Acid-Base Regulation-II

Chapter 31
Unit V

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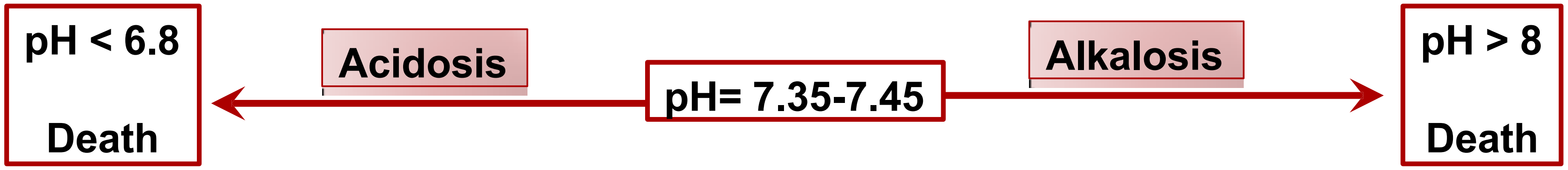
Respiratory regulation of acid-base balance

Alkalosis= excess removal of H+ from the body fluids

Acidosis= excess addition of H+

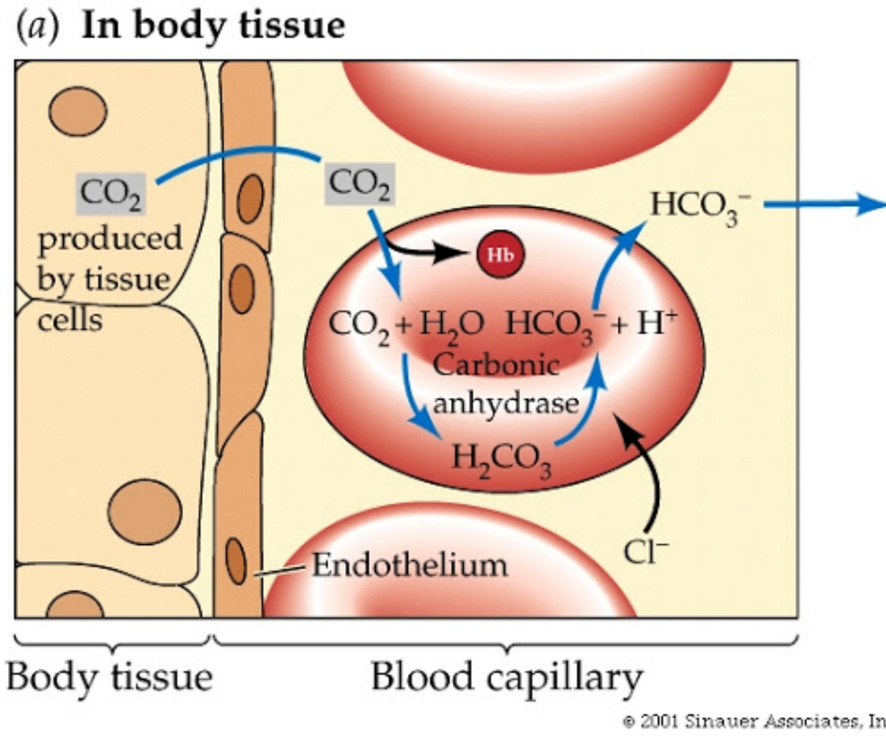


Respiratory Regulation of A/B

- 2nd line of defence against acid-base disturbances in the body.
- By modulating CO_2 excretion.
- Normally, PCO2 = 40 mmHg (35-45 mmHg).
- ↑CO2 formation→ ↑ECF CO2 → ↑ ECF PCO2 &

Vice versa.

↑ECF CO2→ ↑H2CO3→ ↑H+



$$pH \propto \frac{HCO3}{PCO2}$$

Respiratory regulation of A/B

- Response occurs within 3-12 minutes.
- ↑↑ ventilation (RR) → ↓↓ PCO_2 → ↑PH

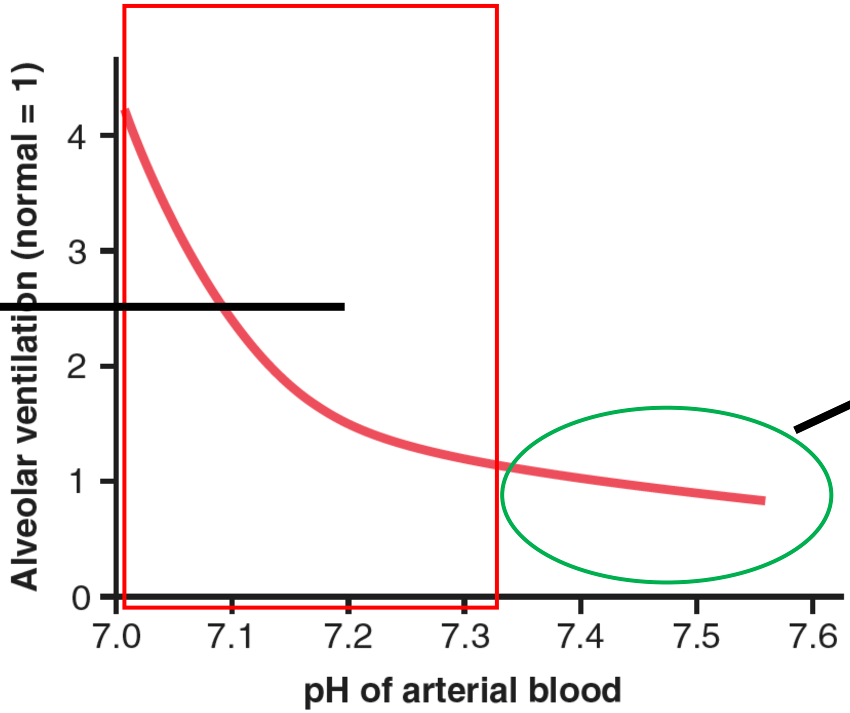
- ↓↓ ventilation (RR) → accumulation of CO_2→↑↑ P_{CO_2}→ ↓PH

Respiratory Regulation of A/B

$$pH \propto \frac{HCO3}{PCO2}$$

- ↓↓ $[H^+]$ → ↑pH → ↓↓ ventilation (RR) → accumulation of CO_2→↑↑ P_{CO_2}.
- ↑↑ $[H^+]$ → ↓pH → ↑↑ ventilation (RR) → ↓↓ P_{CO_2}

More changes in RR at low pH



Less change (↓) in RR with high pH

↓

↓PO2

↓

↑↑ ventilation

Respiratory compensation is less effective at pH increase

Renal Regulation of Acid-Base Balance

- **3rd line of defence against acid-base disturbances and the most powerful.**
- **Kidneys conserve HCO3 - and excrete acidic or basic urine depending on body needs**

↓ ↓

↓ acid in ECF **↓ base in ECF**

- Kidneys eliminate non-volatile acids (H_2SO_4, H_3PO_4) (~ 80 mmol/day)
- Filtration of HCO_3^- (~ 4320 mmol/day)
- Secretion of H^+ (~ 4400 mmol/day)
- Reabsorption of HCO_3^- (~ 4319 mmol/day)
- Production of new HCO_3^- (~ 80 mmol/day)
- Excretion of HCO_3^- (1 mmol/day)

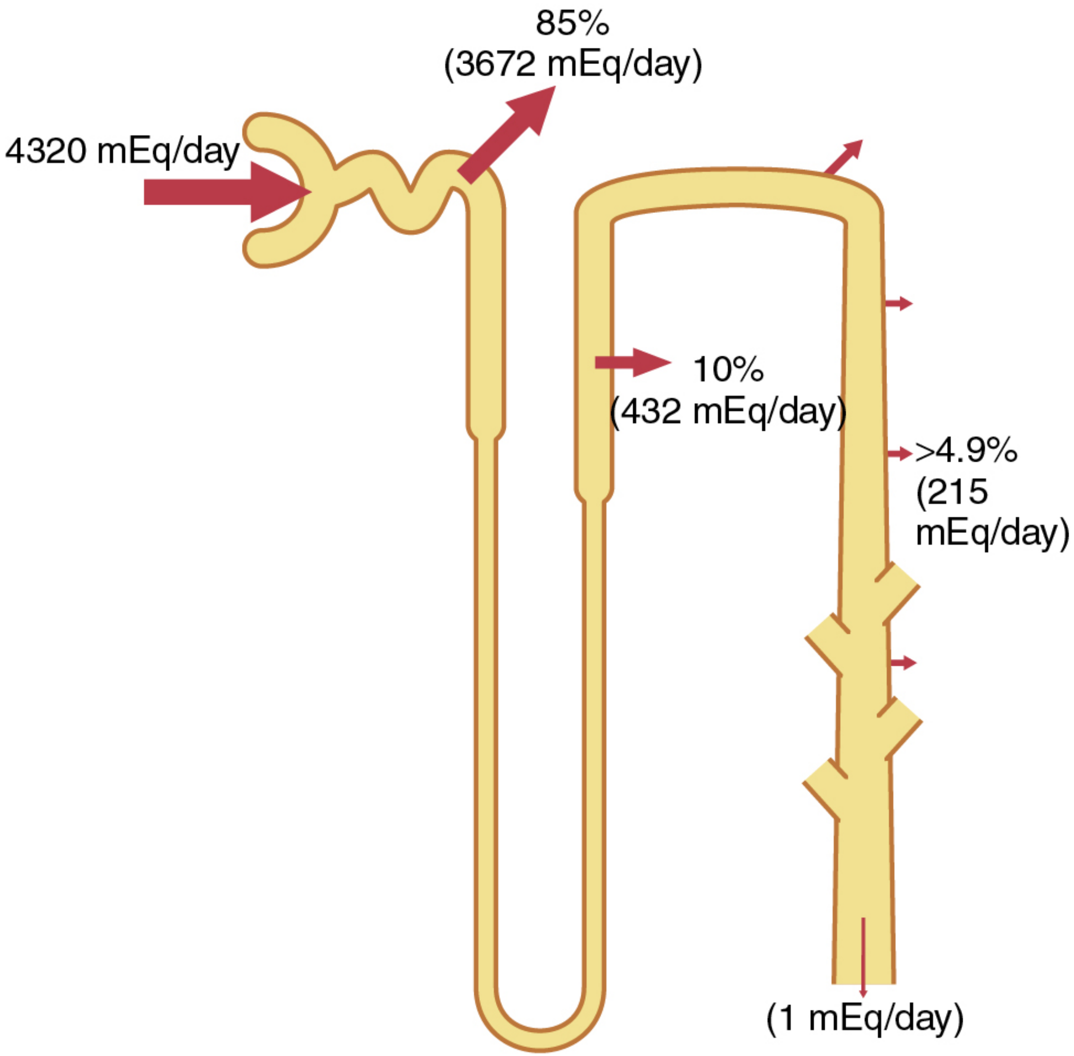
H+ is not excreted as free H+ but rather in combination with other urinary buffers, especially phosphate and ammonia.

Renal compensation of Acid-Base Balance

- Acidosis:
  - increased H^+ secretion
  - increased HCO_3^- reabsorption
  - production of new HCO_3^-

- Alkalosis:
  - decreased H^+ secretion
  - decreased HCO_3^- reabsorption
  - loss of HCO_3^- in urine

HCO3 reabsorption & secretion of H^+ in renal tubule



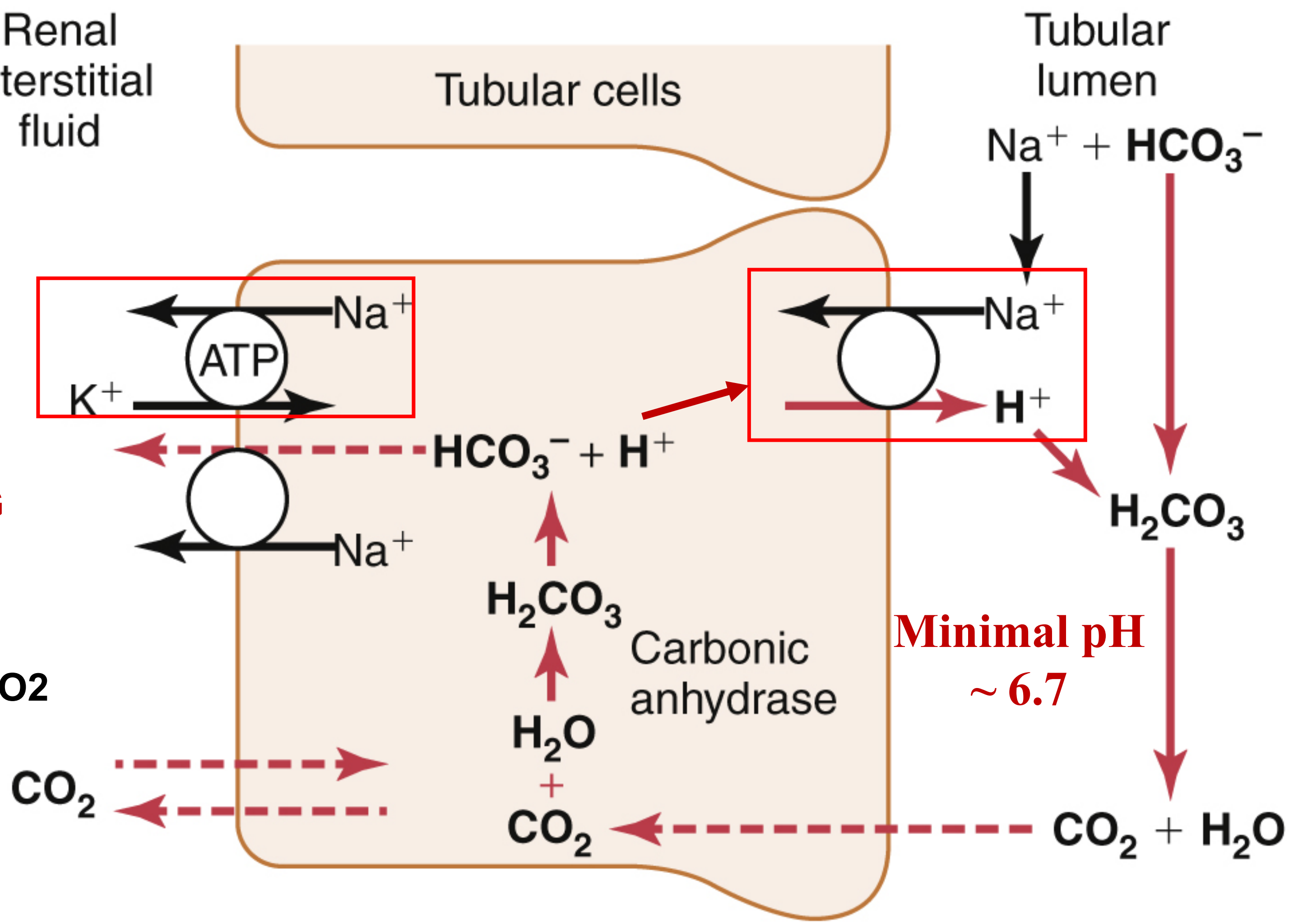
<u>Key point:</u>
For each HCO_3^- reabsorbed, there must be a H^+ secreted

Mechanisms of HCO_3^- reabsorption and Na^+-H^+ exchange in PT, thick loop of Henle & early DT

Na-K ATPase→ Dec. IC Na→ [] gradient
↓
H+ secretion into the tubular fluid by Na-H counter-transport

NO CHANGE IN LUMINAL pH (EXCEPT COLEECTING DUCTS)

HCO3 reabsorption starts with formation of H2CO3→ CO2 reabsorption→ Na-HCO3 co-transport
Replacement of filtered HCO3



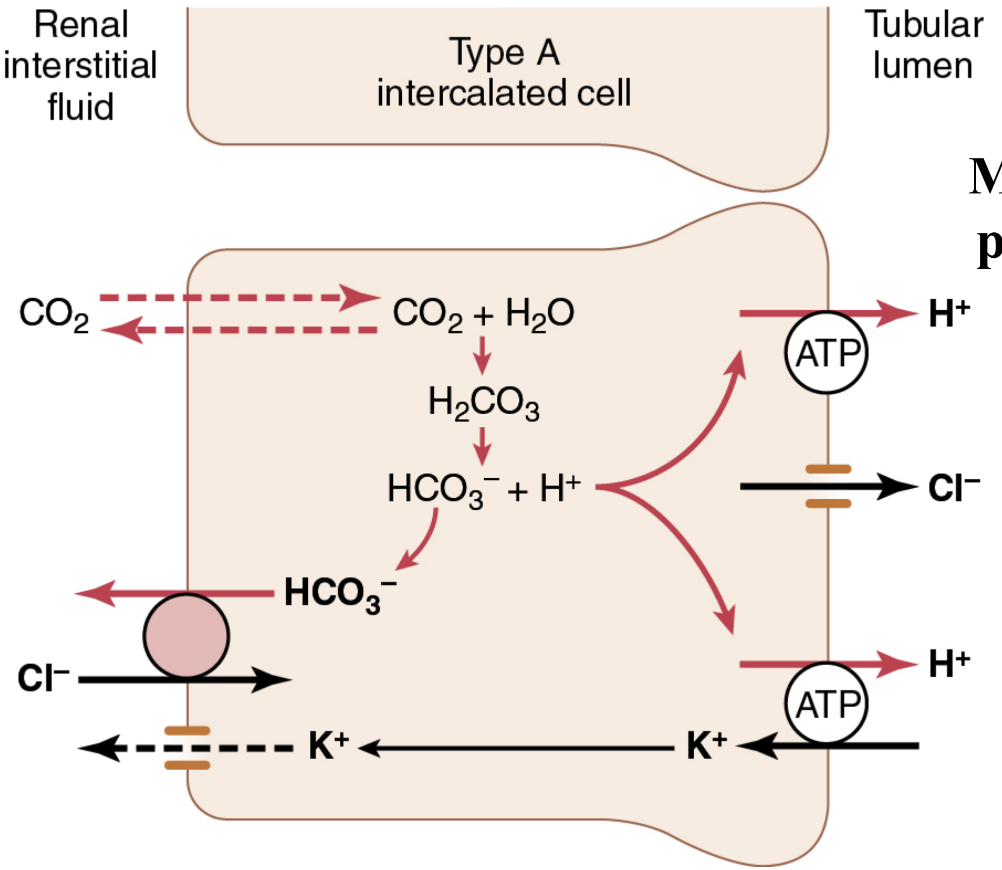
HCO_3^- reabsorption and H^+ secretion in intercalated cells of late distal and collecting tubules

Primary Active secretion of H+ by H+–ATPase & and H+-K+-ATPase

CHANGE IN LUMINAL pH→acidification of U

one HCO3 is absorbed for each H+ secreted→HCO3-Cl counter transport (PT, LH,CD)

one Cl is passively secreted H+.



Minimal pH ~4.5

- Only a limited number of H^+ can be excreted in its free form in urine.
- Lowest possible urine pH=4.5 → ≈ 0.04 mmol/L of free H^+.
- ***How does the kidney excrete the extra H^+?***

Non-Bicarbonate Buffers in the Tubular Lumen

The extra H^+ secreted will need to be buffered in the tubular lumen

2 main non-bicarbonate buffers in the tubule

Filtered

Phosphate buffer system

$$H_2PO_4^- \leftrightarrow HPO_4^{-2} + H^+$$

(acid) *(base)*

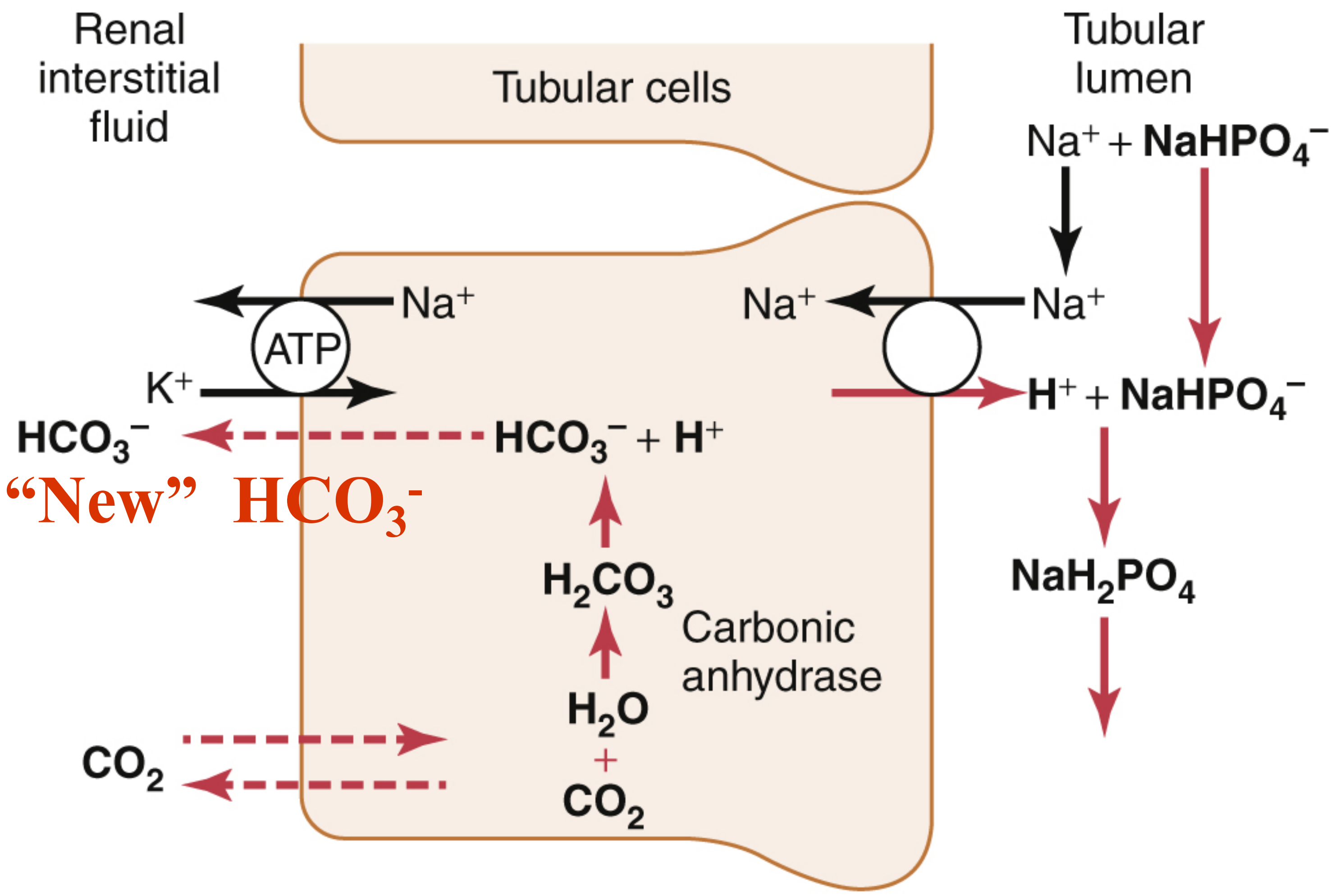
Synthesized

Ammonia buffer system

$$NH_4^+ \leftrightarrow NH_3 + H^+$$

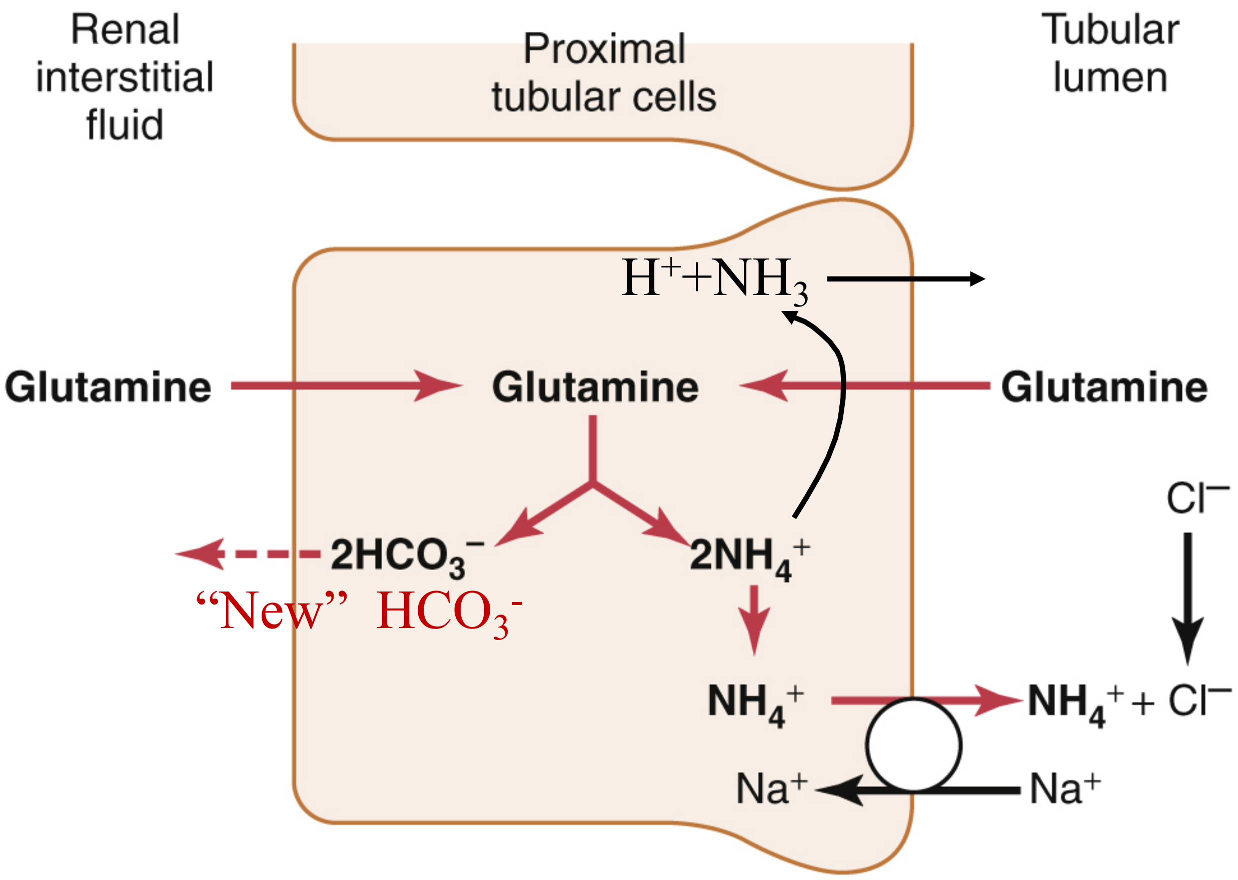
(acid) *(base)*

Buffering of secreted H^+ by filtered phosphate ($NaHPO_4^-$) and generation of "new" HCO_3^-

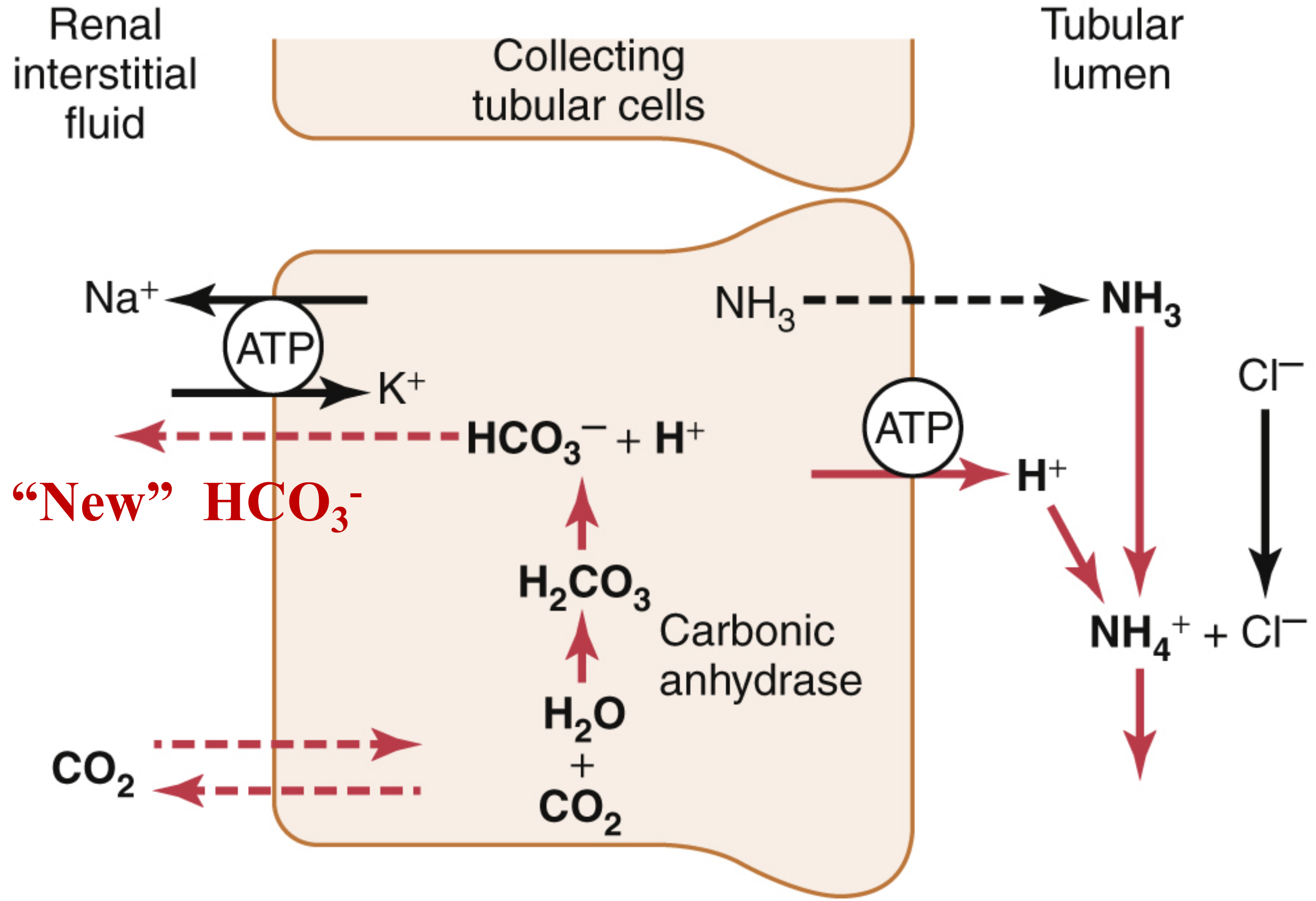


Production and secretion of NH_4^+ and HCO_3^- by proximal, thick loop of Henle and distal tubules

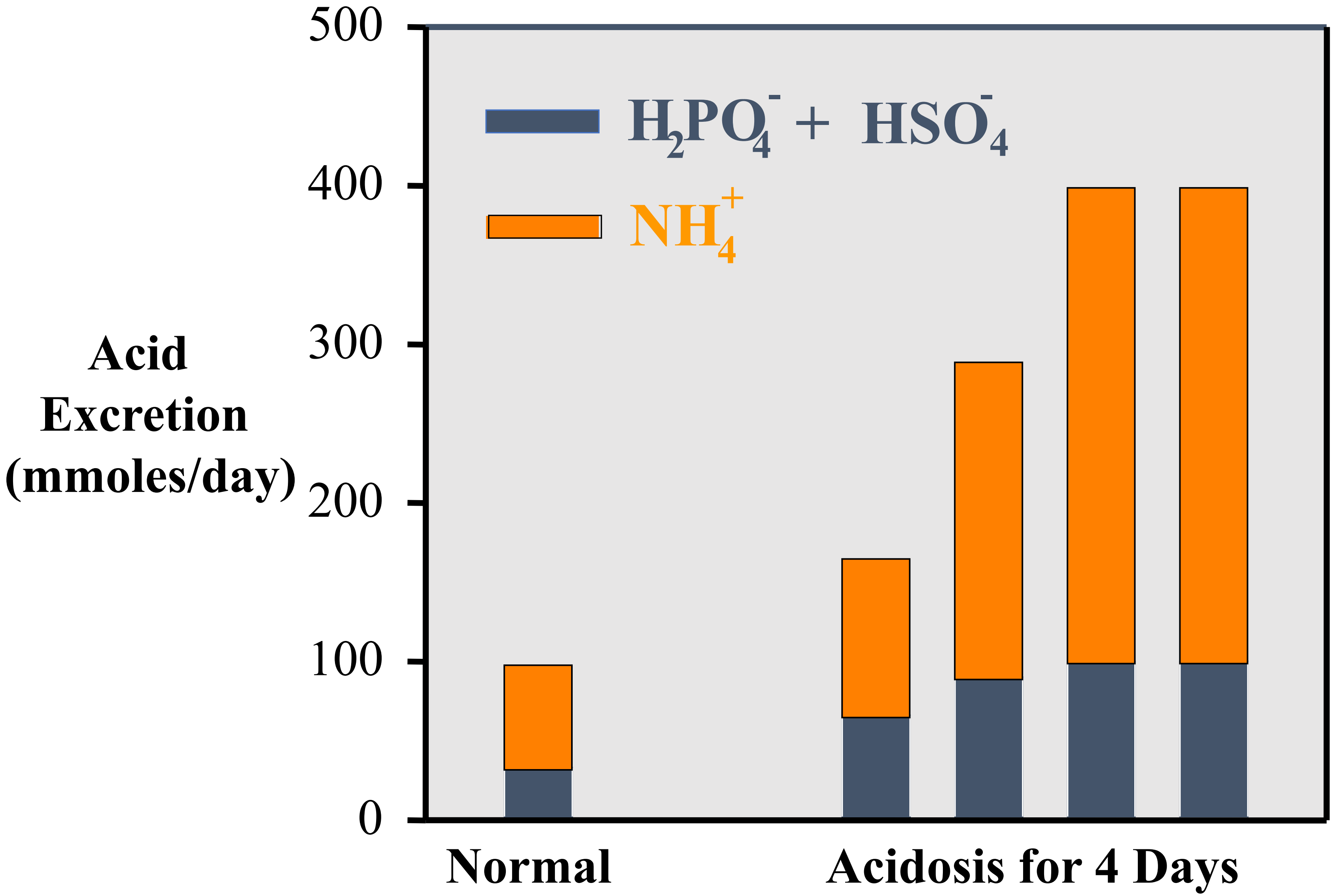
- Quantitatively, NH4+ system is more important than the phosphate buffer system for H^+ excretion in urine.
- It is the most important system in case of **acidosis**.
- Ammoniagenesis→from glutamine



Buffering of H^+ by NH_3 in collecting tubules



Phosphate and Ammonium Buffering In Chronic Acidosis



Quantifying Renal Acid-Base Excretion

HCO_3 excretion=urine flow rate X [$HCO3_U$].
HCO_3 excretion= adding an H^+ to the blood

amount of **new** HCO3 added to blood =H^+ excretion with non-HCO3 buffers

= NH4+ excretion_+phosphate excretion

= V x[NH4u]+ urinary titrable acid ← NaOH, to a pH of 7.4 number of milliequivalents of NaOH= number of milliequivalents of secreted H to combine with phosphate

Net acid excretion= NH4 excretion+ Urinary titratable acid- HCO3 excretion → =adding an H+ to the blood

net acid excretion must equal the nonvolatile acid production in the body.

Quantifying Renal Acid-Base Excretion

Net acid excretion= NH4 excretion+ Urinary titratable acid- HCO3 excretion

In acidosis→net acid excretion??
NH4 excretion ↑↑↑
↓
Net acid excretion ↑
Net acid excretion=HCO3 added to blood

In alkalosis→net acid excretion??
NH4 excretion=0
HCO3 excretion ↑↑↑
↓
Net acid excretion is negative
=HCO3 is lost & NO new HCO3 formation

Table 31-2 Plasma or Extracellular Fluid Factors That Increase or Decrease H^+ Secretion and HCO_3^- Reabsorption by the Renal Tubules

Increase H^+ Secretion and HCO_3^- Reabsorption	Decrease H^+ Secretion and HCO_3^- Reabsorption
↑ P_{CO_2}	↓ P_{CO_2}
↑ H^+, ↓ HCO_3^-	↓ H^+, ↑ HCO_3^-
↓ Extracellular fluid volume	↑ Extracellular fluid volume
↑ Angiotensin II	↓ Angiotensin II
↑ Aldosterone	↓ Aldosterone
Hypokalemia	Hyperkalemia

Renal correction of acidosis

	pH	H^+	P_{CO_2}	HCO_3^-
Normal	7.4	40 mEq/L	40 mm Hg	24 mEq/L
	7.35-7.45		35-45	22-26

Acidosis → ↓pH

$$pH \propto \frac{HCO3}{PCO2}$$

	Acidosis pH< 7.35	
Type	Respiratory	Metabolic
Change	↑PCO2	↓ HCO3
Causes	Hypoventilation- respiratory centers damage Airways obstruction Impaired exchange of gases Neuromuscular dis	excessive acid →Metabolic dis (e.g DM, shock)/Ingestion of Acids→aspirin/Impaired acid secretion HCO3 loss→ diarrhea & RF
Compensation ↑ pH	Renal→↑HCO3 reabsorption	↑HCO3 reabsorption Respiratory→ hyperventilation
Diagnosis	pH ↓ ↑PCO2 ↑HCO3	pH ↓ ↓PCO2 ↓ HCO3

Renal correction of alkalosis

	pH	H^+	PCO_2	HCO_3^-
Normal	7.4	40 mEq/L	40 mm Hg	24 mEq/L
	7.35-7.45		35-45	22-26

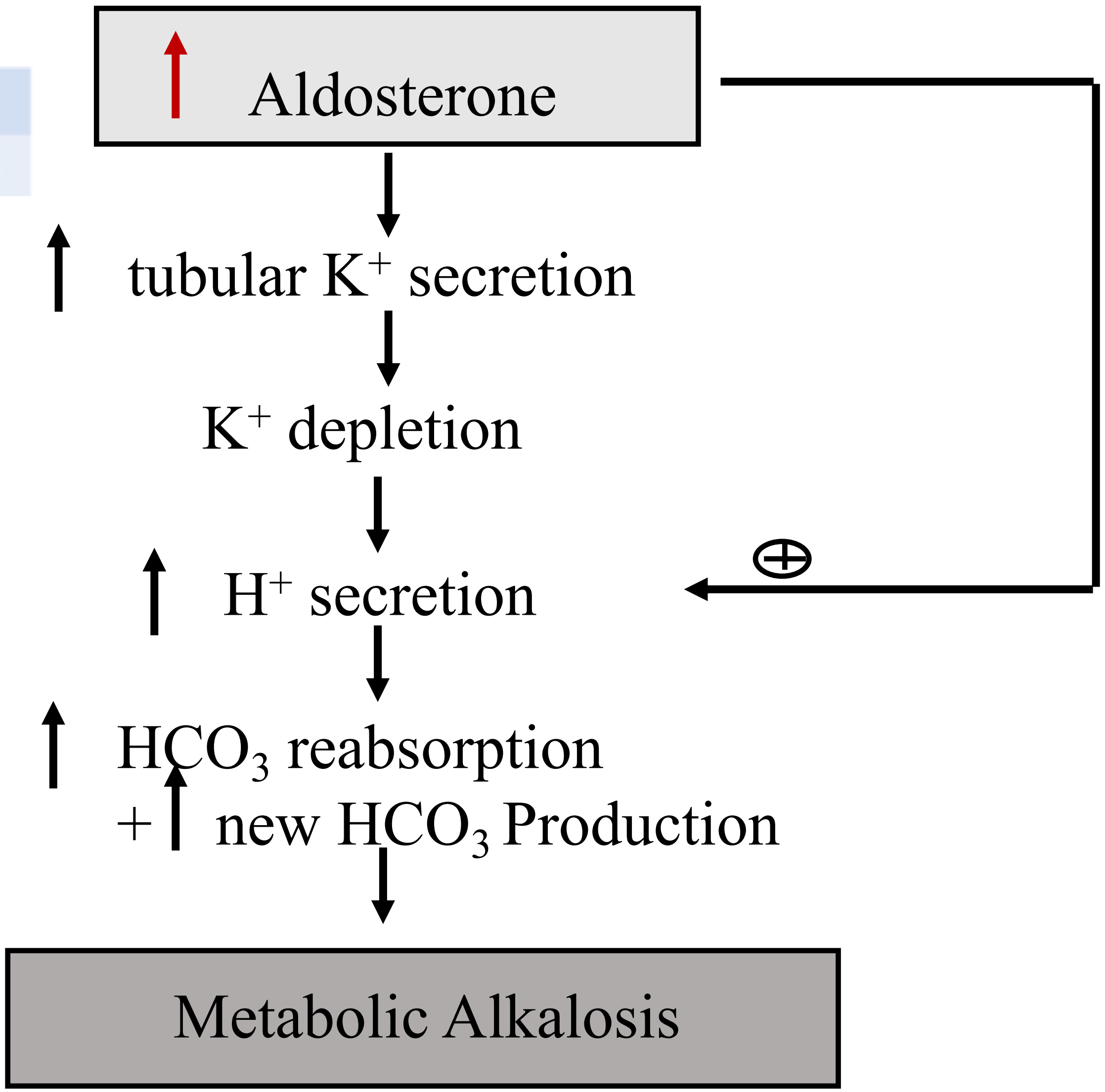
Alkalosis → ↑pH

$$pH \propto \frac{HCO3}{PCO2}$$

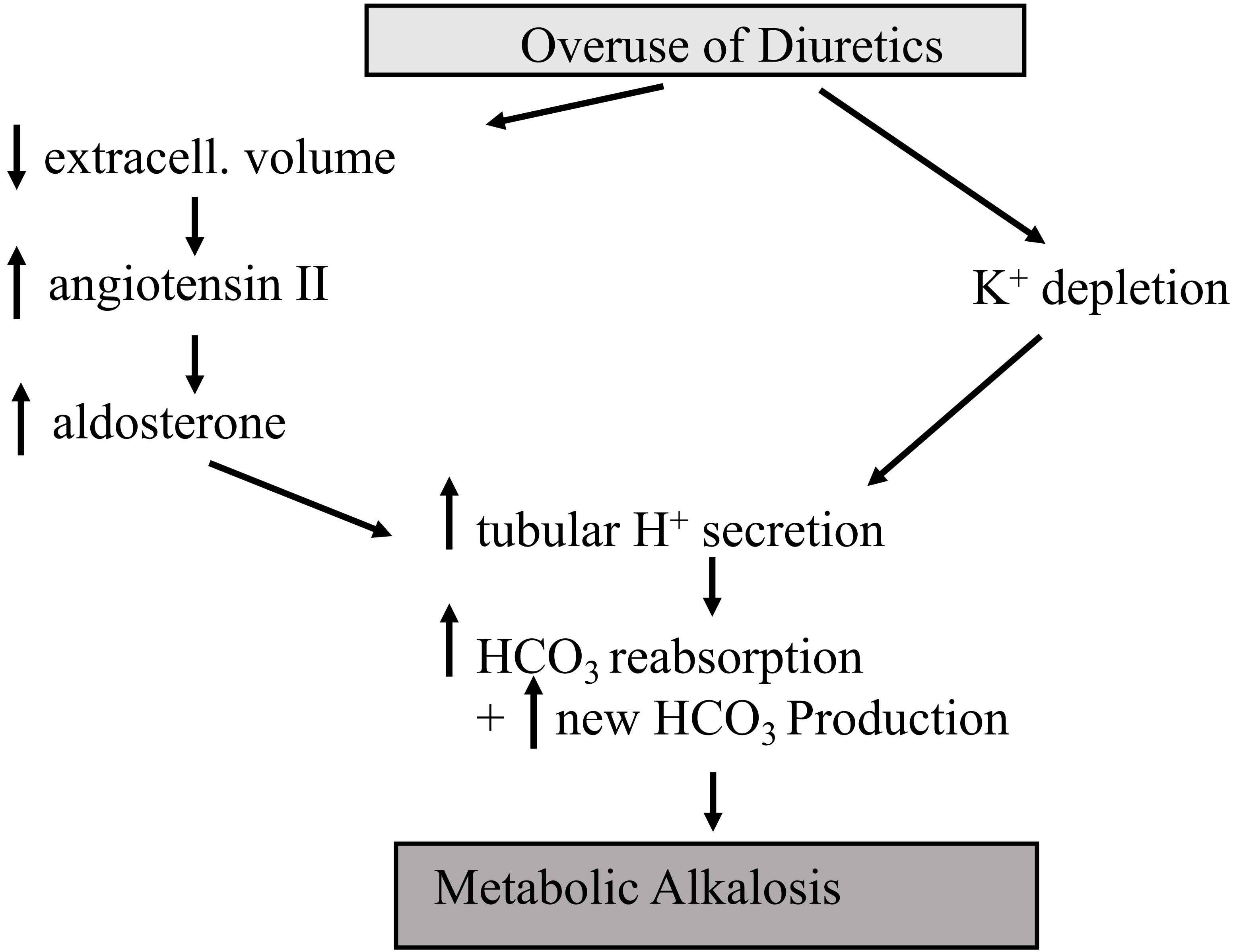
	Alkalosis pH> 7.45	
Type	Respiratory	Metabolic
Change	↓PCO2	↑HCO3
Causes	Hyperventilation-fever, psychoneurosis, meningitis, early exercise, ascending to high altitude	-Acid loss→persistent vomiting -↑HCO3 →thiazides/loop diuretics-Hypovolemia-Ingestion of alkaline drugs (NaHCO3) ↑aldosterone & cortisol
Compensation ↓ pH	Renal→↓HCO3 reabsorption	Renal→↓HCO3 reabsorption Respiratory→ hypoventilation
Diagnosis	pH ↑ ↓PCO2 ↓ HCO3	pH ↑ ↑PCO2 ↑HCO3

Hyperaldosteronism (aldosteronism) and acid base disturbances

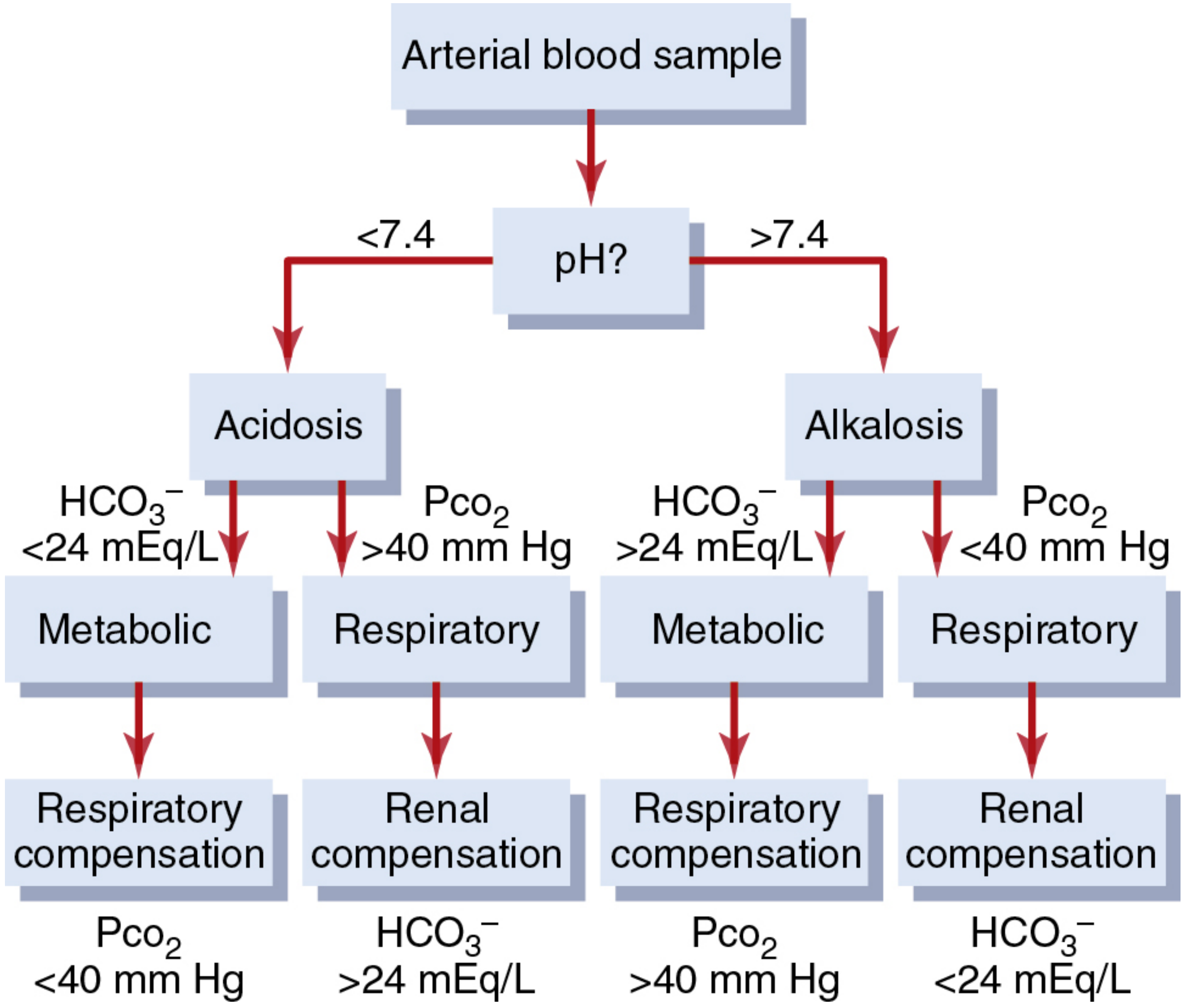
Hormone	Effects
Aldosterone	↑ NaCl, H_2O reabsorption, ↑ K^+ secretion, ↑ H^+ secretion

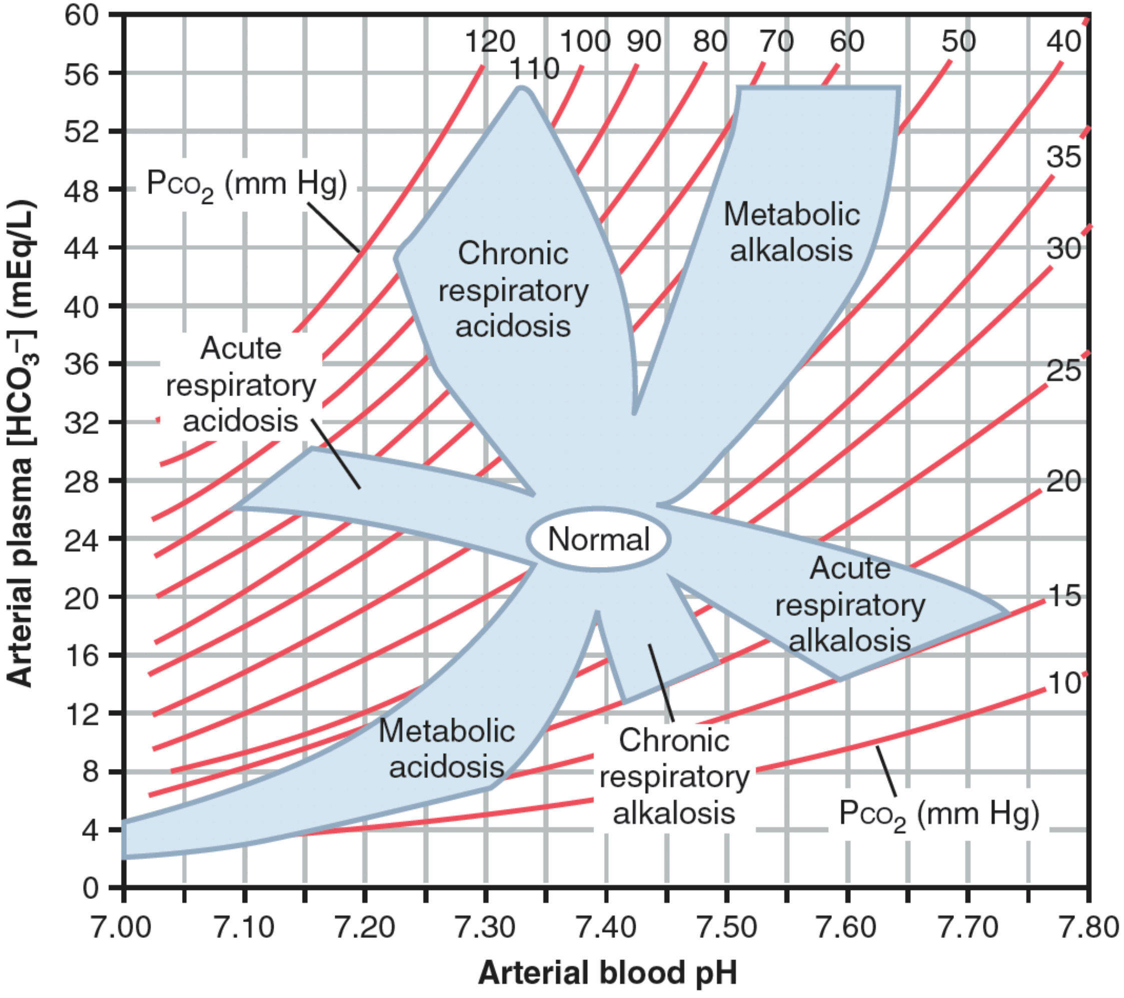


Acid base disturbances caused by overuse diuretics



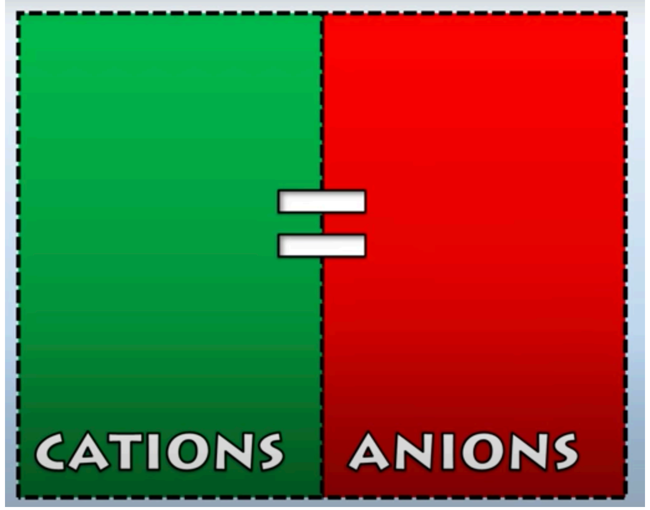
Classification of Acid-Base Disorders from plasma pH, pCO_2, and HCO_3^-





Mixed disorders

Anion Gap as a Diagnostic Tool



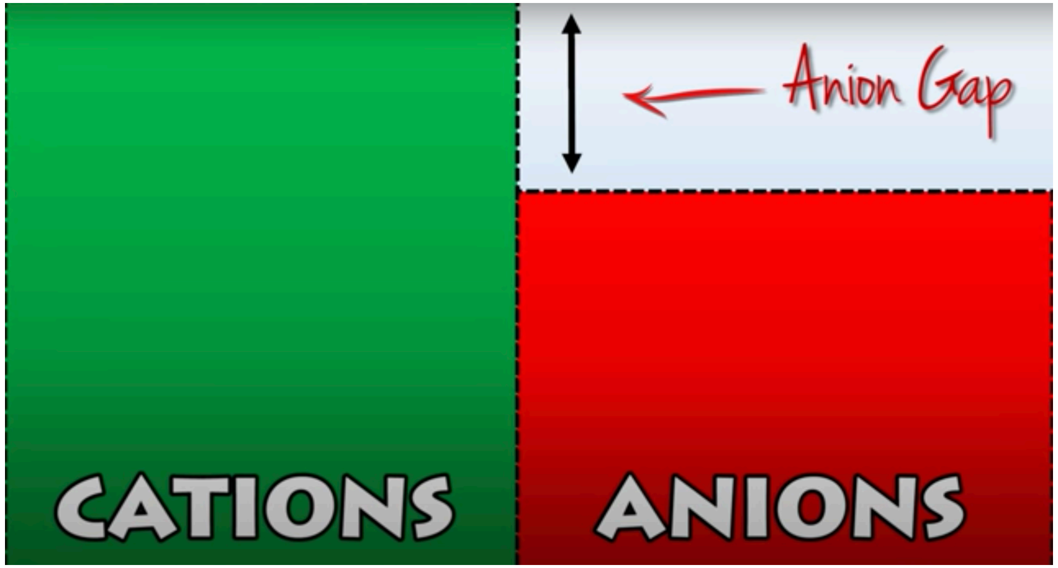
In body fluids: total cations = total anions

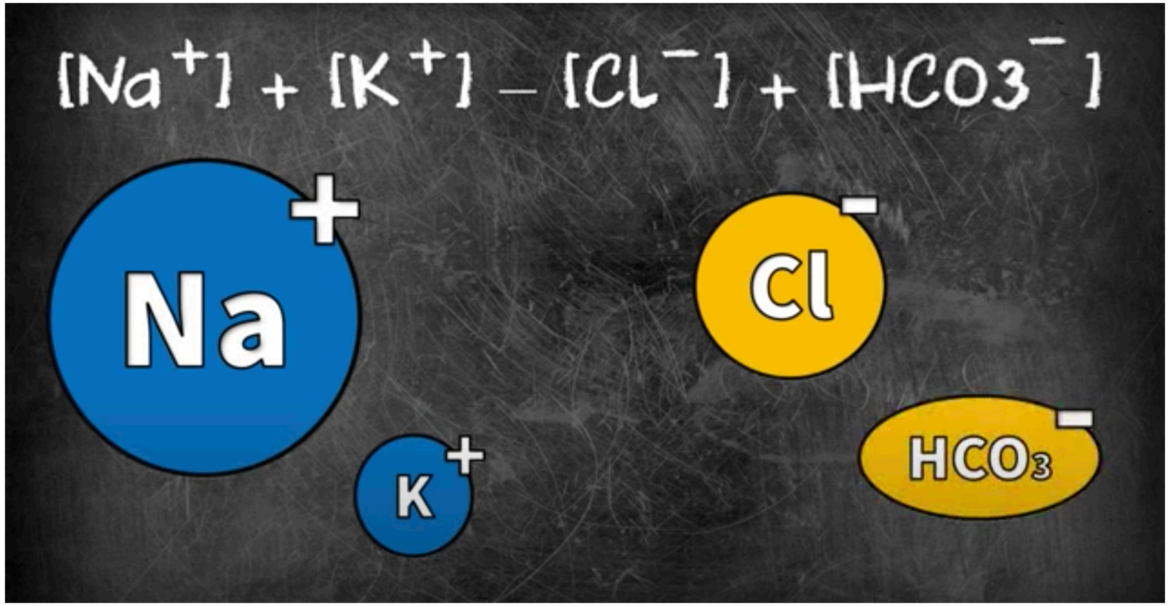
$Na^+ = Cl^- + HCO_3^-$ + unmeasured anions

unmeasured anions = $Na^+ - Cl^- - HCO_3^-$ = anion gap

= 142 - 108 - 24 = 10 mEq/L

Normal anion gap = 8 - 16 mEq / L





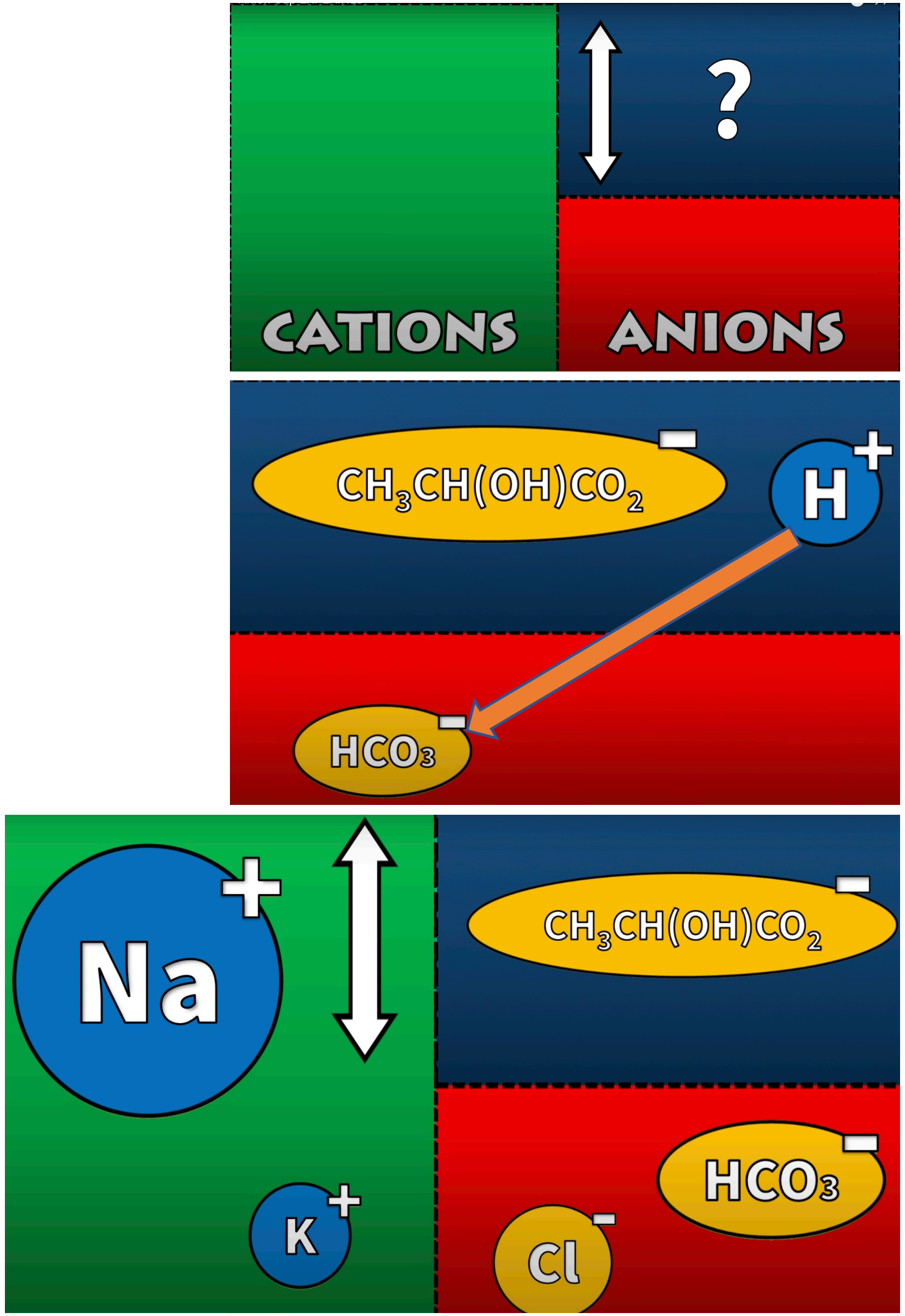
Anion Gap in Metabolic Acidosis

- ↑ anion gap → ↑unmeasured anions (organic acids)

anion gap = Na^+ − Cl^- − ↓ HCO_3^-

normochloremic metabolic acidosis

Increased Anion Gap (Normochloremia)
Diabetes mellitus (ketoacidosis)
Lactic acidosis
Chronic renal failure
Aspirin (acetylsalicylic acid) poisoning
Methanol poisoning
Ethylene glycol poisoning
Starvation

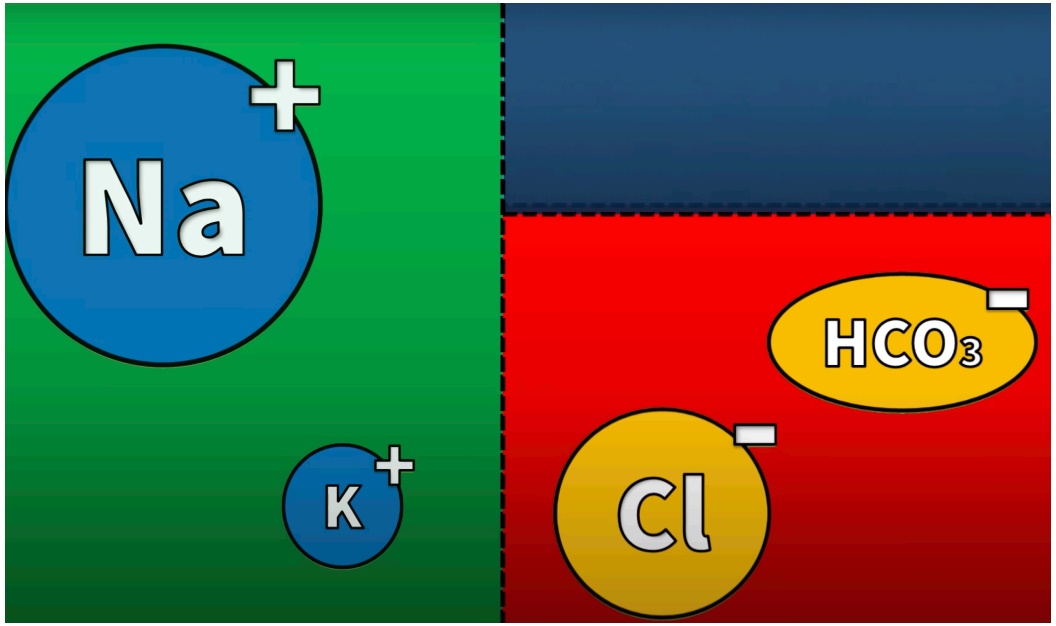


Anion Gap in Metabolic Acidosis

- loss of HCO_3^- = normal anion gap

anion gap = Na^+ - ↑Cl^- - ↓HCO_3^-
hyperchloremic metabolic acidosis

Normal Anion Gap (Hyperchloremia)
Diarrhea
Renal tubular acidosis
Carbonic anhydrase inhibitors
Addison's disease



Question

	pH	H^+	P_{CO_2}	HCO_3^-
Normal	7.4	40 mEq/L	40 mm Hg	24 mEq/L
	7.35-7.45		35-45	22-26

A patient presents in the emergency room and the following data are obtained from the clinical labs:

plasma pH= 7.15, HCO_3^- = 8 mmol/L, pCO_2= 24 mmHg

This patient is in a state of:

1. metabolic alkalosis with partial respiratory compensation
2. respiratory alkalosis with partial renal compensation
3. metabolic acidosis with partial respiratory compensation
4. respiratory acidosis with partial renal compensation

	pH	H^+	P_{CO_2}	HCO_3^-
Normal	7.4	40 mEq/L	40 mm Hg	24 mEq/L
	7.35-7.45		35-45	22-26

Laboratory values for an uncontrolled diabetic patient include the following:

arterial pH = 7.25 ↓
Plasma HCO_3^- = 12 ↓
Plasma P_{CO_2} = 28 ↓
Plasma Cl^- = 102
Plasma Na^+ = 142

Metabolic Acidosis

Respiratory Compensation

What type of acid-base disorder does this patient have?

What is his anion gap?

Anion gap = 142 - 102 - 12 = 28

Which of the following are the most likely causes of his acid-base disorder?

a. diarrhea

b. diabetes mellitus

c. Renal tubular acidosis

d. primary aldosteronism

Increased Anion Gap (Normochloremia)
Diabetes mellitus (ketoacidosis)
Lactic acidosis
Chronic renal failure
Aspirin (acetylsalicylic acid) poisoning
Methanol poisoning
Ethylene glycol poisoning
Starvation

	pH	H^+	P_{CO_2}	HCO_3^-
Normal	7.4	40 mEq/L	40 mm Hg	24 mEq/L
	7.35-7.45		35-45	22-26

Laboratory values for a patient include the following:

arterial pH = 7.34
Plasma HCO_3^- = 15
Plasma P_{CO_2} = 29
Plasma Cl^- = 118
Plasma Na^+ = 142

Metabolic Acidosis
Respiratory Compensation

What type of acid-base disorder does this patient have?
What is his anion gap?

Anion gap = 142 - 118 - 15 = 9 (normal)

Which of the following are the most likely causes of his acid-base disorder?

a. diarrhea

b. diabetes mellitus

c. aspirin poisoning

d. Chronic renal failure

Normal Anion Gap (Hyperchloremia)
Diarrhea
Renal tubular acidosis
Carbonic anhydrase inhibitors
Addison's disease

	pH	H^+	P_{CO_2}	HCO_3^-
Normal	7.4	40 mEq/L	40 mm Hg	24 mEq/L
	7.35-7.45		35-45	22-26

Two or more underlying causes of acid-base disorder.

pH= 7.60

pCO_2 = 30 mmHg

plasma HCO_3^- = 29 mmol/L

What is the diagnosis?

<u>Mixed Alkalosis</u>

- Metabolic alkalosis : increased HCO_3^-
- Respiratory alkalosis : decreased pCO_2

Question

	pH	H^+	P_{CO_2}	HCO_3^-
Normal	7.4	40 mEq/L	40 mm Hg	24 mEq/L
	7.35-7.45		35-45	22-26

A plasma sample revealed the following values in a patient:

$pH = 7.12$

$PCO_2 = 50$

$HCO_3^- = 18$

diagnose this patient's acid-base status:

acidotic or alkalotic? Acidotic

respiratory, metabolic, or both? Both

Mixed acidosis: metabolic and respiratory acidosis

The end