarbonate value from the blood gas (a calculated value) with the bicarbonate from the chemistry panel (a measured value). They are not always exactly the same but they should be close to each other. This only works, however, if your chemistry panel and blood gas were measured at roughly the same time. You cannot do this if the samples were drawn many hours apart.

A more thorough approach is to see if there is consistency between the blood gas and the chemistry panel using the Henderson-Hasselbach equation. The equation is used to calculate the pH you would expect based on the measured PCO₂ and HCO₃⁻. This pH is then compared to the measured pH. If the values are similar, your sample is valid. If the values are far apart, there may be a measurement error.

Because no one can easily remember the full Henderson-Hasselbach equation, there is a modified process that can be used instead. This modified process is as follows:

- Calculate the hydrogen ion concentration using a modified Henderson-Hasselbach equation:

$$[H^+] = 24 \times PCO_2 / HCO_3^-$$

- Use the calculated [H⁺] to determine what the pH should be. pH is a function of the hydrogen ion concentration (pH = -log [H⁺]) but rather than doing the calculation you can refer to the following table:

If the [H ⁺] is...	Then the Calculated pH is...
100	7.00
79	7.10
63	7.20
50	7.30
45	7.35
42	7.38

41	7.39
40	7.40
39	7.41
38	7.42
35	7.45
32	7.50
25	7.60

- Compare the calculated pH to the measured pH. If they are similar, your sample is valid. If the values are far apart, there may be a measurement error.

A Step-Wise Approach to Acid-Base Status Interpretation

As with reading an electrocardiogram or a chest x-ray, it is important to use a system when reading arterial blood gases. Adhering to a system will allow you to identify the primary and compensatory process and any additional disorders that may be present.

A suggested step-wise approach for reading an arterial blood gas is as follows:

- Examine the pH and comparing it to the normal range
- Identify the primary process that led to the change in pH
- Calculate the serum anion gap
- Identify the compensatory process (if one is present)
- Identify if any other disorders are present or there is a mixed acid-base process.

Each of these steps is described below in greater detail. After working through these steps, you should be able to give a one- or two-sentence synopsis of the patient's acid-base status such as "This patient has a primary respiratory acidosis with a compensatory metabolic alkalosis."

As you go through this process, try not to lose track of the clinical scenario that led to the blood gas being drawn in the first place. You will use the results and their interpretation to help you figure out what is going on with the patient. In addition, you should always ask if the results make sense in light of what you know about the patient's case. If the results do not make sense, either your interpretation was wrong or there may be some additional processes at work that were not recognized on the initial analysis.

With that in mind, the main steps in interpreting an arterial blood gas in greater detail are presented below.

- **Step 1: Examine the pH and compare it to the normal range.** As noted above, if the pH is low, the patient has an **acidemia**. If the pH is above this range, the patient has an **alkalemia**. Be aware that patients can have mixed metabolic disorders (eg. concurrent metabolic acidosis and alkalosis) that can give them a pH in the normal range. This will be discussed further below.

- **Step 2: Determine the primary process that led to the change in the pH:**

For a patient with a low pH (acidemia)

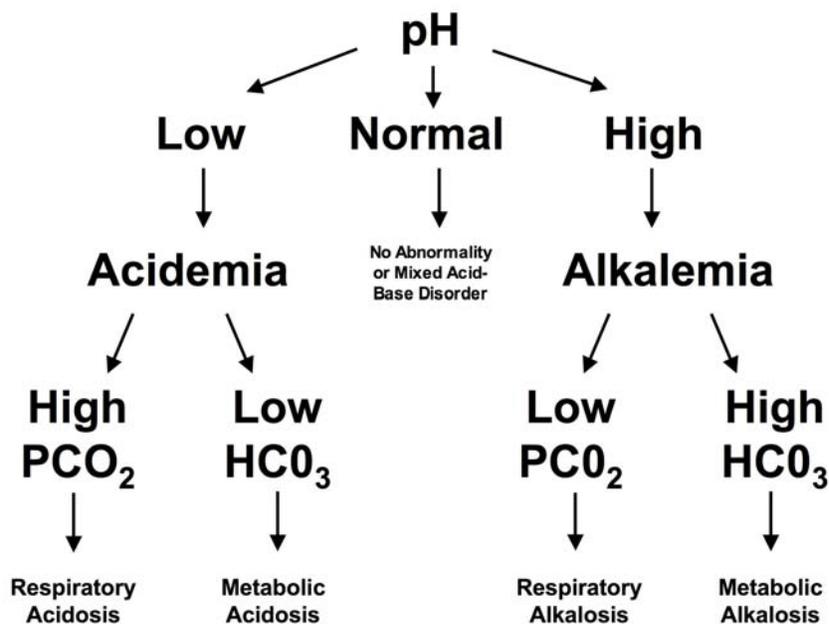
- If the PCO_2 is elevated (> 44), the primary process is a respiratory acidosis
- If the HCO_3^- is low (< 22), the primary process is a metabolic acidosis

For a patient with a high pH (alkalemia)

- If the PCO_2 is low (< 36), the primary process is a respiratory alkalosis
- If the HCO_3^- is high (> 26), the primary process is a metabolic alkalosis

This framework is depicted in Figure 1.

Figure 1: Identifying the Primary Process



Examples of how to work through this step are provided in Example Set 1 below.

- **Step 3: Calculate the serum anion gap (SAG):**

$$\text{Serum Anion Gap (SAG)} = \text{Na}^+ - (\text{Cl}^- + \text{HCO}_3^-)$$

You should use the bicarbonate from the chemistry panel for this calculation. If this value is elevated (> 12), the person is deemed to have an “elevated anion gap.” This implies that the patient has a primary elevated serum anion gap metabolic acidosis

Example Set 1

Case A

A patient is brought back to the floor from the operating room on a patient controlled analgesia (PCA) pump with hydromorphone. The patient hits his PCA button several times in the first hour. Shortly thereafter, the nurse walks in the room and finds him somnolent and difficult to arouse. His S_pO_2 is only 88% so the nurse obtains a blood gas that reveals: pH 7.25, PCO_2 55, PO_2 60 and HCO_3^- 25.

Step 1: pH is low (acidemia)

Step 2: The PCO_2 is high (respiratory acidosis) and the bicarbonate is normal. A low pH with a high PCO_2 indicates that the primary process is a respiratory acidosis.

Summary: In this case, the patient started hypoventilating because he had likely given himself too much narcotic pain medications.

Case B

A patient presents with a one-day history of productive cough, fevers and increasing dyspnea. In the ER, the chest x-ray shows a right middle lobe opacity. His oxygen saturation is 90% on room air and an arterial blood gas is obtained. It reveals a pH 7.55, PCO_2 30, PO_2 63, HCO_3^- 22.

Step 1: The pH is high (alkalemia)

Step 2: The PCO_2 is low (respiratory alkalosis) and the bicarbonate is on the low side of normal. A high pH with a low PCO_2 indicates that the primary process is a respiratory alkalosis.

Summary: In this case, the patient is likely hyperventilating because he is hypoxemic. This is a good example of the hypoxemic ventilatory response.

Case C

A patient with Type I diabetes presents to the ER complaining of feeling poorly two days after running out of his insulin. An arterial blood gas is obtained and shows pH 7.25, PCO_2 28, PO_2 95, HCO_3^- 15.

Step 1: The pH is low (acidemia)

Step 2: The PCO_2 is low (respiratory alkalosis) and the bicarbonate is low (metabolic acidosis). A low pH and low bicarbonate signifies that the metabolic acidosis is the primary process.

Summary: In this case, the patient is likely in diabetic ketoacidosis because he was not taking insulin.

regardless of what other abnormalities you identify or what else is happening with the pH and bicarbonate. There must be an additional disorder because the body

does not generate an anion gap in order to compensate for a primary respiratory disorder.

Be aware, however, that an elevated anion gap acidosis may not be the only primary process. For example, patients with salicylate intoxication may have a primary respiratory alkalosis and a concurrent primary elevated anion gap acidosis at the same time. An example of this situation is provided in Example Set 2.

Example Set 2

A 30 year-old woman is brought into the emergency room with altered mental status. Her friends found her at home with an empty bottle of aspirin by her bedside. Her S_pO_2 is 99% and she is obviously hyperventilating on exam. An arterial blood gas is obtained as part of her initial work-up and reveals: pH 7.56, PCO_2 22, PO_2 110, HCO_3^- 17. On her chemistry panel, her sodium is 137, chloride 99, bicarbonate 18.

Step 1: The pH is high (alkalemia)

Step 2: The PCO_2 is low (respiratory alkalosis) and the bicarbonate is low (metabolic acidosis). A high pH with a low PCO_2 indicates that the primary process is a respiratory alkalosis.

Step 3: The serum anion gap is elevated at 20. As a result, she also has an elevated anion gap acidosis going on at the same time.

Summary: This combination of alkalemia due to a primary respiratory alkalosis with a concurrent elevated anion gap metabolic acidosis is classic for salicylate intoxication.

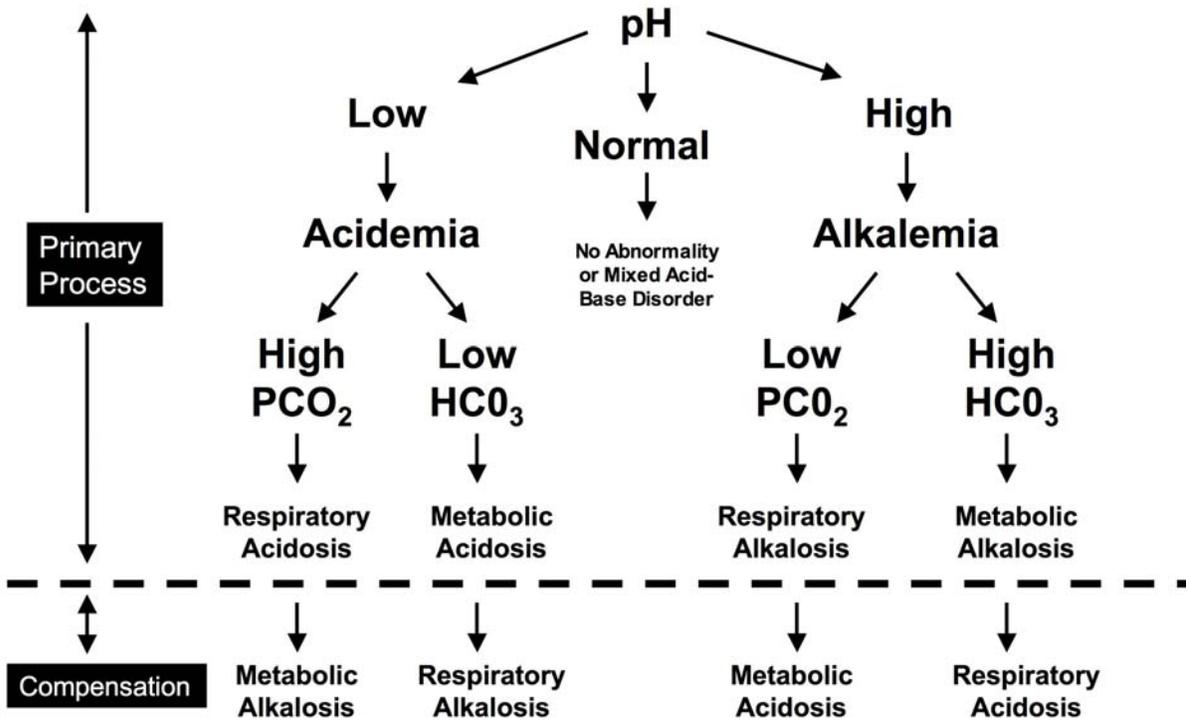
You should also note that the normal anion gap is affected by the patient's serum albumin level. As a general rule of thumb, the normal anion gap is roughly three times the albumin value. By way of example, for a patient with an albumin of 4.0, the normal anion gap would be 12. For a patient with chronic liver disease and an albumin of 2.0, the upper limit of normal for the anion gap would be 6. Other people propose that the ceiling value for a normal anion gap is reduced by 2.5 for every 1g/dL reduction in the plasma albumin concentration.

- **Step 4: Identify the compensatory process (if one is present).** In general, the primary process is followed by a compensatory process, as the body attempts to bring the pH back towards the normal range.
 - If the patient has a primary respiratory acidosis (high PCO_2) leading to acidemia: the compensatory process is a metabolic alkalosis (rise in the serum bicarbonate).

- If the patient has a primary respiratory alkalosis (low PCO_2) leading to alkalemia: the compensatory process is a metabolic acidosis (decrease in the serum bicarbonate)
- If the patient has a primary metabolic acidosis (low bicarbonate) leading to acidemia, the compensatory process is a respiratory alkalosis (low PCO_2).
- If the patient has a primary metabolic alkalosis (high bicarbonate) leading to alkalemia, the compensatory process is a respiratory acidosis (high PCO_2)

The compensatory processes are summarized in Figure 2.

Figure 2: Primary And Compensatory Processes



Examples of how to work through these steps are provided in Example Set 3 on the following page.

Example Set 3

Case A

A 40 year-old mountain climber ascends to an elevation of 15,000 feet. She remains there for a period of 3 weeks as part of a research project. At the end of that time, she has an arterial blood gas drawn which shows pH 7.44, PCO_2 24, PO_2 55, HCO_3^- 16. The serum anion gap was normal (11).

Step 1: The pH is high (alkalemia)

Step 2: The PCO_2 is low (respiratory alkalosis) and the bicarbonate is low (metabolic acidosis). Therefore, the respiratory alkalosis is the primary process.

Step 3: The serum anion gap normal.

Step 4: The metabolic acidosis is the compensatory process for the respiratory alkalosis.

Summary: If you had measured the ABG immediately upon arrival, the bicarbonate would have been close to normal and the pH would have been much higher. This is because it takes several days for metabolic compensation to occur.

Case B

A 65 year-old man with very severe COPD ($\text{FEV}_1 = 25\%$ predicted) has an arterial blood gas done as part of routine pulmonary function testing to help determine if he requires home oxygen therapy. The sample shows pH 7.36, PCO_2 60, PO_2 60, HCO_3^- 36. The anion gap is 8

Step 1: The pH is low (acidemia)

Step 2: The PCO_2 is high (respiratory acidosis) and the bicarbonate is high (metabolic alkalosis). Therefore, the respiratory acidosis is the primary process.

Step 3: The serum anion gap is normal at 8.

Step 4: The metabolic alkalosis is the compensatory process for the respiratory acidosis.

Summary: This patient likely has chronic carbon dioxide retention due to his very severe COPD. Because this is a long-standing process, he has had adequate time for metabolic compensation to occur.

Case C

A 40 year-old woman develops a severe case of diarrhea with multiple loose bowel movements over the course of a one-day period. When she presents to the ER, an arterial blood gas is obtained and shows pH 7.35, PCO_2 32, PO_2 75, HCO_3^- 18. The anion gap is 10

Step 1: The pH is low (acidemia)

Step 2: The PCO_2 is low (respiratory alkalosis) and the bicarbonate is low (metabolic acidosis). Therefore, the metabolic acidosis is the primary process.

Step 3: The serum anion gap is normal at 10. The metabolic acidosis from Step 2, therefore, is a non-gap acidosis.

Step 4: The respiratory alkalosis is the compensatory process for the metabolic acidosis.

Summary: The patient's metabolic acidosis is likely due to her diarrhea as diarrhea leads to bicarbonate loss through the lower gastrointestinal tract. Even though her symptoms have been present for only one day, her pH has come back up towards normal already. That is because respiratory compensation for metabolic processes occurs almost immediately. In severe acidosis, this may not be enough to bring the pH back close to normal but at a minimum respiratory compensation starts quickly.

Important Points Regarding Compensatory Processes

There are several important points to be aware of regarding these compensatory processes:

- *The body never overcompensates for the primary process.* For example, if the patient develops acidemia due to a respiratory acidosis and then subsequently develops a compensatory metabolic alkalosis (a good example of this is the COPD patient with chronic carbon dioxide retention), the pH will move back towards the normal value of 7.4 but will not go to the alkalemic side of normal. This might result in a pH of 7.36, for example but should not result in a pH such as 7.44 or another value on the alkalemic side of normal. If the pH appears to “over-compensate” then an additional process is at work and you will have to try and identify it. This can happen with mixed acid-base disorders, which are described further below.
- *The pace of compensation varies depending on whether it is respiratory or metabolic compensation.* Respiratory compensation for primary metabolic disturbance is almost immediate. For example, if someone infused hydrochloric acid through an IV and gave the patient a metabolic acidosis, the patient would rapidly begin hyperventilating and generate a respiratory alkalosis that would move the pH back towards normal. Metabolic compensation for primary respiratory abnormalities, however, is slow and may take several days. For example, if someone travels to high altitude and begins to hyperventilate due to the low oxygen levels in the atmosphere, initially there will be no metabolic compensation and they will have a high pH. Over several days, however, metabolic compensation will occur and the pH will return back towards normal.
- *Despite the compensatory mechanisms, the pH may not return all the way to normal.* For example, consider the following arterial blood gas in a patient with acute toluene toxicity: pH 6.95, PCO_2 9, HCO_3^- 2. This is a primary metabolic acidosis but despite a huge degree of hyperventilation and a marked compensatory respiratory alkalosis, the pH still remains very low. In other situations (eg. a compensated respiratory acidosis in a patient with obesity hypoventilation, or the compensated respiratory alkalosis in a pregnant woman), the pH will return closer to the normal range
- *What may appear to be a compensatory process may not actually represent true compensation.* For example, consider a patient who develops an acute respiratory acidosis (large rise in the PCO_2). Even though this is an acute process and renal compensation has not occurred, the bicarbonate value may read 27 on the ABG. This appears elevated and would suggest metabolic compensation is starting to occur but may, in fact, not represent true compensation. How does this occur? Remember that a key relationship that governs acid-base physiology is the following:



If there is a large rise in the PCO_2 , this equation will shift towards the right and the levels of bicarbonate will transiently increase. Similarly, a large fall in the PCO_2 would shift the equation to the left and the bicarbonate would transiently decrease. How can you figure out whether the observed changes in bicarbonate represent true compensation or changes due to this relationship? The answer lies in another value you will see reported with the arterial blood gas – the base excess. In general, as you may recall from respiratory physiology, the base excess is defined as the difference between the patient's HCO_3^- after correction to a pH of 7.4 by a change in the PCO_2 and the normal HCO_3^- at pH 7.4. It can be used in the following manner to interpret changes in the HCO_3^- levels.

- If the base excess is between -2 and $+2$ then the observed changes in bicarbonate are due to movement based on the equation above and there is no metabolic acidosis or alkalosis.
- If the base excess is less than -2 , then there is a metabolic acidosis, which may be the compensatory process. Another term for this is a *base deficit*.
- If the base excess is greater than $+2$, then there is a metabolic alkalosis, which may be the compensatory process.

Be aware that if the base excess is less than -2 or greater than $+2$, and therefore, a metabolic process is present, the base excess value itself does not tell you whether this is a primary process or a compensatory process. It only tells you a metabolic process is present. You still need to work through the steps described here to tell whether it is the primary process or the compensatory process.

- *What appears as a lack of compensation may actually represent an acute process on top of a chronic process.* In some cases, patients may live in a chronically compensated state of acid-base disturbance and then deviate from that state due to an acute problem. The best example is the patient with very severe COPD who might have chronic respiratory acidosis with metabolic compensation at baseline. The arterial blood gas for this patient might look like the following: pH 7.35, PCO_2 55, PO_2 70, HCO_3^- 32. Now, suppose the patient develops a severe exacerbation and comes into the ER. At that point in time, an arterial blood gas may show pH 7.25, PCO_2 65, PO_2 62, HCO_3^- 33. The PCO_2 is now 10 mm Hg higher than before and the pH is now much further away from 7.40. If you didn't have the initial blood gas for comparison, you would say this patient has a respiratory acidosis with only partial compensation. However, knowing the prior acid-base status, it would be more

correct to say this patient has an acute-on-chronic respiratory acidosis. The acute worsening of his COPD led to a rise in the PCO_2 but the bicarbonate has not risen further from baseline and the pH has not moved back towards normal because the kidneys have not had time to compensate for the acute change in the patient's condition.

- **Step 5: Determine if a Mixed Acid-Base Disorder is Present.** The 4 steps outlined above allow you to fully classify the patient's acid-base status in the majority of cases. In such cases there is a primary abnormality and, possibly, a compensatory process. There are occasional situations, however, where patients may have more than one disorder going on at the same time. For example, it is possible for patients to have a concurrent metabolic acidosis and metabolic alkalosis or a concurrent elevated anion-gap acidosis and non-anion gap acidosis (The only combination you cannot have is a combined respiratory alkalosis and acidosis as it is impossible for the patient to hyper- and hypoventilate at the same time). These situations are referred to as *mixed acid-base disorders*.

One way to determine if a mixed acid-base disorder is present is to calculate the anticipated response to the primary abnormality. If the actual response deviates from this value then you know an additional process may be at work. There are equations for example, that stipulate that the bicarbonate should change by a certain amount in response to a chronic respiratory acidosis. The problem is that these equations are difficult to remember and, as a result, are tedious to apply in the acute setting. The nomograms that are often presented in respiratory physiology course are also difficult to use, as well as locate, when you need them.

An alternative approach is to calculate what is referred to as the Delta-Delta. This approach, which gives you a sense of whether the body is holding onto or losing more bicarbonate than you would expect simply based on looking at the pH, serum anion gap (SAG) and the bicarbonate values, can be done as follows:

- 1) Calculate the Delta Gap: Measured SAG – Normal SAG (12)
- 2) Calculate the Delta Delta: Add the Delta Gap to the measured bicarbonate (from the chemistry panel)
- 3) Compare the Delta Delta to a normal bicarbonate (22-26):
 - If the Delta Delta < 22, the patient is losing bicarbonate somewhere and there is a *non-gap* acidosis. If you found a non-gap acidosis (either the compensatory or the primary process) in the initial steps above, then the acidosis you identify here represents the same process. If however, you did not identify an acidosis in the earlier steps or you identified a gap acidosis in the initial steps, then this last step reveals the presence of an additional non-gap acidosis.

- If the Delta Delta > 26 , the patient is holding onto bicarbonate and there is an additional metabolic alkalosis. If you found an alkalosis (either the compensatory or the primary process) in the initial step above, then the alkalosis you identify here represents the same process. If however, you identify an acidosis in the initial steps and then this last step reveals the presence of alkalosis, you have found an additional metabolic process.

Be aware that for these calculations to work, the chemistry panel and blood gas must have been drawn at roughly the same time. If, for example, you obtain a blood gas on a patient during a code on a patient at 6PM, you cannot use the morning chemistry panel from 6AM to do these calculations.

Examples of how to work through this last step of the process are provided in Example Set 4 below.

Example Set 4

Case A

You are working in the emergency room when the paramedics bring in a 45 year-old man who was found down in Pioneer Square. He is somnolent but arouseable. He has emesis on his shirt. He is hypotensive and tachycardic. Labs are drawn and reveal the following: room air ABG: pH 7.22, PCO_2 29, PO_2 78, HCO_3^- 11. Chemistry panel: Na^+ 131, Cl^- 90, HCO_3^- 12. Glucose 135.

Step 1: The pH is low (acidemia)

Step 2: The PCO_2 is low (respiratory alkalosis) and the bicarbonate is low (metabolic acidosis). Therefore, the metabolic acidosis is the primary process.

Step 3: The serum anion gap is elevated at 29. There is, therefore, an elevated anion gap acidosis.

Step 4: The respiratory alkalosis is the compensatory process for the metabolic acidosis.

Step 5:

- The Delta Gap = Measured SAG \checkmark Normal SAG = 29 \checkmark 12 = 17
- Calculate the Delta Delta: Delta Gap + measured bicarbonate = 17 + 12 = 29
- Since the Delta Delta is above a normal bicarbonate level, there is a concurrent metabolic alkalosis at work.

Summary: The patient has a primary elevated anion gap acidosis with respiratory compensation (which is not complete) and a concurrent metabolic alkalosis. You would need to sort through the differential diagnosis for an elevated anion gap acidosis to identify the cause of that problem. The metabolic alkalosis is likely due to vomiting.

Example Set 4 (continued)

Case B

A 60 year-old man was recently in the hospital for treatment of aspiration pneumonia for which he was treated with levofloxacin and clindamycin. One week later, he presents to the ER with severe diarrhea, abdominal pain and hypotension. He is admitted to the ICU where an arterial blood gas shows: pH 7.29, PCO₂ 25, PO₂ 89, HCO₃⁻ 10. On his chemistry panel, he has: Na⁺ 129, Cl⁻ 99, HCO₃⁻ 10. Glucose 135.

Step 1: The pH is low (acidemia)

Step 2: The PCO₂ is low (respiratory alkalosis) and the bicarbonate is low (metabolic acidosis). Therefore, the metabolic acidosis is the primary process.

Step 3: The serum anion gap is elevated at 20. There is, therefore, an elevated anion gap acidosis.

Step 4: The respiratory alkalosis is the compensatory process for the metabolic acidosis.

Step 5:

- The Delta Gap = Measured SAG - Normal SAG = 20 - 12 = 8
- Calculate the Delta Delta: Delta Gap + measured bicarbonate = 8 + 10 = 18
- Since the Delta Delta is below the normal bicarbonate level, there is a concurrent non-gap metabolic acidosis at work.

Summary: The patient has a primary elevated anion gap acidosis with respiratory compensation and a concurrent non-gap metabolic acidosis. He likely has sepsis from C.Difficile Colitis as the cause of his elevated anion gap acidosis. The non-gap acidosis may be from his severe diarrhea (a source of bicarbonate loss).

Case C

A 56 year-old woman with chronic kidney disease presents to the emergency room with increasing dyspnea. She is noted to be tachypneic, but is afebrile, has a normal lung exam and a normal appearing chest x-ray. An arterial blood gas is drawn and reveals: pH 7.28, PCO₂ 29, PO₂ 85, HCO₃⁻ 16. On her chemistry panel, the sodium is 131, chloride 105 and HCO₃⁻ 15.

Step 1: The pH is low (acidemia)

Step 2: The PCO₂ is low (respiratory alkalosis) and the bicarbonate is low (metabolic acidosis). Therefore, the metabolic acidosis is the primary process.

Step 3: The serum anion gap is normal at 11. The patient, therefore, does not have an elevated anion gap acidosis

Step 4: The respiratory alkalosis is the compensatory process for the metabolic acidosis.

Step 5:

- The Delta Gap = Measured SAG - Normal SAG = 11 - 12 = -1
- Calculate the Delta Delta: Delta Gap + measured bicarbonate = -1 + 15 = 14
- The Delta Delta is below the normal bicarbonate level. This tells us there is a non-gap acidosis, but in this case, this acidosis is actually the same acidosis that you identified in Steps 2 and 3 and there are no additional metabolic processes at work.

Summary: The patient has chronic kidney disease. Many such patients develop non-gap acidoses due to renal tubular acidosis.

Generating Differential Diagnoses

Identifying the primary process is important because it helps you to generate differential diagnoses and decide on work-up and management. The basic differential diagnoses for the primary acid-base abnormalities are as follows:

- **Elevated Anion Gap Metabolic Acidosis:** It is common for students and physicians to use a mnemonic to remember the common causes of an elevated anion gap acidosis. One common mnemonic is as follows:
 - **M:** Methanol intoxication
 - **U:** Uremia
 - **L:** Lactic acidosis
 - **E:** Ethylene glycol intoxication
 - **P:** Paraldehyde intoxication
 - **A:** Alcoholic Ketoacidosis
 - **K:** Ketoacidosis (diabetic, starvation, alcoholic)
 - **S:** Salicylate intoxication, Seizures, Shock

It is important to recognize that in the case of seizures and shock, it is actually the accumulation of lactic acid that is responsible for the development of the elevated anion gap acidosis.

Some people use an alternative mnemonic:

- **M:** Methanol intoxication
- **U:** Uremia
- **D:** Diabetic Ketoacidosis
- **P:** Paraldehyde intoxication
- **I:** Infection (sepsis)
- **L:** Lactic acidosis
- **E:** Ethylene glycol intoxication
- **S:** Salicylate intoxication, Seizures, Shock

Other diagnoses that don't fit in these mnemonics can also cause an elevated anion gap acidosis and should be considered in cases where your initial work-up does not identify an underlying cause. These other diagnoses would include:

- Cyanide or carbon monoxide poisoning
- Excess inhaled beta-agonists
- Hereditary disorders (eg. glucose-6-phosphatase deficiency)
- D-Lactic acidosis (jejuno-ileal bypass, small bowel resection)
- Medications (iron, isoniazid, zidovudine)
- Toluene intoxication
- Massive Rhabdomyolysis

As noted above, in several of these cases (eg. carbon monoxide poisoning, excess beta-agonists), the elevated anion gap derives from accumulation of lactate.

You should also be aware that there is a differential diagnosis for a low serum anion gap. It includes the following items:

- Fall in unmeasured anions (eg. Hypoalbuminemia)
- Increased unmeasured cations (hyperkalemia, hypercalcemia, hypermagnesemia)
- Lithium
- Multiple Myeloma
- Bromide (found in Pyridostigmine Bromide used in the treatment of myasthenia gravis and some herbal medications)

- **Normal Anion Gap Metabolic Acidosis (non-gap acidosis):** The differential diagnosis includes:

- Gastrointestinal bicarbonate losses:
 - Diarrhea
 - Ureteral Diversion (ileal loop)
- Renal bicarbonate losses:
 - Carbonic anhydrase inhibitors (eg. acetazolamide)
 - Renal tubular acidosis
 - Aldosterone inhibitors or hypoaldosteronism

If the cause of the non-gap acidosis is not clear based on the patient history, you can identify whether the problem is renal or gastrointestinal losses by calculating a urine anion gap:

$$\text{Urine Anion Gap (UAG)} = (\text{Urine Na}^+ + \text{Urine K}^+) - \text{Urine Cl}^-$$

A positive value (UAG > 0) suggests the metabolic acidosis is due to a renal etiology, whereas a negative value (UAG < 0) points to a gastrointestinal source.

- **Metabolic Alkalosis:** The differential diagnosis includes:

Chloride Responsive Alkaloses:

- Vomiting
- Nasogastric suction
- Diuretics

Chloride Unresponsive Alkaloses:

- Hyperaldosteronism
- Cushing's syndrome
- Licorice ingestion
- Bartter's syndrome
- Excess alkali intake (eg. milk alkali syndrome)

If the cause of the metabolic alkalosis is not clear based on the patient history, you can obtain a urine chloride level to help determine the cause. If the urine chloride level is < 15 the patient has a "chloride responsive alkalosis" which can be corrected with saline (NaCl) administration. This typically happens with gastrointestinal losses or intravascular volume depletion (i.e. a contraction alkalosis with diuretic use). If the urine chloride is > 15 , the patient has a "Chloride Unresponsive Alkalosis"

- **Respiratory Acidosis:** A primary respiratory acidosis implies that the patient is hypoventilating or not ventilating enough in the face of high CO_2 production. This can be seen in the following settings:
 - Acute intoxication with narcotics or other sedative medications
 - Severe metabolic encephalopathy
 - Obesity hypoventilation
 - Severe chronic obstructive pulmonary disease
 - Acute upper airway obstruction
 - Neuromuscular disorders (eg. Guillan Barre, Myasthenia Gravis, Botulism, Amyotrophic Lateral Sclerosis)
 - Later stages of a severe asthma exacerbation (eg. the patient is tiring out)
 - Thoracic cage trauma (flail chest)
 - Inappropriately low minute ventilation settings on mechanical ventilation
- **Respiratory Alkalosis:** A primary respiratory alkalosis implies that the patient is hyperventilating. This can be seen in the following settings:
 - Early stages of an asthma exacerbation
 - Anxiety attack
 - Acute hypoxia (hypoxic ventilatory response)
 - Pregnancy or other cases of elevated progesterone
 - Cirrhosis and/or hepatic encephalopathy
 - Salicylate intoxication
 - Central nervous system disease

Use Old Arterial Blood Gas Results to Your Advantage

There are certain clinical situations where a review of the patient's prior arterial blood gas results can be of great value (if the patient did, in fact, have a sample drawn in the past). To see how prior ABG results may be of use, consider the following scenario.

A patient with very severe COPD was found ashen and pulseless on the wards and a Code 199 was called. The initial arterial blood gas revealed pH 7.32, PCO_2 50, PO_2 105, HCO_3^- 25 on an F_iO_2 of 1.0. This patient was acidemic with a high PCO_2 and a normal bicarbonate and it was determined that he had a primary respiratory acidosis without metabolic compensation. That is the correct interpretation if all you have is the information from that one arterial blood gas. However, the patient did have an earlier arterial blood gas, well before his cardiac arrest whose results were as follows: pH 7.38, PCO_2 80 PO_2 72, HCO_3^- 48. These results are consistent with a primary respiratory acidosis and a compensatory metabolic alkalosis that reflects his history of very severe COPD and known carbon dioxide retention. Of note, his baseline bicarbonate is 48, well higher than the “normal” appearing value of 25 that was obtained during the code. If all you did in this situation were look at the ABG drawn during the code, you would see a “normal” bicarbonate and might not realize that he has developed a severe metabolic acidosis. If, however, you have his old blood gas values, you would correctly note that his bicarbonate has fallen dramatically. As a result, he likely has some problem (eg. sepsis) that caused a severe metabolic acidosis and ultimately led to his decompensation.

Oxygenation

The arterial blood gas also provides information about the oxygenation status of the patient. In general, there are two basic pieces of information you can obtain using the PO_2 on a blood gas: insight into the cause of the hypoxemia and an assessment of the adequacy of gas exchange.

Assessing the Cause of Hypoxemia

There are five broad categories of problems that cause hypoxemia:

- Low inspired partial pressure of oxygen (eg. high altitude)
- Hypoventilation
- Shunt
- Low ventilation relative to perfusion (low V/Q)
- Diffusion limitation (rarely an issue at sea-level)

When a patient presents with unexplained hypoxemia, you can begin to sort through the differential diagnosis by calculating the alveolar-arterial oxygen difference (AaO_2 Difference). You begin this calculation by determining the alveolar PO_2 using the alveolar gas equation:

$$P_{\text{AO}_2} = (P_{\text{B}} - 47) F_i\text{O}_2 - P_{\text{aCO}_2}/R$$

Whereby P_{B} = barometric pressure, $F_i\text{O}_2$ = the inspired oxygen concentration and R = the respiratory quotient. If you have trouble remembering the full equation, you can simplify things by remembering the $P_i\text{O}_2$ of room air where you live. The $P_i\text{O}_2$ is the first

term of the alveolar gas equation ($P_{iO_2} = [P_B - 47] F_{iO_2}$). For example, the P_{iO_2} while breathing ambient air at sea level is 150 mmHg whereas if you live in Boise, Idaho, where the average P_B is 695 mmHg, the P_{iO_2} of room air is 135 mmHg.

Once you have calculated this value, the AaO₂ Difference is calculated as follows:

$$AaO_2D = P_{AO_2} - P_{aO_2}$$

The normal value for the AaO₂ Difference is about 10-15 mm Hg. If you determine that the patient has a normal AaO₂ Difference, then the hypoxemia can be attributed to hypoventilation or a low inspired partial pressure of oxygen. If, however, you find that the patient has an elevated AaO₂ difference then they have some process going on that is causing shunt or low V/Q, such as pneumonia, that is contributing to the observed hypoxemia.

There are a few important points to be aware of regarding the use of the AaO₂ Difference.

- In order to use the alveolar gas equation you must have an accurate assessment of the F_{iO_2} . The F_{iO_2} will be accurate when your patient is on room air, non-invasive or invasive mechanical ventilation or is on a high-flow facemask system. When patients are on supplemental oxygen using nasal cannula, regular face masks, Venturi masks or non-rebreather masks, the F_{iO_2} is not reliable; these systems often deliver less gas flow than the patient is requiring for their minute ventilation and, as a result, they end up entraining in a lot of room air which dilutes out the intended inspired oxygen concentration.
- The “normal” AaO₂ Difference increases with age. Some sources state that the upper limit of normal for the AaO₂ Difference is equal to: $2.5 + (0.21 \times \text{age})$.
- The “normal” AaO₂ Difference varies based on the F_{iO_2} . On an F_{iO_2} of 1.0, the normal AaO₂ difference is 100 mmHg. Also, if you go to high altitude, where the barometric pressure is decreased and the P_{iO_2} falls, the normal AaO₂ Difference is lower than 10.
- Make sure you are using the correct value for R. In general, we use a value of 0.8. However, if your patient is on an F_{iO_2} of 1.0, then R is taken to be 1.

Assessing the Adequacy of Gas Exchange

Suppose your patient has P_{aO_2} of 85 that results in an S_{pO_2} around 97-98%. Even though these values are adequate for sustaining the patient, they do not mean that gas exchange is normal. In fact, a patient can have a P_{aO_2} and S_{pO_2} in this range and still have markedly abnormal gas exchange. As a result, whenever you interpret the P_{aO_2} on an arterial blood gas, you must look at that number in light of the amount of oxygen that

is being delivered to the patient. There are several ways you can get a sense of this value:

- **The P/F Ratio:** This is the ratio of the P_aO_2 (in mmHg) to the F_iO_2 (expressed as a decimal). The smaller the value, the worse the patient's gas exchange. For example, consider a patient with a P_aO_2 of 80. If they are on an F_iO_2 of 0.3, the P/F ratio is 266. If they are, instead, on F_iO_2 of 0.8, the P/F ratio is only 100, a much worse value that signifies greater impairment in gas exchange. The P/F ratio is commonly used in patients on mechanical ventilation as part of the assessment of whether they have the Acute Respiratory Distress Syndrome (ARDS). A P/F ratio below 300 is consistent with Acute Lung Injury, while a P/F ratio below 200 is consistent with ARDS (provided the patient meets the other criteria including a CXR with diffuse bilateral opacities and evidence that cardiac function is normal).
- **The AaO₂ Difference:** The same number that is used to help determine the cause of hypoxemia can also be used to determine the adequacy of gas exchange. In patients with an elevated AaO₂ Difference, larger values imply a greater degree of either low V/Q areas and/or shunt. The size of the AaO₂ Difference does not help you distinguish between low V/Q and shunt, however. The way to make that determination is to measure the response to supplemental oxygen administration. The P_aO_2 will rise and the AaO₂ difference will shrink in patients with low V/Q as the primary cause of their hypoxemia (eg. the COPD patient during an exacerbation) whereas in shunt, supplemental oxygen does not lead to improvements in the P_aO_2 .

Both methods for assessing the adequacy of gas exchange require an accurate F_iO_2 measurement, which, as noted above, can only be assured if the patient is on room air, a high flow face mask, non-invasive mechanical ventilation or invasive mechanical ventilation.

Special Situations To Be Aware of In Evaluating the P_aO_2 on an ABG

There are a few special situations of which you should be aware when assessing the P_aO_2 on an arterial blood gas.

- **The Hypothermic Patient:** Hypothermia can affect the accuracy of the P_aO_2 measurement by causing changes in the position of the Hb-O₂ dissociation curve. If you do not inform the laboratory of the patient's body temperature at the time the sample was measured, you may measure an artificially high P_aO_2 . To understand how this happens, consider the following scenario. Suppose you see a patient in the emergency room with a temperature of 32°C and draw an ABG while he is still at that temperature. At this point in time, his Hb-O₂ dissociation curve has shifted to the left and, as a result, for any given oxygen content of the arterial blood, the P_aO_2 is lower than it would be at a normal temperature. When the sample is sent to the lab and placed in the blood gas analyzer, however, the machine will warm the sample to 37°C before doing the measurement. This warming process shifts the Hb-O₂ dissociation curve back to the right. Because the oxygen content of the blood has

not changed, this rightward shift will lead to a higher measured P_aO_2 than if the measurement had taken place without warming the blood. For this reason, you should always notify the lab about the patient's temperature at the time of the measurement if they are hypothermic so they can make the appropriate adjustments in the blood gas analyzer.

- **Leukocyte Larceny:** This is a rare situation that may be seen when working on an oncology service with patients presenting with acute leukemia or other patients with extremely high white blood cell counts. White blood cells are metabolically active and consume oxygen. In the time between when a sample is drawn from the wrist and the measurement is made in the blood gas analyzer, the white blood cells may consume enough oxygen to decrease the P_aO_2 from the actual value at the time the sample was drawn. The net result is you get a P_aO_2 result that is much lower than what you would expect based on the oxygen saturation at the time the sample was drawn. This situation, which may be seen in leukemic patients with WBC counts of 50,000 or greater, can occur even if the sample is cooled immediately and analyzed within 10 minutes. This problem can be avoided by putting the sample on ice and adding potassium cyanide to halt oxygen consumption.

Be aware that there are other situations in which you will see a discrepancy between a high S_pO_2 and a low P_aO_2 on the ABG. These include:

- Spuriously high S_pO_2 value
 - Inadvertent venous blood sampling
 - Excessive time delay in sample analysis
 - Air bubbles left in the blood gas sample
- **Methemoglobinemia:** In leukocyte larceny, the P_aO_2 is lower than you would expect given the S_pO_2 . In methemoglobinemia, the opposite occurs; the patient has a low S_pO_2 (typically in the mid-upper 80% range) but the P_aO_2 is much higher than you would expect from that value. In this case, the P_aO_2 is actually a valid reading and the discrepancy reflects important pathology.

In this situation, there is some insult (usually a medication such as dapsone) that leads to oxidation of the iron in the hemoglobin molecule from the 2+ valence to a 3+ valence. As a result, the hemoglobin molecule changes conformation and does not bind oxygen adequately. Blood with the altered hemoglobin molecule has different light absorption properties that lead you to measure a lower saturation using a pulse oximeter. Under normal circumstances, when the P_aO_2 is high, you expect to see a very high saturation. However, in methemoglobinemia, even though you may have the patient on a lot of supplemental oxygen and the P_aO_2 is very high, the oxygen will not bind to hemoglobin and, as a result, the saturation will continue to be low (Because of the absorption properties of methemoglobin, the saturation typically remains around 87-88%).

The tip-off to this diagnosis comes when you see a patient with a low saturation that remains low despite putting them on supplemental oxygen, but find a high P_aO_2 on their blood gas. If you see this pattern and suspect the diagnosis, the next step is to ask the laboratory to check a methemoglobin level on the blood gas sample.

Once the diagnosis is confirmed, you must then identify and stop the offending agent and, in some case, initiate disease-specific therapies. A useful mnemonic for drugs that have the potential to cause methemoglobinemia is:

- **L**: Lidocaine (and other “-caine” local anesthetics)
- **A**: Anti-malarials
- **N**: Nitrites/Nitrates
- **D**: Dapsone (perhaps the most common offender)