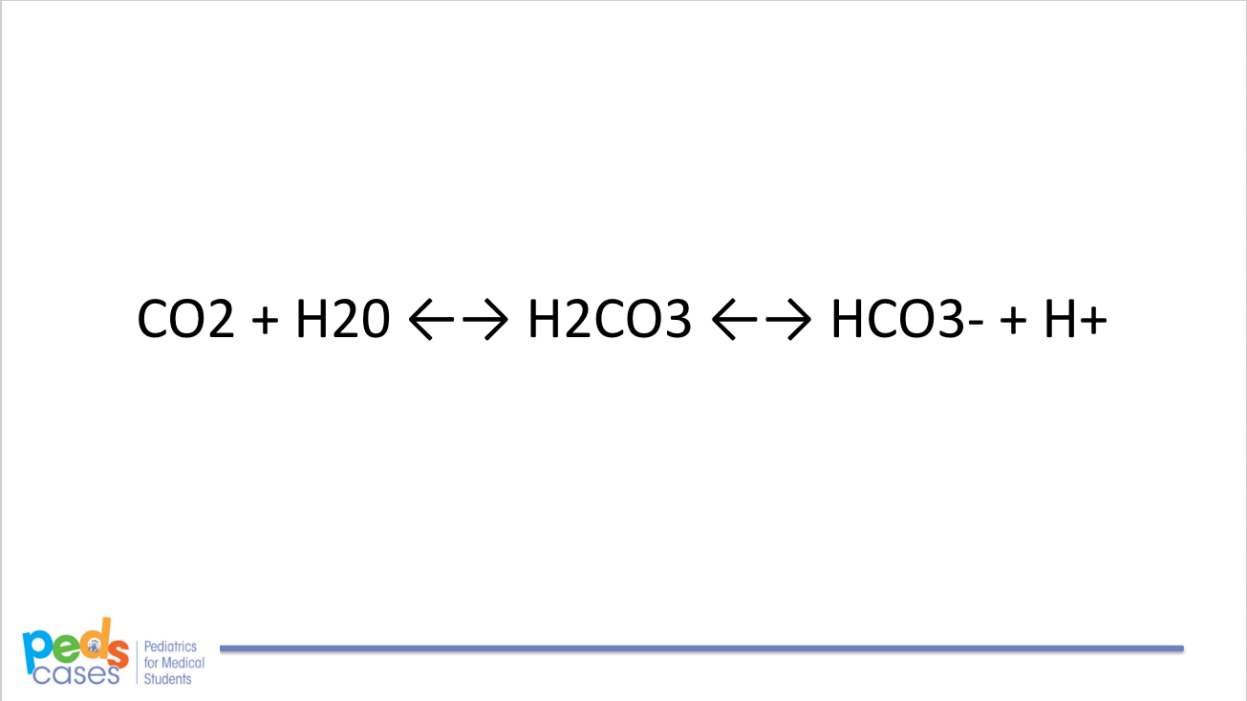

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By the end of this podcast, the learner will be able to:

1. Describe normal acid-base physiology and compensatory mechanisms for acid-base disturbances
2. Interpret an arterial blood gas (ABG) using a standard approach
3. List common causes of metabolic acidosis and metabolic alkalosis.
4. Describe, in general terms, the acute management of acidosis and alkalosis

Let's start with a case:
You are a third-year medical student working in the emergency department during your pediatrics rotation. Tommy is a 2-year-old boy presenting with symptoms that seem consistent with viral gastroenteritis. His parents describe multiple episodes of emesis and diarrhea for two days. He has failed oral rehydration and you clinically assess him as being moderately dehydrated. When you review with your preceptor, you both agree to send off a blood gas to look at Tommy's metabolic status.

Before we interpret our patient's blood gas, let's start by reviewing the basics of acid-base physiology.

Developed by Katie Girgulis and Dr. Karen Forbes for PedsCases.com.
March 17, 2018

The human body does a pretty good job of keeping serum pH regulated within a narrow range – pH is normally maintained between 7.35-7.45. Despite this tight regulation, things can sometimes go awry. When pH < 7.35, it is termed acidosis. When pH >7.45, it is termed alkalosis. We often classify acids in the body as 'respiratory' or 'metabolic'. Respiratory acids (carbon dioxide - CO_2) are controlled by respiration, whereas metabolic acids are not controlled by respiration and instead need to be neutralized or excreted from the body. We will come back to this point later.

When the acid-base balance is shifted, the body has a number of mechanisms for compensation:
organic buffers, respiratory compensation, and compensation at the level of the kidneys. Let's look at each one.

First, organic buffers are usually able to keep pH within the normal range by donating or accepting hydrogen ions. Organic buffers include bicarbonate (HCO_3^-), hydrogen phosphate (HPO_4^{2-}), and protein anions. However, the extent of this compensation is fairly minimal.

Second, let's look at respiratory compensation. If the pH is too low, the respiratory rate can increase – this reduces partial pressure of carbon dioxide (pCO_2) in the blood. Conversely, if pH is too high, the respiratory rate can decrease, thereby increasing pCO_2. These respiratory compensations occur quite quickly. But how does altering pCO_2 affect the pH, you might ask. Carbon dioxide and water combine to form carbonic acid (H_2CO_3), which dissociates to bicarbonate (HCO_3^-) and hydrogen ions (H^+). This reaction is at an equilibrium in the body, so the direction depends on the concentration of reactants and products. For example, when there is plenty of CO_2 around, the direction of the reaction favors the formation of HCO_3^- and H^+, thereby lowering the pH as a result of increased H^+. Conversely, when there is less CO_2, the direction of the reaction favors the formation of H_2CO_3, which uses up HCO_3^- and H^+ thereby raising pH as a result of decreased H^+. Thinking back to the lungs and respiratory compensation, it makes sense that acidosis triggers hyperventilation and alkalosis triggers hypoventilation.

Third, the kidneys can also help compensate by generating HCO_3^- and secreting H^+. When HCO_3^- is above the normal range, we say that there is a 'base excess'. And when HCO_3^- is below the normal range, we say there is a 'base deficit'. Unlike the quick response in the lungs, renal compensation is slower. It involves the generation of ammonia, as well as reabsorption and secretion of HCO_3^- and H^+. However, the full details of what occurs in the kidneys is beyond the scope of this podcast. In broad concept, an acidosis triggers the kidneys to make more HCO_3^- and remove H^+, thus increasing pH into the normal range. On the other hand, alkalosis triggers the opposite.

Tommy's ABG:

pH	7.25
pCO2	36 mmHg
HCO3-	22.5 mmol/L
Na+	135 mmol/L
K+	4.5 mmol/L
Cl-	105 mmol/L

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Now that we have reviewed the basics, let's have a look at Tommy's blood gas.

pH	7.25
pCO2	36 mmHg
HCO3-	22.5 mmol/L
Na+	135 mmol/L
K+	4.5 mmol/L
Cl-	105 mmol/L

Given this blood gas, let's go through an approach to its interpretation.

	Normal values
pH	7.35 - 7.45
pCO2	38 – 42 mmHg
HCO3-	24– 30 mmol/L
Anion Gap	<12 mmol/L

You might be wondering - how do we identify and measure acid-base imbalances in our patients? Clinically, arterial blood gas (ABG) and serum electrolytes are used to analyze a patient's acid-base status. While we will be focusing this discussion on the arterial blood gas, one important thing to note is that, except in the critical care setting, we do not often do an arterial blood gas in pediatric patients. More often, we will substitute with a capillary or venous blood gas, which are much less invasive to obtain. The key difference in these alternate sample types is the interpretation of oxygenation (which is not accurate from a venous sample). The interpretation of the acid-base status from a vGB follows the same general principles as an ABG.

1. The first step for interpreting an ABG is to ensure that you have the correct results for the correct patient (it sounds simple, but it is really important!).
2. Next, you look at the pH – if it is outside the normal range, is there an acidosis (pH <7.35) or alkalosis (pH >7.45)?
3. Next, turn your attention to the pCO2 and compare to normal values (38-42mmHg) – is pCO2 outside the normal range?
    a. If pCO2 is high, is pH low? This is a **respiratory acidosis**
    b. If pCO2 is low, is pH high? This is a **respiratory alkalosis**
4. Now, look at HCO3- and compare to normal values (24-30mmol/L)

. Is the bicarb low? Next, look at pH – if the bicarb is low, suggesting a base deficit, and pH is low, then it is a **metabolic acidosis**

a. Is the bicarb high? Next, look at pH – if the bicarb is high, suggesting a base excess, and pH is high, then it is a **metabolic alkalosis.**

b. When trying to classify the acid-base disturbance as respiratory or metabolic, I like to think – does the pH align with the level of CO2? If the answer is yes, then the

primary problem is respiratory. If the answer is no, then the problem is primarily metabolic.

5. Then determine if any compensation has occurred. If the acid-base disturbance is acute, compensation likely has not kicked in yet. But if the disturbance is more chronic, you will note changes in the ABG that reflect compensatory mechanisms. For example:

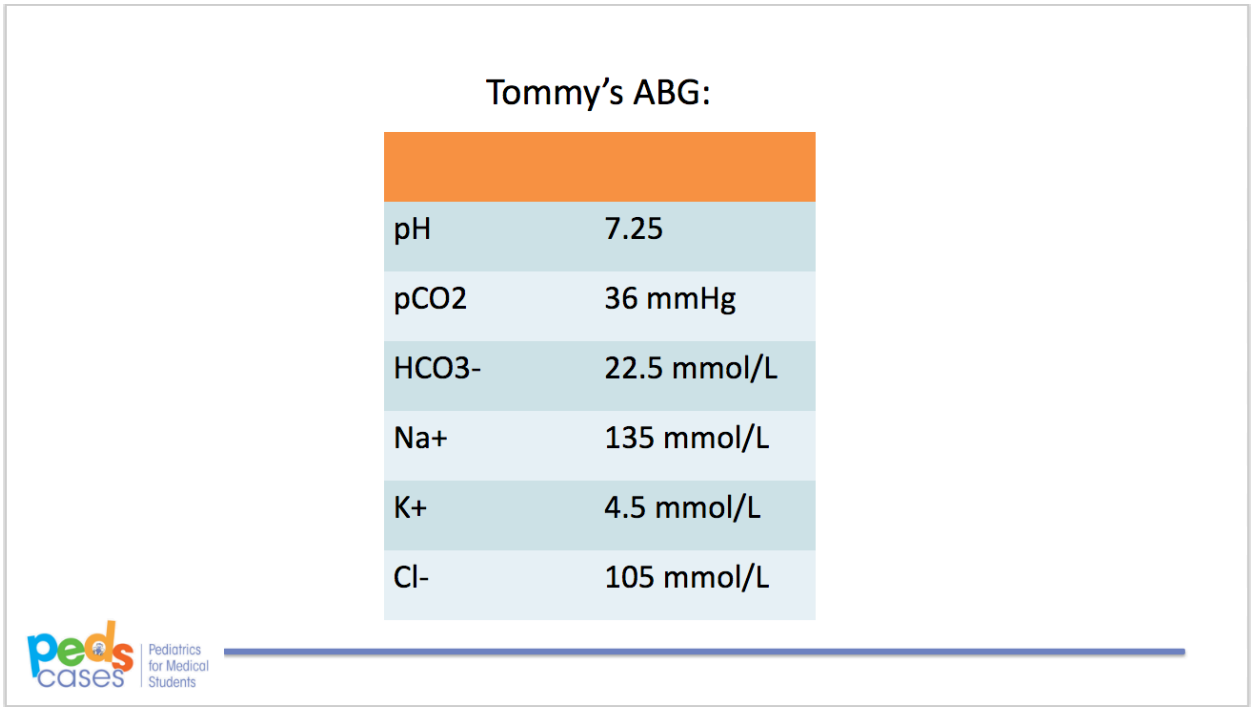
. With a metabolic acidosis: respiratory compensation triggers hyperventilation, which lowers pCO2

a. With respiratory acidosis: metabolic compensation triggers ammoniagenesis, increasing H+ secretion into the urine and HCO3- production and retention in the blood (causing a base excess)

6. The next step only applies if there is a metabolic acidosis. In order to further classify the acidosis, you calculate the anion gap.

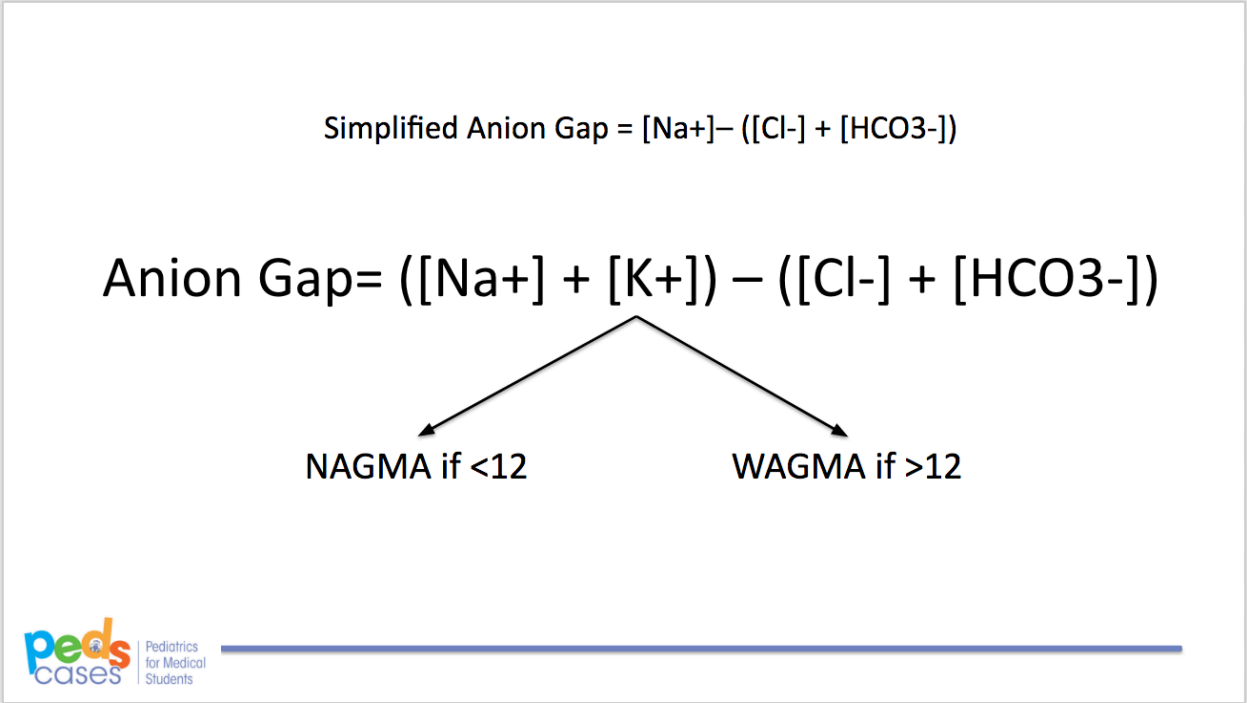
. **Anion gap** compares the amount of measured cations to the amount of measured anions in the body. We do this to look for the presence of unmeasured anions in the body. If you think back to your chemistry knowledge, we are interested in these anions because they represent the conjugate base of an acid in the body that is contributing to the low pH. So, a large (or "wide") anion gap is a surrogate marker suggesting that an acid was added to the body.

a. Anion gap = ([Na+] + [K+]) – ([Cl-] + [HCO3-]). Or, the simplified of [Na+] – ([Cl-] + [HCO3-]) is often used. *Normal is <12 mmol/L.*



Let's apply this approach to our patient's blood gas:

1. We have double-checked to ensure that we are interpreting Tommy's results from today's visit to the emergency department
2. pH of 7.25 is below the normal range, so Tommy has an acidosis
3. pCO2 is close to the normal range, so it is unlikely to be a respiratory acidosis
4. HCO3- is below the normal range – there is a base deficit. This suggests that Tommy has a metabolic acidosis
5. There may be some respiratory compensation (hyperventilation), as pCO2 is at the lower limit of normal
6. The anion gap is [135 + 4.5] – [105 + 22.5] = 12. This is a normal anion gap metabolic acidosis (NAGMA).



Once you have calculated the anion gap, consider – is this a normal anion gap metabolic acidosis (NAGMA; AG <12), or is this a wide anion gap metabolic acidosis (WAGMA; AG >12)

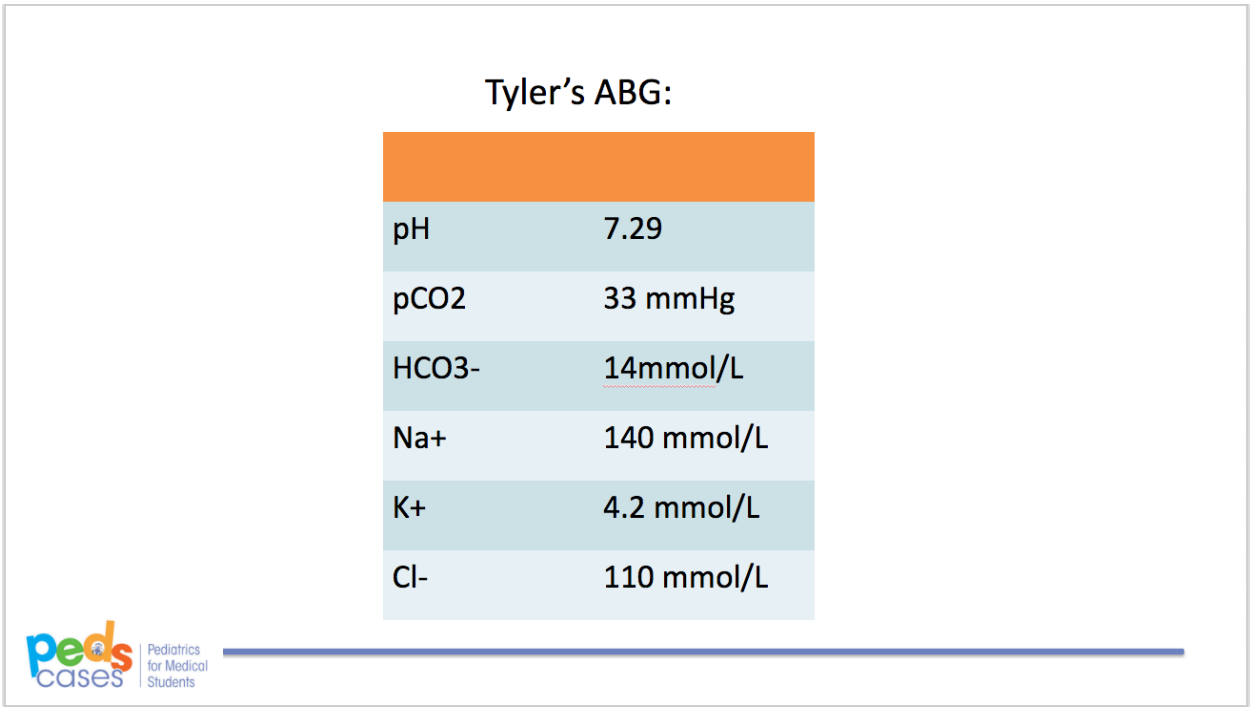
NAGMA

- If the anion gap is normal, this indicates that there is an intrinsic problem with regulating H+ and HCO3-, due to reduced H+ excretion, or more commonly, increased HCO3- loss. There are two sites where this can occur: the GI tract or the kidneys. In event of GI losses of HCO3-, if the kidneys are functioning well and the GI losses are chronic and mild, renal compensation can often work to prevent acidosis. However, in the setting of severe GI loss, the kidneys may be unable to compensate quickly enough. This is what happened with Tommy – he was losing lots of HCO3- in his stool, and renal compensation was unable to keep up, so he developed a metabolic acidosis.
- The NAGMA could also be due to renal problems (i.e. inability to make HCO3- or excrete H+), such as is seen with renal tubular acidosis. There are different types of renal tubular acidosis, depending on where the issue is in the tubule. However, this is beyond the scope of the podcast.

WAGMA

- The wide anion gap indicates that there are unmeasured anions in the blood (i.e. acids that have been converted to their conjugate base) – this is the reason for the acidosis. A common mnemonic used to remember possible causes is "MUDPILES":
    - M = methanol, metformin
    - U = uremia
    - D = diabetic ketoacidosis

    - P = propylene glycol, paraldehyde, paracetamol
    - I = iron, isoniazid, isopropyl alcohol, infection
    - L = lactic acid
    - E = ethylene glycol
    - S = salicylates
- *Hopefully the patient history and clinical context will help direct you about the possible etiology of the WAGMA.*
- In pediatric patients, lactic acidosis, DKA, and salicylate ingestion are the most common causes of WAGMA. Some clinicians find the mnemonic “KULT” easier to remember and more applicable to pediatrics.
    - K = ketones
    - U = uremia
    - L = lactate
    - T = toxins (i.e. salicylates, paracetamol, alcohols)



Now let's consider a different scenario. Tyler, a 3-year-old boy, has come in to the emergency department after getting into the medicine cabinet and eating some of his parent's pain-relief medications. The results of his ABG indicate a metabolic acidosis.

pH	7.29
pCO2	33 mmHg
HCO3-	14 mmol/L
Na+	140 mmol/L
K+	4.2 mmol/L
Cl-	110 mmol/L

Now, let's use the approach to classify his metabolic acidosis.

Anion gap = (140 + 4.2) – (14 + 110) = 20.2

- Thus, Tyler has a WAGMA – likely due to salicylate ingestion. One of the next steps would be to obtain a plasma salicylate concentration to confirm.

So far, we have focused on metabolic acidosis. Let's turn our attention to alkalosis. If you work through the approach to acid-base and determine that there is a metabolic alkalosis, then there are two things to consider. (1) What started the alkalosis (how was it initiated)?; and (2) why is the alkalosis persisting (how is it being maintained)?

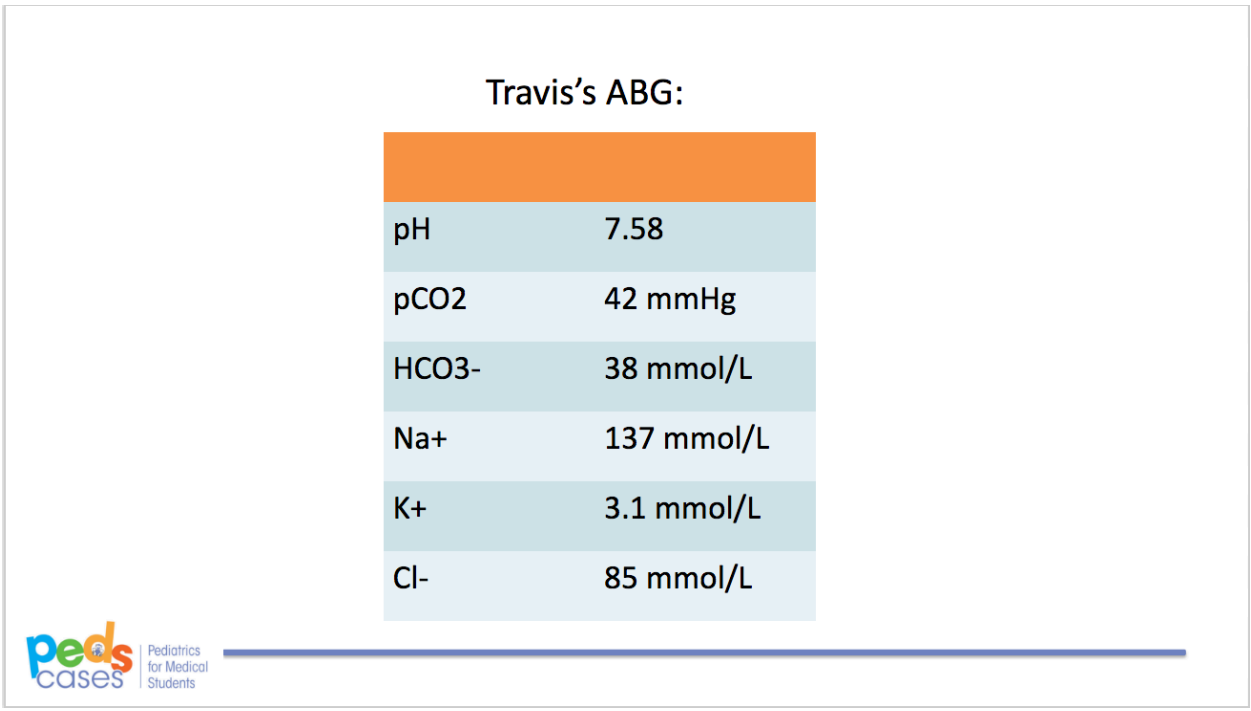
Initiation:

- There are many possible causes for a metabolic alkalosis. Thus, it is easier to start by thinking: was there an addition of HCO3- or a loss of H+? For example:
  - HCO3- can be added due to an ingestion or a citrate administration (blood transfusion).
  - H+ can lost due to emesis, H+ being shifted into cells (as in a patient with hypokalemia), or renal H+ loss.

- Renal loss could result from hypovolemia, thiazide or loop diuretics, or mineralocorticoid excess. All of these processes lead to increased Na+ reabsorption in the distal tubule and ultimately H+ secretion into the lumen and therefore loss in the urine.

Maintenance:

- In a normal and healthy patient, the body will be able to respond to a metabolic alkalosis and return the pH to the normal range. Thus, a continual process must be occurring that perpetuates the alkalosis. Again, we can categorize the possible etiology into two categories: volume dependent or volume independent.
    - Volume-dependent: this means that the patient has low intravascular volume and the kidneys are stimulated to reabsorb Na+ (as previously mentioned, this can lead to H+ loss)
    - Volume-independent: if the problem isn't low volume, then something else must be going on. This could be a mineralocorticoid excess (which stimulates the Na/K ATPase) or low GFR (leading to an impairment in HCO3- excretion).



Now, consider another patient. Travis is a 5-week-old infant brought in by his parents with non-bilious vomiting that has progressively increased over the past week. He vomits forcefully after he feeds, and he seems hungry and irritable through the day. On exam, Tommy is severely dehydrated. He is 200g below his birthweight. On physical exam, you palpate a small mass in the RUQ of the abdomen. His lab work show:

pH	7.58
pCO2	42 mmHg
HCO3-	38 mmol/L
Na+	137 mmol/L
K+	3.1 mmol/L
Cl-	85 mmol/L

The high pH and high bicarb (base excess) tells us that this is a metabolic alkalosis. Why does Travis have a metabolic alkalosis? Recall that he was brought in after several days of vomiting with poor oral intake. The initiation of the alkalosis was likely due to loss of H+ from vomiting. The maintenance is likely volume-dependent and related to his dehydration – as his kidneys are trying to retain Na+, H+ is being lost. Moreover, Travis has a hypokalemic hypochloremic metabolic alkalosis, and his clinical picture is suspicious for pyloric stenosis.

	pH	pCO2	HCO3-	Examples
Respiratory acidosis	< 7.35	> 42 mmHg	Normal **	Severe asthma, sleep apnea, CNS depressants
Respiratory alkalosis	> 7.45	< 38 mmHg	Normal **	Hyperventilation during a panic attack
Metabolic acidosis	< 7.35	Normal * *then <38 mmHg*	< 22 mmol/L	Diarrhea, salicylate ingestion, lactic acidosis, DKA
Metabolic alkalosis	> 7.45	Normal * *then >42 mmHg*	>28 mmol/L	Vomiting, NG suction, diuretics, glucocorticoid/ mineralocorticoid excess

** Normal initially, until respiratory compensation occurs*
*** Normal initially, until renal compensation occurs*

Next, we will move on to learn about the general initial management of alkalosis and acidosis. Of course, the definitive management involves identifying and treating the cause.

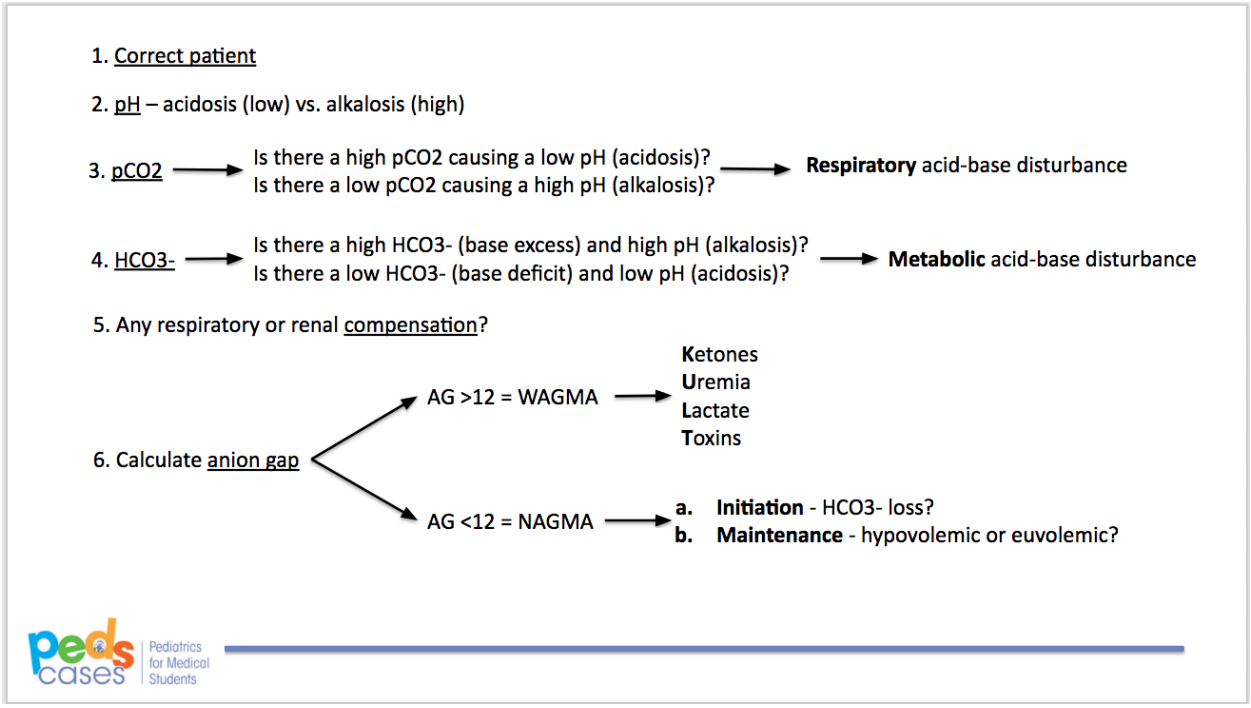
- Acidosis. *Note- IV bicarbonate administration is controversial. It is generally reserved for very severe or chronic acidosis, or in the critical care setting.*
    - **Respiratory acidosis:** Assess and stabilize the patient's airway and breathing (i.e. bag-mask ventilation, intubation, bronchodilators). Reverse any sedative medications slowing respiration rate
    - **Metabolic acidosis:** Some etiologies require urgent and specific treatment (i.e. insulin for DKA, fluid resuscitation for lactic acidosis due to shock, activated charcoal for some acute ingestions). In the context of renal failure, dialysis may be required.
- Alkalosis
    - **Respiratory alkalosis:** respiratory rate needs to be slowed (i.e. reassurance, anxiolytic, pain control)
    - **Metabolic alkalosis:** Again, treatment is aimed at the etiology. Some simple measures might include reducing vomiting, stopping a diuretic or citrate administration, correcting hypokalemia, or giving IV fluids.

Back to the cases:

1. When Tommy came in with metabolic acidosis due to diarrhea and dehydration, we would want to correct his fluid deficit with IV rehydration. His acidosis will resolve once his diarrhea settles down.
2. When Tyler came in with a metabolic acidosis due to ingesting his parent's Aspirin (salicylates), the initial management may include activated charcoal.

Supportive care and alkalinization of the urine are important in the treatment of salicylate ingestions.

3. When Travis came in with a metabolic alkalosis due to vomiting, we would want to first correct his fluid and electrolyte deficits. Surgical management would be the definite treatment if we confirmed the diagnosis of pyloric stenosis.



Thank you for listening to this podcast, I hope you now have a better understanding of acid-base physiology and how we can use that to interpret blood gases in the context of our patients.

You should be able to:

1. Describe normal acid-base physiology and compensatory mechanisms for acid-base disturbances
2. Interpret an arterial blood gas (ABG) using a standard approach
3. List common causes of metabolic acidosis and metabolic alkalosis.
4. Describe, in general terms, the acute management of acidosis and alkalosis

Next, check out the companion Acid-Base case on Pedscases.com. Here you can test your knowledge by working through clinical scenarios, interpreting lab results, and answering practice questions.