A Case-Based Approach to Acid-Base Disorders

Justin Muir, PharmD
Clinical Pharmacy Manager, Medical ICU
NewYork-Presbyterian Hospital
Columbia University Irving Medical Center
jum9081@nyp.org

Disclosures

None

Objectives

At the completion of this activity, pharmacists will be able to:

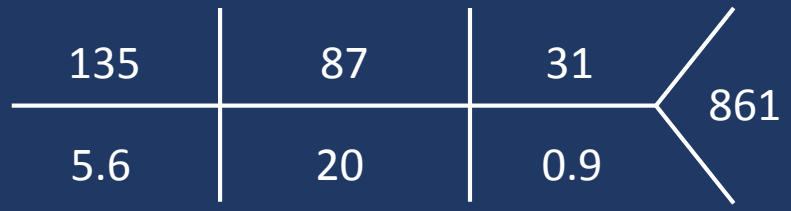
1. Describe acid-base physiology and disease states that lead to acid-base disorders.
2. Demonstrate a step-wise approach to interpretation of acid-base disorders and compensatory states.
3. Analyze contemporary literature regarding the use of sodium bicarbonate in metabolic acidosis.

At the completion of this activity, pharmacy technicians will be able to:

1. Explain the importance of acid-base balance.
2. List the acid-base disorders seen in clinical practice.
3. Identify potential therapies used to treat acid-base disorders.

Case

A 51 year old man with history of erosive esophagitis, diabetes mellitus, chronic pancreatitis, and bipolar disorder is admitted with several days of severe nausea, vomiting, and abdominal pain.



pH 7.46 / pCO_2 29 / pO_2 81
BE -3.8 / HCO_3^- 18 / SaO_2 96

- What additional data should be obtained?
- What acid base disturbance(s) is/are present?

Introduction

- Acid base status is tightly regulated to maintain normal biochemical reactions and organ function
- Body uses multiple mechanisms to maintain homeostasis
- Abnormalities are extremely common in hospitalized patients with a higher incidence in critically ill with more complex pictures
- A standard approach to analysis can help guide diagnosis and treatment

Important acid-base determinants

Blood gas generally includes at least:

Measurement	Description	Normal range (arterial blood)
pH	-log [H^+]	7.35-7.45
pCO_2	partial pressure of dissolved CO_2	35-45 mmHg
pO_2	partial pressure of dissolved O_2	80-100 mmHg
Base excess	calculated measure of metabolic acid/base deviation from normal	-3 to +3
SO_2	calculated measure of Hgb O_2 saturation based on pO_2	95-100%
HCO_3^-	calculated measure based on relationship of pH and pCO_2	22-26 mEq/L

Haber RJ. West J Med 1991;155:146-51

Definitions

Acidemia	Alkalemia
A state of low blood pH (< 7.35)	A state of high blood pH (> 7.45)

Haber RJ. West J Med 1991;155:146-51

Definitions

Acidosis	Alkalosis
A process tending to acidify body fluids	A process tending to alkalinize body fluids

Haber RJ. West J Med 1991;155:146-51

Definitions

Metabolic	Respiratory
Relating to gain/loss of acid or bicarbonate (HCO_3^-)	Relating to gain/loss of carbon dioxide (CO_2)

Haber RJ. West J Med 1991;155:146-51

Definitions

Acute	Chronic
Occurring over minutes to hours	Occurring over days

Haber RJ. West J Med 1991;155:146-51

Consequences of acidemia	Consequences of alkalemia
Cardiovascular	
• Increased pulmonary vascular resistance • Reduced cardiac output, blood pressure • Reduced responsiveness to catecholamines • Arrhythmias	• Arteriolar constriction • Reduction in coronary blood flow • Arrhythmias
Respiratory	
• Hyperventilation • Respiratory muscle fatigue	• Hypoventilation
Metabolic	
• Increased metabolic demand • Insulin resistance • Inhibition of anaerobic glycolysis • Hyperkalemia	• Stimulation of anaerobic glycolysis • Hypokalemia, hypomagnesemia, hypophosphatemia • Ionized hypocalcemia
Cerebral	
• Altered mental status, coma	• Reduction in cerebral blood flow • Tetany, seizures

Adrogue HJ. N Engl J Med 1998;338:26-35
Adrogue HJ. N Engl J Med 1998;338:107-11

Henderson-Hasselbalch equation

$$CO_2 + H_2O \leftrightarrow H_2CO_3 \leftrightarrow H^+ + HCO_3^-$$

$$pH = Pk + log_{10}\left(\frac{HCO_3^-}{0.03\ (PaCO_2)}\right)$$

- Used by blood gas analyzers to calculate HCO_3^-
- May be used to check the internal consistency of a blood gas

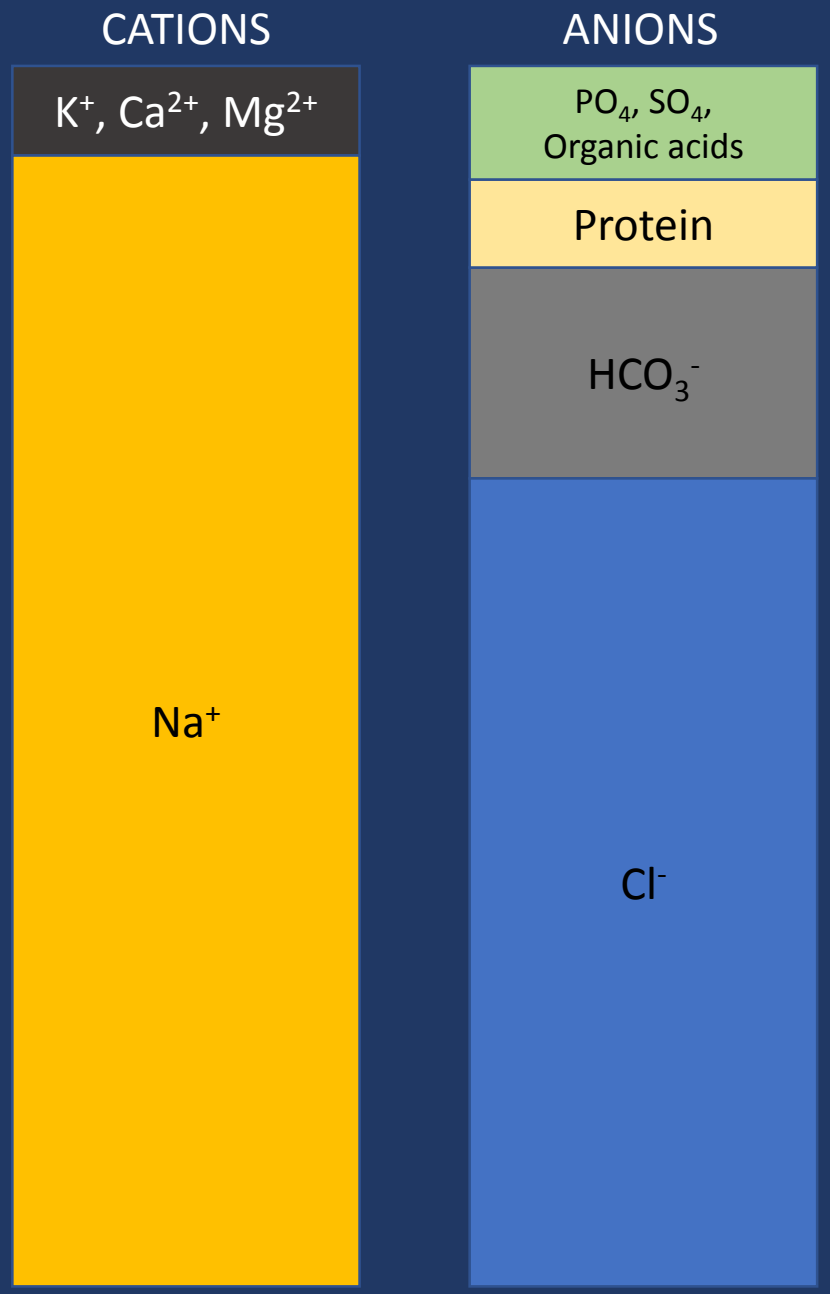
pH – log of hydrogen ion concentration [H^+]
Pk – acid dissociation constant
$PaCO_2$ – partial pressure of arterial carbon dioxide
0.03 – solubility of CO_2 in blood

Berend K. N Engl J Med 2014;371:1434-45

Ionic components of plasma

Cations	mEq/L	Anions	mEq/L
Na^+	140	Cl^-	100
K^+	4	CO_2	25
Ca^{2+}	2	Protein	15
Mg^{2+}	2	Phosphate	2
		Sulfate	1
		Organic acids	5
Total cations	~148	Total anions	~148

CO_2 on a metabolic panel represents *total* CO_2 (tCO_2), including HCO_3^-, pCO_2, and other organic compounds. Generally $tCO_2 \approx HCO_3^-$ but may be slightly higher with severe hypercapnia. More than 95% of tCO_2 and HCO_3^- results are within 3 points of each other.



Morris CG. Anaesthesia 2008;63:294-301
Kumar V. Clin Chem 2008;54:1586-7

Endogenous acids

Type	Substances	Approximate Quantity	Elimination
Volatile	CO_2	15,000 mmol H^+ equivalents per day	Lungs
Organic acids	Primarily ketones and lactate	Several thousand mmol per day	Primarily liver
Inorganic acids	Primarily sulfate and phosphate	1.5 mmol/kg per day	Primarily renal

Morris CG. Anaesthesia 2008;63:294-301

Maintenance of homeostasis

- Plasma buffer system (HCO_3^-, Hgb, phosphate)
- Respiratory system – increase/decrease pCO_2
  - Fast – seconds to minutes
- Renal system – increase/decrease HCO_3^-
  - Slow – hours to days

Metabolic acidosis

- Gain of anion
  - Hyperchloremic
  - Anion gap acidosis
  - Hyperphosphatemic
- Loss of cation (Na^+, K^+)
  - Renal – renal tubular acidosis, natriuretic agents, hypoaldosteronism, excretion of sodium with non-chloride/nonbicarbonate anions (lactate, hippurate, ketones)
  - Gastrointestinal – diarrhea, vomiting pancreatic secretions

Seifter JL. N Engl J Med 2014;371:1821-31

Anion gap

- Estimation of unmeasured anions (esp. phosphate, sulfate, organic anions, plasma proteins)

$$AG = [Na^+] - ([Cl^-] + [HCO_3^-])$$

$$AG = [Na^+] - [Cl^-] - [HCO_3^-]$$

- Other measured ions (K^+, Mg^{2+}, Ca^{2+}, PO_4^{3-}) are assumed to be unmeasured
- Normal value < 12 ± 4 mEq/L

Berend K. N Engl J Med 2014;371:1434-45

Anion gap metabolic acidosis (AGMA) mnemonics

MUDPILES		KUSMALE		GOLDMARK	
M	Methanol	K	Ketoacidosis	G	Glycols (ethylene, propylene)
U	Uremia	U	Uremia	O	Oxoproline (pyroglutamic acid)
D	Diabetic ketoacidosis	S	Salicylate	L	L-lactate
P	Paraldehyde	M	Methanol	D	D-lactate
I	Isoniazid, iron	A	Aldehyde	M	Methanol
L	Lactate	L	Lactate	A	Aspirin
E	Ethylene glycol	E	Ethylene glycol	R	Renal failure
S	Salicylates			K	Ketoacidosis

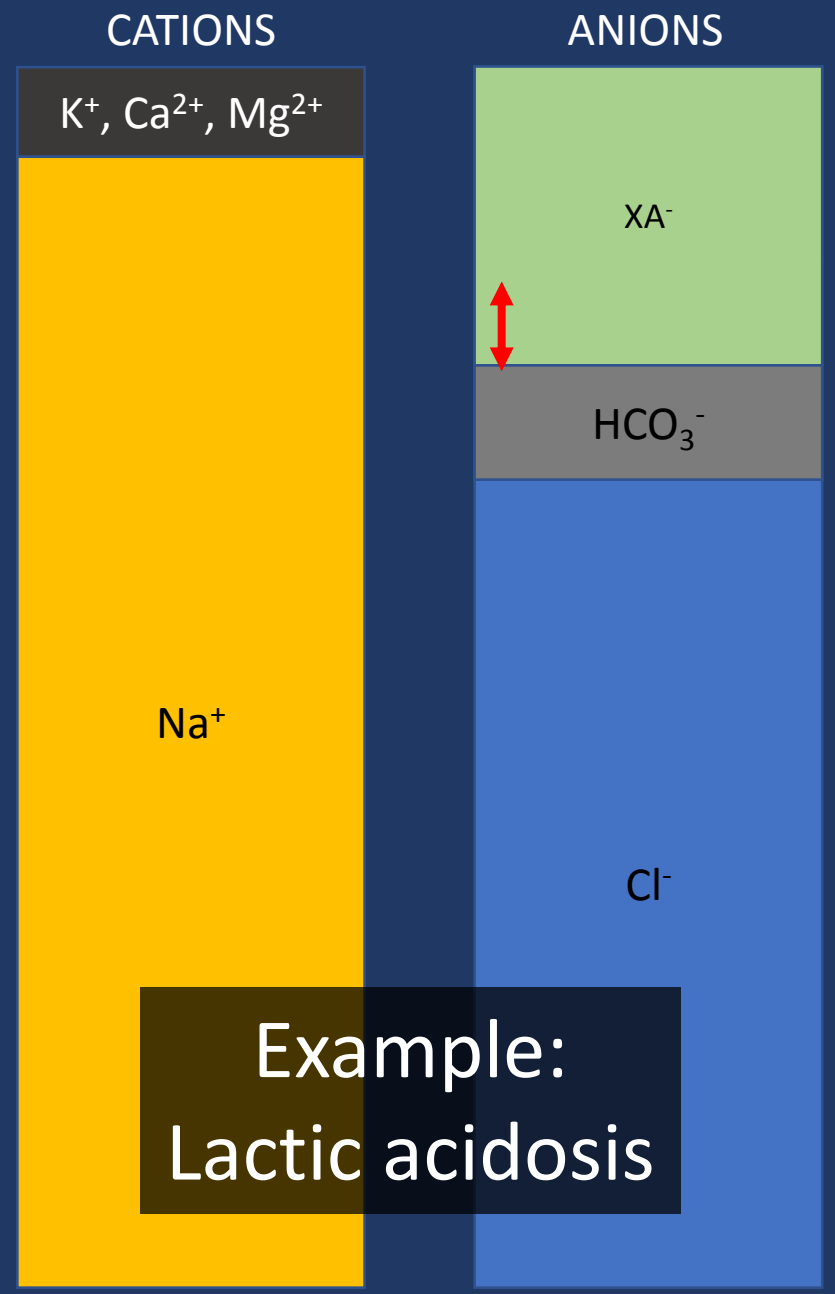
Critique

- Some intoxications outdated e.g. paraldehyde
- Some drugs listed cause AGMA via lactate (other lactate-inducing drugs/conditions missing)
- Ketoacidosis is not exclusively diabetic
- Glycols other than ethylene glycol
- Oxoproline missing (chronic acetaminophen use/glutathione depletion)
- Reminder of different forms of lactic acidosis

Mehta AN. Lancet 2008;372:892

Anion gap metabolic acidosis

- Addition of unmeasured anions (XA^-)
- XA^- increases and HCO_3^- decreases



XA^- = unmeasured anions

Morris CG. Anaesthesia 2008;63:294-301

Non-anion gap metabolic acidosis (NAGMA) mnemonics

HARDUP

- **H** Hyperchloremia
- **A** Acetazolamide, Addison's
- **R** Renal tubular acidosis
- **D** Diarrhea
- **U** Ureteroenterostomy
- **P** Pancreatoenterostomy

ACCRUED

- **A** Ammonium chloride / acetazolamide
- **C** Chloride intake
- **C** Cholestyramine
- **R** Renal tubular acidosis
- **U** Urine diverted into intestine
- **E** Endocrine disorders (e.g. Addison's)
- **D** Diarrhea

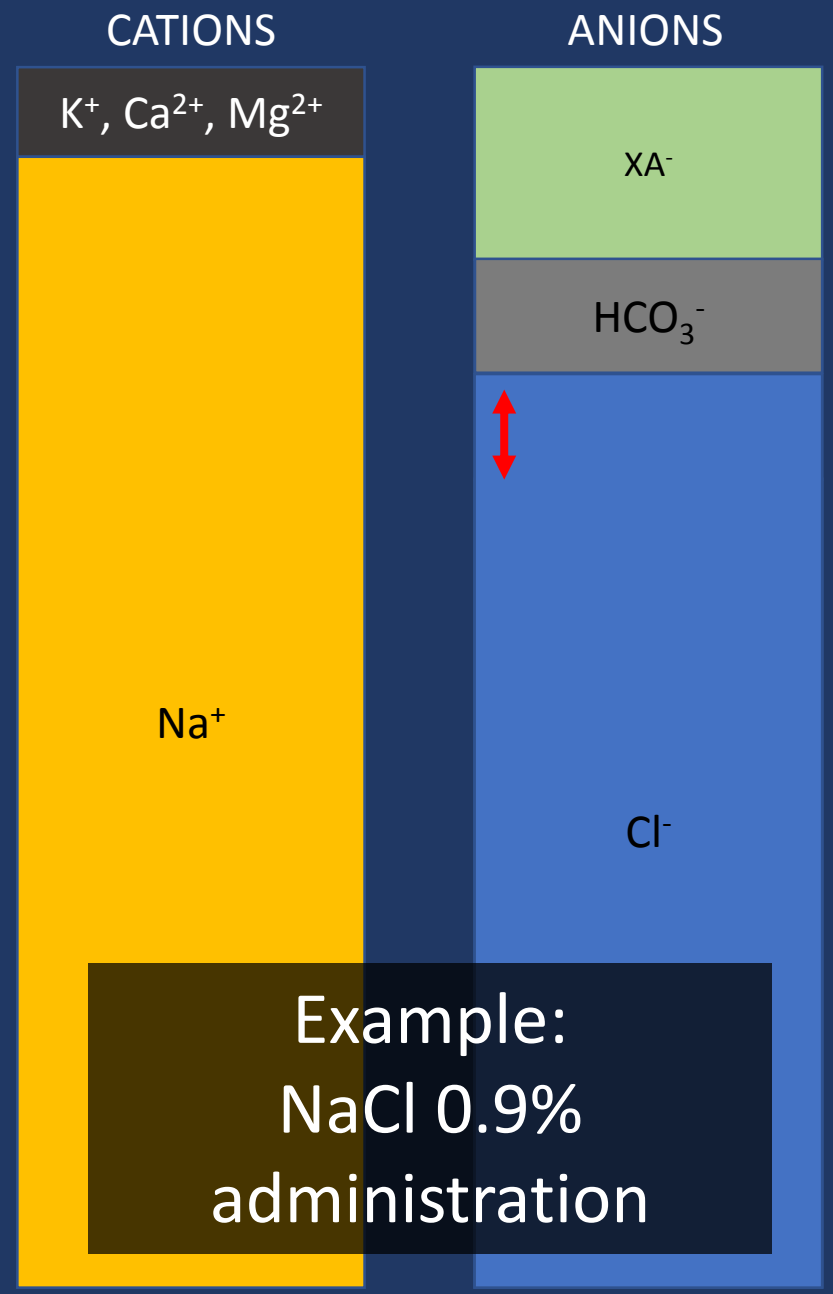
PANDA RUSH

- **P** Pancreatic secretion loss
- **A** Acetazolamide
- **N** Normal saline intoxication
- **D** Diarrhea
- **A** Aldosterone antagonists
- **R** Renal tubular acidosis
- **U** Ureteric diversion
- **S** Small bowel fistula
- **H** Hyperalimentation

All involve gain of chloride or loss of bicarbonate (i.e. measured ions)

Non-anion gap metabolic acidosis

- *Measured ions* are relevant here
- Addition of chloride, direct loss of HCO_3^-
- No change in XA^-



XA^- = unmeasured anions

Morris CG. Anaesthesia 2008;63:294-301

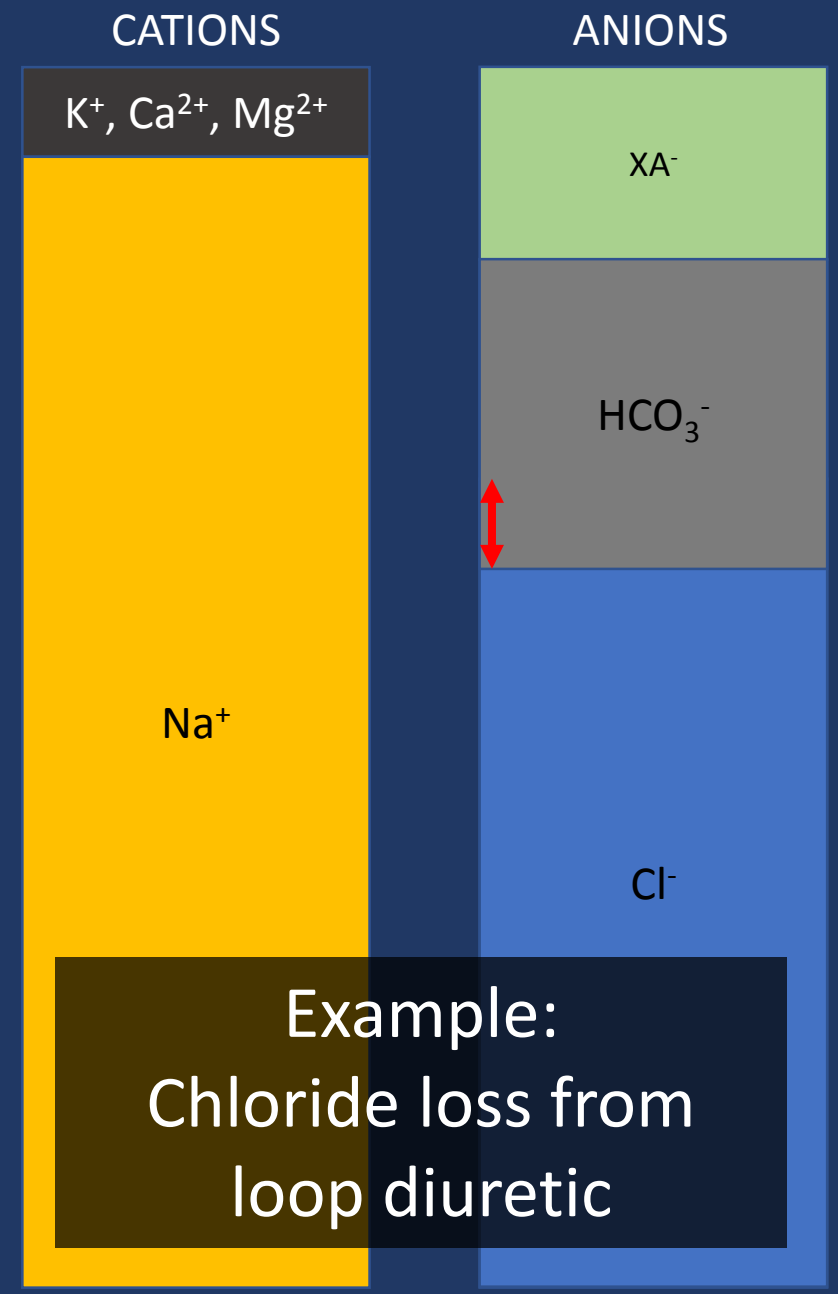
Metabolic alkalosis

- Loss of anion
  - Gastrointestinal – vomiting, villous adenoma, chloride secretory diarrheas
  - Renal – chloruretic agents (loop or thiazide diuretics), chloride channelopathies, hypokalemia
  - Sweat – cystic fibrosis
  - Hypoalbuminemic state, malnutrition
- Gain of cation
  - Sodium bicarbonate/lactate/acetate/citrate
  - Hypernatremia (hyperaldosteronism)
  - Hypercalcemia (milk alkali syndrome, calcium carbonate)

Seifter JL. N Engl J Med 2014;371:1821-31

Metabolic alkalosis

- Addition of HCO_3^-, direct loss of chloride, (loss of XA^-)



XA^- = unmeasured anions

Morris CG. Anaesthesia 2008;63:294-301

Respiratory acidosis

Acute	Chronic
CNS depression	Chronic lung disease
Neuromuscular disorders	Chronic neuromuscular disorders
Acute airway obstruction	Chronic respiratory center depression
Severe pneumonia or pulmonary edema	
Impaired lung motion (e.g. pneumothorax)	
Flail chest	
Ventilator dysfunction	

Respiratory alkalosis

Etiologies	
Anxiety	Pregnancy
Hypoxemia	Liver disease
Lung diseases (e.g. asthma, pneumonia, PE)	Sepsis
CNS diseases	Hepatic encephalopathy
Drugs – salicylates, catecholamines, progesterone	Mechanical ventilation

Haber RJ. West J Med 1991;155:146-51

Acid-base analysis methods

- Bicarbonate-pH-pCO_2 aka physiological method

  "Boston method"
- Base excess method

  "Copenhagen method"
- Physicochemical method

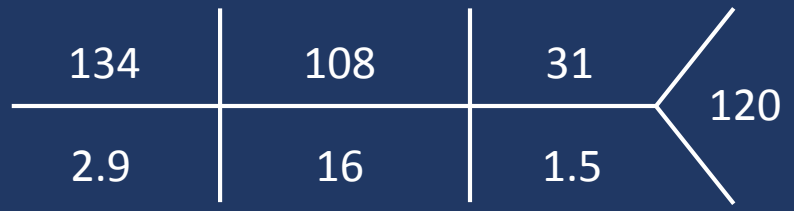
  "Stewart/strong ion difference method"

Important caveats and principles

- Results tend to be more qualitative than quantitative
- The body does not overcompensate
- At most there can be 3 acid-base processes
  - Respiratory acidosis OR alkalosis
  - Anion gap metabolic acidosis
  - Non-anion gap metabolic acidosis OR metabolic alkalosis
- Assigning diagnoses becomes challenging in the setting of mechanical ventilation, ECMO

Case

- AL is a 44-year-old man with a history of HIV, nonadherent to medications, and smoking (30 pack year history) admitted to the ED with a two-day history of severe diarrhea.

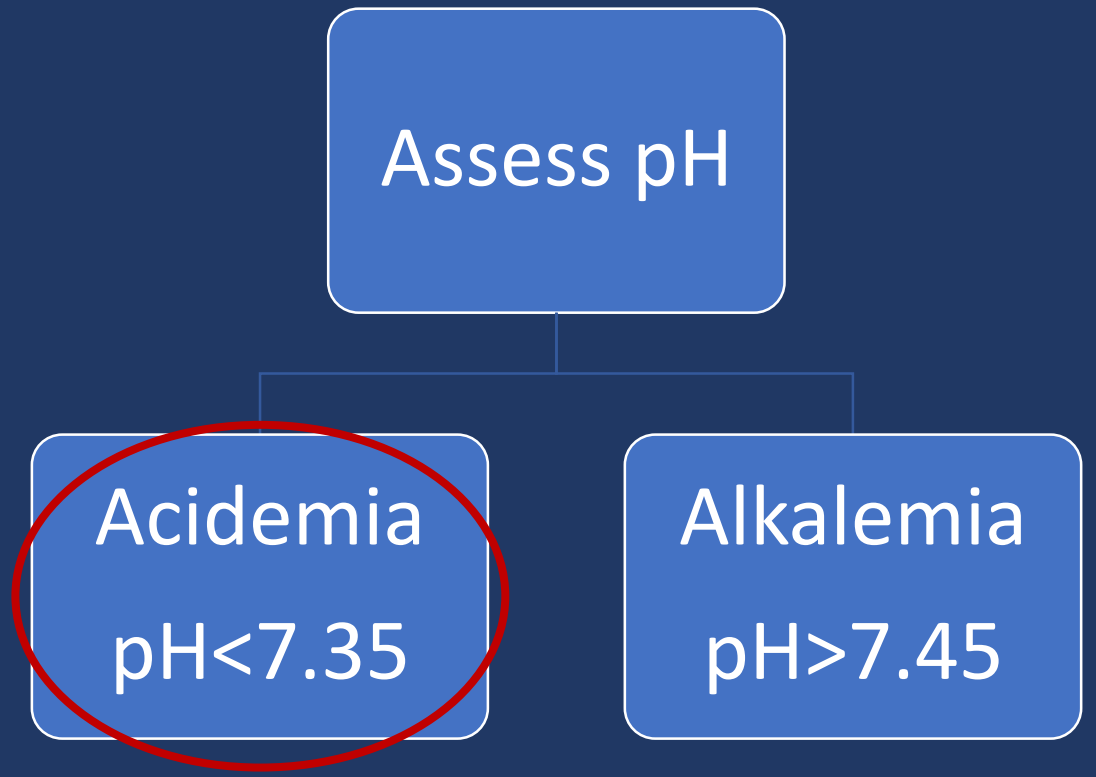


pH 7.19 / pCO_2 43 / pO_2 77 / BE -9
HCO_3^- 15 / SaO_2 94% / Lactate 2.2

Albumin 4.1 g/dL

Acid-base interpretation steps

1. Acidemia or alkalemia



134	108	31	120
2.9	16	1.5	

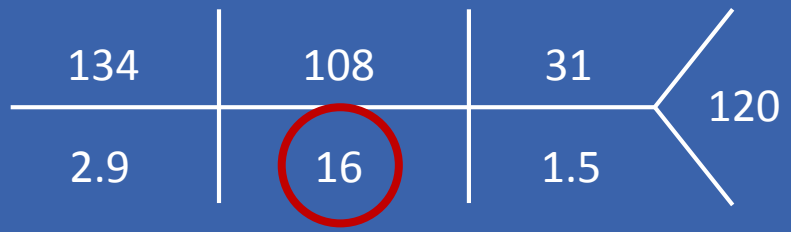
pH 7.19 / pCO_2 43 / pO_2 77 / BE -9
HCO_3 15 / SaO_2 94% / Lactate 2.2

Albumin 4.1 g/dL

Haber RJ. West J Med 1991;155:146-51

Acid-base interpretation steps

1. Acidemia or alkalemia
2. Primary disturbance



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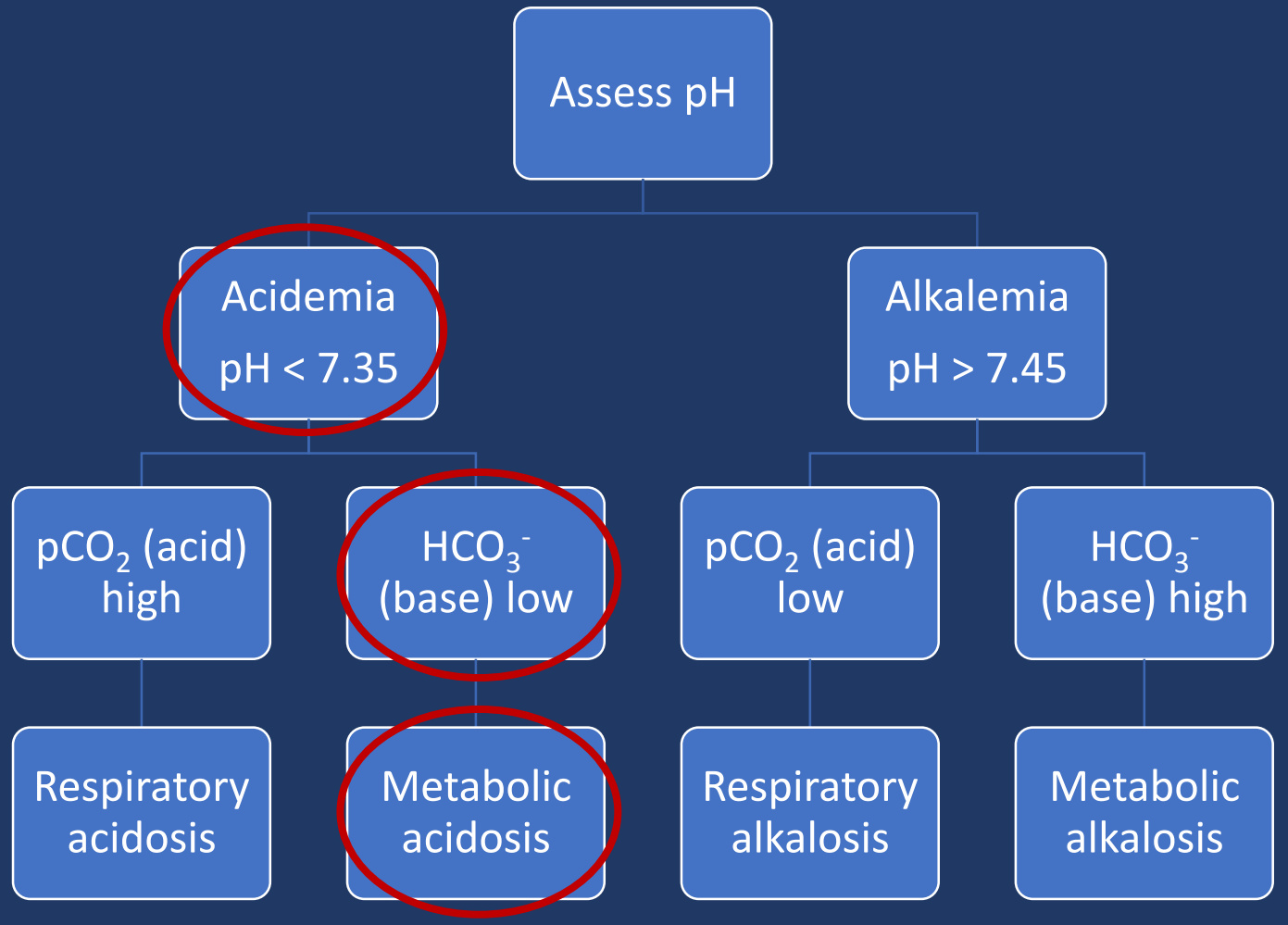
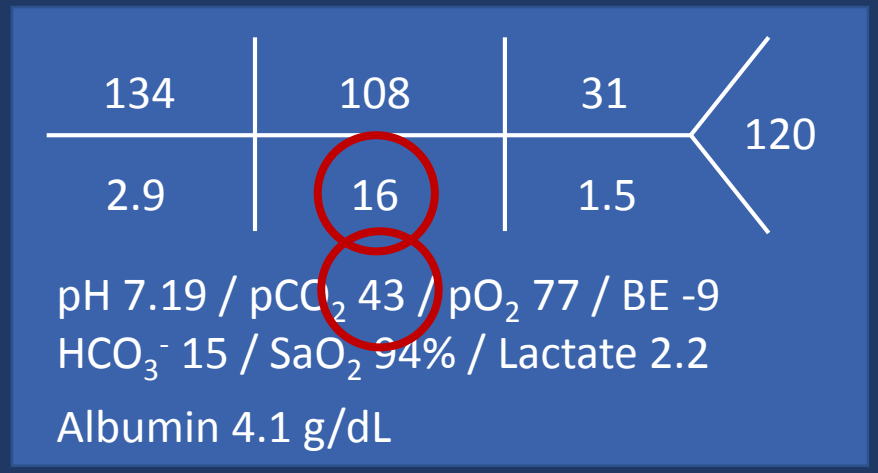


Haber RJ. West J Med 1991;155:146-51

Acid-base interpretation steps

1. Acidemia or alkalemia
2. Primary disturbance
3. Assess compensation



Metabolic acidosis: Winter's formula

$$Expected\ pCO_2 = 1.5\ x\ HCO_3^- + 8 \pm 2$$

$$Expected\ pCO_2 = 1.5\ x\ 16 + 8 \pm 2$$

$$= 28\text{-}34$$

Inadequate compensation
↑ pCO_2 = respiratory acidosis

Haber RJ. West J Med 1991;155:146-51

Acid-base interpretation steps

1. Acidemia or alkalemia
2. Primary disturbance
3. Assess compensation

pH 7.32 / pCO_2 70 / pO_2 165 / BE 9
HCO_3^- 38 / SaO_2 99% / Lactate 1.2

Albumin 3.5 g/dL

Respiratory acidosis:
Assess acute (not compensated) vs chronic (compensated)

Acute: pH ↓ 0.08 for every 10 mmHg ↑ pCO2 from 40 mmHg
HCO_3^- increases 1 for every 10

Chronic: pH ↓ 0.03 for every 10 mmHg ↑ pCO2 from 40 mmHg
HCO_3^- increases 4 for every 10

If *acute*, (70-40)/10 x 0.08 = 0.24 ↓ in pH = pH 7.16
HCO_3^- should ↑ 3

If *chronic*, (70-40)/10 x 0.03 = 0.09 ↓ in pH = pH 7.31
HCO_3^- should ↑ 12

pH 7.32 ≈ expected 7.31; appears chronic

Haber RJ. West J Med 1991;155:146-51

Acid-base interpretation steps

1. Acidemia or alkalemia
2. Primary disturbance
3. Assess compensation

Compensation formulas exist for:

Acute and chronic respiratory acidosis: effect on pH and HCO_3^-
Acute and chronic respiratory alkalosis: effect on pH and HCO_3^-
Metabolic acidosis: expected pCO_2
Metabolic alkalosis: expected pCO_2

Haber RJ. West J Med 1991;155:146-51

Acid-base interpretation steps

1. Acidemia or alkalemia
2. Primary disturbance
3. Assess compensation
4. Calculate anion gap

Haber RJ. West J Med 1991;155:146-51

Anion gap

- Estimation of unmeasured anions (esp. phosphate, sulfate, organic anions, plasma proteins)

$$AG = [Na^+] - ([Cl^-] + [HCO_3^-])$$

$$AG = [Na^+] - [Cl^-] - [HCO_3^-]$$

- Other measured ions (K^+, Mg^{2+}, Ca^{2+}, PO_4^{3-}) are assumed to be unmeasured
- Normal value < 12 ± 4 mEq/L

Berend K. N Engl J Med 2014;371:1434-45

AG correction for albumin

- Albumin is a major component of AG
- Hypoalbuminemia will lower the AG, potentially masking accumulation of other unmeasured anions

$$AG_{corr} = AG_{measured} + 2.5\ (4 - albumin)$$

2.5 = estimated net negative charge of 1 g/dL albumin
Has been measured to be 2.3-2.5 mEq/L

Normal albumin assumed to be 4-4.4 g/dL

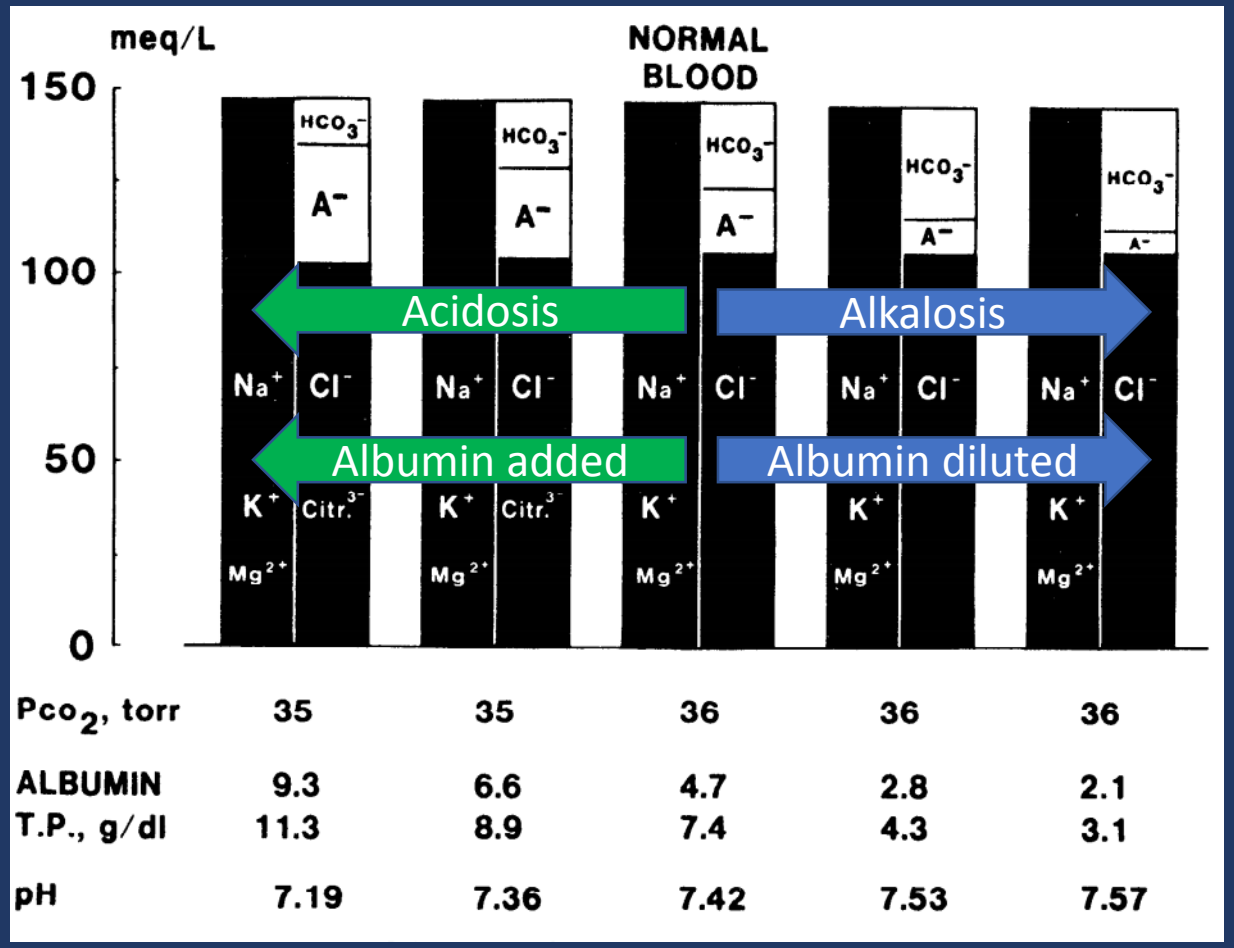
Kraut JA. Clin J Am Soc Nephrol 2007;2:162-74

Causes of low or negative AG

- Lab error
- Hypoalbuminemia
- Sodium measurement error (e.g. severe hyperNa)
- Gammopathy (e.g. MGUS); multiple myeloma
- Intoxications – bromide, iodide, lithium
- Hypercalcemia or hypermagnesemia

Kraut JA. Clin J Am Soc Nephrol 2007;2:162-74

Albumin's effects on pH and bicarbonate



Pco_2, torr	35	35	36	36	36
ALBUMIN	9.3	6.6	4.7	2.8	2.1
T.P., g/dl	11.3	8.9	7.4	4.3	3.1
pH	7.19	7.36	7.42	7.53	7.57

In vitro manipulation of human blood

Rossing TH. J Appl Physiol 1986;61:2260-5

Acid-base interpretation steps

1. Acidemia or alkalemia
2. Primary disturbance
3. Assess compensation
4. Calculate anion gap
5. Delta gap

Haber RJ. West J Med 1991;155:146-51

Delta gap / “Delta Delta”

- AGMA may overlap with NAGMA or metabolic alkalosis
- [HCO_3^-] decreases ~ 1 point for every point increase in AG
- Various methods exist to assess the additional metabolic component
  - Corrected bicarbonate
  - Expected bicarbonate
  - $\Delta AG - \Delta HCO_3^-$ (difference)
  - $\Delta AG / \Delta HCO_3^-$ (ratio)
  - Sodium-chloride effect
- No need to conduct if AG normal (Na-Cl effect could still be used)

Delta gap (corrected HCO_3^- method)

- Estimates what [HCO_3^-] would be if anion gap process was removed

$$\Delta AG = AG_{corr} - 12$$

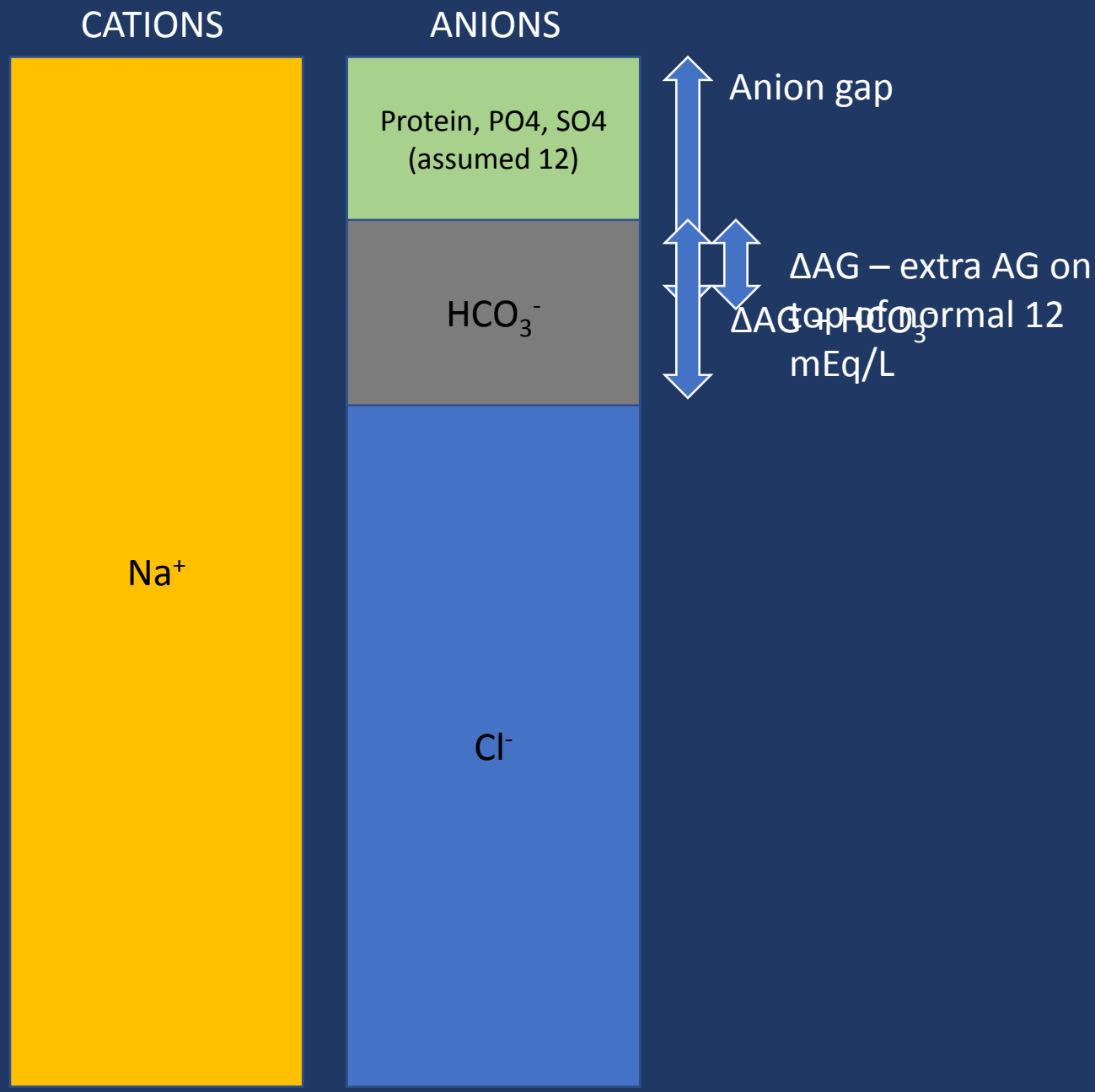
$$[HCO_3^-] + \Delta AG = \text{“corrected”}\ [HCO_3^-]$$

- “Corrected” [HCO_3^-] elevated i.e. > 28-30: metabolic alkalosis
- “Corrected” [HCO_3^-] reduced i.e. < 20: NAGMA

Haber RJ. West J Med 1991;155:146-51

Corrected HCO_3^-

This is not a real number but estimates what the bicarbonate would be if there was no anion gap process



Delta gap (Na-Cl effect method)

- Sodium-chloride effect is a derivation of Δ gap = ΔAG – ΔHCO_3^-

$$\Delta\ Gap = \Delta\ AG - \Delta\ HCO_3^-$$

$$\Delta\ Gap = ([Na^+] - [Cl^-] - [HCO_3^-]) - 12 - (24 - HCO_3^-)$$

$$\Delta\ Gap = [Na^+] - [Cl^-] - 36$$

< -6 suggests NAGMA

> +6 suggests metabolic alkalosis

Tsapenko MV. Oman Med J 2013;28:73-4

Urinary charge gap / urinary anion gap

$$\text{Urine gap} = [U_{Na}^{+}] + [U_{K}^{+}] - [U_{Cl}^{-}]$$

- Negative urine gap
  - Increased excretion of unmeasured cation ammonium
  - Alkalinizing effect via chloride excretion
  - Suggests etiology of NAGMA not intrinsic to kidneys (e.g. GI, diuretics, saline)

- Positive urine gap
  - Increased excretion of unmeasured anions (bicarbonate, lactate, hippurate, ketones)
  - Acidifying effect via chloride retention
  - Suggests renal etiology of NAGMA (e.g. RTA)

Seifter JL. N Engl J Med 2014;371:1821-31

Urine chloride in metabolic alkalosis

Urine chloride low (< 10-25 mEq/L) ("chloride-responsive alkalosis")	Urine chloride high (> 20-40 mEq/L) ("chloride-nonresponsive alkalosis")
Vomiting, nasogastric suctioning	Excess mineralocorticoid activity
Diuretic use in the past	Ongoing diuretic use
Posthypercapnia	Excess alkali administration
Contraction alkalosis	Refeeding alkalosis

Kellum JA. Crit Care 2000;4:6-14

Buffer therapy

Buffer	Dosage forms	Comment
Sodium bicarbonate	IV, PO	Most common
Sodium acetate	IV Contained in Plasmalyte, Normosol	Mostly used for TPN Risk of cardiovascular toxicity with rapid administration
Sodium or potassium citrate	PO	Treatment of chronic metabolic acidosis
Sodium lactate	Contained in Lactated Ringer's	Potential increase in lactate if unable to metabolize
Tromethamine (THAM, tris-hydroxymethyl aminomethane)	IV	Not CO_2-based No longer manufactured
Carbicarb	IV	Equimolar mixture of Na_2CO_3 and $NaHCO_3$ Not available in US

Bicarbonate deficit

$$Bicarbonate\ Deficit = 0.5\ x\ Wt\ x\ (desired\ \Delta HCO_3^-), \text{ or}$$

$$Bicarbonate\ Deficit = \left(0.4 + \frac{2.6}{HCO_3^-}\right) x\ Wt\ x\ (desired\ \Delta HCO_3^-)$$

For example, to increase HCO_3^- from 8 to 15 mEq/L for a 70 kg person

= 0.5 x 70kg x (15-8) = 245 mEq

Alternatively, [0.4 + (2.6/8)] x 70kg x (18-5) = 355 mEq

- May be used to guide bicarbonate replacement
- Caution with overshooting if buffering a process that is clearing (e.g. lactate, ketoacidosis, renal failure) → typically safest to only administer until pH is out of a dangerous range (e.g. pH > 7.2, HCO_3^- > 10-12 mEq/L)

Fernandez PC. Kidney Int 1989;36:747-52

Potential harms with bicarbonate

- Increasing pCO_2
  - Especially if unable to ventilate extra load (obstructive lung disease, paralyzed, low tidal volume ventilation, cardiac arrest)
  - Intracellular/CSF acidosis – largely based on animal data
  - Severity may relate to rate of infusion
- Stimulation of lactate / impaired clearance
- Fluid/sodium load
- Hypokalemia, hypocalcemia

Forsythe SM. Chest 2000;117:260-7

BICAR-ICU Trial

Design	Randomized, controlled trial
Location	26 French ICUs
Population	389 adult patients with severe acidemia (pH ≤ 7.2; PaCO2 ≤ 45 mm Hg) and SOFA score ≥ 4 or lactate ≥ 2 mmol/L
Intervention	Sodium bicarbonate vs no sodium bicarbonate • Administered 4.2% $NaHCO_3$ in 62.5-125 mEq doses over 30 minutes • ABG checked 1-4 hours after bicarbonate, repeated if pH < 7.3 • Max 500 mEq per 24 hours • Central line recommended (1000 mOsm/L) • Goal pH ≥ 7.30
Primary outcome	• Composite of 28-day mortality and ≥ 1 organ failure at 7 days • Standardized indications for mechanical ventilation and RRT

Jaber S. Lancet 2018;392:31-40

Baseline characteristics

	Control (n=194)	Bicarbonate (n=195)
Age	65 (55-75)	66 (55-75)
SAPS II	60 (48-73)	59 (49-73)
SOFA	10 (7-13)	10 (7-13)
Sepsis	115 (59)	123 (63)
AKIN 0-1	104 (54)	103 (53)
AKIN 2-3	90 (46)	92 (47)
Cause of acidemia		
- Cardiac arrest	18 (9)	18 (9)
- Septic shock	98 (51)	107 (55)
- Hemorrhagic shock	40 (21)	45 (23)
- Others	38 (20)	25 (13)
Mechanical ventilation	160 (82)	164 (84)
Vasopressors	156 (80)	154 (79)

Data represented as n (%) or median (IQR)

SAPS, simplified acute physiology score; SOFA, sequential organ failure assessment; AKIN, Acute Kidney Injury Network

Jaber S. Lancet 2018;392:31-40

Baseline acid/base characteristics

	Control (n=194)	Bicarbonate (n=195)
Arterial pH	7.15 (7.11-7.18)	7.15 (7.09-7.18)
PaO_2/FiO_2 ratio	229 (142-355)	264 (114-403)
$PaCO_2$, mmHg	37 (32-42)	38 (33-42)
Bicarbonate, mEq/L	13 (10-15)	13 (10-15)
Lactate, mmol/L	5.3 (3.4-9)	6.3 (3.6-9.7)
Lactate ≥ 2 mmol/L	152 (78)	168 (86)
Creatinine, mg/dL	1.8 (1.2-2.5)	1.7 (1.1-2.3)

Data represented as n (%) or median (IQR)

26% vs 60% achieved pH > 7.3 and maintained for at least 36 hours

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Results

	Control (n=194)	Bicarbonate (n=195)	Difference	P value
Primary: composite of mortality and ≥ 1 organ failure at day 7	138 (71)	128 (66)	-5.5 (-15.2 to 4.2)	0.24
Day 28 mortality	104 (54)	87 (45)	-9 (-19.4 to 1.4)	0.07
≥ 1 organ failure	134 (69)	121 (62)	-2.8 (-15.4 to 9.8)	0.15
AKIN 2-3				
Composite outcome	74/90 (82)	64/92 (70)	-12.3 (-26 to -0.1)	0.046
Mortality	57/90 (63)	42/92 (46)	-17.7 (-33 to -2.3)	0.027
≥ 1 organ failure	74/90 (82)	61/92 (66)	-15.9 (-28.4 to -3.4)	0.014
Renal replacement therapy				
Overall	100 (52)	68 (35)	-16.7 (-26.4 to -7)	0.001
AKIN 2-3	66/90 (73)	47/92 (51)	-22.2 (-36 to -8.5)	0.002
Dialysis dependent at ICU discharge				
Overall	11/32 (34)	7/32 (22)	-12.5 (-34.3 to 9.3)	0.26
AKIN 2-3	10/21 (48)	5/25 (20)	-27.6 (-54.1 to -1.1)	0.047

-No difference in any mechanical ventilation, vasopressor, length of stay, or infectious outcomes
-Heterogeneous effects between AKIN 0-1 and 2-3 (p=0.007) and presence of sepsis (p=0.008)

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Safety

- Alkalemia (pH > 7.45): 16% (bicarbonate) vs 9% (control)
  - Severe alkalemia (pH > 7.5): 9% vs 2%
- Hyperkalemia (K > 5 mmol/L): 32% vs 49%
- Hypernatremia (Na > 145 mmol/L): 49% vs 29%
- Hypocalcemia (iCa < 0.9 mmol/L): 24% vs 15%
- No difference in hypokalemia

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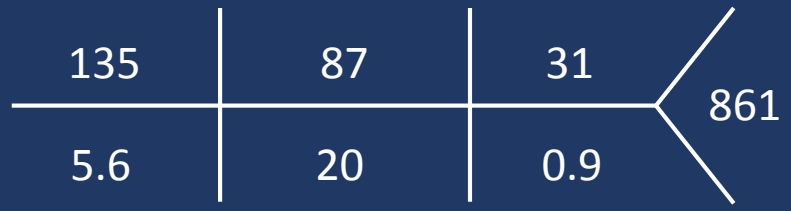
BICAR-ICU discussion

- No overt outcome benefits in overall population (though effects potentially diluted from ~25% crossover)
- Reduced need for RRT – indications seemed reasonable
- Patients with AKIN scores 2-3 may have improvements in mortality, dialysis dependence
  - What is the mechanism for improved mortality?
- No obvious signs of significant harm (i.e. bicarbonate for lactic acidosis) but patients with very high lactate levels not explored

Case

A 51 year old man with history of erosive esophagitis, diabetes mellitus, chronic pancreatitis, and bipolar disorder is admitted with nausea, vomiting, abdominal pain, and shortness of breath.

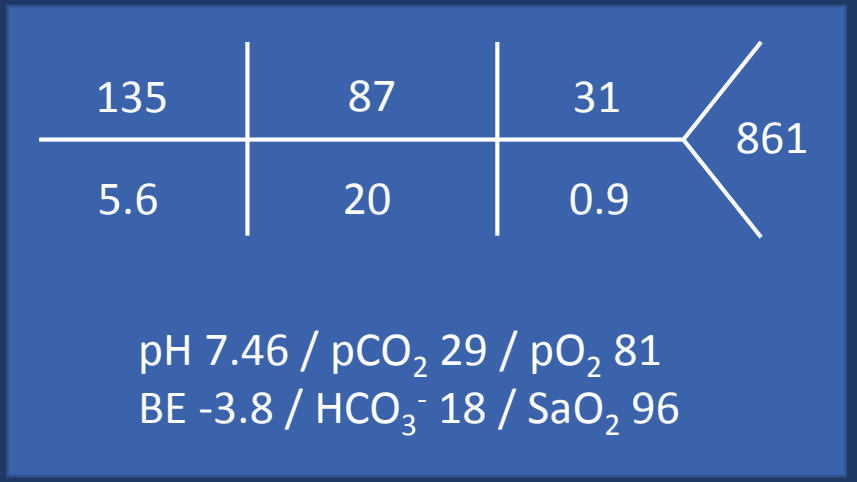


pH 7.46 / pCO_2 29 / pO_2 81
BE -3.8 / HCO_3^- 18 / SaO_2 96

- What additional data should be obtained?
- What acid base disturbance(s) is/are present?

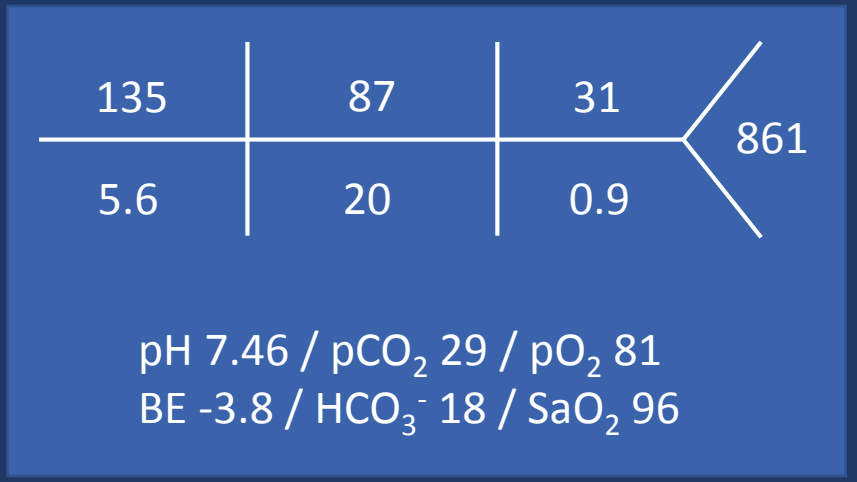
Case

1. Acidemia or alkalemia
2. Primary disturbance
3. Assess compensation
4. Calculate anion gap
5. Delta gap



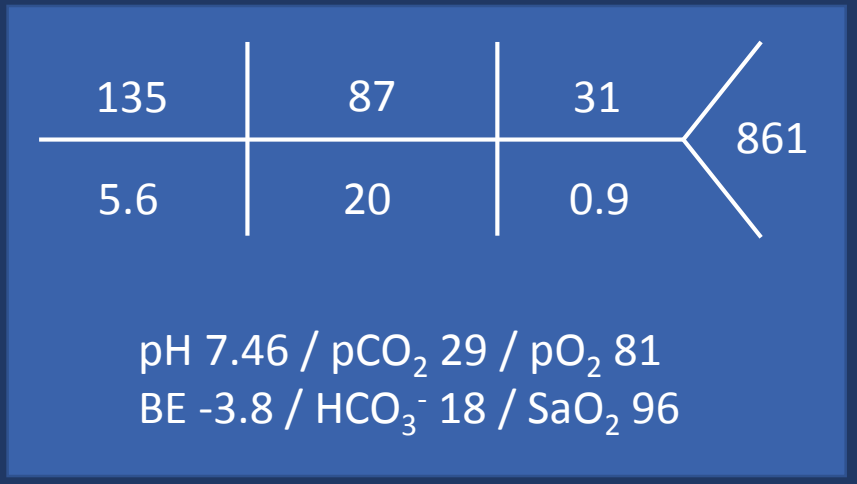
Case

1. Acidemia or alkalemia
2. Primary disturbance
3. Assess compensation
4. Calculate anion gap
5. Delta gap



Case

1. Acidemia or alkalemia
2. Primary disturbance – respiratory alkalosis (?)
3. Assess compensation
4. Calculate anion gap
5. Delta gap



Case

135	87	31	861
5.6	20	0.9	

pH 7.46 / pCO_2 29 / pO_2 81
BE -3.8 / HCO_3^- 18 / SaO_2 96

1. Acidemia or alkalemia
2. Primary disturbance – respiratory alkalosis (?)
3. Assess compensation – acute-on-chronic respiratory alkalosis (?)
4. Calculate anion gap
5. Delta gap

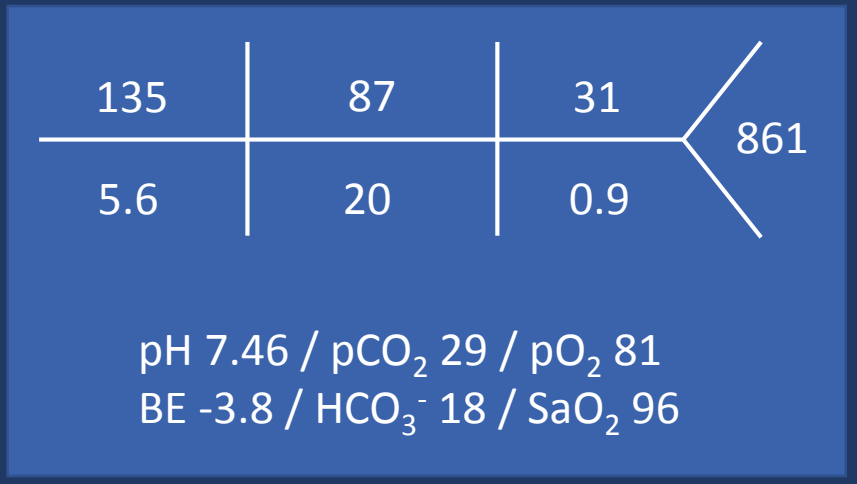
Case

135	87	31	861
5.6	20	0.9	

pH 7.46 / pCO_2 29 / pO_2 81
BE -3.8 / HCO_3^- 18 / SaO_2 96

1. Acidemia or alkalemia
2. Primary disturbance – respiratory alkalosis (?)
3. Assess compensation – acute-on-chronic respiratory alkalosis
4. Calculate anion gap – 135-87-20 = 28 (high = AGMA)
5. Delta gap

Case



1. Acidemia or alkalemia
2. Primary disturbance – respiratory alkalosis (?)
3. Assess compensation – acute-on-chronic respiratory alkalosis
4. Calculate anion gap – 135-87-20 = 28 (high = AGMA)
5. Delta gap – (28-12) + 20 = 36 (high = metabolic alkalosis)

Case

135	87	31	861
5.6	20	0.9	

pH 7.46 / pCO_2 29 / pO_2 81
BE -3.8 / HCO_3^- 18 / SaO_2 96

Diagnoses:

Respiratory alkalosis, anion gap metabolic acidosis, metabolic alkalosis

Next steps:

Evaluate causes of AGMA – low level ketosis; lactate 9.5

Evaluate causes of metabolic alkalosis – likely from recent vomiting (chloride 87)

Problem can also be assessed using metabolic acidosis as the primary problem which will give you the same diagnoses and is more pertinent to the patient rather than focusing on the mild respiratory alkalosis

Summary

- Acid base problems can be assessed in a systematic way to identify simple or mixed disorders
- Sodium bicarbonate therapy remains controversial but can be considered in critically ill patients with severe acidosis – especially those with renal dysfunction
- Acid base analyses need to be interpreted in the context of the clinical picture of the patient. Not every disorder requires treatment.

A Case-Based Approach to Acid-Base Disorders

Justin Muir, PharmD
Clinical Pharmacy Manager, Medical ICU
NewYork-Presbyterian Hospital
Columbia University Irving Medical Center
jum9081@nyp.org