ABG interpretation

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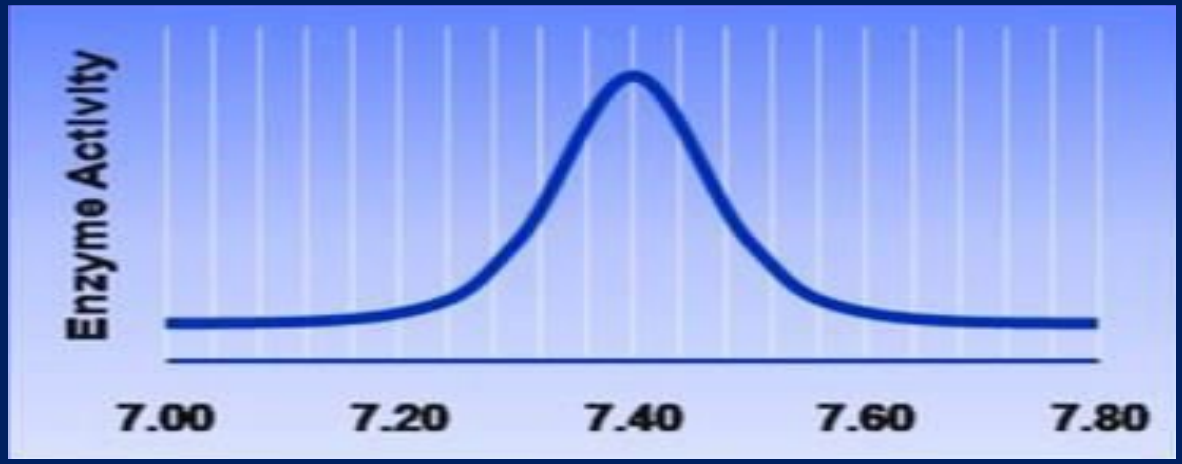
Role of Acid-Base Balance

Maintains stable pH at **7.40 (7.35 - 7.45)** .

"Physiologic pH" necessary to prevent enzyme inactivation and denaturing.



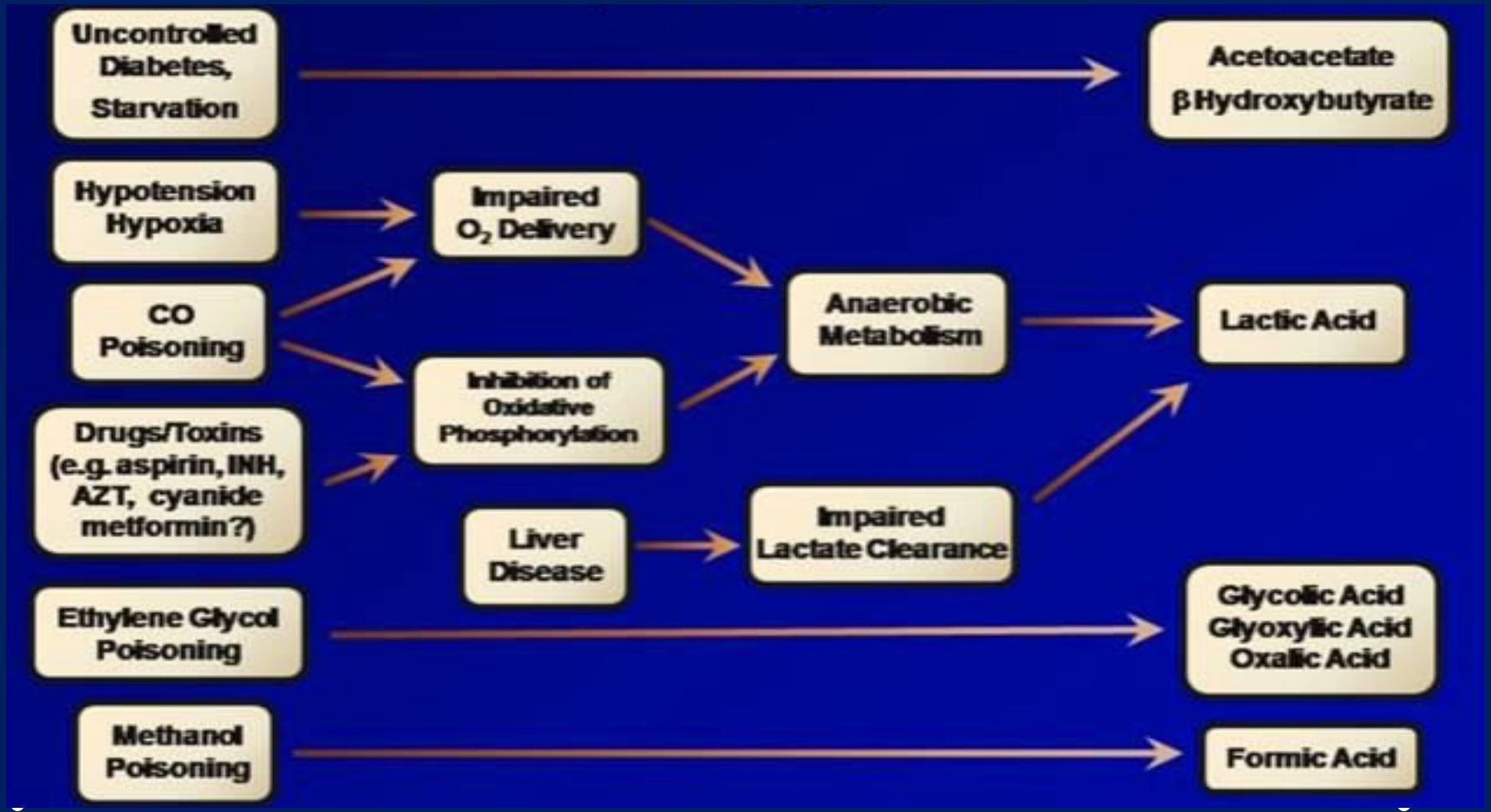
Role of Acid-Base Balance

Clinical consequences of dysregulation of acid-base balance:

- Poor vascular tone
  - Myocardial pump failure
  - Increased risk of arrhythmias
  - Skeletal muscle weakness
  - Electrolyte abnormalities
- Delirium / Coma
- Impaired cellular respiration

Production of Acid (Pathologic)

Accumulated Acids



Intravascular Transport of Acid

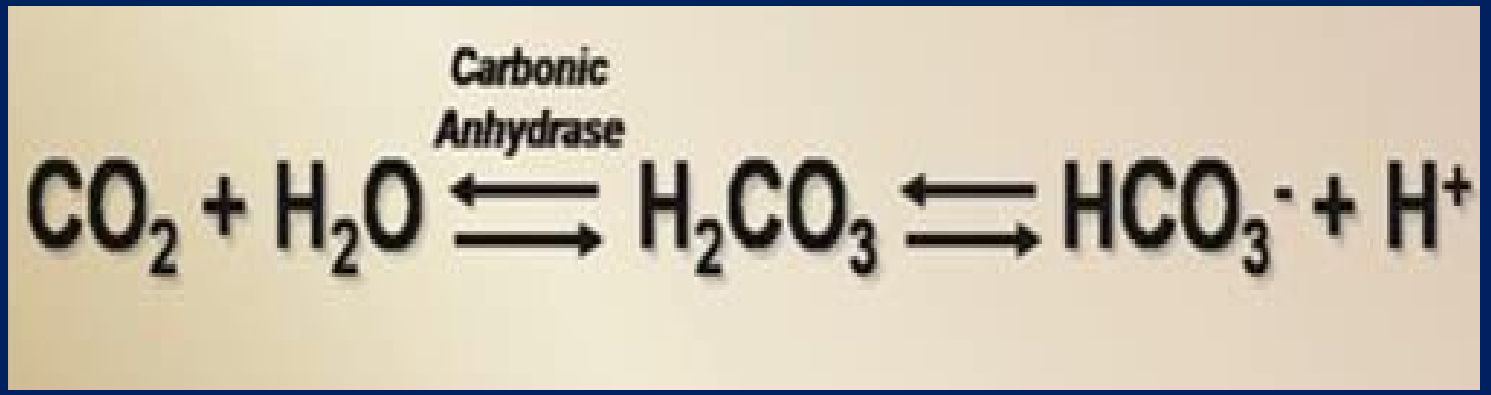
To prevent sudden and large swings in pH, buffers are necessary.

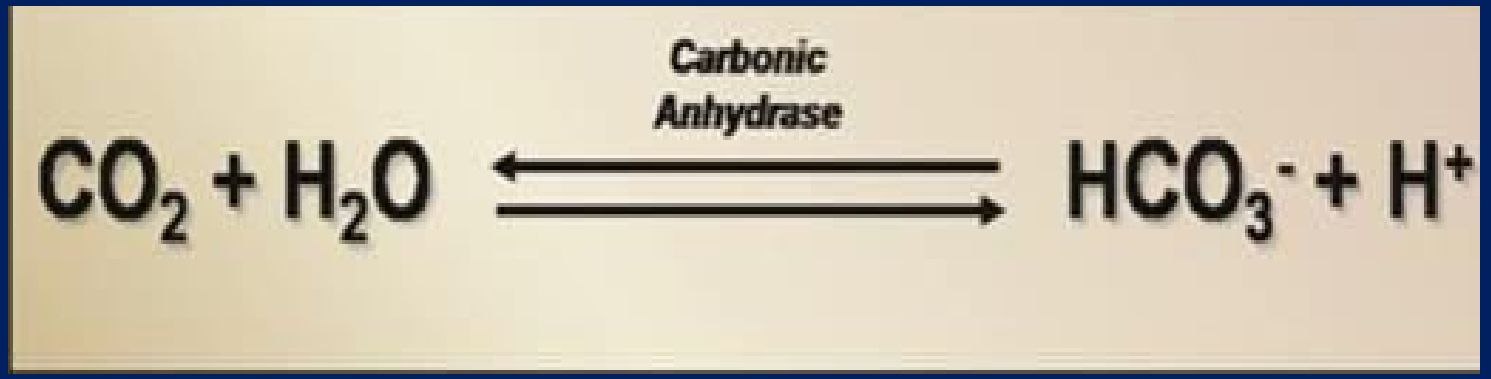
Buffers have two major characteristics:

1. Consist of either a weak acid (H+ donor) and its conjugate base, or a weak base (H+ acceptor) and its conjugate acid.

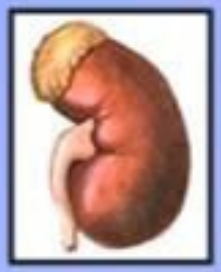
2. Resist changes in pH.

HCO3-/ CO2 Buffering System

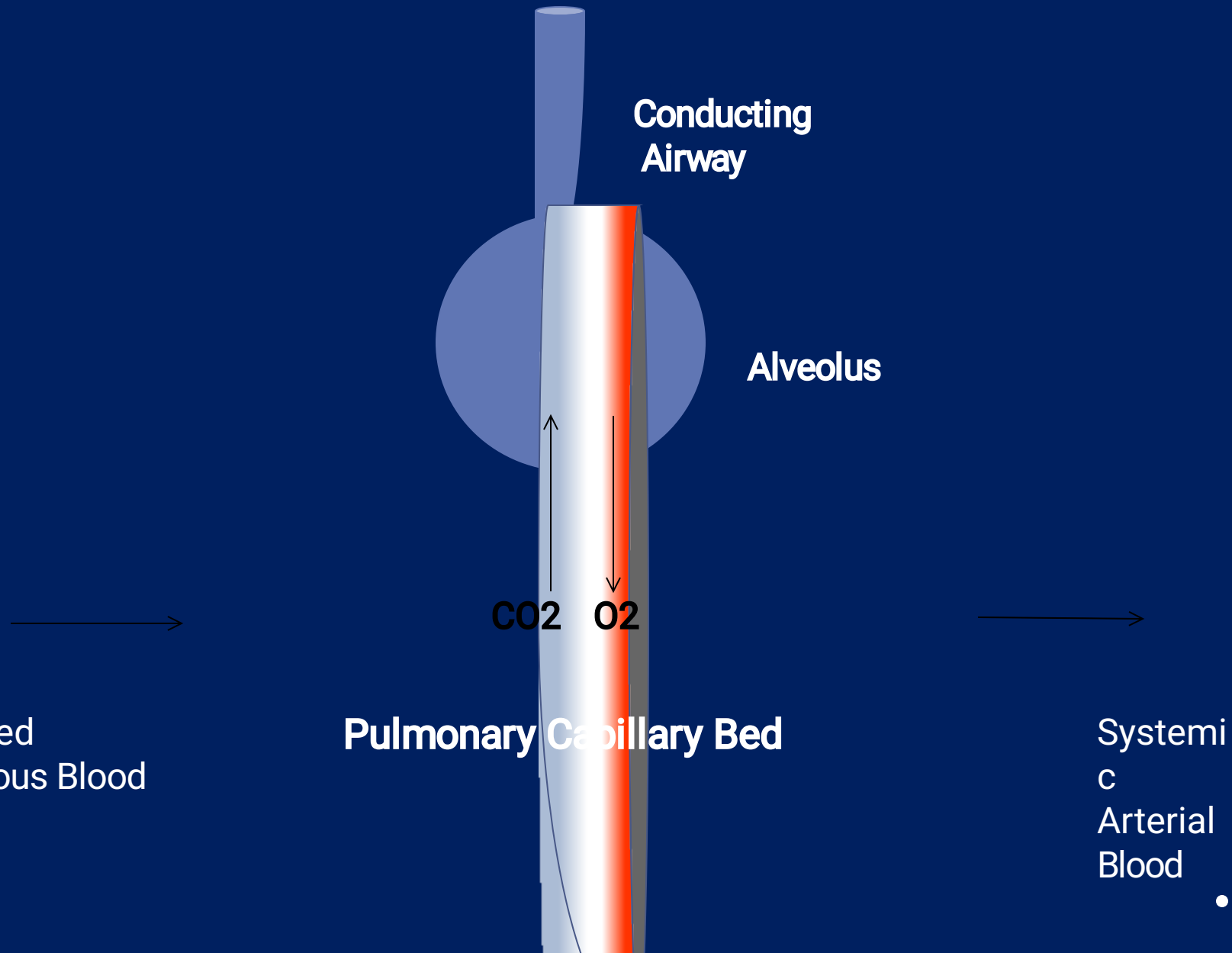




How is Acid Eliminated ?

Site		Mechanism
Lungs 		Expiration of CO_2
Kidneys 	Proximal Tubule	Reabsorption of HCO_3^-
	Distal Tubule / Collecting Duct	Excretion of H^+ as titratable acid (e.g. $H^+ + HPO_4^{2-} \rightarrow H_2PO_4^-$)
		Excretion of NH_4^+

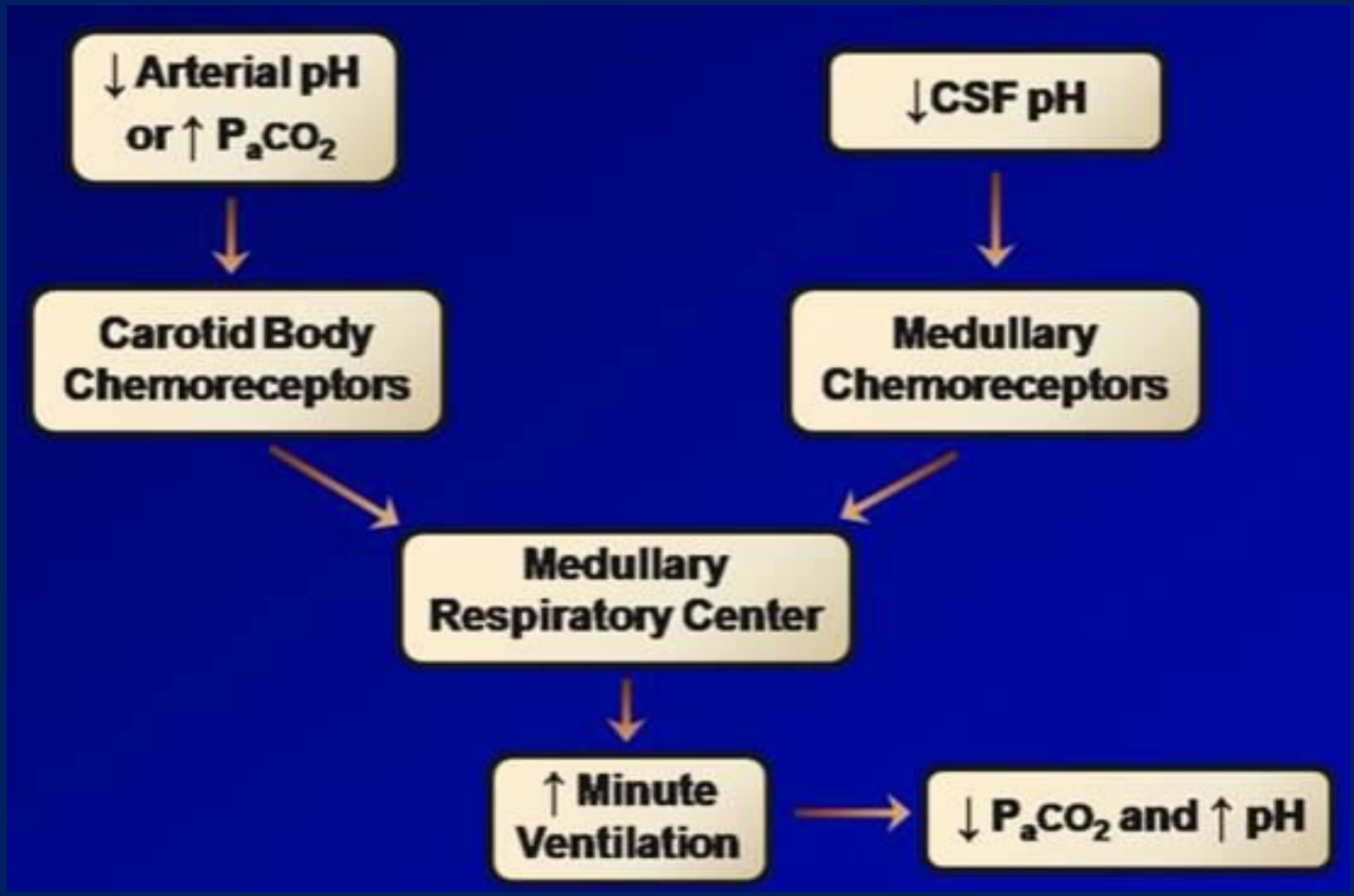
Lungs' role in acid base balance

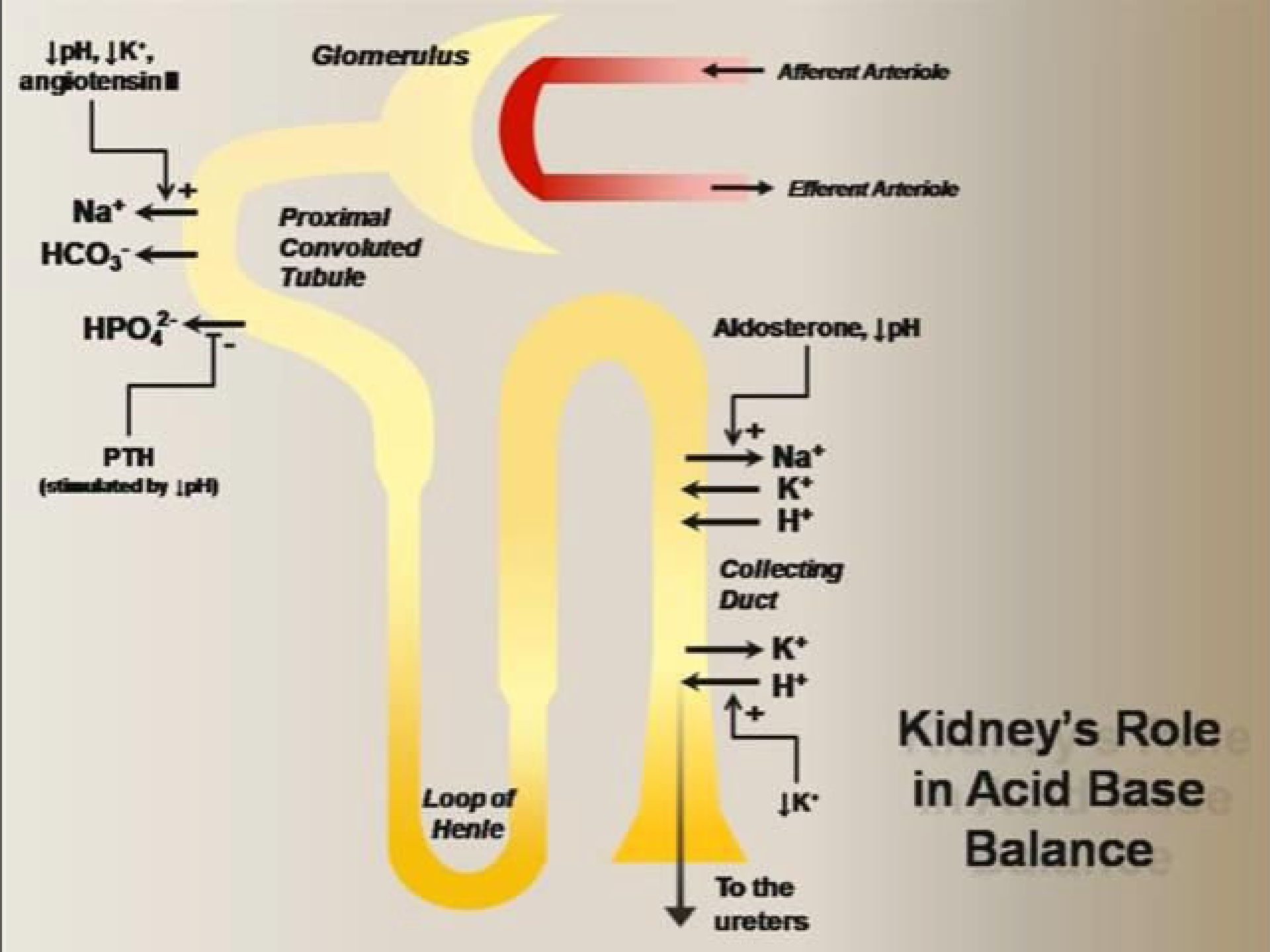


Lungs' role in acid base balance

Peripheral

Central





Kidney's Role in Acid Base Balance

K+ /H+ Exchange

In the presence of acid-base disturbances, H4 can move across the cell membrane in exchange for K+.

Most pronounced with metabolic acidoses.

Once intracellular, H4 are buffered by organic phosphates (e.g. ATP and 2,3-DPG) and intracellular proteins (e.g. hemoglobin).

Can result in apparent abnormalities of K+ balance that don't represent total K+ stores.

K+ /H+ Exchange

Acidemia → Hyperkalemia

For every 0.1 drop in pH, serum K+ increases ~0.6 mEq/L
(0.2-1.7 mEq/L)

Alkalemia → Hypokalemia

Acidemia vs. Acidosis
Alkalemia vs. Alkalosis

Acidemia and alkalemia refer to a physiologic state dependent solely upon arterial pH.

Acidemia is present if the pH is < 7.35

Alkalemia is present if the pH is >7.45

Acidemia vs. Acidosis
Alkalemia vs. Alkalosis

A patient can be acidemic or alkalemic, but not both.

However, a patient can have one or more acidosis, and one or more alkalosis, which can directly offset one another.

Disorders that affect pH resulting in an acidosis or alkalosis are acid- base disorders. Primary acid-base disorders are either respiratory or metabolic in origin:

Primary respiratory disorders: The change in $PaCO_2$ causes the initial change in pH; and the kidney slowly responds in an opposite direction by dumping or holding on to HCO_3^-.

Primary metabolic disorders: The change in HCO_3^- causes the initial change in pH; and the respiratory rate immediately increases or decreases.

Again: The kidneys respond **slowly** to changes in pH while the respiratory rate responds **immediately**.

MECHANISMS

There is really only 1 chemical equation you must know to calculate and understand all acid-base problems.

This is the Henderson-Hasselbalch equation. It is derived from the bicarbonate buffer equation shown here:

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

This equation tells us that the body has only 2 ways to control the serum pH:

1- Regulate the respiratory rate and tidal volume; thus, control the P.CO2.

2- Regulate the kidney's reabsorption of HCO3 -. It further shows that it is the ratio of P.CO2 to HCO3- that determines pH and not the absolute levels

Remember:

Significant alkalemia of any etiology can cause the diffuse paresthesia/numbness and muscle spasms we usually associate with acute hyperventilation; the high pH increases the fraction of bound calcium.

The resulting decrease in ionized calcium produces these symptoms of hypocalcemia. There is no change in total serum calcium (ionized + bound). This effect also can be induced by rapid overload with intravenous HCO_3^- or with citrate (massive blood transfusion).

On the other hand, patients with both metabolic acidosis and hypocalcemia are protected from the hypocalcemia since acidosis decreases the fraction of bound calcium and increases the ionized calcium.

Correction of acidosis prior to correction of hypocalcemia in this setting removes the protective effect of the acidosis, and can precipitate seizures

Respiratory vs. Metabolic Disorders

Respiratory Disorders	**Pathologic processes which disrupt acid-base balance due to their effects on the lungs (i.e. alveolar ventilation).** **Respiratory Acidosis** P_aCO_2 too high (i.e. hypoventilation) **Respiratory Alkalosis** P_aCO_2 too low (i.e. hyperventilation)
Metabolic Disorders	**Pathologic processes which disrupt acid-base balance due to their effects on anything other than the lungs (i.e. kidneys, GI tract, cellular respiration, etc…)** **Metabolic Acidosis** $[HCO_3^-]$ too low **Metabolic Alkalosis** $[HCO_3^-]$ too high

Compensation

A primary metabolic disorder will result in respiratory compensation.

A primary respiratory disorder will result in metabolic compensation.

Compensation

Compensation does not return the pH to normal.

Patients never “overcompensate “

Compensation

Acid-Base Disorder	Mechanism of Compensation
Metabolic Acidosis ($\downarrow HCO_3^- \rightarrow \downarrow pH$)	**Increased minute ventilation** ($\downarrow PCO_2 \rightarrow \uparrow pH$)
Metabolic Alkalosis ($\uparrow HCO_3^- \rightarrow \uparrow pH$)	**Decreased minute ventilation** ($\uparrow PCO_2 \rightarrow \downarrow pH$)
Respiratory Acidosis ($\uparrow PCO_2 \rightarrow \downarrow pH$)	**$\uparrow$ Reabsorption of HCO_3^- and $\uparrow$ Excretion of H^+ by the kidneys** ($\uparrow HCO_3^- \rightarrow \uparrow pH$)
Respiratory Alkalosis ($\downarrow PCO_2 \rightarrow \uparrow pH$)	**$\downarrow$ Reabsorption of HCO_3^- and $\downarrow$ Excretion of H^+ by the kidneys** ($\downarrow HCO_3^- \rightarrow \downarrow pH$)

Compensation

How fast does it occur?

	Timing of peak compensation
Respiratory compensation for a primary metabolic disorder	1 — 24 hrs
Metabolic compensation for a primary respiratory disorder	12 hrs — 5 days?

Compensation

1° Metabolic Acidosis
HCO3- = 10 mEq/L

Predicted →

Respiratory Compensation
PCO2=~ 23 mmHg

Actual →

Measured PCO2= 35 mmHg

Explanation?

A second, primary acid-base disorder is present. (A primary respiratory acidosis)

Compensation Formulas

Initial Disorder	Compensation Formula
Metabolic Acidosis	$P_aCO_2 \approx 1.5\,(HCO_3^-) + 8$ (Winters' Formula)
Metabolic Alkalosis	$P_aCO_2 \approx 40 + [\,0.7\,(HCO_3^- - 24)\,]$
Respiratory Acidosis	Acute: $HCO_3^- \approx 24 + \frac{(P_aCO_2 - 40)}{10}$ Chronic: $HCO_3^- \approx 24 + 4\left(\frac{(P_aCO_2 - 40)}{10}\right)$
Respiratory Alkalosis	Acute: $HCO_3^- \approx 24 - 2\left(\frac{(40 - P_aCO_2)}{10}\right)$ Chronic: $HCO_3^- \approx 24 - 5\left(\frac{(40 - P_aCO_2)}{10}\right)$

Alternative to Calculating Compensation for Respiratory Disorders

	Acute	Chronic
Respiratory Acidosis	$[HCO_3^-]$ ↑ 1mEq/L for each 10mmHg PCO_2 is above 40 mmHg	$[HCO_3^-]$ ↑ 4mEq/L for each 10mmHg PCO_2 is above 40 mmHg
Respiratory Alkalosis	$[HCO_3^-]$ ↓ 2mEq/L for each 10mmHg PCO_2 is below 40 mmHg	$[HCO_3^-]$ ↓ 5mEq/L for each 10mmHg PCO_2 is below 40 mmHg

METABOLIC ACIDOSIS

Etiology

Metabolic acidosis occurs with the following:

1. Overproduction of lactic acid or ketoacids
2. HCO_3^- wasting (renal tubular acidosis [RTA] or diarrhea)
3. Failure to excrete daily acid production (renal failure)
4. Ingestion of agents that are acids (salicylates) or are metabolized to acids (methanol, ethylene glycol, paraldehyde) or cause a lactic/ketoacidosis (salicylates, isoniazid, and iron)

Normal Anion Gap Metabolic Acidosis

Normal Anion Gap Metabolic Acidosis ([NAGMA]; also called "hyperchloremic" acidosis) has a commensurate increase in Cr with the decrease in HCO3-. The Cr is retained to maintain electrical neutrality.

The 3 causes of NAGMA:

1- Usual: Loss of HCO3- due to diarrhea or proximal RTA

2- Increased organic acids (NH4 +; e.g., patients on total parenteral nutrition)

3- Inability of the kidney to excrete endogenous acids (renal failure or distal RTA)

Again, the main causes of NAGMA are diarrhea and RTA. NAGMA plus hyperkalemia, think Type 4 RTA (hypoaldosteronism).

NAGMA plus hypokalemia is caused by:

1- GI loss (sometimes)

2- RTA Types 1 (distal) and 2 (proximal)

On the rare occasion when you cannot distinguish RTA from diarrhea (or other GI loss of HCO3-, such as a urinary fistula), calculate the UAG. Again:

1- UAG is positive with NAGMA due to RTA.

2- UAG is negative with NAGMA due to GI losses.

Remember: neGUTive- negative UAG in bowel cases.

High Anion Gap Metabolic Acidosis

With high anion gap metabolic acidosis (HAGMA), no equivalent increase in CL is observed. Because the net charge in the serum is always neutral, there must be an increase in the unmeasured anions. These tests should be performed immediately in a patient with unexplained HAGMA:

Funduscopic exam
Toxicology screen
Serum glucose; urine and serum ketones
Lactic acid level
Serum osmolality with calculation of the osmolal gap (high in methanol and ethylene glycol ingestions)
U/ A to assess for calcium oxalate crystals

Table 4-3: HAGMAs and NAGMAs

Common Causes of HAGMA

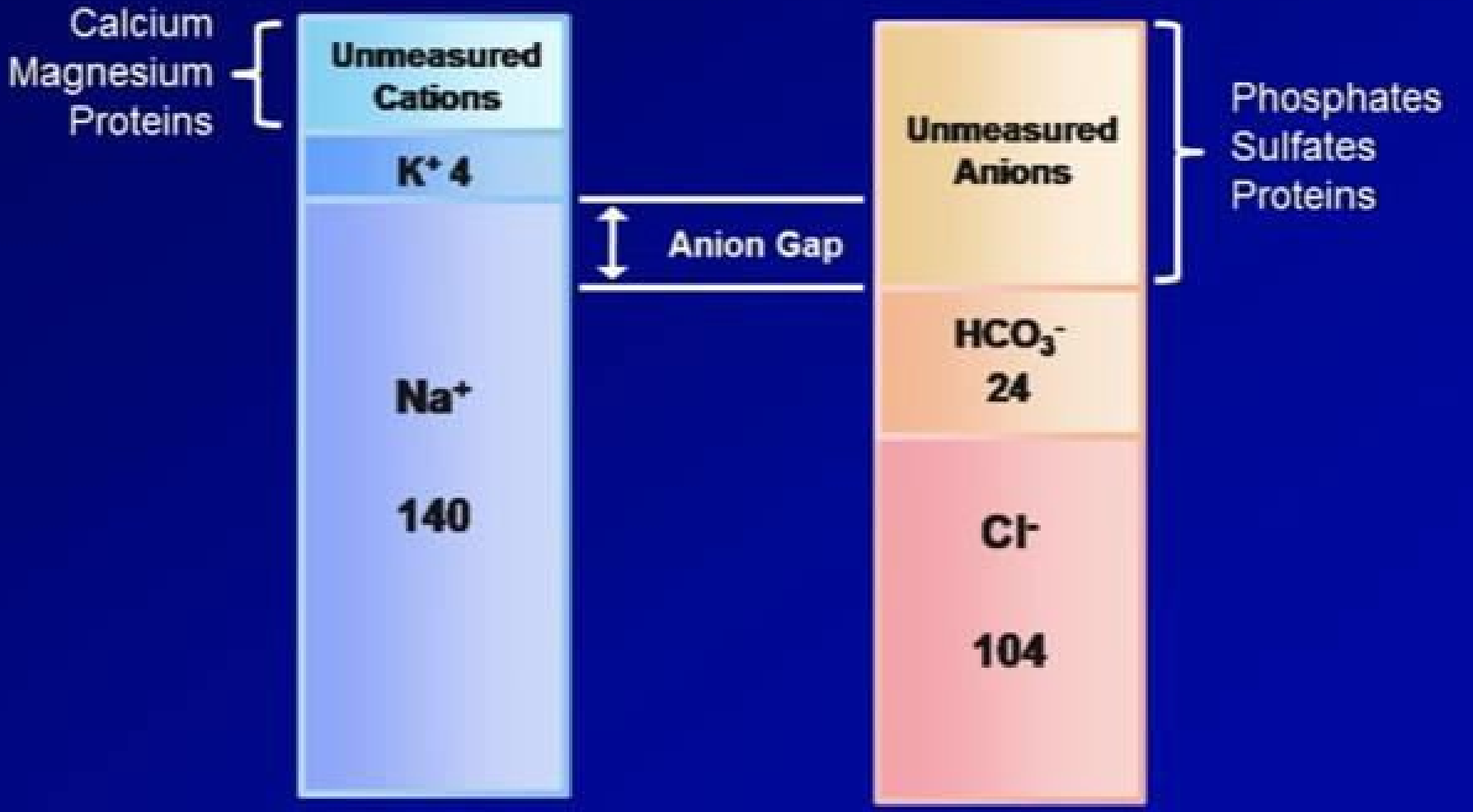
Severe CKD: decreased acid (especially NH_4) excretion—most common
Uremia: sulfate, phosphate, urate
Ketoacidosis: diabetic, alcoholic, starvation
Lactic acidosis: drugs, toxins, circulatory compromise
Poisonings: salicylates, methanol, ethylene glycol, propylene glycol

Common Causes of NAGMA

Renal tubular acidosis
Diarrhea
Carbonic anhydrase inhibitors
Hyperalimentation with TPN

[Cations] = [Anions]

(Positive Charge) (Negative Charge)



Calculation of the Anion Gap

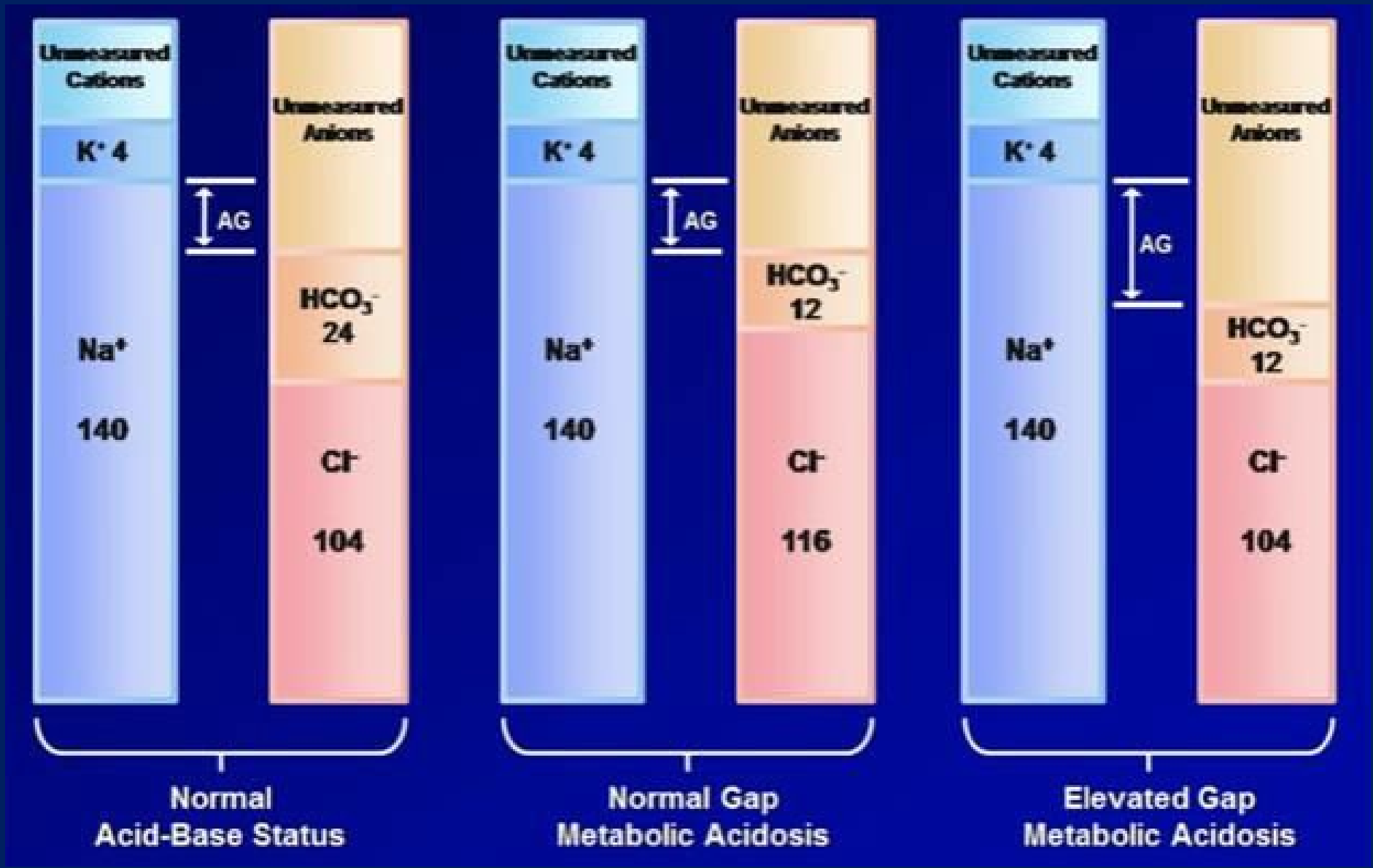
$$\text{Anion Gap} = [Na^+] - \left([Cl^-] + [HCO_3^-]\right)$$

Normal Range: ~8–12 mEq/L (lab specific)

Uncommon Alternative

$$\text{Anion Gap} = \left([Na^+] + [K^+]\right) - \left([Cl^-] + [HCO_3^-]\right)$$

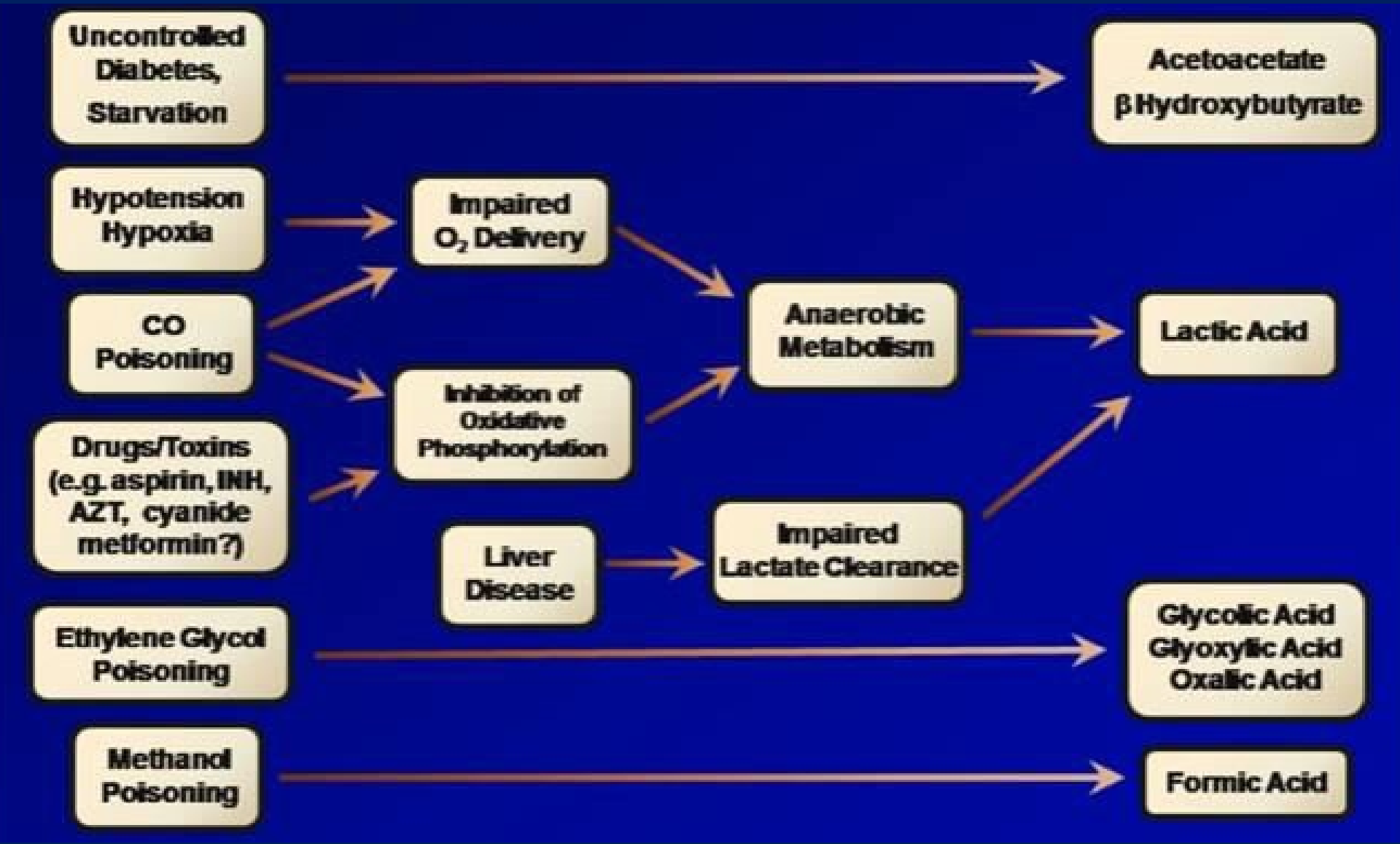
Normal Gap vs. Elevated Gap Acidosis



Etiologies of a Normal Gap Acidosis

Loss of HCO_3^-	Decreased Renal H^+ Excretion
Diarrhea / GI drainage	Renal Failure
Type 2 RTA	Type 1 RTA
Acetazolamide	Type 4 RTA (Hypoaldosteronism)
Ureteral Diversion	

Etiologies of an Elevated Gap Acidosis



Etiology of an Elevated Gap Acidosis

Pathologic Process	Accumulated Anion(s)
Lactic Acidosis	Lactic Acid
Ketoacidosis (DKA, EtOH)	Acetoacetate, B
Methanol Ingestion	Formic Acid
Ethylene Glycol	Glycolic Acid
Toluene Inhalation	Hippuric Acid
Renal Failure (CRF)	Phosphates, Sulfates, Uric Acid

Alterations in Anion Gap Unrelated to a Metabolic Acidosis

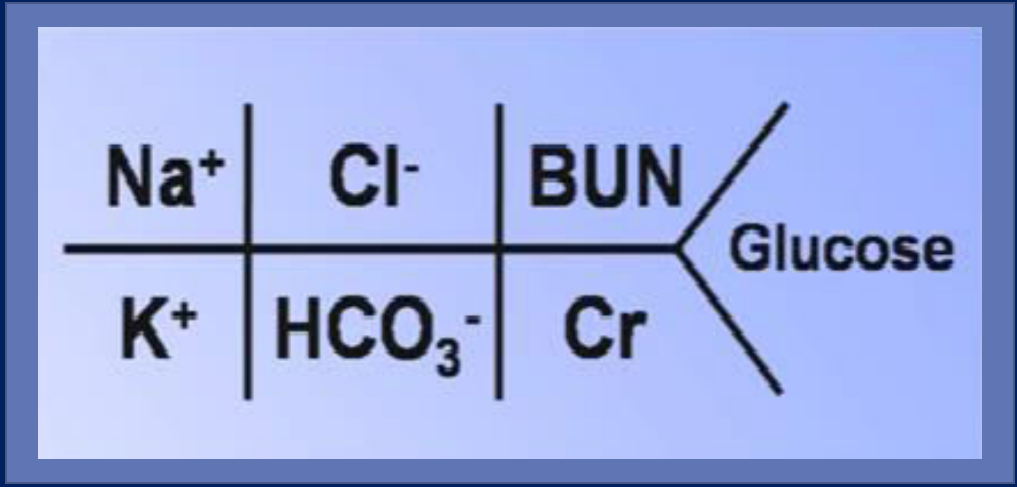
High Anion Gap	Low Anion Gap
Metabolic Alkalosis	↑ ↑ ↑ Hypoalbuminemia

- K+ / Ca+ / Mg+

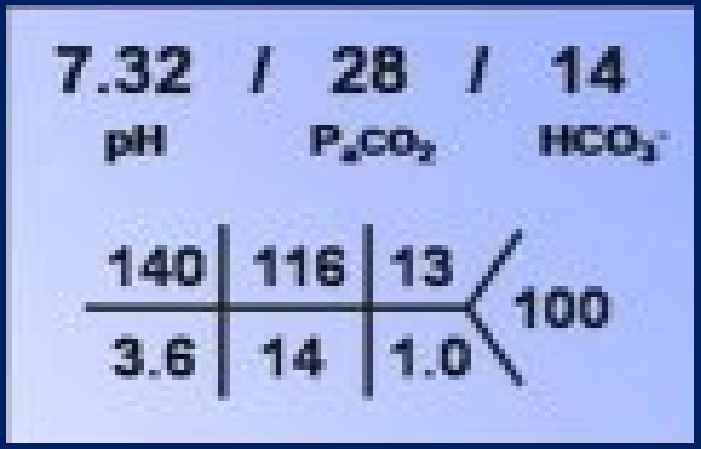
Hypoalbuminemia

$$AG_{adjusted} = AG_{measured} + 2.5\left(4 - [Alb]\right)$$

Example :



Example #1



Step 1: Check pH → Acidemia

Step 2: Check PCO → Metabolic process → Metabolic acidosis

Step 3: Evaluate compensation

PCO2 =~ 1.5 (HCO3-) + 8

Appropriate compensation

Step 4: Calculate anion gap

AG = Na+ _ (Cl- + HCO3-)

AG = 10 mEq/L

Normal Gap Metabolic Acidosis

Example #2

Step 1: Check pH ⟶ Acidemia

Step 2: Check PCO2 ⟶ Metabolic process
⟶ Metabolic acidosis

Step 3: Evaluate compensation
PCO2 = 1.5 (HCO3-) + 8

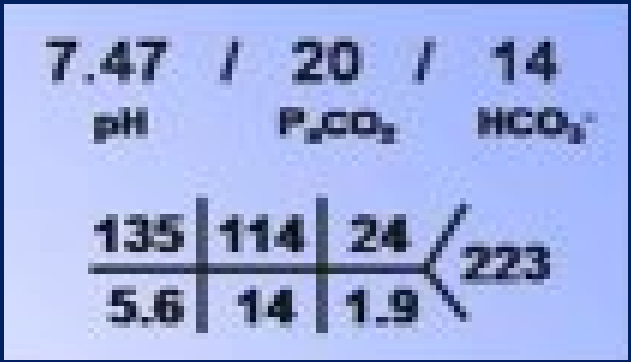
Appropriate compensation

Step 4: Calculate anion gap
AG = Na+— (Cl- + HCO3-)
AG = 22 mEq/L

Elevated Gap Metabolic Acidosis

Example #3

A 58 y/o man with DM and CKD presents with abrupt onset of dyspnea x 2 hrs.



Step 1: Check pH ⟶ Alkalemia

Step 2: Check PCO2 ⟶ Respiratory process ⟶ Respiratory Alkalosis

Step 3: Evaluate compensation
Is HCO3- ↓ by 2 for every 10 PCO2 <40?

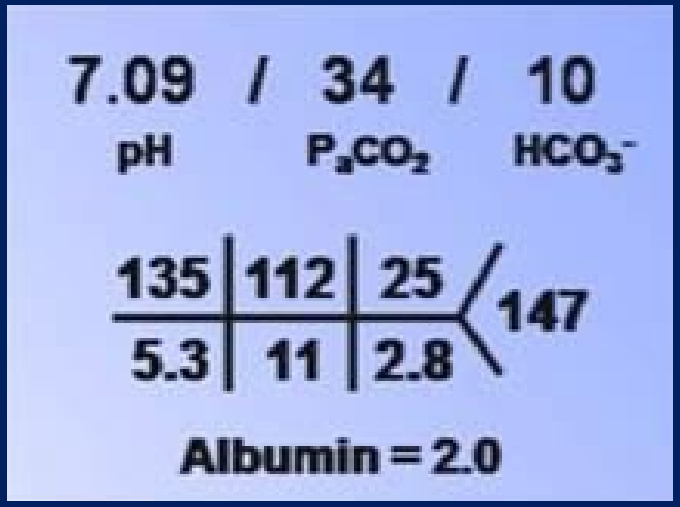
No ⟶ Not appropriate
HCO3 - lower than expected
Additional: **Metabolic Acidosis**

Step 4:
Calculate anion gap
AG = Na+ — (Cl- + HCO3-)
AG = 7 mEq/L

Respiratory Alkalosis + Normal Gap Metabolic Acidosis

Example #4

A 48 y/o woman is found unconscious next to an empty pill bottle at home.



Elevated Gap Metabolic Acidosis + Respiratory Acidosis

Step 1: Check pH → Acidemia

Step 2: Check PCO2 → Metabolic process → Metabolic acidosis

Step 3: Evaluate compensation

PCO- = 1.5 (HCO3-) + 8

Not appropriate

PCO2 higher than expected

Additional: Respiratory Acidosis

Step 4: Calculate anion gap

AG = Na+ — (Cl- + HCO3)

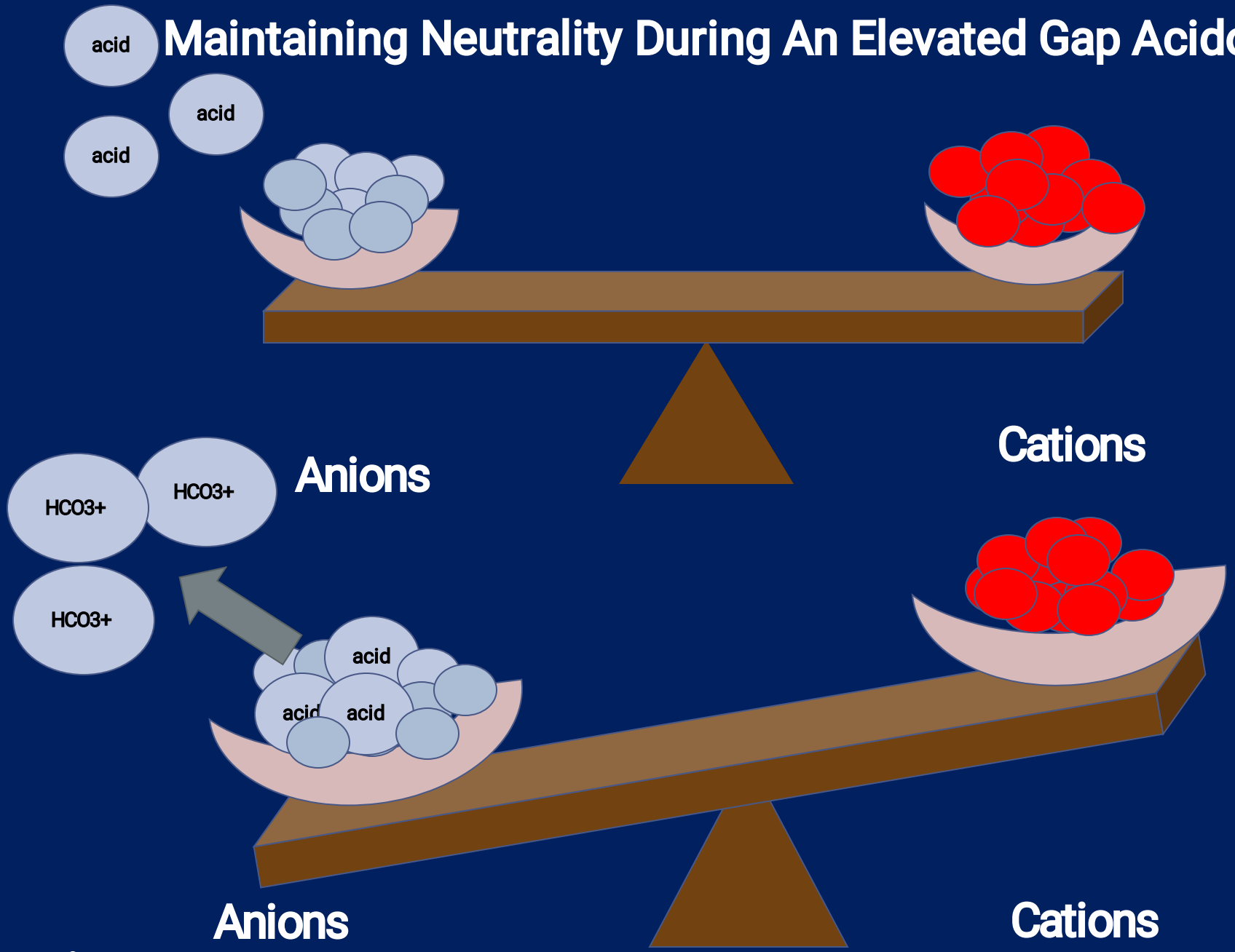
AG = 12 mEq/L

Adjust for ↓ albumin:

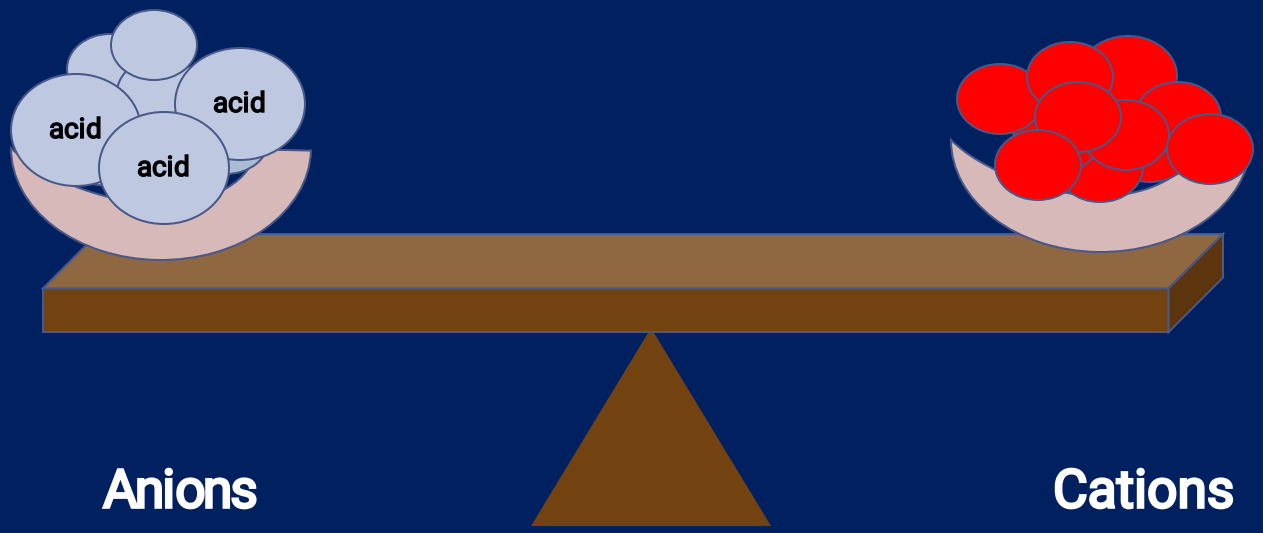
AG adjusted = AG measured + 2.5 (4 — Alb)

AG adjusteri = 17 mEq/L

Maintaining Neutrality During An Elevated Gap Acidosis



Maintaining Neutrality During An Elevated Gap Acidosis



Suggests there should be a 1:1 ratio between ↑ anion gap (AG), and ↓ HCO3-

The 4 common causes of HAGMA include:

1- **Ketosis** (diabetic, alcoholic, and starvation):

Check 13- hydroxybutyrate and urine ketones.

- Diabetic ketoacidosis (DKA):

  Classic findings include volume depletion, a normal cr, hyperglycemia, and HAGMA in a diabetic. DKA responds to restoration of intravascular volume, replacement of electrolytes, and insulin.

- Alcoholic ketoacidosis (AKA): Key clue is an alcoholic who presents with HAGMA. Classic findings include HAGMA, hypophosphatemia, and hypoglycemia in a known alcoholic. AKA responds well to dextrose infusion.

2- **Uremia** causes an accumulation of anions, including sulfate, phosphate, and urate. (Check BUN and creatinine.)

3- **Lactic acidosis** (check blood lactic acid level):

Type A is due to muscle hypoperfusion during shock, cardiac failure, or sepsis.

Type B (findings of systemic hypoperfusion are lacking) can be caused by drug- induced mitochondrial dysfunction (zidovudine, metformin, propofol), tumor-induced lactic acidosis (leukemia, lymphomas), and alcoholism.

Propofol-related infusion syndrome:

a High doses of propofol for more than 48 hours can result in type B lactic acidosis and a syndrome associated with renal failure, rhabdomyolysis, hyperlipidemia, J-point elevation on EKG, and various arrhythmias.

D-lactic acidosis

can occur in patients with short bowel syndrome; they present with typical neurologic abnormalities, from slurred speech to obtundation. D-lactic acid is not the normal L-lactic acid seen with anaerobic metabolism. D-lactic acid takes much longer to break down and therefore accumulates more quickly and hangs around longer.

4- Toxins (salicylates, ethylene glycol [makes glycolic and oxalic acid], methanol [makes formic acid], and propylene glycol):

Salicylate overdose :

Key clue is mixed respiratory alkalosis+ HAGMA. Salicylate intoxication initially causes the respiratory alkalosis, then additionally, the HAGMA. Suspect in elderly patients taking medications for arthritis.

Ethylene glycol :

Key clue is calcium oxalate crystals in the urine. Ethylene glycol forms glycolic acid and oxalic acid, resulting in HAGMA

Methanol	Propylene glycol
Key clue is visual symptoms. Methanol metabolizes to formaldehyde and formic acid, resulting in HAGMA. **Patients** present with nausea, vomiting, abdominal pain, and may have visual complaints described as "walking through a snowstorm.“ **Formic acid** is directly toxic to the optic nerve. Methanol and ethylene glycol are toxic because of their metabolites. Like **ethanol**, these substances are metabolized by alcohol dehydrogenase. The previous treatment was to start an ethanol drip to act as a competitive inhibitor of alcohol dehydrogenase. **Fomepizole +dialysis** now make up the standard of care for both of these ingestions.	is used as a solvent for intravenous lorazepam. Continuous infusion or large IV doses of lorazepam can cause propylene glycol toxicity, which manifests as HAGMA with an osmolal gap.

Treat :

Treat HAGMA by correcting the underlying cause of the acidosis, including removal of toxic alcohols via dialysis if necessary.

Treat propofol-related infusion syndrome by discontinuing the propofol; and in cases with AKI and severe acidosis, initiate hemodialysis.

Always treat salicylate poisoning with aggressive sodium bicarbonate therapy, as alkalemia protects the CNS from the salicylate.

DON'T :

Do not treat DKA with bicarbonate unless the pH is< 7.0.

Do not treat lactic acidosis with bicarbonate unless the pH is< 7.1.

Chronic acetaminophen use

(pyroglutamic acidosis) at therapeutic doses rather than in the setting of an overdose, can result in an elevated anion gap metabolic acidosis.

The accumulating acid is pyroglutamic acid

(also called 5- oxoproline). Chronic illness and malnutrition are the 2 big risk factors. The pathogenesis is thought to be related to chronic glutathione deficiency. Treat acetaminophen overdose with n- acetylcysteine (NAC), which blocks the hepatotoxic effects caused by acetaminophen.

METABOLIC ALKALOSIS

Metabolic alkalosis commonly results from volume contraction caused by diuretics or vomiting/gastric suction. Metabolic alkalosis always involves a generation phase (initial H+ loss or HCO3- gain) and maintenance phase (failure of the kidney to excrete HCO3- to correct the alkalosis):

- With vomiting and NG suction, HCl is lost via gastric secretions.
- With primary hyperaldosteronism, there is renal acid loss.
- With diuretic-induced "contraction" alkalosis, there is renal l oss of bicarb-free fluid, resulting in reduction in the extracellular fluid volume around a fixed quantity of extracellular bicarbonate.

The maintenance of the alkalosis is the failure of the kidney to excrete the excess HCO3-.
This is most often mediated by volume depletion, which leads to decreased distal Cl- delivery and high aldosterone levels.
Aldosterone enhances distal sodium reabsorption by activating distal tubular Na+/ H+ and Na+/K+ pumps, at the expense of H+ loss (alkalosis) and K+ loss (hypokalemia).
This can result in "paradoxical aciduria," a low urine pH in the setting of metabolic alkalosis. Also in alkalemia, K+ shifts from the extracellular space to the intracellular space in exchange for H+, exacerbating hypokalemia.

The 2 types of metabolic alkalosis,

chloride responsive or chloride resistant, are based on the urinary chloride measurement. UNa and FENa are elevated during metabolic alkalosis even in the face of volume depletion because bicarbonaturia results in Na being excreted as the accompanying cation. In cases of volume depletion, urinary cr is < 10 mEq!L because NaCl is avidly reabsorbed to maintain intravascular volume. If urinary cr is > 10, think of other causes of alkalosis such as **Cushing syndrome**, Bartter syndrome, Gitelman syndrome, primary hyperaldosteronism, Liddle syndrome, licorice ingestion, severe hypokalemia, or increased intake of HCO3- (i.e., milk-alkali syndrome).

In chloride-responsive alkalosis (when urinary cr < I 0),

aim treatment at restoration of volume with IV fluids (with either NaCl and/or KCl) and interruption of the cycle, which causes persistent volume loss. Potassium correction is integral to resolving the alkalosis, as well. Both interventions interrupt aldosterone production.

The carbonic anhydrase inhibitor, acetazolamide, which increases sodium bicarbonate excretion, can be used in patients who have alkalosis with contraindications to saline or potassium administration (e.g., severe edematous states such as decompensated heart failure).

Severe metabolic alkalosis (> 7.55) can be treated with HCl, which must be infused over an extended period of time through central venous access. This is done only in rare circumstances and usually only in the I CU.

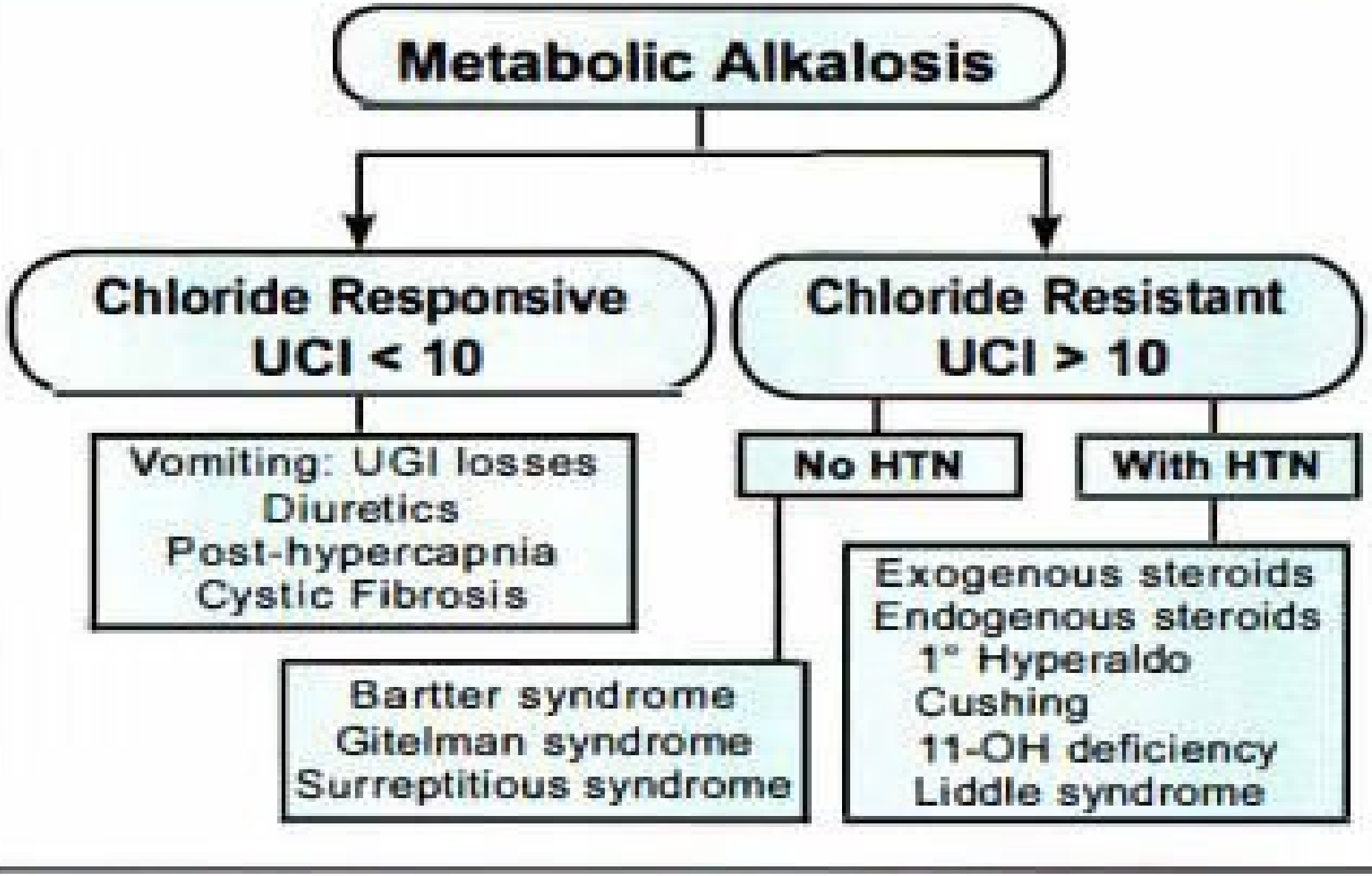


Figure 4-1: Metabolic Alkalosis: Chloride Responsive vs. Chloride Resistant Causes

Urine Anion Gap

The Urine Anion Gap (UAG) is used to evaluate the etiology of NAGMA to differentiate between gastrointestinal loss of HCO3- and renal tubular acidosis .

UAG is determined using the measured ions in the urine:

Na+, K+, and CL, expressed in mEq/L. UAG=Na++K+-CL

UAG is an estimate of the unmeasured ions in the urine, the most important one being NH4 +:

Normal value of UAG is close to 0.

A positive UAG value suggests low urinary NH4 + (e.g., RTA Type 4).

A negative UAG value suggests high urinary NH4 + (e.g., diarrhea).

Remember neGUTive UAG in cases of diarrhea.

In the setting of metabolic acidosis due to extra-renal bicarbonate losses, renal H+ excretion should be high, and H+ is excreted in the form of NH4+.

OSMOLAL GAP

The osmolality of the blood is determined mainly by **concentrations** of Na+, glucose, and urea.

The osmolal gap (OG) helps you determine whether unmeasured osmotically active substances (osmoles) are circulating in the blood (and possibly causing an acidosis). The OG is the difference between the measured serum osmolality (from the lab) and a calculated estimation of what the osmolality ought to be-if the only effective osmoles present are the normal ones (sodium, glucose, and urea).

Use the following formula to calculate the serum osmolality:

$$Osmcalc = 2[Na+] + (BUN/2.8) + (glucose/18)$$

Subtract this value from the lab-measured serum osmolality to get the OG.

Therefore:

OG = Osmmeas - Osmc alc

OG = Osmmeas-(2[Na+] + BUN/3 + glucose/20)

Know that a normal OG is< 10.

Important causes to know specifically are methanol and ethylene glycol ingestions and propylene glycol. Chronic kidney disease causes a high OG from retention of small solutes. Similarly, lactic acidosis and ketoacidosis cause a high OG from the accumulation of unknown small solutes and not from the actual lactic acid or ketoacids.

Know that :

Isopropyl alcohol ingestion is not associated with acidosis, even though the osmolal gap is increased (so the AG is normal). Nontoxic causes of an increased OG and normal AG are mannitol, sorbitol, and glycerol.

The main use of OG is in the workup of a patient with possible acid alcohol ingestion (e.g., ethylene glycol, methanol, or propylene glycol). Especially consider these possible poisonings if the OG > 25 mOsm!kg:

- Ethylene glycol is a common primary ingredient in radiator antifreeze solutions.
- Propylene glycol is a solvent used in IV lorazepam. It may cause a HAGMA + OG if the lorazepam is given as a continuous infusion
- Methanol is a common ingredient in paint thinners and deicing solutions (e.g., windshield washer fluids). Rarely, methanol is an inadvertent contaminant of "moonshine." Methanol is a by-product of grain fermentation.

Table 4-2: AG and OG in the Obtunded Patient

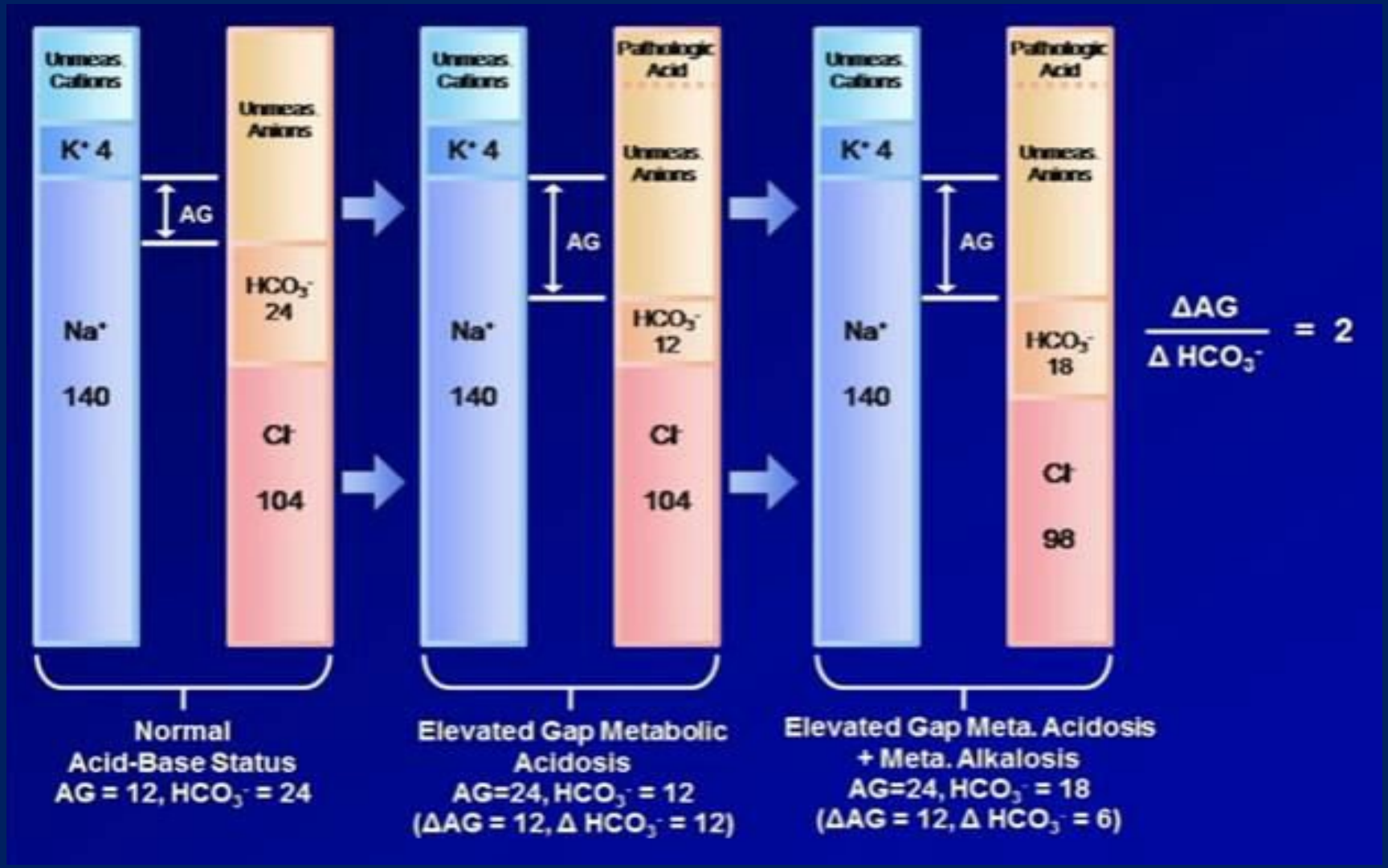
Anion Gap	Osmolal Gap	Consider
High	Very High	Methanol and ethylene glycol; ketoacidosis and lactic acidosis; chronic kidney disease
High	High	Ketoacidosis and lactic acidosis; chronic kidney disease
High	Normal	Salicylate poisoning; methanol or ethylene glycol ingestion after substrates have been converted to acid metabolites.
Normal	High	Isopropyl alcohol, acetone, or ethanol ingestion
Normal	Normal	Think carbon monoxide poisoning—before lactic acidosis develops.

The Delta Ratio

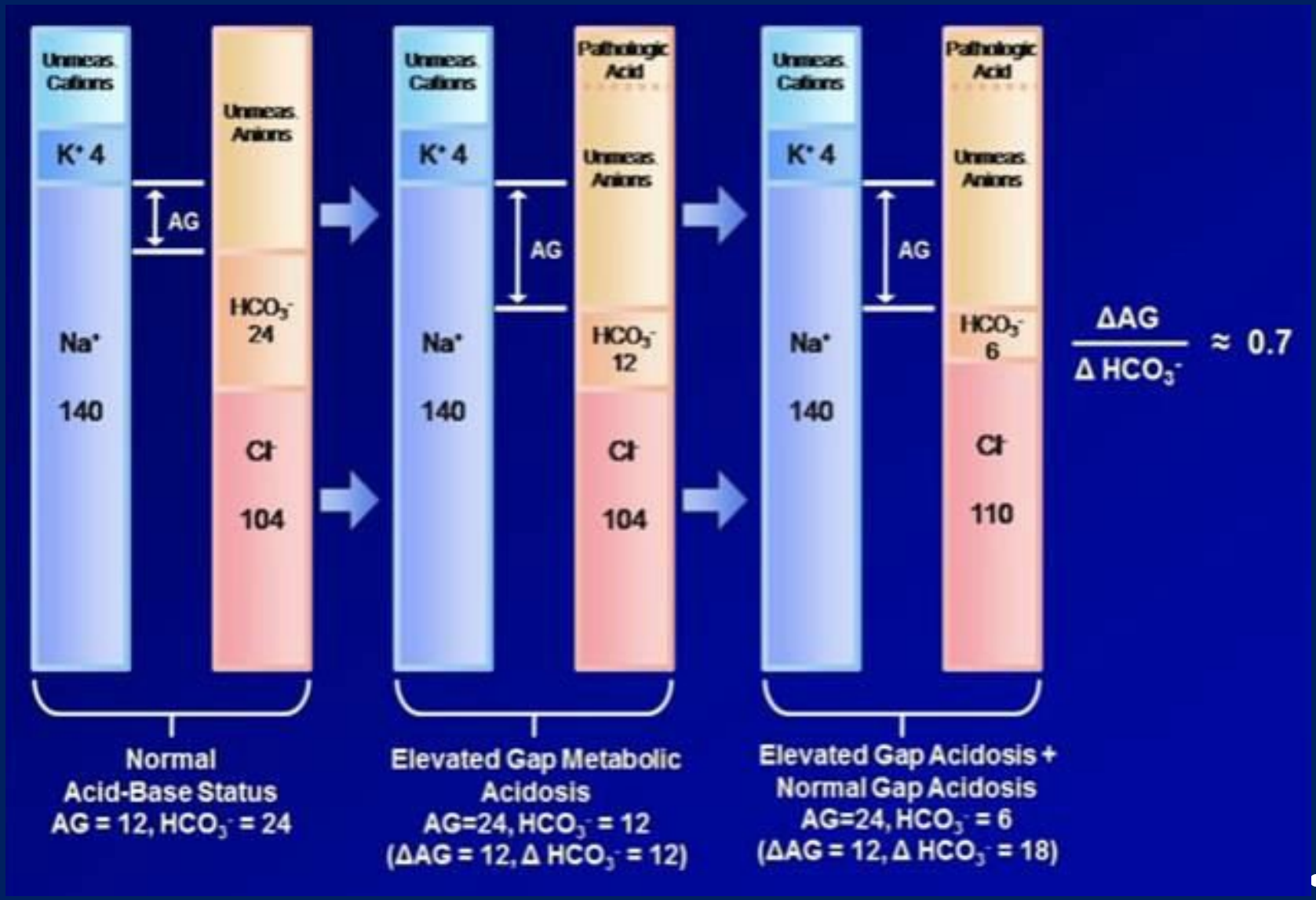
The expected "delta ratio" during an elevated gap metabolic acidosis depends upon the etiology of the elevated gap.

Pathologic	Expected
Lactic Acidosis	1.6 (1.0 — 2.0)
Ketoacidosis	1.0 (0.8 — 1.2)
Kidney Disease	Variable (depends on
Methanol, Ethylene Glycol	Unknown (Probably

Elevated Gap Acidosis + Metabolic Alkalosis



Elevated Gap Acidosis + Normal Gap Acidosis



The Delta Ratio

Measured Delta Ratio	Pathologic Metabolic Disorder(s)
Lower Than Expected Range	Elevated Gap Metabolic Acidosis + Normal Gap Metabolic Acidosis
Within Expected Range	Elevated Gap Metabolic Acidosis Only
Higher Than Expected Range	Elevated Gap Metabolic Acidosis + Metabolic Alkalosis

Example #1

A 75 y/o woman from a SNF presents with fever and profuse diarrhea x 2 days. Vital signs: T 38.5°, HR 130, BP 78/30.

7.29 / 30 / 14
pH P_aCO_2 HCO_3^-

128	94	20	140
3.2	14	1.6	

Step 1: Check pH → Acidemia

Step 2: Check PCO_2 → Metabolic Acidosis

Step 3: Evaluate compensation

$PCO_2 \approx 1.5\ (HCO_3^-) + 8$

Appropriate compensation

Step 4: Calculate anion gap

AG = 128 – (94 + 14)

AG = 20 mEq/L

Elevated Gap Metabolic Acidosis

Step 5: If AG is elevated, calculate delta ratio

$$\text{Delta Ratio} = \frac{\Delta AG}{\Delta HCO_3^-} = \frac{8}{10} = 0.8$$

Since the etiology of ↑AG is likely lactic acidosis, and the delta ratio < 1.0, there is also a Normal Gap Metabolic Acidosis.

Elevated Gap Metabolic Acidosis + Normal Gap Metabolic Acidosis

Example #2

A 34 y/o type 1 diabetic man comes to the ER with fever, nausea, vomiting, and abdominal pain for 1 day.

7.27 / 27 / 12
pH P_aCO_2 HCO_3^-

140	98	20	355
4.8	12	1.6	

Step 1: Check pH → Acidemia

Step 2: Check PCO_2 → Metabolic Acidosis

Step 3: Evaluate compensation

$PCO_2 \approx 1.5\ (HCO_3^-) + 8$

Appropriate compensation

Step 4: Calculate anion gap

AG = 140 – (98 + 12) = 30 mEq/L

Elevated Gap Metabolic Acidosis

Step 5: If AG is elevated, calculate delta ratio

$$\text{Delta Ratio} = \frac{\Delta AG}{\Delta HCO_3^-} = \frac{18}{12} = 1.5$$

Since delta ratio > 1.2, in the setting of probable ketoacidosis, there is also a Metabolic Alkalosis.

Elevated Gap Metabolic Acidosis + Metabolic Alkalosis

Example #3

A 48 y/o alcoholic man is found unconscious in his apartment, soiled with vomit. He was last seen leaving a party 6 hrs prior.

7.17 / 65 / 22

pH P_aCO_2 HCO_3^-

136	98	19	84
3.4	22	2.2	

Albumin = 1.6

Step 1: Check pH → Acidemia

Step 2: Check PCO_2 → Respiratory Acidosis

Step 3: Evaluate compensation

Is HCO_3^- ↑ by 1 for every 10 PCO_2 > 40?

No → Not appropriate

HCO_3^- ↓ than expected → Met. Acidosis

Step 4: Calculate anion gap

$AG = 136 - (98 + 22) = 16$ mEq/L

$AG_{adjusted} = AG_{measured} + 2.5\ (4\text{-Alb}) = 22$

Elevated Gap Metabolic Acidosis

Step 5: If AG is elevated, calculate delta ratio

$$\text{Delta Ratio} = \frac{\Delta AG}{\Delta HCO_3^-} = \frac{10}{2} = 5$$

Since the delta ratio > 2, irrespective of the etiology of the ↑AG, there is also a Metabolic Alkalosis.

Respiratory Acidosis + Elevated Gap Metabolic Acidosis + Metabolic Alkalosis

Patterns of Mixed Disorders

PCO_2	HCO_3^-	Anion Gap	Mixed Disorder
High	High	Normal	Respiratory acidosis + metabolic alkalosis
High	High	High	Respiratory acidosis + metabolic alkalosis + elevated gap metabolic acidosis
Low	Low	Normal	Respiratory alkalosis + normal gap metabolic acidosis
Low	Low	High	Respiratory alkalosis + elevated gap metabolic acidosis +/- another metabolic disorder
Normal	Normal	High	Elevated gap metabolic acidosis + metabolic alkalosis

Example #1

A 61 y/o morbidly obese man with COPD and CHF has an ABG and metabolic panel checked during routine pulmonary function tests.

7.41 / 55 / 34

pH / P_aCO_2 / HCO_3^-

133	92	21
3.4	34	1.2

123

PCO_2	HCO_3^-	AG	Mixed Disorder
High	High	Normal	Respiratory Acidosis + Metabolic Alkalosis
High	High	High	Resp. acidosis + meta. alkalosis + ↑ AG meta. acidosis
Low	Low	Normal	Respiratory Alkalosis + Normal Gap Meta. Acidosis
Low	Low	High	Resp. alkalosis + ↑ AG meta. acidosis ± other meta. disorder
Normal	Normal	High	↑ AG Meta. Acidosis + Metabolic Alkalosis

Example #1

A 61 y/o morbidly obese man with COPD and CHF has an ABG and metabolic panel checked during routine pulmonary function tests.

7.41 / 55 / 34

pH P_aCO_2 HCO_3^-

133	92	21	123
3.4	34	1.2	

Step 1: Check pH → Normal

Step 2: Check PCO_2 → Respiratory Acidosis

Step 3: Evaluate compensation

Normal pH → Opposite 1° disorder → Metabolic alkalosis

Step 4: Calculate anion gap

AG = 133 – (92 + 34) = 7 mEq/L

↑AG Metabolic Acidosis is *not* present.

Step 5: If AG is elevated, calculate delta ratio

Respiratory Acidosis + Metabolic Alkalosis

Example #1

A 61 y/o morbidly obese man with COPD and CHF, has an ABG and metabolic panel checked during routine pulmonary function tests.

7.41 / 55 / 34

pH P_aCO_2 HCO_3^-

133	92	21	123
3.4	34	1.2	

Respiratory Acidosis + Metabolic Alkalosis

Example #2

A 14 y/o girl with bulimia is brought to the ER after being found unresponsive at home with an empty pill bottle nearby.

7.39 / 22 / 13

pH P_aCO_2 HCO_3^-

139	88	15	75
3.1	13	0.8	

PCO_2	HCO_3^-	AG	Mixed Disorder
High	High	Normal	Respiratory Acidosis + Metabolic Alkalosis
High	High	High	Resp. acidosis + meta. alkalosis + ↑ AG meta. acidosis
Low	Low	Normal	Respiratory Alkalosis + Normal Gap Meta. Acidosis
Low	Low	High	Resp. alkalosis + ↑ AG meta. acidosis ± other meta. disorder
Normal	Normal	High	↑ AG Meta. Acidosis + Metabolic Alkalosis

Example #2

A 14 y/o girl with bulimia is brought to the ER after being found unresponsive at home with an empty pill bottle nearby.

7.39 / 22 / 13

pH P_aCO_2 HCO_3^-

139	88	15	75
3.1	13	0.8	

Step 1: Check pH → Normal

Step 2: Check PCO_2 → Respiratory Alkalosis

Step 3: Evaluate compensation

Opposite 1° disorder → Metabolic Acidosis

Step 4: Calculate anion gap

AG = 139 – (88 + 13) = 38 mEq/L

Elevated Gap Metabolic Acidosis

Step 5: If AG is elevated, calculate delta ratio

$$\text{Delta Ratio} = \frac{\Delta AG}{\Delta HCO_3^-} = \frac{26}{11} \approx 2.2$$

Since the delta ratio > 2, irrespective of the etiology of the ↑AG, there is also a Metabolic Alkalosis.

Respiratory Alkalosis + Elevated Gap Metabolic Acidosis + Metabolic Alkalosis

Example #2

A 14 y/o girl with bulimia is brought to the ER after being found unresponsive at home with an empty pill bottle nearby.

7.39 / 22 / 13

pH P_aCO_2 HCO_3^-

139	88	15	75
3.1	13	0.8	

Respiratory Alkalosis + Elevated Gap Metabolic Acidosis + Metabolic Alkalosis

Example #3

A 32 y/o pregnant woman comes to the ER with 4 days of "non-stop" vomiting. Vitals on admission: T 37.0°, HR 145, BP 78/42.

7.41 / 42 / 26

pH P_aCO_2 HCO_3^-

146	92	19	84
3.2	26	2.2	

Step 1: Check pH → Normal

Step 2: Check PCO_2 → Normal

Step 3: Evaluate compensation

Step 4: Calculate anion gap

AG = 146 – (92 + 26) = 28 mEq/L

Elevated Gap Metabolic Acidosis

Step 5: If AG is elevated, calculate delta ratio

$$\text{Delta Ratio} = \frac{\Delta AG}{\Delta HCO_3^-} = \frac{16}{-2} = -8\ ?$$

Negative delta ratio with normal pH → Metabolic Alkalosis

Elevated Gap Metabolic Acidosis + Metabolic Alkalosis

Example #3

A 32 y/o pregnant woman comes to the ER with 4 days of "non-stop" vomiting. Vitals on admission: T 37.0°, HR 145, BP 78/42.

7.41 / 42 / 26

pH P_aCO_2 HCO_3^-

146	92	19	84
3.2	26	2.2	

Elevated Gap Metabolic Acidosis + Metabolic Alkalosis

Etiologies of an Elevated Gap Acidosis

Methanol

Uremia

Diabetic ketoacidosis

Paraldehyde

INH, iron, intoxication, infection, etc...

Lactic acidosis

Ethylene glycol, ethanol

Salicylic acid

Etiologies of an Elevated Gap Acidosis

- Glycols
  - Oxoproline
  - L – lactate
  - D - lactate
- Methanol
- Aspirin
- Renal
  - Ketoacidosis
- Uremia
  - Lactic acidosis
- Toxins

Case :

A 78-year old female has been in the ICU for 2 weeks because of cholecystitis , Gram Neg sepsis, hypotension, and ARDS requiring MV. Patient was found to have a persistent low serum bicarb. Her medications include imipenem, acetaminophen, dopamine. and noradrenaline

Arterial pH	7.27
Arterial PCO2	41 mm Hg
Serum bicarbonate	18 mEq/L

Blood urea nitrogen	14 mg/dL
Serum creatinine	1.4 mg/dL
Serum lactate	1.6 mmOl/L
Serum Osmolality	289

Serum sodium	134 mEq/L
Serum potassium	3.8 mEq/L
Serum chloride	99 mEq/L
Serum glucose	187 mg/dL

Step 1: pH is 7.27 >>> Acidemia

Step2: HCO_3 18 , PCO_2 41 >> Metabolic Acidosis

Step 3: Compensation

Winter Formula, expected PCO_2 = 35, actual PCO_2 is 41 >>> Resp Acidosis

Step 4: AG = 134 - 99 - 18 = 17 >> AGMA

Step 5: delta/delta

Gap excess is 7, it should consume 7 bicarb.

HCO_3 is 18.

$\Delta AG/\Delta HCO_3$ = (17-10 (/(24-18) ~ 1

No additional metabolic disorder

Step 6: OG

Calculated = = 2(134) + 187/18 + 14/2.8 = 283

Measured = 289

OG = 6

Respiratory Acidosis

AG Metabolic Acidosis

Step 7: What is the underlying cause?

Which of the following are appropriate in the management of this patient's acid-base disturbance:

(A) CT scan rule out ischemic bowel

(B) Discontinue acetaminophen

(C) Add colistin to cover CR Enterobacteriaceae

(D) Alkaline diuresis

(E) A and C

Pyroglutamic acidemia (5-oxoprolinemia)

3/4 of cases are female, usually critically ill

Risk factors include: Sepsis, SIRS ,liver dysfunction, renal failure and malnutrition, Rx with acetaminophen, and flucloxacillin.

All have anion gap acidosis with elevated blood and urine pyroglutamic acid

Discontinue acetaminophen , flucloxacillin, supportive care

Case:

A 48-year-old male patient in the ICU, intubated for respiratory failure due to severe pneumonia and is paralysed with vecuronium and sedated with lorazepam. He is hemodynamically stable and on no pressor. Morning labs showed

Arterial pH	7.40
Arterial PCO2	24 mm Hg
S. Bicarbonate	16 mEq/L

Serum sodium	143 mEq/L
Serum potassium	4.9 mEq/L
Serum chloride	109 mEq/L

Blood urea nitrogen	12 mg/dL
Serum creatinine	1.1 mg/dL
Serum glucose	194 mg/dL
Serum lactate	8 mmol/L
Serum osmolality	312 mOsm/kg

Step 1: pH is 7.40

Step 2: HCO_3 16, PCO_2 = 24 >> Metabolic Acidosis

Step 3: Compensation

Winter Formula, expected PCO_2 = 32, actual PCO_2 is 24 >>> Respiratory Alkalosis

Step 4: AG = 143 - 109 - 16 = 18 >>> AGMA

Step 5: delta/delta

Gap excess is 8, it should consume 8 bicarb. HCO_3 is 16.

Δ AG/ Δ HCO_3 = (18-10)/(24-16) = 1

No additional disturbances

Step 6: OG
Calculated = 2(143) + 194/18 + 12/2.8 = 301

Measured = 312

OG = 312 - 301 = 11 (normal < 10)

AG Metabolic Acidosis and Res Alk with OG

The most appropriate next step in the management of this patient is:

(A) Dopamine

(B) Dobutamine

(C) Abdominal computed tomography

(D) Discontinue vecuronium

(E) Discontinue Lorazepam

Commonly used IV drugs containing Propylene glycol

Drug	% by volume
Lorazepam, 2mg/ml	80
Phenobarbital 30-130 mg/ml	70
Diazepam 5 mg/ml	40
Pentobarbital 50mg/ml	20-40
Phenytoin 50mg/ml	40
Bactrim 16:80 mg/ml	40
Etomidate 2mg/ml	35
Nitroglycerin 5mg/ml	30
Esmolol 250mg/ml	25

A 24-year-old woman was found down in the street by some bystanders. The medics were called and, upon arrival, found her with an oxygen saturation of 88% on room air and pinpoint pupils on exam. She was brought into the ER. A room air ABG and serum electrolytes as below

Arterial pH 7.24

Arterial PCO_2 60 mm Hg

Arterial PO_2 65 mm Hg

Bicarbonate 26 mEq/L

Serum sodium 137 mEq/L

Serum potassium 4.3 mEq/L

Serum chloride 100 mEq/L

Acute respiratory acidosis	↑ $HCO_3 = 0.1 \times \Delta P_aCO_2$ (also, ↓ $pH = 0.008 \times \Delta P_aCO_2$)
Chronic respiratory acidosis	↑ $HCO_3 = 0.35 \times \Delta P_aCO_2$ (also, ↓ $pH = 0.003 \times \Delta P_aCO_2$)

Step 1 : Acidemia → Step 2: Respiratory acidosis

Step 3:
HCO3 = 0.1 x 20 = 2
HCO3 = 0.35 x 20 = 7
actual HCO3 is 26 = Acute

→ Change in PH
PH = 0.008 x20 = 0.16
PH = 0.003 x20 = 0.06 Actual PH 7.24

Step 4: AG =11 →

- Acute Respiratory acidosis
- Appropriate metabolic alkalosis compensation

Primary disorder	Expected compensation
Metabolic acidosis	Each 1 mEq/L ↓ HCO_3^- → 1.2 mm Hg ↓ P_{CO2}
Metabolic alkalosis	Each 1 mEq/L ↑ HCO_3^- → 0.7 mm Hg ↑ P_{CO2}
Respiratory acidosis	
Acute	Each 1 mm Hg ↑ P_{CO2} → 0.1 mEq/L ↑ HCO_3^-
Chronic	Each 1 mm Hg ↑ P_{CO2} → 0.3 mEq/L ↑ HCO_3^-
Respiratory alkalosis	
Acute	Each 1 mm Hg ↓ P_{CO2} → 0.2 mEq/L ↓ HCO_3^-
Chronic	Each 1 mm Hg ↓ P_{CO2} → 0.4 mEq/L ↓ HCO_3^-

A 65-y/o man is brought into the hospital with complaints of nausea and weakness. He has hx of peptic ulcer disease and he has been having similar pain for the past two weeks. He has been drinking significant quantities of milk and consuming large quantities of TUMS (calcium carbonate). On his initial laboratory studies, he is found to have a calcium level of 11.5 mg/dL, a creatinine of 1.4 mg/dl

Serum sodium 139 mEq/L
Arterial PCO2 48 mm Hg
Serum chloride 95 mEq/L

S. Bicarbonate 34 mEq/L
Arterial pH 7.45

Metabolic alkalosis	$\uparrow P_aCO_2 = 0.7 \times \Delta HCO_3$

Step1 : Alkalemia

Step 2 : Metabolic alkalosis

Step3 :

PCO2 = 0.7 x 10=7

Actual PCO2 is 48 - – compensated

Step 4: AG = 10

Metabolic Alkalosis

Appropriate Res acidosis compensation

A 60-year-old man with amyotrophic lateral sclerosis is brought into clinic by his family who are concerned that he is more somnolent than normal. On further history, they report that he has been having problems with morning headaches and does not feel very refreshed when he wakes up. An arterial blood gas is performed and reveals:

Arterial pH 7.34

Arterial PCO_2 60 mm Hg

Arterial PO_2 70 mm HG

Bicarbonate 31 mEq/L

Acute respiratory acidosis	$\uparrow HCO_3 = 0.1 \times \Delta P_aCO_2$ (also, $\downarrow pH = 0.008 \times \Delta P_aCO_2$)
Chronic respiratory acidosis	$\uparrow HCO_3 = 0.35 \times \Delta P_aCO_2$ (also, $\downarrow pH = 0.003 \times \Delta P_aCO_2$)

Step 1: Acidemia → Step 2: Respiratory acidosis

Step 3: HCO3 = 0.1 x 20 = 2
HCO3 = 0.35 x 20 = 7
actual HCO3 is 31 = Chronic → Change in PH
PH = 0.008 x20 = 0.16
PH = 0.003 x20 = 0.06
Actual PH is 7.34

→ Chronic Respiratory acidosis
Appropriate metabolic
alkalosis compensation

A climber is coming down from the summit of Mt. Everest. At an altitude of 8,400 m, he has a blood gas drawn while breathing ambient air as part of a research project. The blood gas reveals

Arterial Ph	7.55
Arterial PCO2	12 mm Hg
PaO2	30 mm Hg
Bicarbonate	11 mEq/L

Acute respiratory alkalosis	$\downarrow HCO_3 = 0.2 \times \Delta P_aCO_2$ (also, $\uparrow pH = 0.008 \times \Delta P_aCO_2$)
Chronic respiratory alkalosis	$\downarrow HCO_3 = 0.4 \times \Delta P_aCO_2$

Step 1: Alkalemia → Step 2: Respiratory Alkalosis

Step 3:
HCO3 = 0.2 x 28 = 5.6
HCO3 = 0.4 x 28 = 11.2
actual HCO3 is 11 = Chronic

→ Change in PH
PH = 0.008 x28 = 0.22
Actual PH is 7.55 and not 7.62

→ Chronic Respiratory alkalosis
Appropriate metabolic acidosis compensation

A 57 year-old woman presents with 2 days of fevers, dyspnea and a cough productive of rust-colored sputum. Her room air oxygen saturation in the emergency room is found to be 85% and the intern decides to obtain a room air arterial blood gas while they are waiting for the chest x-ray to be done. The blood gas reveals:

Arterial pH	7.54
Arterial PCO2	25 mm Hg
PaO2	65 mm Hg
Bicarbonate	22 mEq/L

Acute respiratory alkalosis	$\downarrow HCO_3 = 0.2 \times \Delta P_aCO_2$ (also, $\uparrow pH = 0.008 \times \Delta P_aCO_2$)
Chronic respiratory alkalosis	$\downarrow HCO_3 = 0.4 \times \Delta P_aCO_2$

Step 1: Alkalemia → Step 2: Respiratory Alkalosis

Step 3: HCO3 = 0.2 x 15 =
3 HCO3 = 0.4 x 15 = 6
actual HCO3 is 22 = Acute

Change in PH
PH = 0.008 x15 = 0.12
Actual PH is 7.54

Acute Respiratory alkalosis
Appropriate metabolic acidosis compensation

A 45-year-old woman with a history of inhalant abuse presents to the emergency room complaining of dyspnea. She has an Sp02 of 99% on room air and is obviously tachypneic on exam with what appears to be Kussmaul's respirations. A room air arterial blood gas is performed and reveals:

Arterial pH 6.95

Arterial PCO2 9 mm Hg

PaO2 128 mm Hg

S. Bicarbonate 2 mEq/L

Serum sodium 130 mEq/L

Serum chloride 98 mEq/L

Metabolic acidosis	$\downarrow P_aCO_2 = 1.2 \times \Delta HCO_3$ or $P_aCO_2 = (1.5 \times HCO_3) + 8 \pm 2$ (Winters' formula)

Step 1: Acidemia → Step 2: Metabolic acidosi

Step 3: PCO2 = 1.5 x2 + 8 = 11 Actual PCO2 is 11-- compensated → Step 4: AG =30 AGMA

→

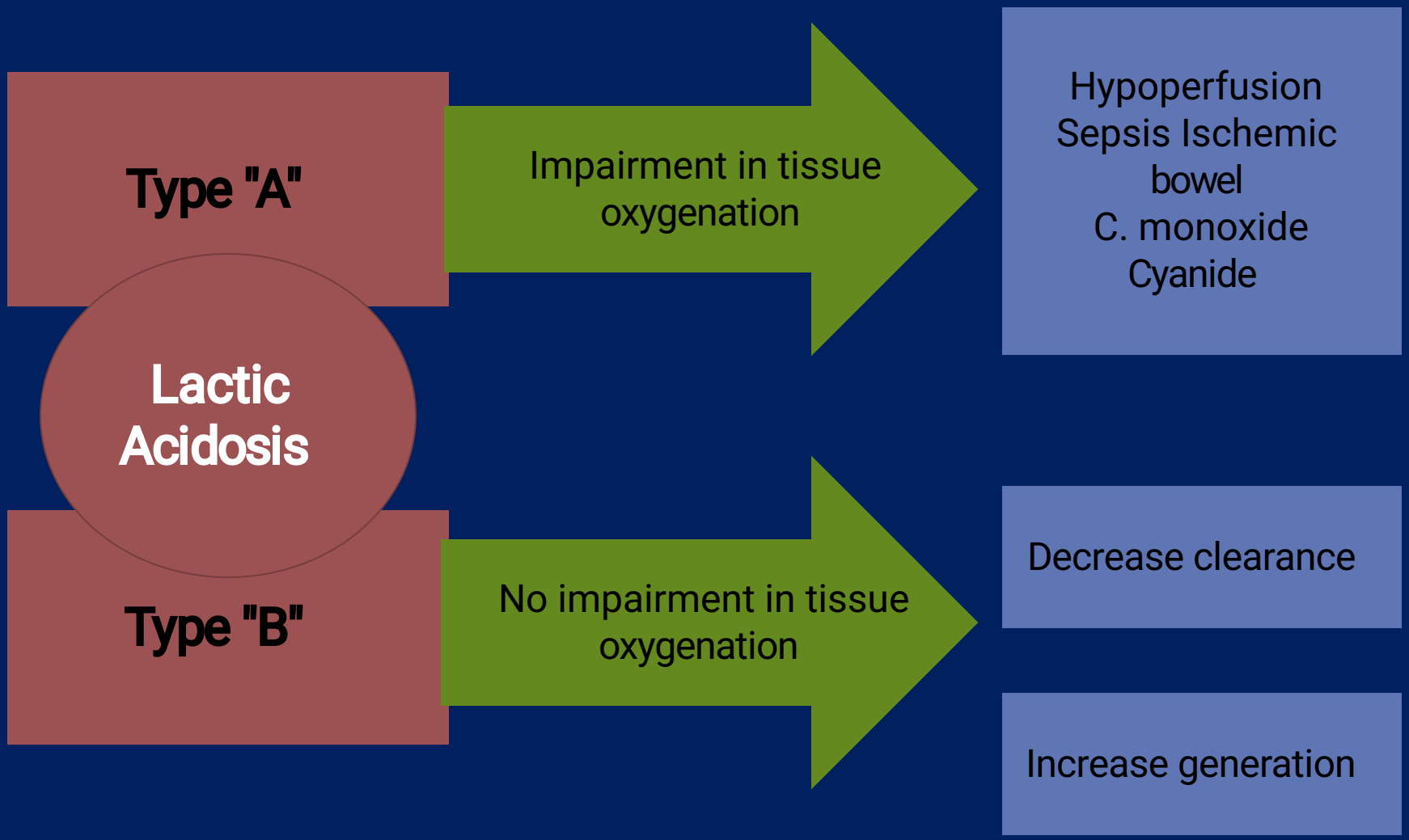
- AG Metabolic Acidosis
- Appropriate Respiratory compensation

Case : A 16-year-old male has a witnessed grand mal seizure and is brought immediately to the emergency room. He is post- ictal and has vomitus on his shirt. BP 120/83, HR 105

Arterial pH	7.30
Arterial PCO2	33 mm Hg
Serum bicarbonate	14 mEq/L

Blood urea nitrogen	12 mg/dL
Serum creatinine	1.1 mg/Dl
Serum creatine kinase	35 Mu/Ml
Serum osmolality	289 mOsm/kg
Toxicology screen	Negative
Urine ketones	Negative

Serum sodium	139 mEq/L
Serum potassium	4.2 mEq/L
Serum chloride	95mEq/L
Serum glucose	75 mg/Dl


Lactic Acidosis
Type "A"
Impairment in tissue oxygenation
Hypoperfusion
Sepsis Ischemic bowel
C. monoxide
Cyanide
Type "B"
No impairment in tissue oxygenation
Decrease clearance
Increase generation

Type B lactic acidosis:

Seizures

Malignancy (acute leukemia, lymphoma, solid tumor with liver metastases

Liver failure

Vitamin deficiency (thiamine, riboflavin)

Drugs/toxins (ethanol, methanol, ethylene glycol, propylene glycol, salicylates, metformin, NTRI, isoniazid, linezolid)

D-lactic acidosis

Pathogenesis :

1- Carbohydrates in gut + bacterial overgrowth
In colon -> generation of D-lactic acid

Both AGMA and NGMA