ACID-BASE ANALYSIS

Outline

- Basic concepts
- Stepwise approach to acid-base analysis
- The gaps
  - The anion gap
  - The gap-gap ratio

Hydrogen Ion Concentration and pH

- The power of hydrogen: pH=-log[H+]
  - The normal pH of plasma is indicated as 7.40, which corresponds to a [H+] of 40 nEq/L.
- The equilibrium: [H+]=24x(PCO2/HCO3)
  - [H+]: the concentration of hydrogen in extracellular fluid
  - PCO2: the partial pressure of carbon dioxide
  - HCO3: the concentration of bicarbonate

Primary and Secondary Acid-Base Disorders

Table 31.2 Primary Acid-Base Disorders and Secondary Responses

$\Delta[H^+] = \Delta PCO_2/\Delta HCO_3$

Primary Disorder	Primary Change	Secondary Response†
Respiratory Acidosis	$\uparrow PCO_2$	$\uparrow HCO_3$
Respiratory Alkalosis	$\downarrow PCO_2$	$\downarrow HCO_3$
Metabolic Acidosis	$\downarrow HCO_3$	$\downarrow PCO_2$
Metabolic Alkalosis	$\uparrow HCO_3$	$\uparrow PCO_2$

Primary and Secondary Acid-Base Disorders

Metabolic		Respiratory			
Acidosis	Alkalosis	Acidosis		Alkalosis	
5/4	4/5	0.1	0.3	0.2	0.4

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EXAMPLE.
Q. Consider a case where the **PaCO2 = 23 mm Hg**, the **pH = 7.32**, and the **HCO3 = 16 mEq/L**.
A. This is a primary **metabolic/respiratory** acidosis **+/-** a secondary **metabolic/respiratory acidosis/alkalosis**.

This is a primary metabolic acidosis with a secondary respiratory alkalosis.

Primary and Secondary Acid-Base Disorders

Metabolic		Respiratory			
Acidosis	Alkalosis	Acidosis		Alkalosis	
5/4	4/5	0.1	0.3	0.2	0.4

EXAMPLE.
Q. Consider a case where the **PaCO2 = 23 mm Hg**, the **pH = 7.52**, and the **HCO3 = 16 mEq/L**.
A. This is a primary **metabolic/respiratory** acidosis **+/-** a secondary **metabolic/respiratory acidosis/alkalosis**.

This is a chronic respiratory alkalosis with an appropriate (completed) renal response.

The Gaps

- The anion gap (AG): AG = UA-UC = Na-(Cl-HCO3).
  - Ref: 12±2 (mEq/L)
- Influence of Albumin: AGc = AG + 2.5x(4.5-[Albumin (g/dL)])
  - Low albumin concentration lowers AG, masking the presence of unmeasured anion that is contributing to a metabolic acidosis.

The Gaps

- Influence of Albumin: AGc = AG + 2.5x(4.5-[Albumin (g/dL)])

Table 31.3 Determinants of the Anion Gap

Unmeasured Anions	Unmeasured Cations
Albumin (15 mEq/L)	Calcium (5 mEq/L)
Organic Acids (5 mEq/L)	Potassium (4.5 mEq/L)
Phosphate (2 mEq/L)	
Sulfate (1 mEq/L)	Magnesium (1.5 mEq/L)
Total UA: (23 mEq/L)	Total UC: (11 mEq/L)
Anion Gap = UA – UC = 12 mEq/L	

The Gaps

- **Normal AG:** The loss of HCO3 is counterbalanced by a gain of chloride ions, i.e., hyperchloremic metabolic acidosis.
- **High AG:** HCO3 decreases too rapidly to be counterbalanced.

Table 31.4 Classification of Metabolic Acidosis with the Anion Gap (AG)

High AG	Normal AG
Lactic Acidosis	Diarrhea
Ketoacidosis	Isotonic Saline Infusion
End-Stage Renal Failure	Early Renal Insufficiency
Methanol Ingestion	Renal Tubular Acidosis
Ethylene Glycol Ingestion	Acetazolamide
Salicylate Toxicity	Ureteroenterostomy

The Gaps

- **High AG:** HCO3 decreases too rapidly to be counterbalanced.

- (+) Ketone: DM, alcoholic, starvation.
- (+) Lactate: Sepsis, hypoperfusion
- Ingestion. Calculate
  - Osmolal gap = Measured osmoles - 2*Na+Glu/18+BUN/2.8
  - Osmolal gap > 10: 甲醇、乙醇、乙二醇、異丙醇
  - Osmolal gap < 10: 乙醛、水楊酸、阿斯匹靈

The Gaps

- **Normal AG:** The loss of HCO3 is counterbalanced by a gain of chloride ions, i.e., hyperchloremic metabolic acidosis.

- Calculate urine anion gap (UAG): $\mathbf{U_{Na}} + \mathbf{U_{K}} - \mathbf{U_{Cl}}$ =UA-UC
  - UC is mostly NH4+.
  - UAG<0 → 腎臟排**NH4**正常 → HCO3 loss → Diarrhea or RTA type 2
    - RTA type 2: Acidosis with hypokalemia. Fanconi syndrome. No kidney calcinosis.
  - UAG>0 → 腎臟無法排**NH4** → RTA type 1 & 4
    - RTA type 1: Acidosis with hypokalemia. Due to AIR (Sjogren syn, SLE). Low $\mathbf{U_{NH4}}$.
    - RTA type 4: Acidosis with hyperkalemia. Due to hypoRAAS. Due to Spironolactone.

The Gaps

- 19 下列何者不是高陰離子間隙代謝性酸中毒（high-anion-gap metabolic acidosis）的原因？

  (A)lactic acidosis

  (B)ketoacidosis

  (C)diarrhea

  (D)salicylate intoxication

The Gaps

- 26 下列那一個病例較符合所列之動脈血氣體分析和血清電解質的檢查結果？pH 7.32，PaO_2 110 mmHg， $PaCO_2$ 30 mmHg，HCO_3^- 18 mEq/L；Na^+ 138，K^+ 3.5，Cl^- 97（電解質的單位是 mmol/L）

  (A) 70 歲病人因便秘嚴重，服用 magnesium sulfate 導致腹瀉數天

  (B) 28 歲病人診斷為修格連氏症候群（Sjögren’s syndrome），無意間發現腎鈣化（nephrocalcinosis），尿液 酸鹼值為 6.5；給予 NH4Cl（0.1 g/kg 體重）後，尿液酸鹼值為 6.0

  (C) 20 歲病人第一型糖尿病病史 5 年，血糖控制不佳，最近因為期末考胰島素注射次數減少

  (D) 60 歲病人因膽道阻塞放置引流管引流膽汁

The Gap-Gap Ratio

- **The Gap-Gap Ratio: △AG/△HCO3**
  - Mnemonic: 酸酸小，酸鹼大
  - DG > 2: High AG acidosis with metabolic alkalosis. (額外的鹼)
  - DG < 1. High AG acidosis with non-AG metabolic acidosis. (額外的酸)

The Gap-Gap Ratio: A Case Study

- A patient with diabetic ketoacidosis (DKA) is associated with improvement in the blood glucose and the clinical condition of the patient, but the acidosis persists. What should we do next?
- We can measure the patient's gap-gap ratio.
- When HCO3 remains low with the gap-gap ratio falls below 1, it indicates that the acidosis is switching from a high AG to a normal AG acidosis. Thus, monitoring the serum HCO3 alone will create a false impression that the DKA is not resolving, while the gap-gap ratio provides an accurate measure of the acid-base status of the patient

METABOLIC ALKALOSIS

- Pathogenesis
- Clinical manifestations
- Evaluation
  - Chloride-Responsive Alkalosis
  - Chloride-Resistant Alkalosis
  - Severe K+ Depletion.
- Management

Metabolic alkalosis

- Defined as an increase in [HCO3] concentration in extracellular fluid that is not an adaptive response to hypercapnia.
- This condition can be the result of any of the following:
  - (a) loss of hydrogen ions (H+) from extracellular fluid,
  - (b) a gain in bicarbonate ions in extracellular fluid, or
  - (c) a decrease in extracellular volume.
- Once developed, metabolic alkalosis is sustained by
  - a decrease in HCO3 excretion in the urine, which is the result of both an increase in HCO3 reabsorption and a decrease in HCO3 secretion in the distal nephron.

Renal Mechanisms

- Bicarbonate Reabsorption (top)
- Bicarbonate Secretion (bottom)
- Chloride Depletion (2 effects)
- Hypokalemia: intracellular pH ↓ .
- Aldosterone: stimulates H+ pump.

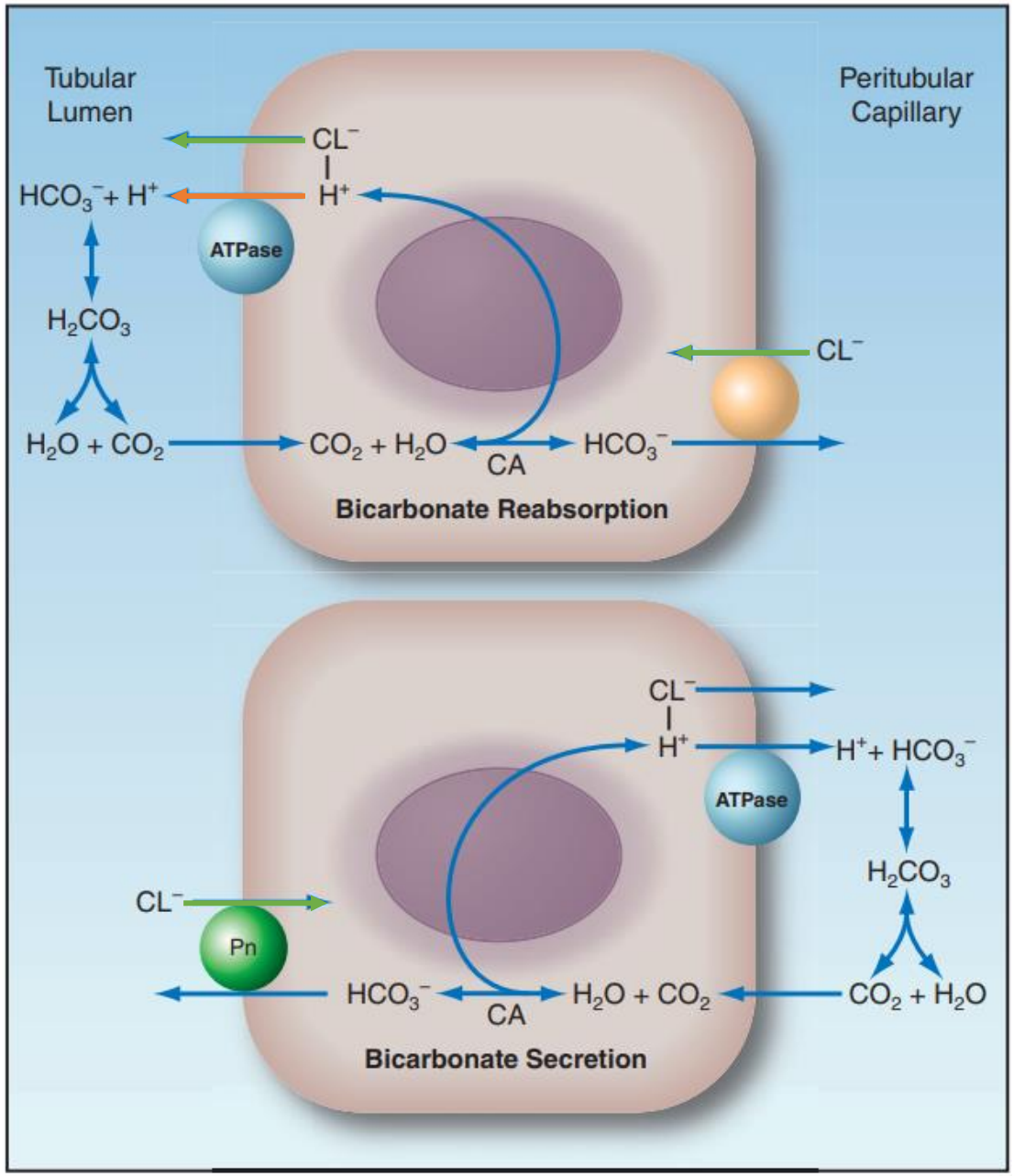


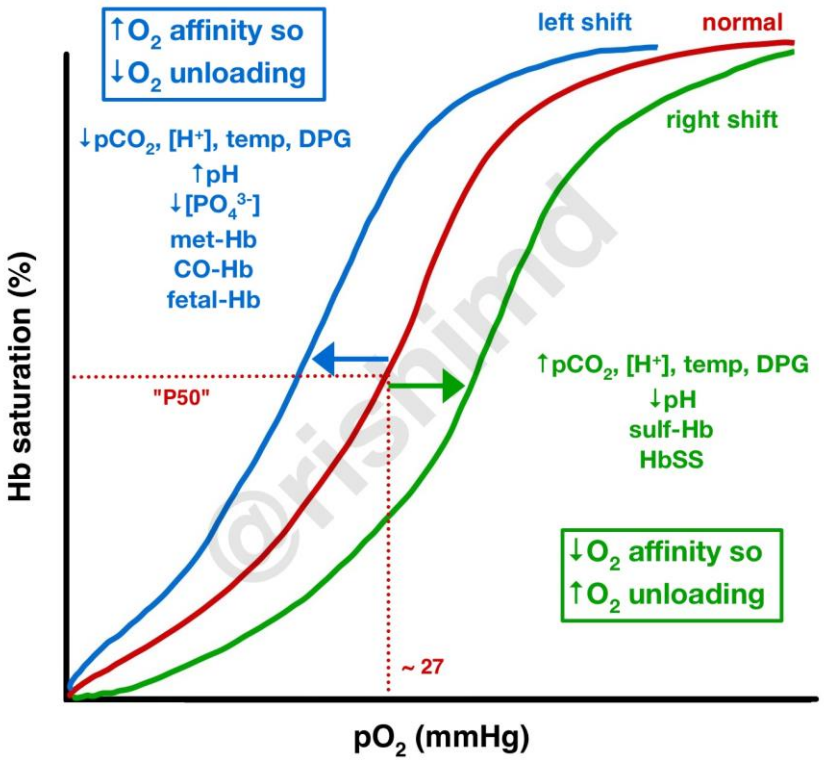
FIGURE 33.1 Mechanisms of bicarbonate reabsorption and secretion in the renal collecting tubules. CA = carbonic anhydrase, Pn = pendrin (the chloride-bicarbonate exchanger). See text for explanation.

Predisposing Conditions

- **Volume Loss.** Activate RAAS.
- **Loss of Gastric Acid.** Nasogastric suction results in loss of gastric secretions, which are rich in H+, Cl, and K+.
  - Loss of H+ will initiate a metabolic alkalosis, while loss of CL– and K+ will sustain the alkalosis.
- **Diuretics**. Thiazide diuretics and “loop” diuretics promote metabolic alkalosis via chloride and potassium depletion.
  - By increasing sodium loss in urine (natriuresis), and an equivalent amount of chloride is also lost in urine (chloruresis) because urinary chloride excretion usually matches urinary sodium excretion.

Clinical Manifestations

- **Neurologic Manifestations:** depressed consciousness, generalized seizures, paresthesias, and carpopedal spasms.
- Hypoventilation
- Oxyhemoglobin Dissociation Curve



Classification

Table 33.1 Classification of Metabolic Alkalosis

Category	Criteria	Conditions
Chloride-Responsive volume depletion	Urine [CL^-] <15 mEq/L	Vomiting Nasogastric suction Choluretic diuretics Volume depletion Laxative abuse
Chloride-Resistant Volume expansion.	Urine [CL^-] >25 mEq/L	Primary aldosteronism Licorice ingestion Severe hypokalemia (plasma K^+ <2 mEq/L)

Chloride-Resistant Alkalosis

- Hypertensive:

Renin	Aldosterone	
Low	High	Primary hyperaldosteronism
High	Low	Secondary hyperaldosteronism
Low	Low	High cortisol: Cushing syndrome. Liddle's syndrome: Spironolactone-resistant, pseudo-aldosteronism.

- Hypo- or normotensive
  - Bartter syndrome: similar to excessive use of loop diuretic.
  - Gittleman syndrome: similar to excessive use of thiazide diuretic. 有高血鈣低尿鈣

Management

- Saline Infusion
- Saline-Resistant Alkalosis
  - Potassium Chloride
  - Acetazolamide
  - Hydrochloric Acid Infusion

Management

- **Saline Infusion**
- Saline-Resistant Alkalosis
  - Potassium Chloride
  - Acetazolamide
  - Hydrochloric Acid Infusion

Table 33.2 Saline Infusions for Metabolic Alkalosis

Step 1. Estimate the chloride deficit:

$$Cl^- \text{ deficit (mEq)} = 0.2 \times \text{wt (kg)} \times (100 - \text{plasma } [Cl^-])$$

Step 2. Determine the replacement volume of saline:

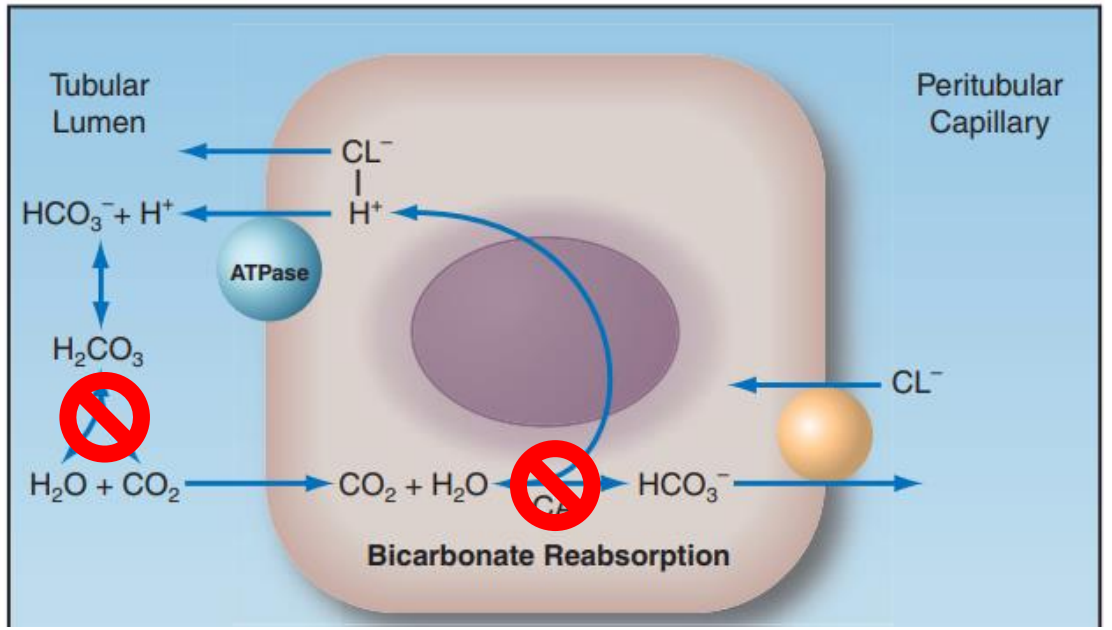
$$\text{Volume of 0.9\% NaCl (L)} = \frac{Cl^- \text{ deficit}}{154}$$

Step 3: Rate of replacement: 100 mL/hr > hourly fluid losses.

Management

- Saline Infusion
- **Saline-Resistant Alkalosis**
  - Potassium Chloride
  - Acetazolamide
  - Hydrochloric Acid Infusion

It is important to emphasize that diuretic-induced hypokalemia can be resistant to potassium replacement if there is concurrent magnesium depletion



A FINAL WORD

It's Chloride

The final word in metabolic alkalosis is *chloride*, the principal element in both the maintenance and correction of metabolic alkalosis in ICU patients. Chloride plays an important role in metabolic acidosis as well. In addition to its role in acid-base balance, chloride is the second most abundant electrolyte in the extracellular fluid, and is a major factor in determining the osmolality and volume of extracellular fluid. In light of chloride's participation in numerous physiological processes, a recent review of chloride suggested that it is the "queen of electrolytes" (24). Although a more appropriate term might be warranted, it highlights an increasing awareness that chloride is much more than sodium's passive partner in the extracellular fluid.