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Diagnosis of metabolic acid-base disorders

September 12, 2019 by **Josh Farkas**

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getting started: metabolic vs. respiratory abnormalities

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metabolic vs. respiratory pH disorders

- Metabolic disorders involve a primary change in the serum bicarbonate and/or anion gap.
- Respiratory disorders involve primary changes in the pCO2 (due to changes in CO2 removal by the lungs).

ABG/VBG isn't needed to evaluate metabolic pH disorders

- *Complete* analysis of pH status requires blood gas analysis, but all you need to determine the *metabolic* pH disorders is an electrolyte panel.
- Analysis of the metabolic pH disorders is usually the most important component (and frequently sufficient to guide treatment).
- Metabolic pH analysis should be performed on *every* set of electrolytes obtained from every patient. Additional evaluation with ABG/VBG may be performed more selectively.

the anion gap

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basic properties of the anion gap

- Anion Gap (AG) = Na – Bicarb – Chloride
- A normal anion gap is roughly 4-12 mM.
  - *Historically,* the normal range of anion gap was often quoted as being higher (e.g. up to ~16 mM). However, with newer electrolyte analyzers, the upper limit of normal has decreased to ~11-12 mM (24766940 (https://www.ncbi.nlm.nih.gov/pubmed/24766940)). This may vary between laboratories however, so the best practice is to be familiar with normal values at your hospital.
- Comparison with a *baseline* anion gap might be helpful, if that is available. For example, a patient with chronic renal insufficiency may have a chronically elevated anion gap at 14 mM. If this represents no change from previous labs, it is less likely to represent an acute and dangerous process.

you don't need to correct for albumin

- Albumin is a negatively charged protein, which will theoretically tend to increase the anion gap.
- Most literature and textbooks on acid-base status recommend correction of anion gap for the albumin. However, my experience is that clinicians actually *don't* do this in real life (because measurement of the albumin is often unavailable).
- Correcting the anion gap for albumin makes theoretical sense, but it is supported by no clinical evidence.
  - Correcting for albumin shifts the anion gap *upwards* by ~4 mM. Thus, a higher cutoff value must be needed for the detection of an anion-gap metabolic acidosis if correction is made for albumin.
  - Using an un-corrected anion gap with a cutoff value of >10 mM has the *same performance* for detecting anion gap metabolic acidosis as using a corrected anion gap with a higher cutoff value of ~14 mM (16858097 (https://www.ncbi.nlm.nih.gov/pubmed/16858097) , 18431828 (https://www.ncbi.nlm.nih.gov/pubmed/18431828) , 19087326 (https://www.ncbi.nlm.nih.gov/pubmed/19087326)). Different cutoffs may affect sensitivity and specificity, but *the overall performance of the test is unchanged* (i.e. same area under the Receiver Operator Curve). So correcting for the albumin is an extra step which provides no improved clinical utility to this test.
  - If you feel compelled to correct the anion gap for albumin that's fine, but you need to use a higher cutoff value.
- Further discussion of this here (https://emcrit.org/pulmcrit/mythbusting-correcting-the-anion-gap-for-albumin-is-not-helpful/) .

causes of an *elevated* anion gap

- This generally indicates the presence of an anion-gap metabolic acidosis (AGMA).
- More on the differential diagnosis of this in a forthcoming chapter on AGMA.

performance of anion gap in detecting lactic acidosis

- Anion gap is *not* reliable for detecting mild degrees of lactic acidosis (e.g. lactate of 2-4 mM). This is because a normal anion gap spans a range of ~10 mM. If the patient begins with a baseline anion gap at the lower limit of normal (e.g. 4 mM), they could easily develop a substantial lactic acidosis while still having an anion gap within the normal range (17699401 (https://www.ncbi.nlm.nih.gov/pubmed/17699401)).
- Studies vary in the precise sensitivity and specificity of anion gap for lactate detection (and this will likely vary between laboratories as well). One study found that an anion gap >10 mM could detect a lactate level >2.5 mM with a sensitivity of 63% and specificity of 65% (19087326 (https://www.ncbi.nlm.nih.gov/pubmed/19087326)).
- If there is a specific concern regarding whether the patient might have lactic acidosis, the best strategy is to check lactate directly. An anion gap cannot be relied upon to exclude elevated lactate. However, an anion gap remains a useful *surveillance* test for the detection of marked lactic acidosis.

causes of a *reduced* anion gap

- This might be defined as an anion gap below ~4 mM.
- Potential causes
  - **Laboratory error** (possibly the most common). This may occur due to severe hypernatremia, or severe hyperlipidemia (causing pseudohyponatremia).
  - Increased levels of cations: **hyperkalemia**, **hypercalcemia**, **hypermagnesemia,** or **lithium**.
  - Elevated levels of immunoglobulins (**multiple myeloma**, polyclonal gammopathy).
  - Cationic drugs (polymixin B), administration of ammonium chloride.

- **Pseudohyperchloremia**: Bromide or Iodide may cause chloride level to be incorrectly measured as crazy high. A similar phenomenon may occur with salicylates (29344509 (https://www.ncbi.nlm.nih.gov/pubmed/29344509)).

diagnostic approach to metabolic pH abnormalities

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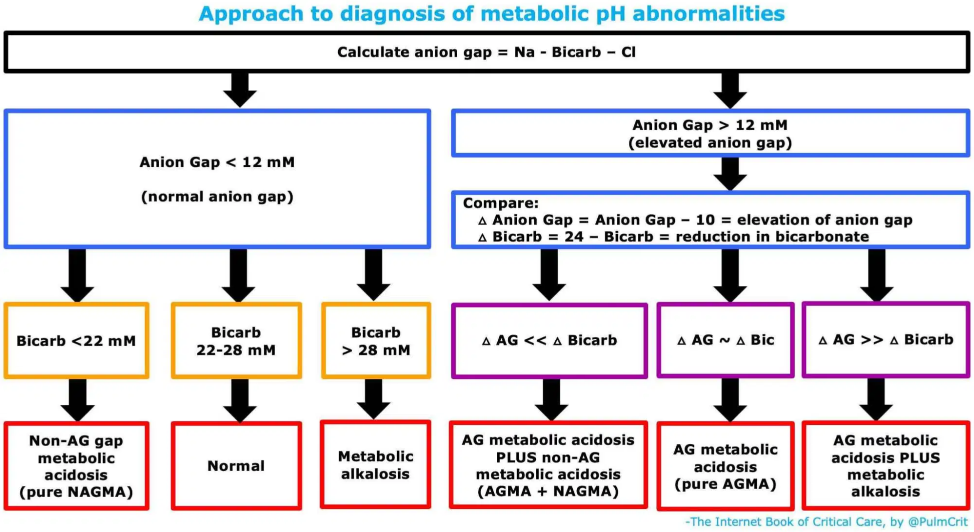

1. determination of the anion gap to evaluate for anion gap metabolic acidosis (AGMA)

- More on the anion gap above (#the_anion_gap) .

2. if the anion gap is normal, just look at the bicarbonate

- Bicarbonate <22 mM with a normal anion gap indicates a pure non-anion-gap metabolic acidosis (NAGMA).
- Bicarbonate >28 mM with a normal anion gap indicates a pure metabolic alkalosis.
- A bicarbonate of 22-28 mm with a normal anion gap indicates a normal metabolic pH status.

3. if the anion gap is elevated, determine the "delta delta"

- What are these?
  - Delta anion gap = (Anion Gap) – 10. This is roughly the degree of *elevation* of the anion gap.
  - Delta bicarbonate = 24 – bicarbonate. This is roughly the degree of *reduction* of the serum bicarbonate.
- Comparing these values can help determine if there is an additional process, in combination with the anion gap metabolic acidosis. Specifically:
  - (1) If delta anion gap is roughly equal to the delta bicarbonate, then no other process is present. This is about what we would expect for an isolated, pure anion gap metabolic acidosis.
  - (2) If the delta anion gap is much *higher* than the delta bicarbonate, then a second process is present which is increasing the bicarbonate level. This reveals a combination of an anion gap metabolic acidosis plus a metabolic alkalosis.
  - (3) If the delta anion gap is much *lower* than the delta bicarbonate, then this reveals a second process which is decreasing the bicarbonate. This indicates a combined anion gap metabolic acidosis plus a non-anion-gap metabolic acidosis.

respiratory pH analysis & how much does this help us?

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An ABG/VBG will provide information about respiratory pH abnormalities. Although this is traditionally considered a mandatory component of pH analysis, the amount of useful information provided by this analysis is unclear. Blood gas analysis can answer essentially two questions:

1. Is there adequate compensation?
2. Is there a primary respiratory disorder?

#1) is there adequate respiratory compensation?

- Patients with metabolic pH abnormalities should "normally" be expected to develop respiratory compensation, as shown in the left side of the table below:
  - Metabolic alkalosis may be compensated for by mild hypoventilation (secondary respiratory acidosis)
  - Metabolic acidosis may be compensated for by hyperventilation (secondary respiratory alkalosis)
- By determining whether the patient is obeying these rules, we could theoretically determine whether their ventilation is intact (or whether it is proportionally inadequate or excessive).
- In practice, ventilation in critically ill patients is generally influenced by *numerous* factors (e.g. anxiety, opioids, mechanical ventilation settings). Compensation equations are historically based on fairly stable patients *without* multiple active problems. It's unclear how well these equations function in the context of modern critically ill patients, who frequently have numerous active medical problems.
- Overall, it's murky how information about respiratory compensation should affect our management of critically ill patients. Specifically, decisions regarding intubation or selection of respiratory support devices are generally made on the basis of clinical assessment and diagnosis (not blood gas values).

pH compensation cheat sheet

RESPIRATORY COMPENSATION	
Primary Problem: Abnormal Bicarbonate	Compensatory pCO_2
>40	Not >50-55
40	49
39	48
38	48
37	47
36	46
35	46
34	45
33	44
32	43
31	43
30	42
29	41
28	41
27	40
Normal Range	
22	42
21	41
20	39
19	38
18	36
17	35
16	33
15	31
14	30
13	28
12	27
11	25
10	24
9	22
8	21
7	19
6	18
5	16 Not < 10-15

METABOLIC COMPENSATION		
Primary problem: Abnormal pCO_2	Acute compensation: Bicarbonate	Chronic compensation: Bicarbonate
100	30	Not > 45
97	30	44
94	29	43
91	29	42
88	29	41
85	29	40
82	28	39
79	28	38
76	28	37
73	27	36
70	27	35
67	27	34
64	26	32
61	26	31
58	26	30
55	26	29
52	25	28
49	25	27
46	25	26
Normal Range		
36	23	22
35	23	22
34	23	21
33	23	21
32	22	20
31	22	20
30	22	19
29	22	19
28	22	18
27	21	18
26	21	17
25	21	17

This table incorporates all compensatory equations into a single, easy-to-use format. No need to memorize formulas - just look at this an you're all set. Unfortunately, these formulas *aren't* well validated and their overall significance is *dubious* – so use them with caution and exercise judgement.

-The Internet Book of Critical Care, by @PulmCrit

(https://emcrit.org/ibcc/ph/)

#2) is there a primary respiratory disorder?

- This is undoubtedly more important than whether there is adequate respiratory compensation (#1).
- If we detect a metabolic pH abnormality, there is a possibility that it represents a *secondary* compensatory response to a respiratory abnormality (the right side of the chart above). Specifically:
  - (a) Metabolic acidosis could be due to a chronic respiratory alkalosis
  - (b) Metabolic alkalosis could be due to a chronic respiratory acidosis
- Sorting this out is important, because it leads to an entirely different diagnosis and management.
- From a practical standpoint:
  - (a) Metabolic acidosis due to chronic respiratory alkalosis is extremely rare (unless a patient is being mismanaged on mechanical ventilation). This is a bit of a zebra.
  - (b) Metabolic alkalosis due to chronic respiratory acidosis is common in patients with hypercapnia of any etiology (most commonly COPD, obesity hypoventilation syndrome, or possibly chronic opioid use). This can generally be diagnosed based on a compatible clinical history, as well as review of archival labs (which show a *chronic* metabolic alkalosis).

so, what does the blood gas analysis really add to a clinically relevant analysis of pH?

- As explored above, blood gas analysis usually won't have a substantial effect on our diagnosis and management of the patient (assuming that we have fully evaluated the electrolyte panel and performed a thoughtful history and physical examination).
- Occasionally, blood gas analysis may reveal a chronic respiratory acidosis as the cause of a metabolic alkalosis (2b) – but in most cases this would already have been suspected on the basis of clinical history and/or prior laboratory studies.
- So, in sum, blood gas analysis isn't mandatory when analyzing a patient's acid-base status. It may be obtained on a *selective* basis, rather than broadly being ordered for any patient with a pH abnormality. This is preferable for the following reasons:
  - (1) Acid-base abnormalities are extremely common among critically ill patients (present in perhaps a majority of patients). If we take the attitude that any acid-base abnormality mandates a blood gas analysis, then we are going to be subjecting our patients to *lots* of blood gas analyses (at considerable pain and expense).
  - (2) Treatment decisions can often be made directly on the basis of the electrolytes (metabolic acid-base analysis). This allows for the streamlining of clinical management (without a delay for blood gas analysis).
- French guidelines do recommend measurement of arterial blood gas in every patient with decreased plasma bicarbonate level. However, they cite no high-quality evidence to support this recommendation (31418093 (https://www.ncbi.nlm.nih.gov/pubmed/31418093)).

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etiologies are more important than numbers

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types of information from pH analysis

- (1) Diagnostic information – clues as to the underlying diagnosis.
- (2) Severity information – how severe is the pH abnormality?

Generally, the most critical aspect of pH analysis is to identify unexpected *diagnoses* (#1). The precise severity of the disorder is less important. As long as we have correctly identified the underlying diagnosis and we are treating it appropriately, the exact pH numbers are often relatively unimportant.

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other approaches to pH analysis

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- There are *numerous* approaches to pH analysis, most of which are much more complex (e.g. Stewart's Acid-Base approaches). However, different strategies of analysis will generally yield the same conclusions.
  - Choice of various models remains controversial. There's no solid evidence that one model is clinically superior to the other (22976522 (https://www.ncbi.nlm.nih.gov/pubmed/22976522)). Most comparisons of various models are theoretical rather than actually field-tested.
  - iPhone apps based on Stewart Acid-Base analysis may provide misleading information (Nicholson et al 2016 (https://www.atsjournals.org/doi/pdf/10.1513/AnnalsATS.201604-234LE)).
- Any approach which you understand and apply in a consistent fashion is great. The above approach is easy to perform and widely used by clinicians (which may facilitate communication with colleagues). However, if you already have a method that you are using, there is no reason to switch.
- The main problem occurs when people fail to apply *any* pH analysis at all (for example, failing to note that the anion gap is elevated).

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podcast

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questions & discussion

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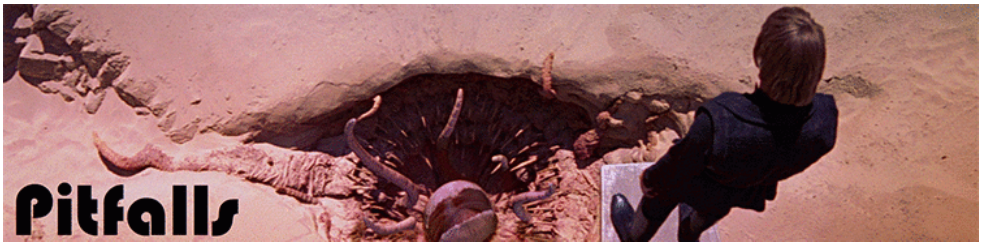
To keep this page small and fast, questions & discussion about this post can be found on another page ***here*** (https://emcrit.org/pulmcrit/ph/) .



(https://i1.wp.com/emcrit.org/wp-content/uploads/2016/11/pitfalls2.gif)

- The anion gap should be calculated *whenever* evaluating any set of chemistries (if your computer system doesn't do this for you automatically).
- An anion gap elevation in a critically ill patient should be considered to likely represent lactic acidosis and a life-threatening process, until proven otherwise.
- Many approaches to acid-base physiology make this unnecessarily difficult and confusing. Avoid this. For example, you don't need to correct the anion gap for albumin, potassium, or anything else.

The Internet Book of Critical Care is an online textbook written by Josh Farkas (@PulmCrit), an associate professor of Pulmonary and Critical Care Medicine at the University of Vermont.