Acidosis and Alkalosis

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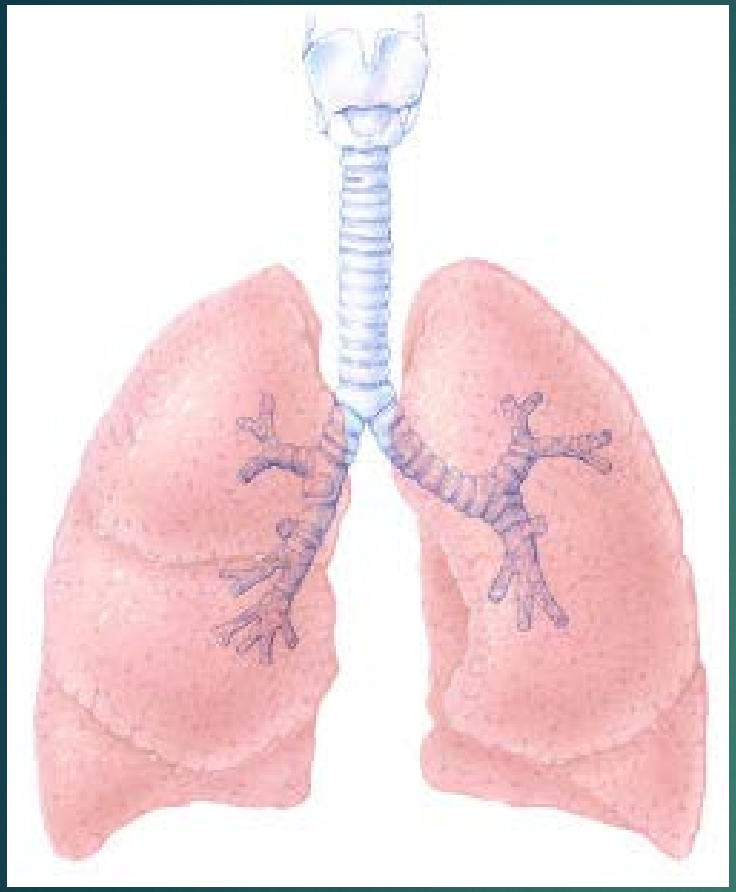
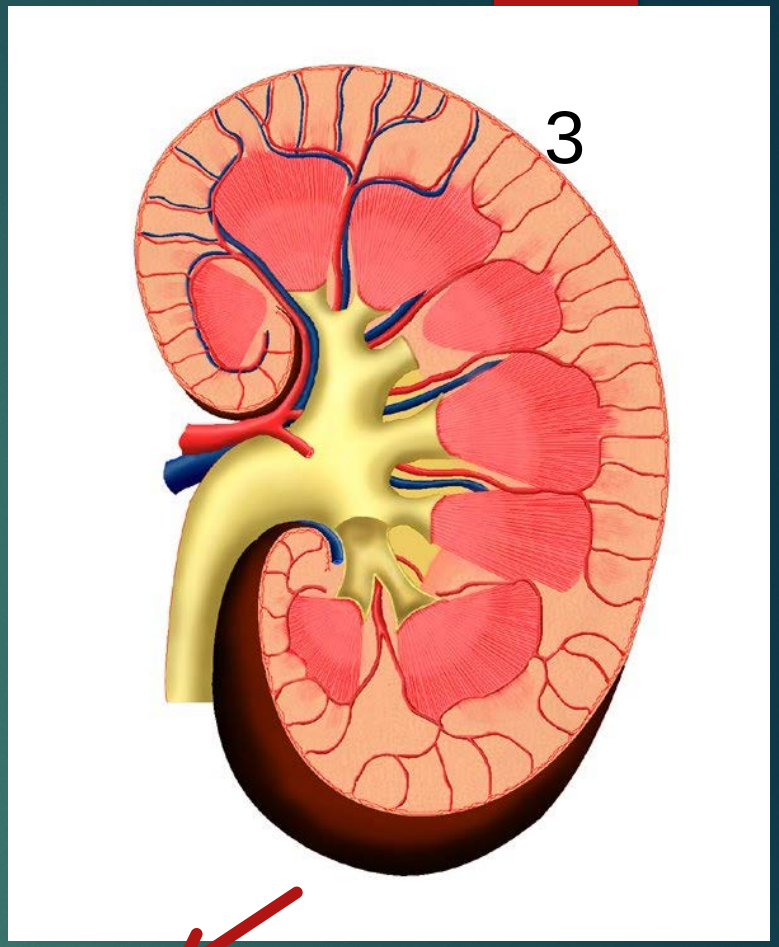
Outline

- Compensation
- Anion gap
- Metabolic acidosis





pH

P CO2

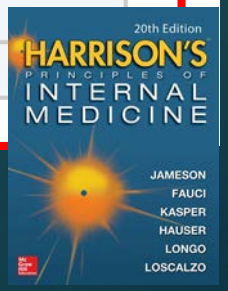
$HCO3^-$

Systemic arterial pH is maintained between 7.35 and 7.45 by extracellular and intracellular chemical buffering together with respiratory and renal regulatory mechanisms.

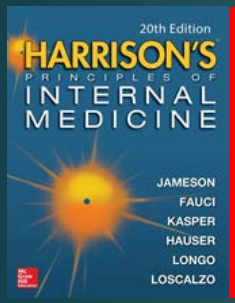
TABLE 51-1

Prediction of Compensatory Responses to Simple Acid-Base Disturbances and Pattern of Changes

Disorder	Prediction of Compensation	Range of Values		
		pH	HCO_3^-	$PaCO_2$
Metabolic acidosis	$PaCO_2 = (1.5 \times HCO_3^-) + 8 \pm 2$ *or* $PaCO_2$ will ↓ 1.25 mmHg per mmol/L ↓ in $[HCO_3^-]$ *or* $PaCO_2 = [HCO_3^-] + 15$	Low	Low	Low
Metabolic alkalosis	$PaCO_2$ will ↑ 0.75 mmHg per mmol/L ↑ in $[HCO_3^-]$ *or* $PaCO_2$ will ↑ 6 mmHg per 10 mmol/L ↑ in $[HCO_3^-]$ *or* $PaCO_2 = [HCO_3^-] + 15$	High	High	High
Respiratory alkalosis		High	Low	Low
Acute	$[HCO_3^-]$ will ↓ 0.2 mmol/L per mmHg ↓ in $PaCO_2$			
Chronic	$[HCO_3^-]$ will ↓ 0.4 mmol/L per mmHg ↓ in $PaCO_2$			
Respiratory acidosis		Low	High	High
Acute	$[HCO_3^-]$ will ↑ 0.1 mmol/L per mmHg ↑ in $PaCO_2$			
Chronic	$[HCO_3^-]$ will ↑ 0.4 mmol/L per mmHg ↑ in $PaCO_2$			



- pH: 6.83



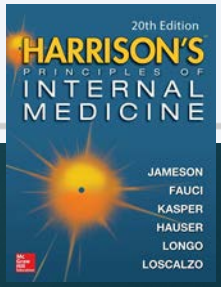
changes in PaCO and [HCO] in opposite directions indicate a mixed acid-base disturbance.

- Pco2: 50

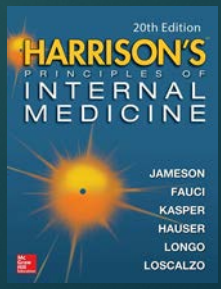
TABLE 51-1

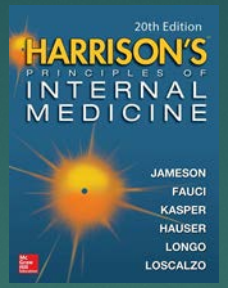
Prediction of Compensatory Responses to Simple Acid-Base Disturba Changes

Disorder	Prediction of Compensation
Metabolic acidosis	$PaCO_2 = (1.5 \times HCO_3^-) + 8 \pm 2$ *or* $PaCO_2$ will ↓ 1.25 mmHg per mmol/L ↓ in $[HCO_3^-]$ *or* $PaCO_2 = [HCO_3^-] + 15$
Metabolic alkalosis	$PaCO_2$ will ↑ 0.75 mmHg per mmol/L ↑ in $[HCO_3^-]$ *or* $PaCO_2$ will ↑ 6 mmHg per 10 mmol/L ↑ in $[HCO_3^-]$ *or* $PaCO_2 = [HCO_3^-] + 15$



	$PaCO_2$ ... $[HCO_3^-]$ ...
Respiratory alkalosis	
Acute	$[HCO_3^-]$ will ↓ 0.2 mmol/L per mmHg ↓ in $PaCO_2$
Chronic	$[HCO_3^-]$ will ↓ 0.4 mmol/L per mmHg ↓ in $PaCO_2$
Respiratory acidosis	
Acute	$[HCO_3^-]$ will ↑ 0.1 mmol/L per mmHg ↑ in $PaCO_2$
Chronic	$[HCO_3^-]$ will ↑ 0.4 mmol/L per mmHg ↑ in $PaCO_2$





Compensatory responses return the pH toward, but not to, the normal value.

- pH: 7.13
- HCO3: 8

Chronic respiratory alkalosis when prolonged is an exception to this rule and may return the pH to a normal value.

Compensation

	Primary event	Compensation	Timing	$[HCO_3^-]$ / 10 Pa_{CO2}
Respiratory acidosis	↑P CO_2	↑HCO_3	Acute	1
			Chronic	4
Respiratory alkalosis	↓P CO_2	↓HCO_3	Acute	2
			Chronic	4

Compensation

	Primary event	Compensation	
Metabolic acidosis	$\downarrow HCO_3$	$\downarrow P\,CO_2$	$Pa_{CO2} = (1.5 \times HCO_3^-) + 8 \pm 2$ $Pa_{CO2} = [HCO_3^-] + 15$
Metabolis alkalosis	$\uparrow HCO_3$	$\uparrow P\,CO_2$	Pa_{CO2} will $\uparrow 0.75$ / $\uparrow [HCO_3^-]$ $Pa_{CO2} = [HCO_3^-] + 15$

Example:

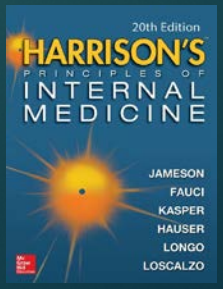
- A 60 y/o man with severe vomiting and BUN:130, Crt: 12 mg/dl.

When the pH is normal, an elevated anion gap reliably denotes the presence of an AG metabolic acidosis.

- $HCO3^-$, 25
- Pa_{co2}, 40
- AG, 20

AG = Na - (Cl + HCO3)

The “normal” ranges from 6 to 12 mmol/L, with an average of ~10 mmol/L.



Mixed Acid-Base Disorders

- A discrepancy in the AG and the HCO_3^- indicates the presence of a mixed high-gap acidosis—metabolic alkalosis

$$\Delta AG > \Delta HCO_3$$

$$AG\text{-}10 > 25\text{-}HCO_3$$

Mixed high-AG—normal-AG acidosis

- $\Delta HCO3^-$ accounted for by combined change in Δ AG and Δ Cl^-.
- Na^+, 135;
- Cl^-, 110;
- $HCO3^-$, 10;
- AG, 15;
- Pa_{co2}, 25;
- pH, 7.20

ANION GAP

Na^+ + Unmeasured cations = Cl^- + HCO_3^- + Unmeasured anions

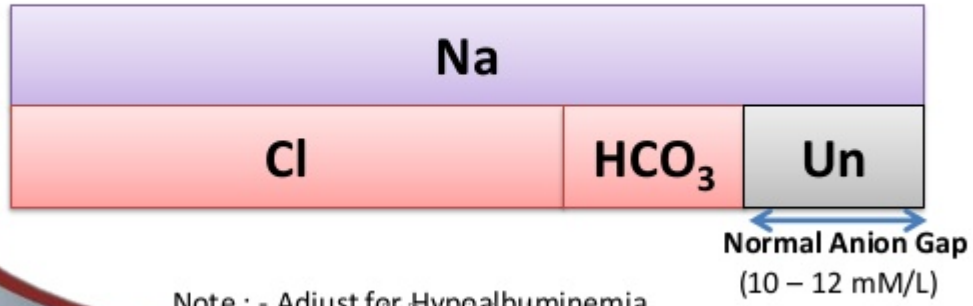
Or, Unmeasured anions – Unmeasured cations = Na^+ - (Cl^- + HCO_3^-)

Anion Gap = Na^+ - (Cl^- + HCO_3^-)

Definition

Anion gap is Quantity of anions not balanced by cations

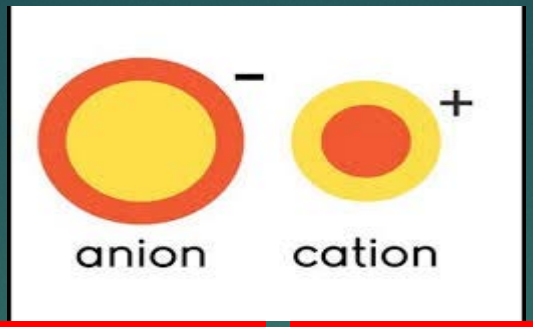
- usually due to the **NEGATIVELY CHARGED PLASMA PROTEINS** as the charges of the other unmeasured cations and anions tend to balance out.



Note : - Adjust for Hypoalbuminemia

Anion Gap

↑ AG	↓ AG
↑unmeasured anions ↓unmeasured cations	↓ ↑unmeasured anions ↑ unmeasured cations

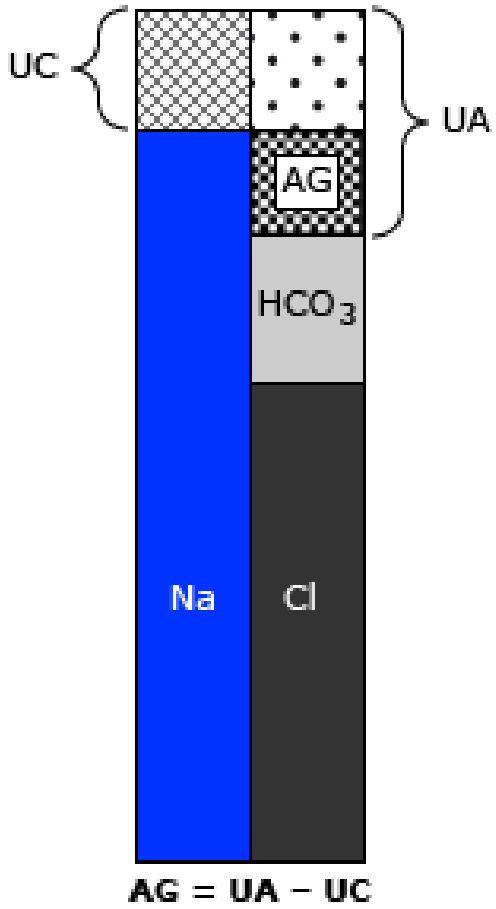


Unmeasured anions

- Albumin
- Phosphate
- Sulfate
- Organic anions: acetoacetate and lactate, salicylate

Unmeasured cations

- Calcium
- Magnesium
- Potassium
- Lithium (lithium intoxication)
- Cationic immunoglobulins (plasma cell dyscrasias)



AG = UA − UC

]

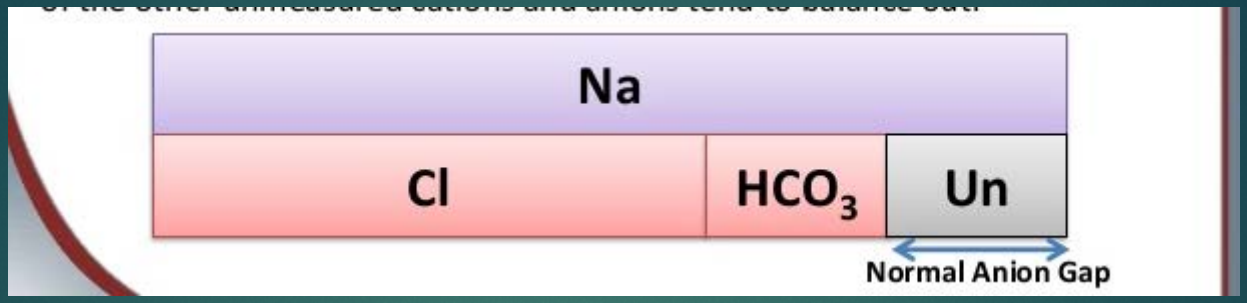
Anion Gap

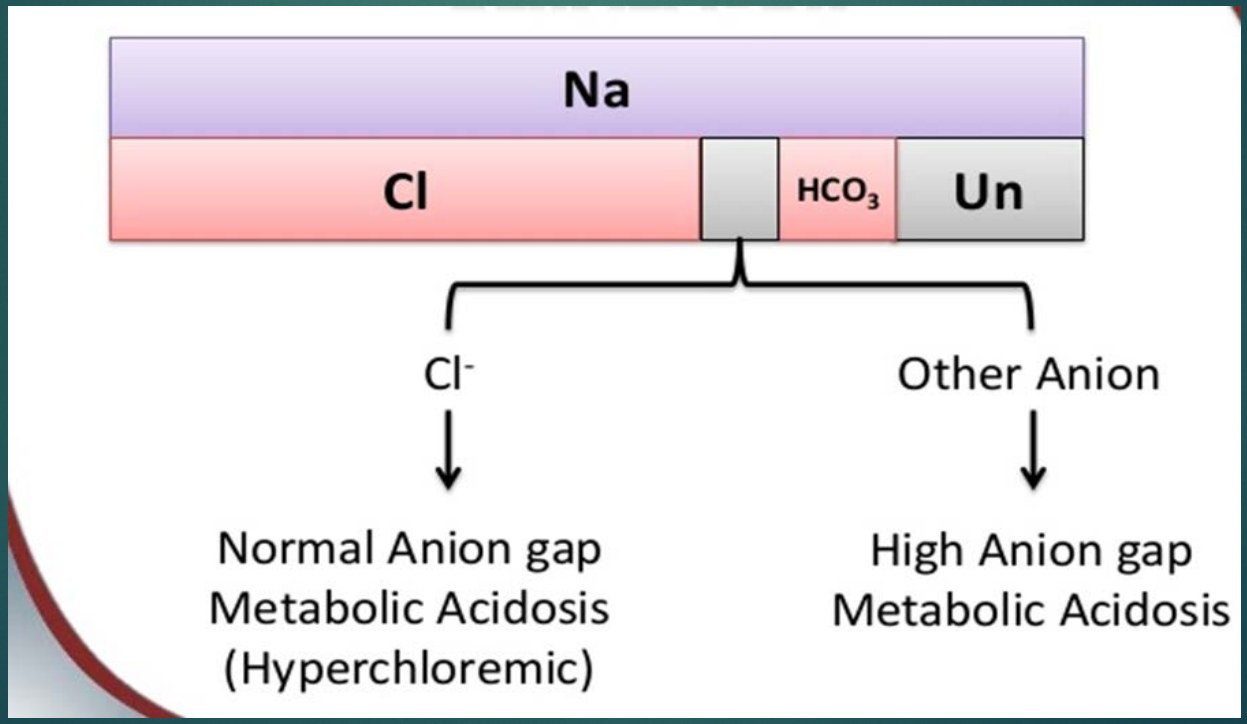
- For each g/dL of serum albumin below the normal value (4.5 g/dL), 2.5 mmol/L should be added to the reported (uncorrected) AG.

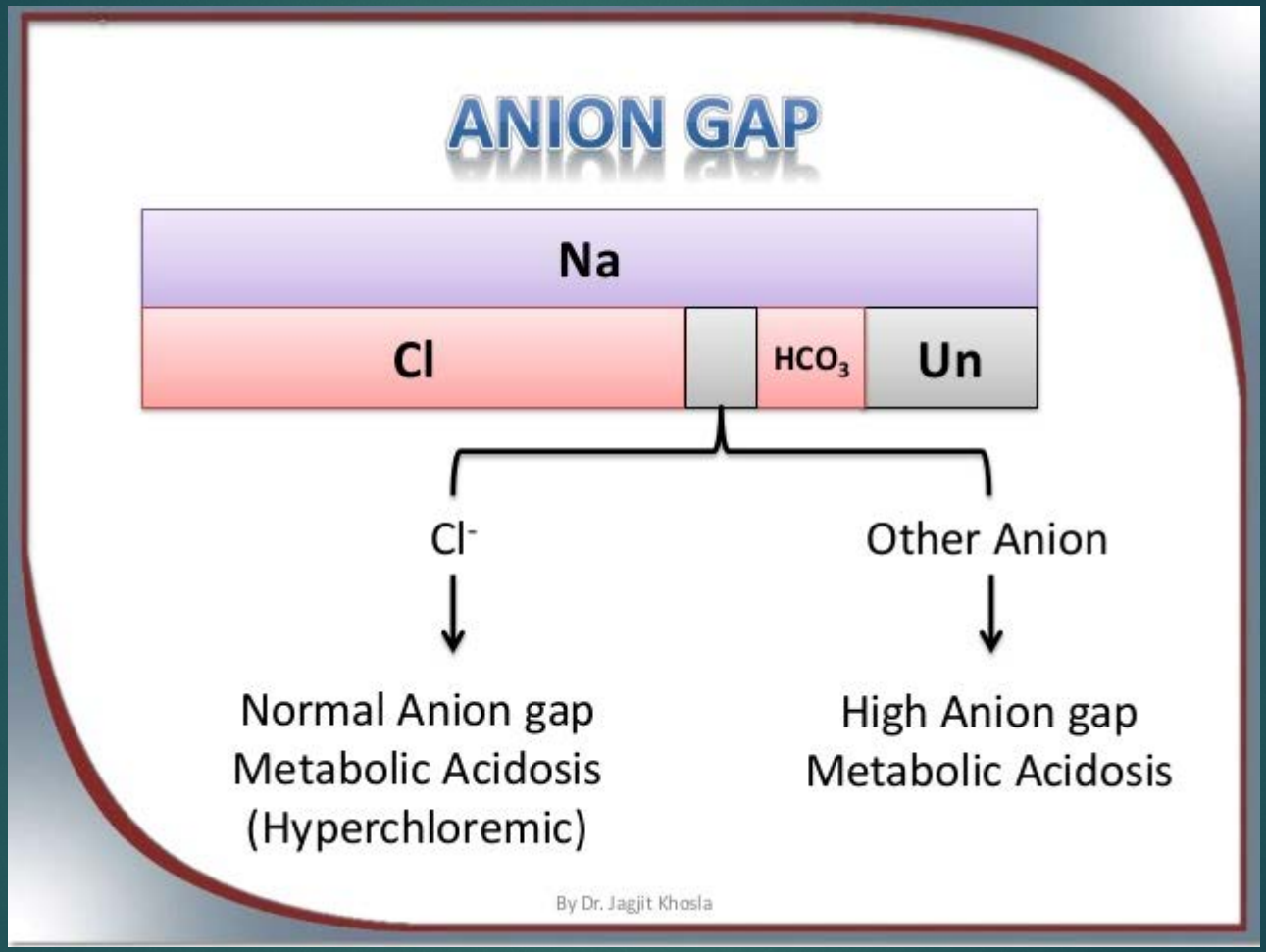
Corrected AG = AG + [(4.5 – Albumin) × 2.5]

Anion Gap

- Normal values for [HCO3-], PaCO2, and pH do not ensure the absence of an acid-base disturbance.
  - An alcoholic who has been vomiting may develop a metabolic alkalosis with a pH of 7.55, PaCO2 of 48 mmHg, [HCO3-] of 40 mmol/L, [Na+] of 135, [Cl-] of 80, and [K+] of 2.8. If such a patient were then to develop a superimposed alcoholic ketoacidosis with a ß-hydroxybutyrate concentration of 15 mM, arterial pH would fall to 7.40, [HCO3-] to 25 mmol/L, and the PaCO2 to 40 mmHg.
  - Although these blood gases are normal, the AG is elevated at 30 mmol/L, indicating a mixed metabolic alkalosis and metabolic acidosis.


Na
Cl
HCO_3
Un
Normal Anion Gap


Na
Cl
HCO_3
Un
Cl^-
Other Anion
Normal Anion gap
Metabolic Acidosis
(Hyperchloremic)
High Anion gap
Metabolic Acidosis


ANION GAP
Na
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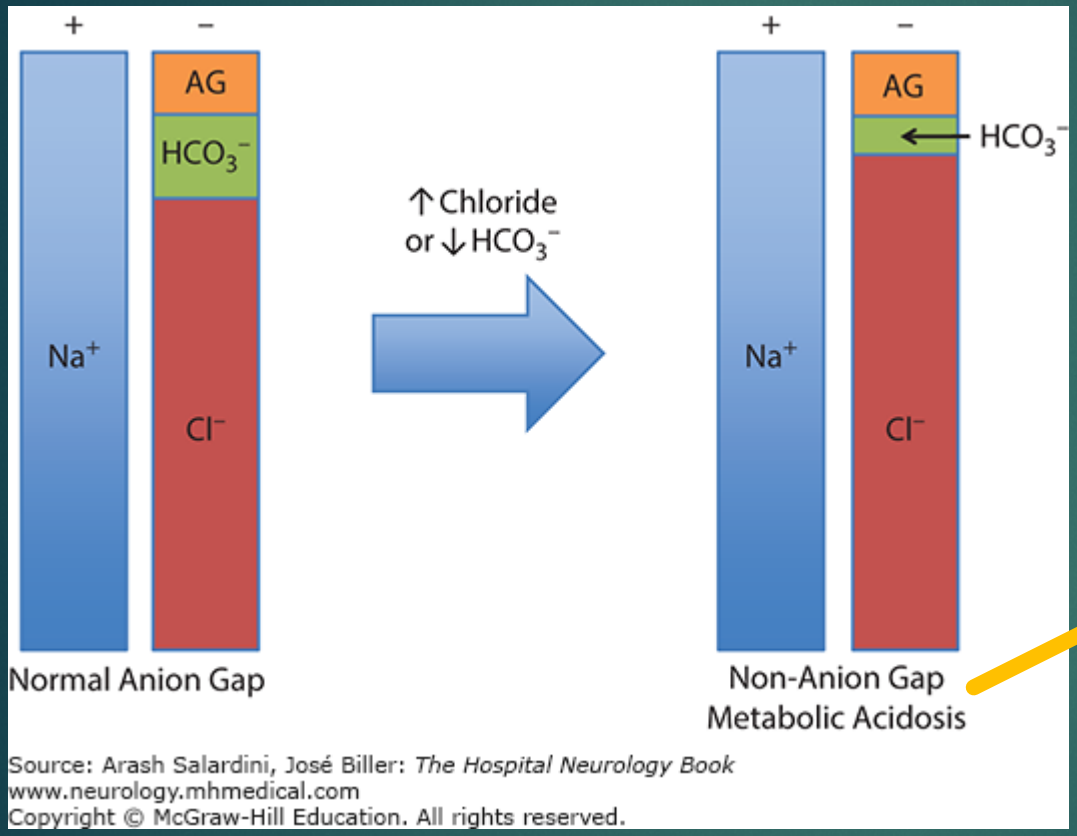
Metabolic Acidosis
By Dr. Jagjit Khosla



Source: Arash Salardini, José Biller: *The Hospital Neurology Book*
www.neurology.mhmedical.com

hyperchloremic acidosis

Categories of clinical metabolic acidosis

- High-anion-gap (AG)
- Normal-AG, or hyperchloremic acidosis

METABOLIC ACIDOSIS

↑AG

- Lactic acidosis
- Ketoacidosis
- Ethylene glycol
- Methanol
- Salicylates
- Propylene glycol
- Pyroglutamic acid (5-oxoproline)
- Renal failure (acute and chronic)

Nl AG

- Diarrhea
- RTA
- Ureterosigmoidostomy, jejunal loop, ileal loop

Effects of metabolic acidosis

- Kussmaul respiration
- Intrinsic cardiac contractility may be depressed, but inotropic function can be normal because of catecholamine release.
- Peripheral arterial vasodilation and central venoconstriction
- Pulmonary edema with even minimal volume overload.
- Central nervous system function is depressed, with headache, lethargy, stupor, and, in some cases, even coma. Glucose intolerance may also occur

TREATMENT

- Treatment of metabolic acidosis with alkali should be reserved for:
  - Severe acidemia (pH <7.10)
  - No "potential HCO_3^-" in plasma: metabolizable acids (i.e., β-hydroxybutyrate, acetoacetate, and lactate).

TREATMENT

- It must be determined if the acid anion in plasma is metabolizable (i.e., ß-hydroxybutyrate, acetoacetate, and lactate) or nonmetabolizable (anions that accumulate in chronic kidney disease and after toxin ingestion).

- Potential [HCO3-] can be estimated from the increment in the AG

  (ΔAG = patient's AG - 10).

TREATMENT

- Alkali therapy, either orally or intravenously in an amount necessary to slowly increase the plasma [HCO3-] into the 20 to 22 mmol/L range:
  - Normal AG acidosis
  - AG attributable to a nonmetabolizable anion in the face of renal failure

Severe acidosis (pH <7.10)

- Intravenous administration of NaHCO3 IV administration of 50 meq of NaHCO diluted in 300 mL of sterile water over 30–45 min, during the initial 1–2 h of therapy.

- The goal is to increase the [HCO3-] to 10 meq/L and the pH to 7.20, not to increase these values to normal.

bicarbonate deficit

- Estimation of the “bicarbonate deficit” by calculation of the volume of distribution of bicarbonate is often taught but is unnecessary and may result in administration of excessive amounts of alkali.

METABOLIC ACIDOSIS

↑AG	Nl AG
▶ Lactic acidosis ▶ Ketoacidosis ▶ Ethylene glycol ▶ Methanol ▶ Salicylates ▶ Propylene glycol ▶ Pyroglutamic acid (5-oxoproline) ▶ Renal failure (acute and chronic)	▶ Diarrhea ▶ RTA ▶ Ureterosigmoidostomy, jejunal loop, ileal loop

ALCOHOLS

ALCOHOLS

- **Osmolal gap**:
  - Posm = 2Na+ + Glu/18 + BUN/2.8
  - The calculated and determined osmolality should agree within 10 to 15 mmol/kg H2O
  - **Osmolal gap >10 to 15:**
    - **<u>The serum sodium is spuriously low:</u>**
      - Hyperlipidemia or hyperproteinemia (pseudohyponatremia
    - **<u>Osmolytes other than sodium salts, glucose, or urea have accumulated in plasma:</u>**
      - Mannitol, radiocontrast media, isopropyl alcohol, ethylene glycol, ethanol, methanol, and acetone.

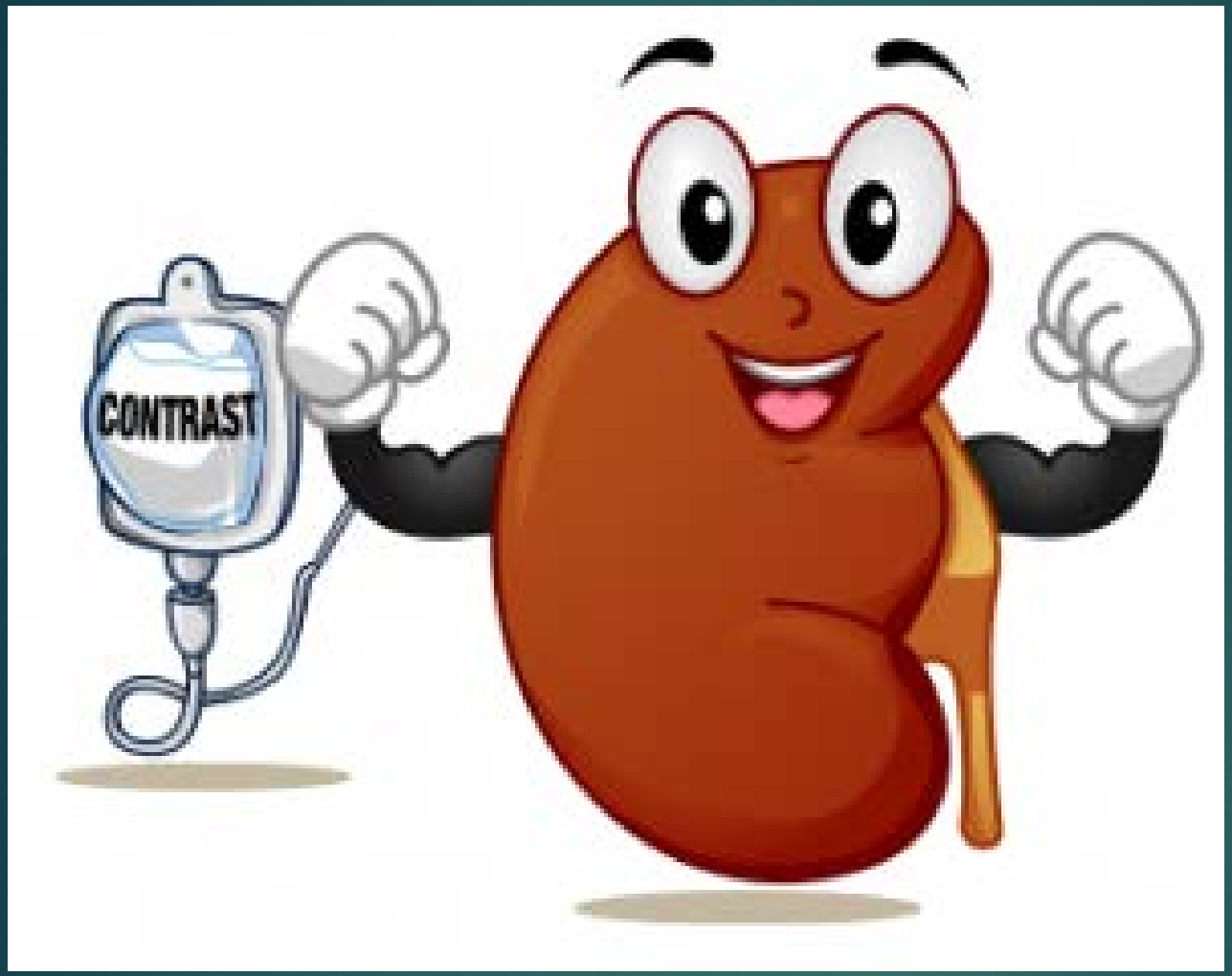
ALCOHOLS

- Three alcohols may cause fatal intoxications: ethylene glycol, methanol, and isopropyl alcohol.
- All cause an elevated osmolal gap, but only the first two cause a high-AG acidosis.

	Elevated osmolal gap	High-AG acidosis
Ethylene Glycol	+	+
methanol	+	+
isopropyl alcohol	+	-

Ethylene Glycol

- Oxalate crystals in the urine
- Osmolar gap in serum
- High-AG acidosis
- Hemodialysis is indicated when the arterial pH is <7.3, or the osmolar gap exceeds 20 mOsm/kg.



1. ~~CRRT~~
2. ~~HD~~
3. ~~PD~~

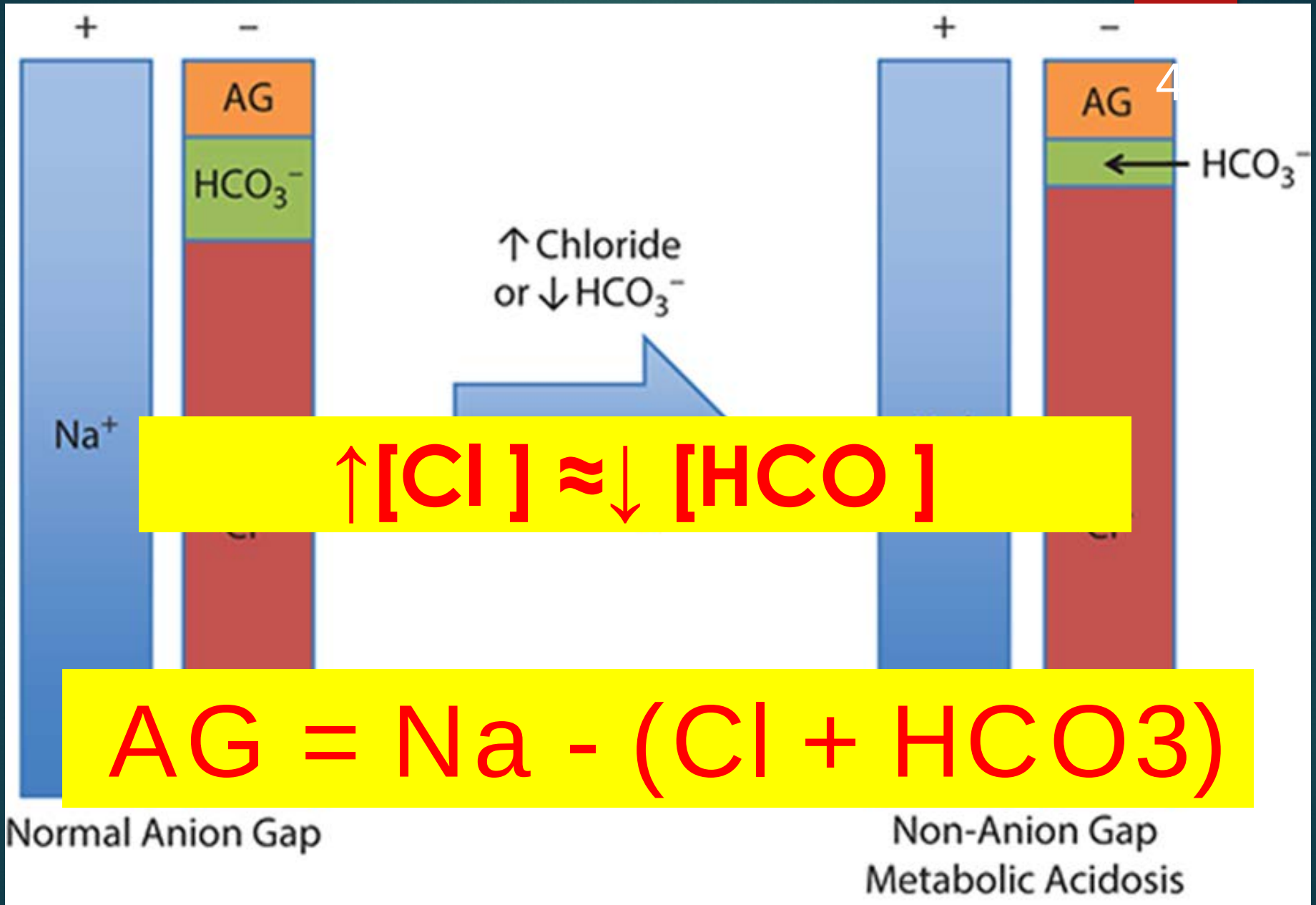
RENAL FAILURE

- Moderate renal insufficiency : Nl AG acidosis
- Advanced renal failure(Stages 4 and 5) : high AG acidosis

- TREATMENT:
  - Oral alkali replacement to maintain the [HCO] to 25 mmol/L.

HYPERCHLOREMIC (NONGAP)

METABOLIC ACIDOSES



↑[Cl] ≈↓ [HCO]

AG = Na - (Cl + HCO3)

Source: Arash Salardini, José Biller: *The Hospital Neurology Book*
www.neurology.mhmedical.com

Causes of non-Anion-Gap Acidosis

- A. Diarrhea
- RTA
- B. External pancreatic or small-bowel drainage
- C. Ureterosigmoidostomy . jejunal loop, ileal loop
- D. Drugs
  - Calcium chloride (acidifying agent)
  - Magnesium sulfate (diarrhea)
  - Cholestyramine (bile acid diarrhea)

Causes of non-Anion-Gap Acidosis

- Drug-induced hyperkalemia (with renal insufficiency)
  - A. Potassium-sparing diuretics (amiloride, triamterene,spironolactone)
  - B. Trimethoprim
  - C. Pentamidine
  - D. ACEI & ARBs
  - E. NSAIDS
  - F. Cyclosporine

Causes of non-Anion-Gap Acidosis

- Other
  - Acid loads (amnnonium chloride . hyperalimentation)
  - loss off potential bicarbonate : ketosis with ketone excretion
  - Expansion acidosis (rapid saline administration)
  - Hippurate
  - Cation exchange resins

I. Gastrointestinal bicarbonate loss

- A. Diarrhea
- B. External pancreatic or small-bowel drainage
- C. Ureterosigmoidostomy, jejunal loop, ileal loop
- D. Drugs
  1. Calcium chloride (acidifying agent)
  2. Magnesium sulfate (diarrhea)
  3. Cholestyramine (bile acid diarrhea)

II. Renal acidosis

A. Hypokalemia

1. Proximal RTA (type 2)

   Drug-induced: acetazolamide, topiramate

2. Distal (classic) RTA (type 1)

   Drug-induced: amphotericin B, ifosfamide

B. Hyperkalemia

1. Generalized distal nephron dysfunction (type 4 RTA)

   a. Mineralocorticoid deficiency

   b. Mineralocorticoid resistance (PHA I, autosomal dominant)

   c. Voltage defect (PHA I, autosomal recessive, and PHA II)

   d. Tubulointerstitial disease

C. Normokalemia

1. Chronic progressive kidney disease

III. Drug-induced hyperkalemia (with renal insufficiency)

- A. Potassium-sparing diuretics (amiloride, triamterene, spironolactone, eplerenone)
- B. Trimethoprim
- C. Pentamidine
- D. ACE-Is and ARBs
- E. Nonsteroidal anti-inflammatory drugs
- F. Calcineurin inhibitors
- G. Heparin in critically ill patients

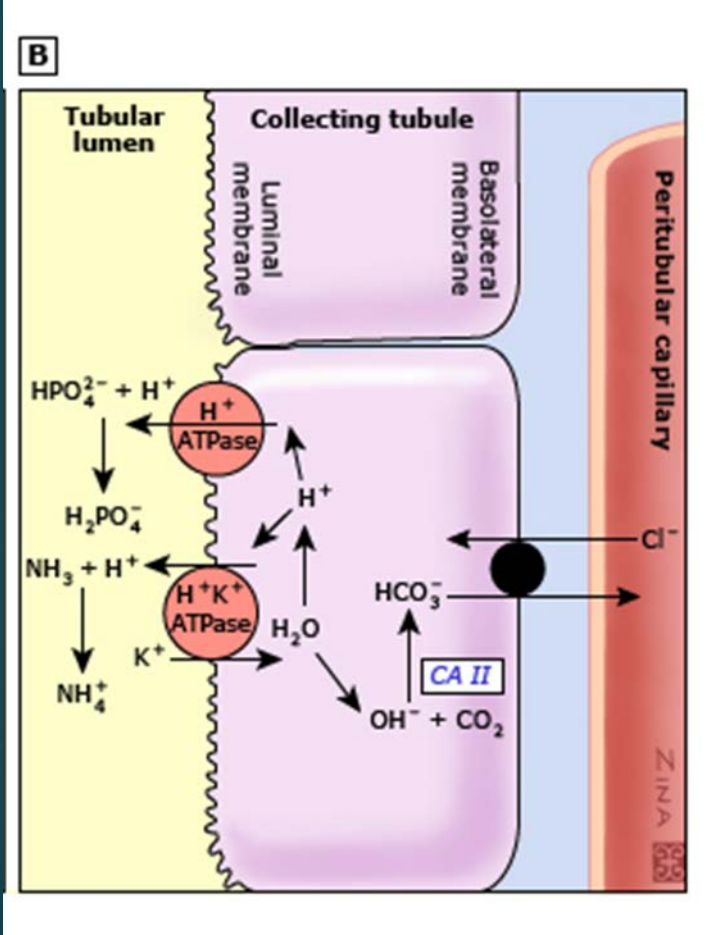
IV. Other

- A. Acid loads (ammonium chloride, hyperalimentation)
- B. Loss of potential bicarbonate: ketosis with ketone excretion
- C. Expansion acidosis (rapid saline administration)
- D. Hippurate
- E. Cation exchange resins

Causes of non-Anion-Gap Acidosis

- Diarrhea
- RTA
- Ureterosigmoidostomy

Diarrhea → metabolic acidosis



↑ renal NH_4^+

↑ urine pH>6

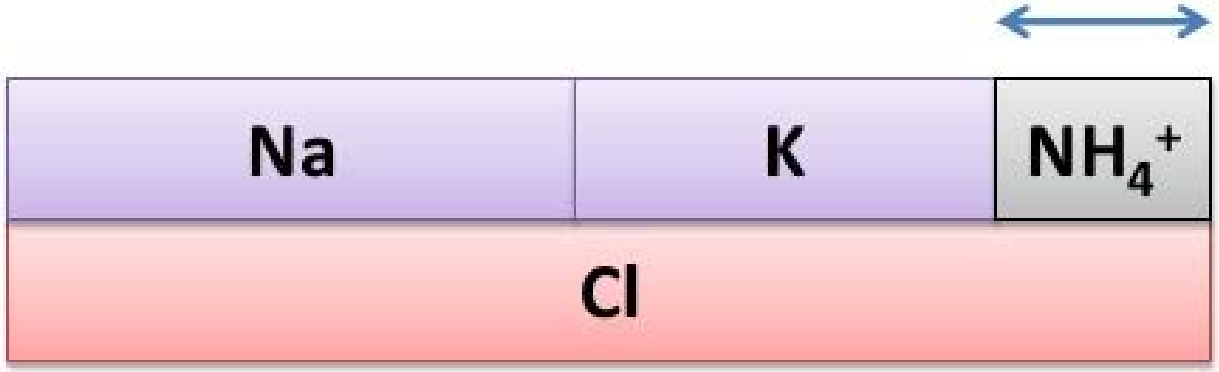
URINE ANION GAP

$U_{Na+} + U_{K+}$ + Unmeasured cations = U_{Cl-} + Unmeasured anions

Or, Unmeasured anions – Unmeasured cations = $(U_{Na+} + U_{K+}) - U_{Cl-}$

Urine Anion Gap (UAG) = $(U_{Na+} + U_{K+}) - U_{Cl-}$

- **NH_4^+** is the primary unmeasured cation which is not balanced by anions.
- **UAG as indirect assay for renal NH4+ excretion**



URINE ANION GAP

Negative

↓

Increased renal NH4+ excretion (Response to acidemia)

Positive

↓

Failure of Kidneys to secrete NH_4^+

Urine anion gap

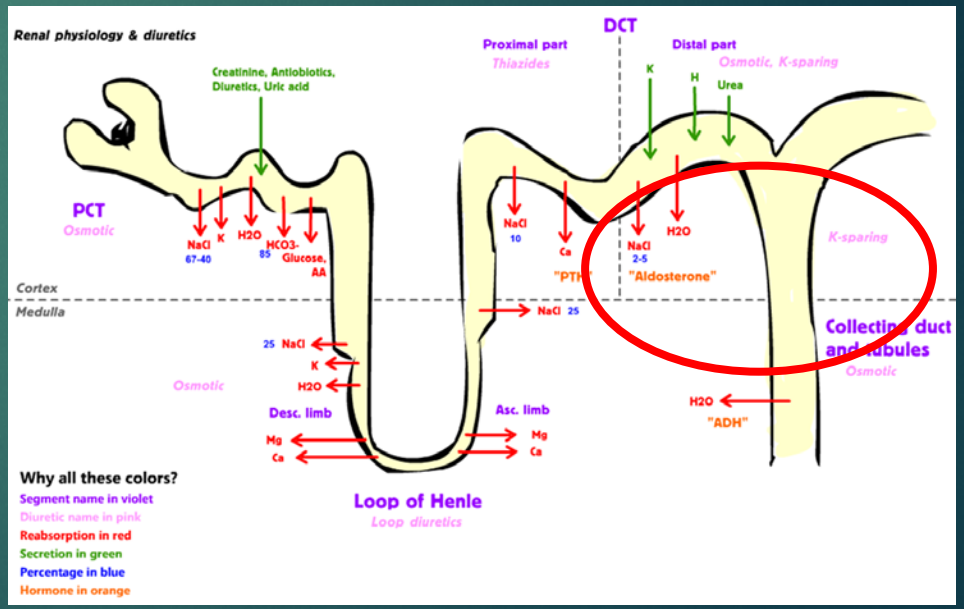
- UAG = $[Na + K]_u - [Cl]_u$
  - - UAG → Diarrhea
    - High U $NH4^+$
    - Extrarenal cause
  - +UAG
    - Low U $NH4^+$ → RTA
    - Renal cause


RENAL TUBULAR
ACIDOSIS

	RTA 1	RTA 2	RTA 4	Diarrhea
Location	Distal	Proximal	Adrenal	GI
Urine pH	**> 5.5**	**<5.5**	**<5.5**	**>6**
Urine AG	**+**	**+**	**+**	**-**
K	↓	↓	↑	↓
Nephrocalcinosis	**+**	**-**	**-**	**-**
Fanconi syndrome	**-**	**+**	**-**	**-**
fractional excretion of [HCO]		**>10-15%**		

TYPE 1 (DISTAL) RTA

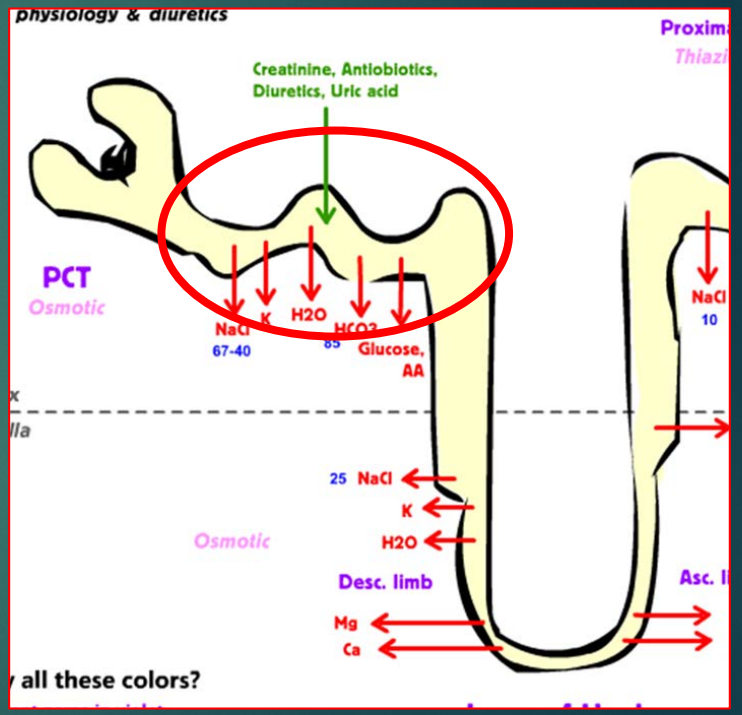
- Distal nephron does not lower urine pH normally
- Hypercalciuria
- Bone disease
- Low urine citrate
- Calcium phosphate stones and nephrocalcinosis



TYPE 2 (PROXIMAL) RTA

- Bicarbonate reabsorption in the proximal tubule is defective

- Features of Fanconi syndrome:
  - glycosuria, generalized aminoaciduria, and phosphaturia



RTA 4

- Hyporeninemic hypoaldosteronism most commonly in older adults with DM or TID and renal insufficiency.

III. Drug-induced hyperkalemia (with renal insufficiency)

A. Potassium-sparing diuretics (amiloride, triamterene, spironolactone, eplerenone)

B. Trimethoprim

C. Pentamidine

D. ACE-Is and ARBs

E. Nonsteroidal anti-inflammatory drugs

F. Calcineurin inhibitors

G. Heparin in critically ill patients

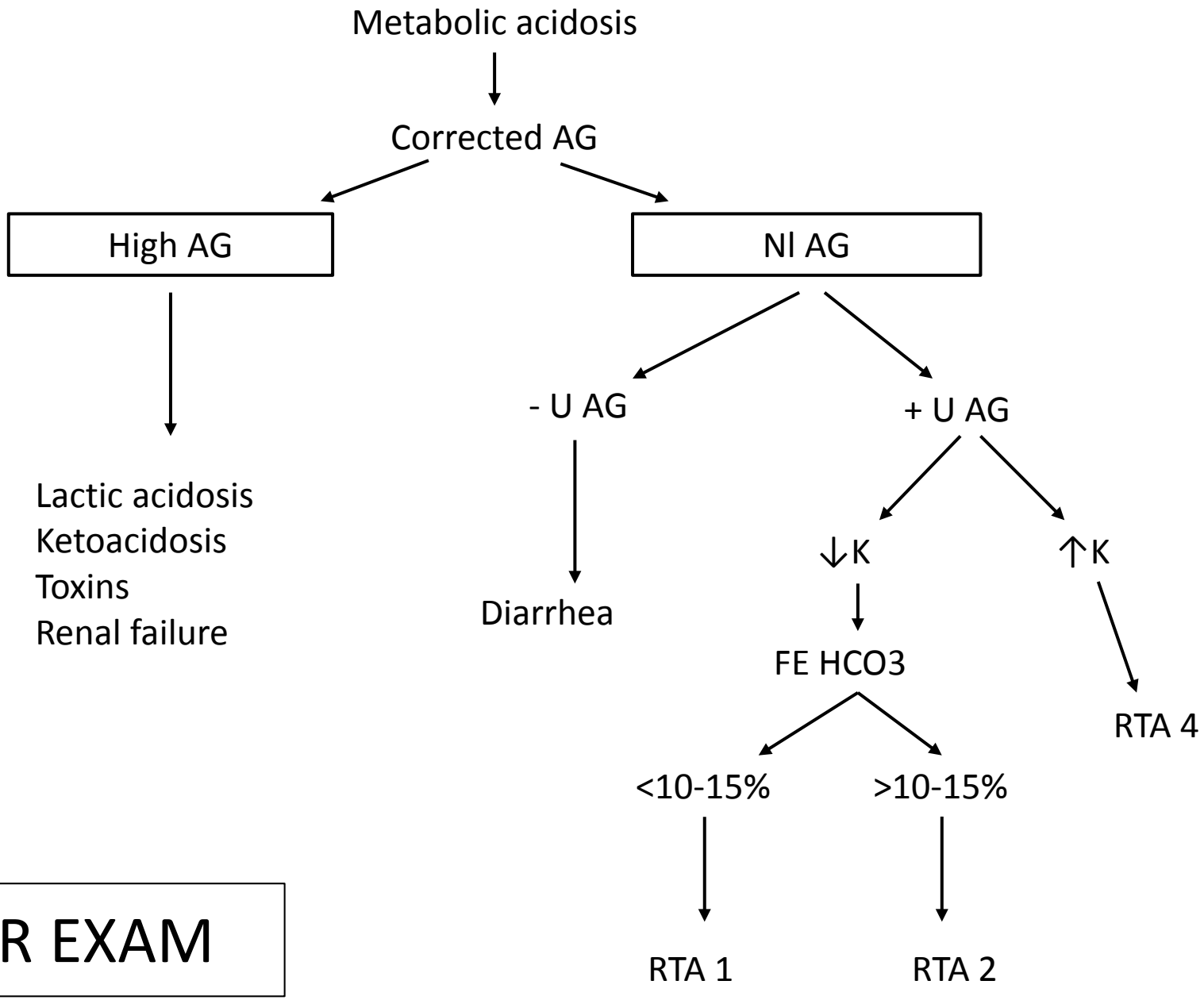
کلیه

۱۰۷- خانم ۶۰ ساله با ضعف و بیحالی بستری می گردد و شرح حال اسهال نمی دهد. آزمایشات به شرح ذیل می باشد:

PH: 7.20 HCO_3: 14 mmol/L PCO_2: 35 mmHg
K: 2.5 meq/L A.G: Normal
Urine: (Na: 20, K^+: 15, Cl^-: 60 mmol/L)

اطلاعات فوق با کدام بیماری بیشتر مطابقت دارد؟

الف: Diarrhea
ب: Distal RTA
ج: Proximal RTA
د: Acetazolamide use


Metabolic acidosis
Corrected AG
High AG
Nl AG
Lactic acidosis
Ketoacidosis
Toxins
Renal failure
- U AG
+ U AG
Diarrhea
↓K
↑K
FE HCO3
RTA 4
<10-15%
>10-15%
RTA 1
RTA 2

FOR EXAM

PRACTICE

Metabolic acidosis

↓

Exclude:
- Lactic acidosis
- Ketoacidosis
- Toxins
- Renal failure
- Diarrhea

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Negative

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- RTA

If Nl AG acidosis+ hypokalemia

	Elevated osmolal gap	High-AG acidosis
Ethylene Glycol	+	+
methanol	+	+
isopropyl alcohol	+	-