Acid Base lecture

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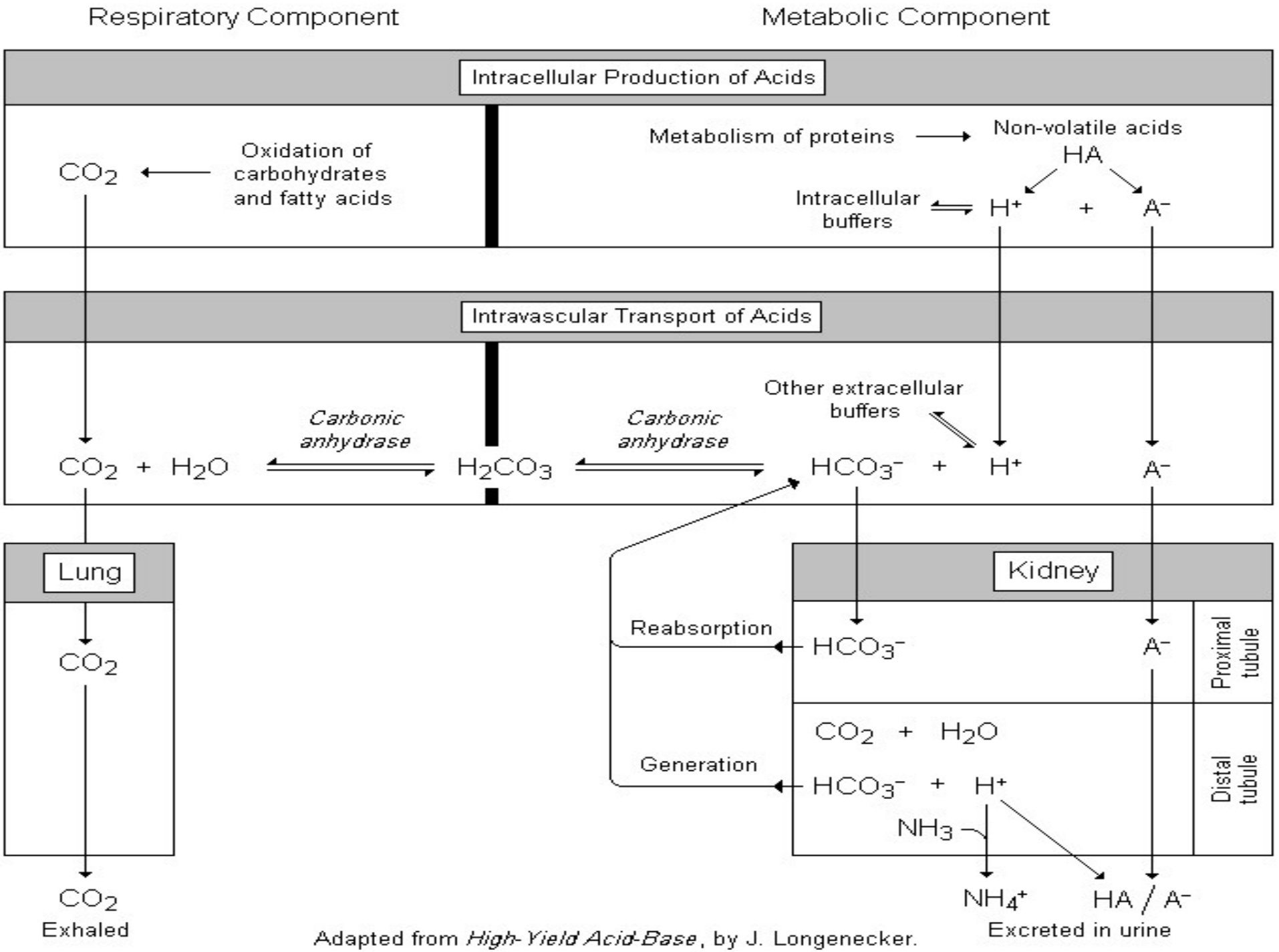


Adapted from *High-Yield Acid-Base*, by J. Longenecker.

$$pH = pK_a + \log \frac{[A^-]}{[HA]} \longrightarrow pH = pK_a + \log \frac{[HCO_3^-]}{[H_2CO_3]} \longrightarrow pH = 6.1 + \log \frac{[HCO_3^-]}{(0.03 \times pCO_2)}$$

Henderson-Hasselbalch Equation

Henderson-Hasselbalch Equation

MASS ACTION EQUATION $$H^+ + HCO_3^- = H_2CO_3 = CO_2 + H_20$$

HENDERSEN-HASSELBACH EQUATION $$pH = pK + \log \frac{HCO_3^-}{.03\,pCO_2}$$

KASSIRER-BLEICH MODIFICATION $$H^+ = 24 \frac{CO_2}{HCO_3^-}$$

pH	7.0	7.1	7.2	7.3	7.4	7.5	7.6	7.7	7.8	7.9	8
H^+	100	80	64	51	40	32	26	20	16	13	10

NORMAL BLOOD GAS VALUES

	ARTERIAL	VENOUS
pH	7.40	< 7.35
pCO_2	40	> 40
HCO_3	24	24
pO_2	> 70	< 60

As dictated by the Henderson-Hasselbalch equation, disturbances in either the respiratory component (pCO_2) or metabolic component (HCO_3^-) can lead to alterations in pH.

Metabolic Acidosis (Too little HCO_3^-)	Metabolic Alkalosis (Too much HCO_3^-)
Respiratory Acidosis (Too much CO_2)	Respiratory Alkalosis (Too little CO_2)

Primary Acid-Base Disorders

Compensation

When a primary acid-base disorder exists, the body attempts to return the pH to normal via the "other half" of acid base metabolism.

Primary metabolic disorder → Respiratory compensation

Primary respiratory disorder → Metabolic compensation

Compensation (continued)

Primary Disorder	Compensatory Mechanism
Metabolic acidosis	Increased ventilation
Metabolic alkalosis	Decreased ventilation
Respiratory acidosis	Increased renal reabsorption of HCO_3^- in the proximal tubule Increased renal excretion of H in the distal tubule
Respiratory alkalosis	Decreased renal reabsorption of HCO_3^- in the proximal tubule Decreased renal excretion of H^+ in the distal tubule

The Four Primary Acid-Base Disturbances

Type of Disturbance	Primary Alteration	Secondary Response	Mechanism of Secondary Response
Metabolic acidosis	Decrease in plasma $[HCO_3^-]$	Decrease in Pa CO_3	Hyperventilation
Metabolic alkalosis	Increase in plasma $[HCO_3^-]$	Increase in $PaCO_3$	Hypoventilation
Respiratory acidosis	Increase in PaCO3	Increase in plasma $[HCO_3^-]$	Acid titration of tissue buffers; transient increase in acid excretion and sustained enhancement of HCO_3^- reabsorption by kidney
Respiratory alkalosis	Decrease in Pa CO_3	Decrease in plasma $[HCO_3^-]$	Alkaline titration of tissue buffers; transient suppression of acid excretion and sustained reduction in bicarbonate reabsorption by kidney

Rules of Thumb for Bedside Interpretation of Acid-Base Disorders

Metabolic acidosis	**$PaCO_2$ should fall by 1.0 to 1.5 X the fall in plasma HCO_3^- concentration**
Metabolic alkalosis	**$PsCO_2$ should rise by 0.25 to 1.0 X the rise in plasma HCO_3^- concentration**
Acute respiratory acidosis	**Plasma HCO_3^- concentration should rise by about 1 mmole per liter for each 10 mm Hg increment in $PaCO_2$ ($\pm$ 3 mmoles per liter).**
Chronic respiratory acidosis	**Plasma HCO_3^- concentration should rise by about 4 mmoles per liter for each 10 mm Hg increment in $PaCO_2$ ($\pm$ 4 mmoles per liter).**
Acute respiratory alkalosis	**Plasma HCO_3^- concentration should fall by about 1 to 3 mmoles per liter for each 10 mm Hg decrement in the $PaCO_2$, usually not to less than 18 mmoles per liter.**
Chronic respiratory alkalosis	**Plasma HCO_3^- concentration should fall by about 2 to 5 mmoles per liter per 10 mm Hg decrement in $PaCO_2$ but usually not to less than 14 mmoles per liter.**

REGULATION OF CO_2 (Read also the separate article in the syllabus)

Plasma CO_2 is determined by the rate of metabolic CO_2 production and by alveolar ventilation:

$$pCO_2 = \frac{CO_2 \text{ production}}{\text{alveolar ventilation}} \times .84$$

- *H2 O*  *H+ +OH–*
- Only 1 in 14 million H2O molecules is ionized to H+ and OH-

- When [H+] = [OH-] solution is neutral

$$K = [H^+][OH^-] = 1\text{x}10^{-14}$$

$$K = [H^+]^2 = 1\text{x}10^{-14}$$

In a neutral solution [H+] = $1\text{x}10^{-7}$ M

$$pH = \log\frac{1}{[H^+]} = -\log[H^+]$$

pH of a neutral solution = $-\log(1\text{x}10^{-7}) = 7$

- If pH of solution is <7, acidic
- • If pH of solution is > 7, basic

solution	pH
1M NaOH	14
Human blood	7.4
Coffee	5
Coke	3
1M HCl	0

Acids are compounds that *donate a H+ to* solution

$$HCl \rightleftharpoons H^+ + Cl^-$$

Bases are compounds that accept H+ from solution

$$H^+ + HCO_3^- \rightleftharpoons H_2CO_3$$

So what's the big deal with H+?

- • H+ is very reactive
- • Almost all aspects of cell function can be
- influenced by H+
- • Enzyme reactions are particularly sensitive to [H+]; there is an optimal pH above or below which the enzyme functions poorly
- • Normal extracell pH=7.4
- • Acidosis pH<7.4 (death <6.8)
- • Alkalosis pH>7.4

- The body normally produces some acids:
- – Metabolism of proteins
- – Lactic acid from muscle

- Disturbances of Acid-Base Balance

1. **Respiratory** – changes in CO2

2. Metabolic – no change in CO2

Metabolic Acid-Base Disturbance

1. Metabolic Acidosis

A. Causes
- Diarrhea (loss of HCO_3^-)
- Acid ingestion (aspirin – acetylsalicylic acid)
- Kidney failure to secrete H^+

B. Effects
- CNS depression and coma, death

2. Metabolic Alkalosis

A. Causes
- Vomiting (loss of H^+)

B. Effects
- CNS excitability, muscle tetanus, death

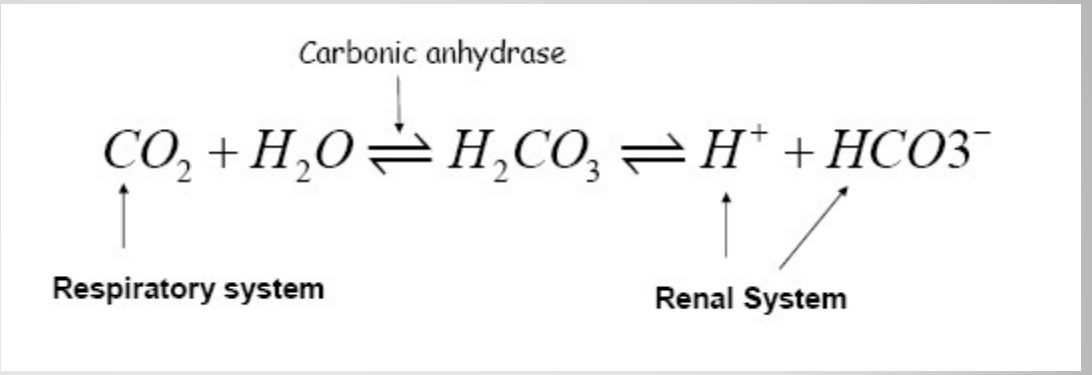
- 1. Fluid Buffering systems
- 2. Kidney
- 3. Respiratory

Acid-Base balance

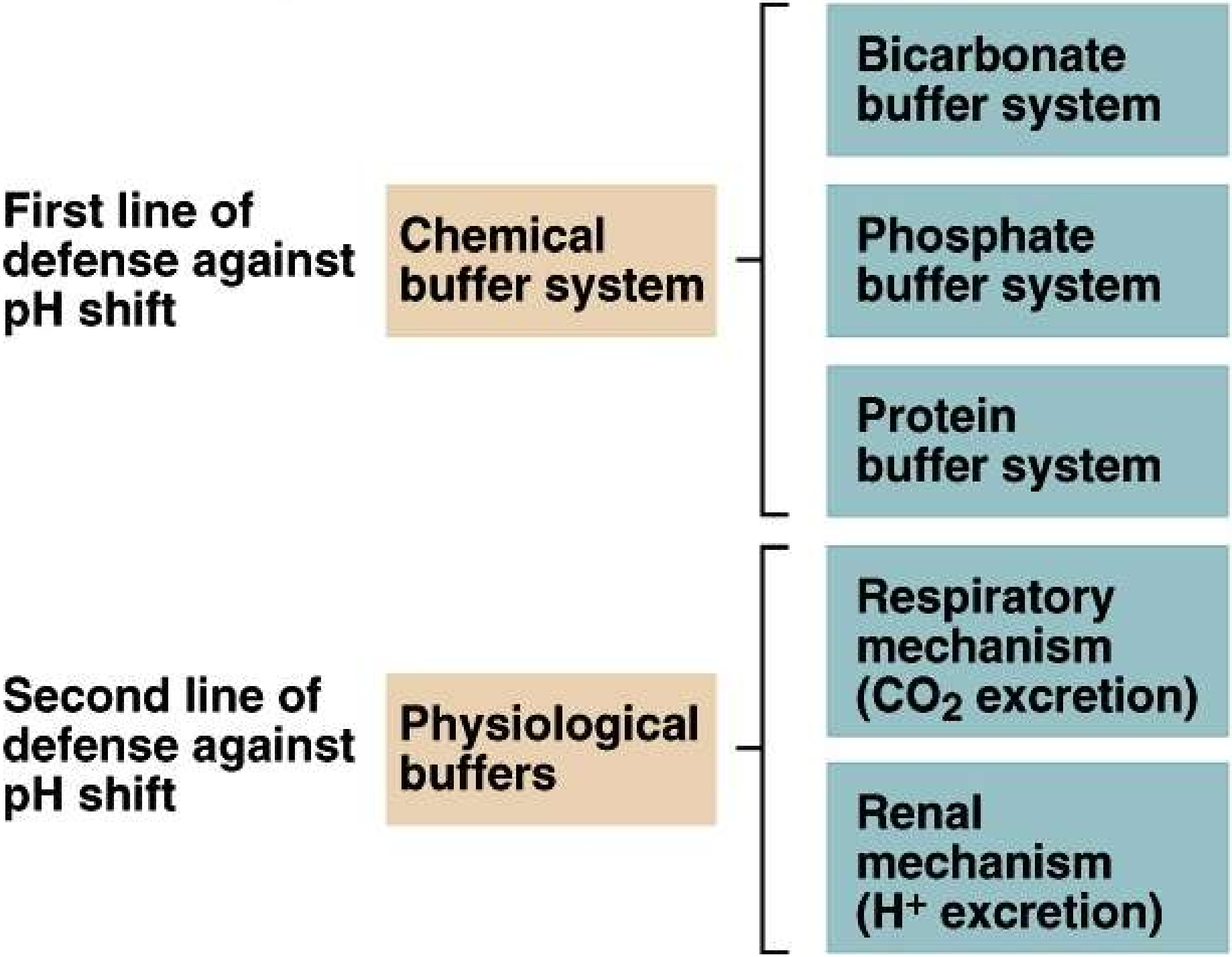
- consists of a mixture of a weak acid and its base
- **Resists changes in pH when small amounts of H+ or OH- are added**

Major physiologically important buffer in blood plasma:

a) Bicarbonate



A buffering system


First line of defense against pH shift
Chemical buffer system
Bicarbonate buffer system
Phosphate buffer system
Protein buffer system
Second line of defense against pH shift
Physiological buffers
Respiratory mechanism (CO_2 excretion)
Renal mechanism (H^+ excretion)

General strategy

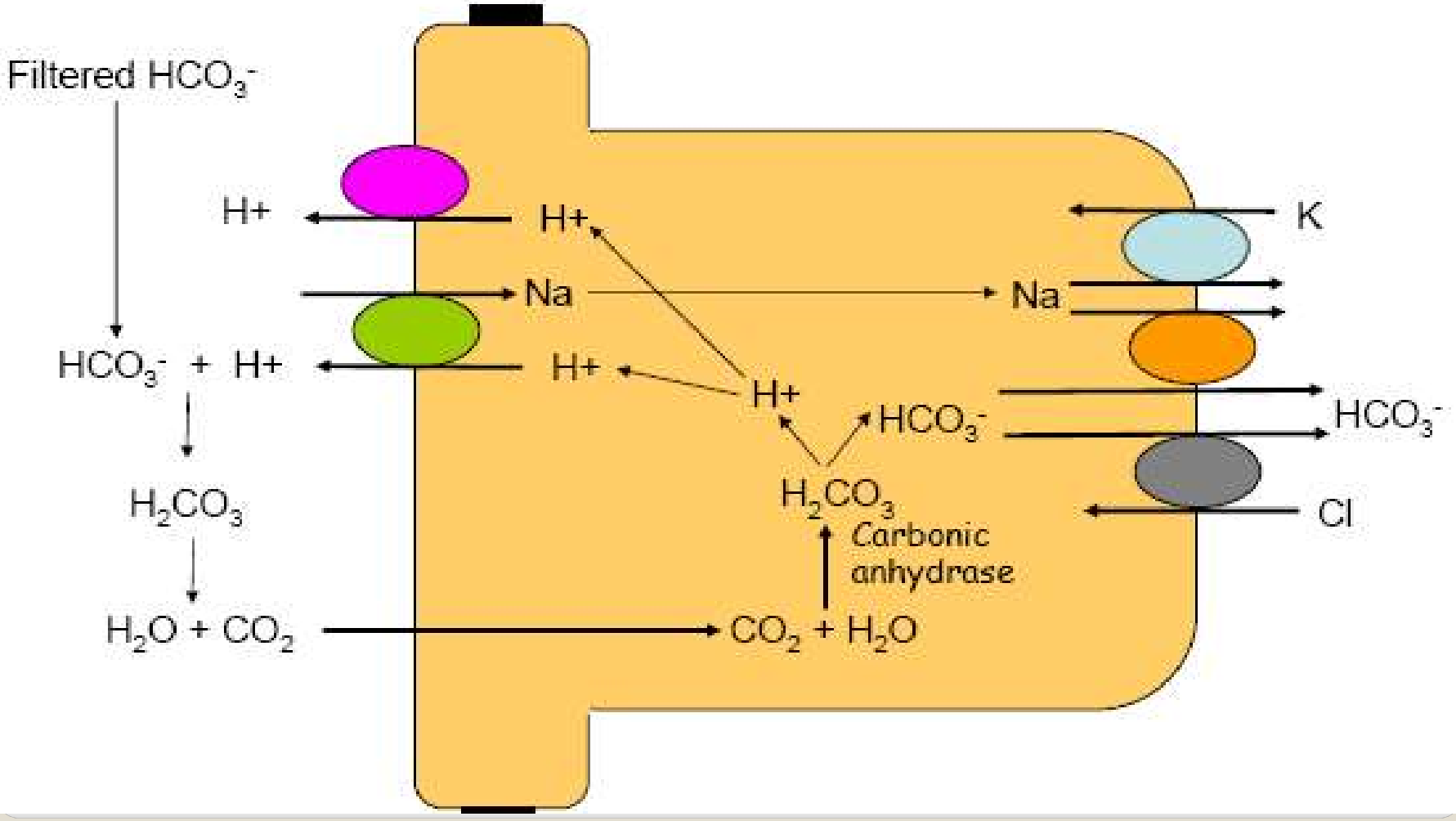
1. Balance the H+ intake and production with H+ excretion

2. Recover HCO3 to preserve buffering capability

Renal regulation of H+ and HCO3

Basic Renal HCO_3^- handling

Almost all the HCO_3^- in the plasma is filtered



1. CO_2 and H_2O form H_2CO_3, which splits into H^+ and HCO_3^-

2. HCO_3^- moves to the interstitial fluid and blood

3. H^+ is secreted into tubule, where it reacts with filtered HCO_3^- to regenerate CO_2 and H_2O

4. For every HCO_3^-
- filtered, an HCO_3^- is formed within the tubular cell & transported to the interstitial fluid and blood

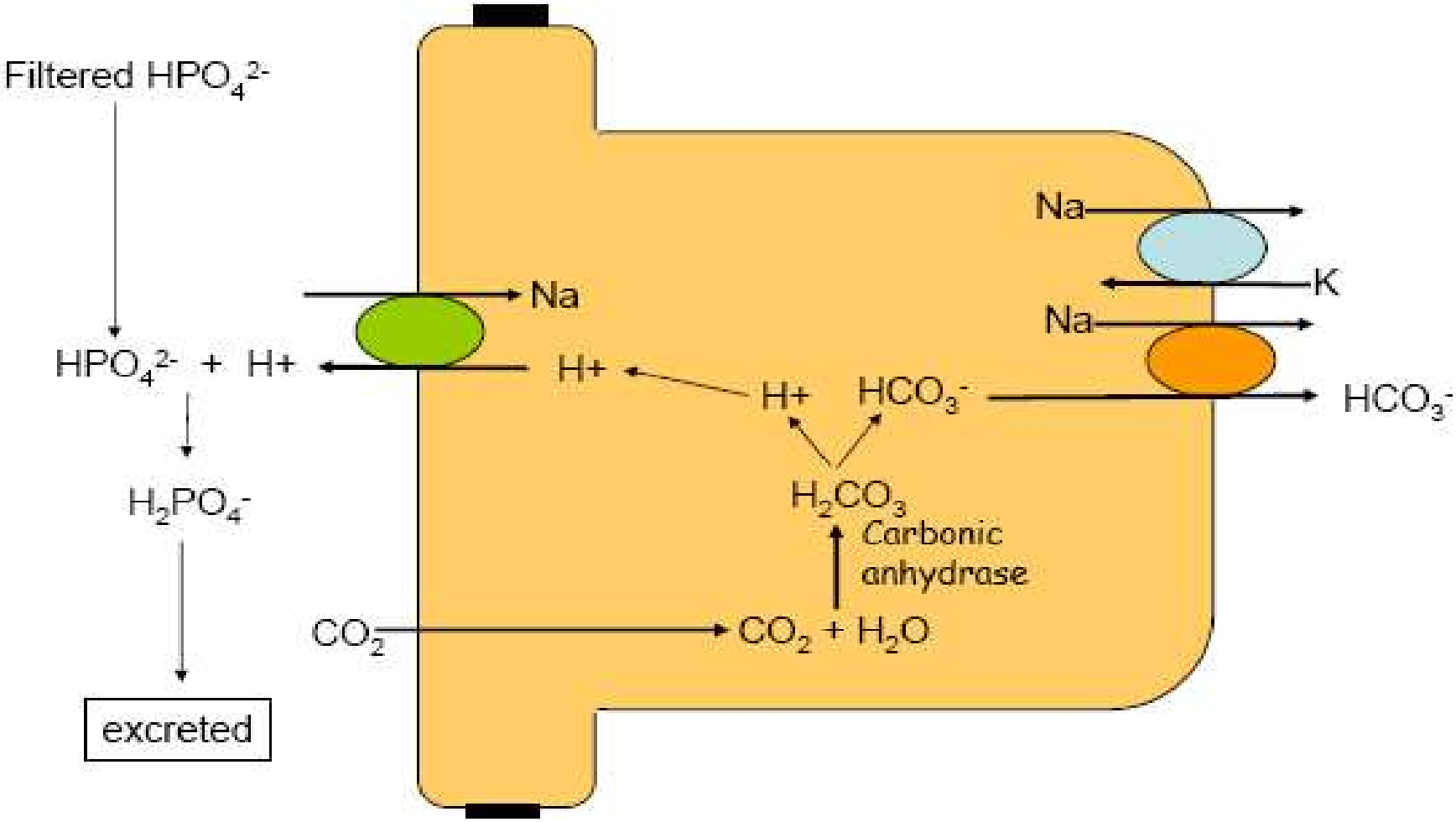
• **"HCO_3^- reabsorption"**

• A second important buffer in the tubular fluid is the ***phosphate system***
• Works in the tubular fluid to buffer H^+ and allows for production of ***new HCO_3^-***

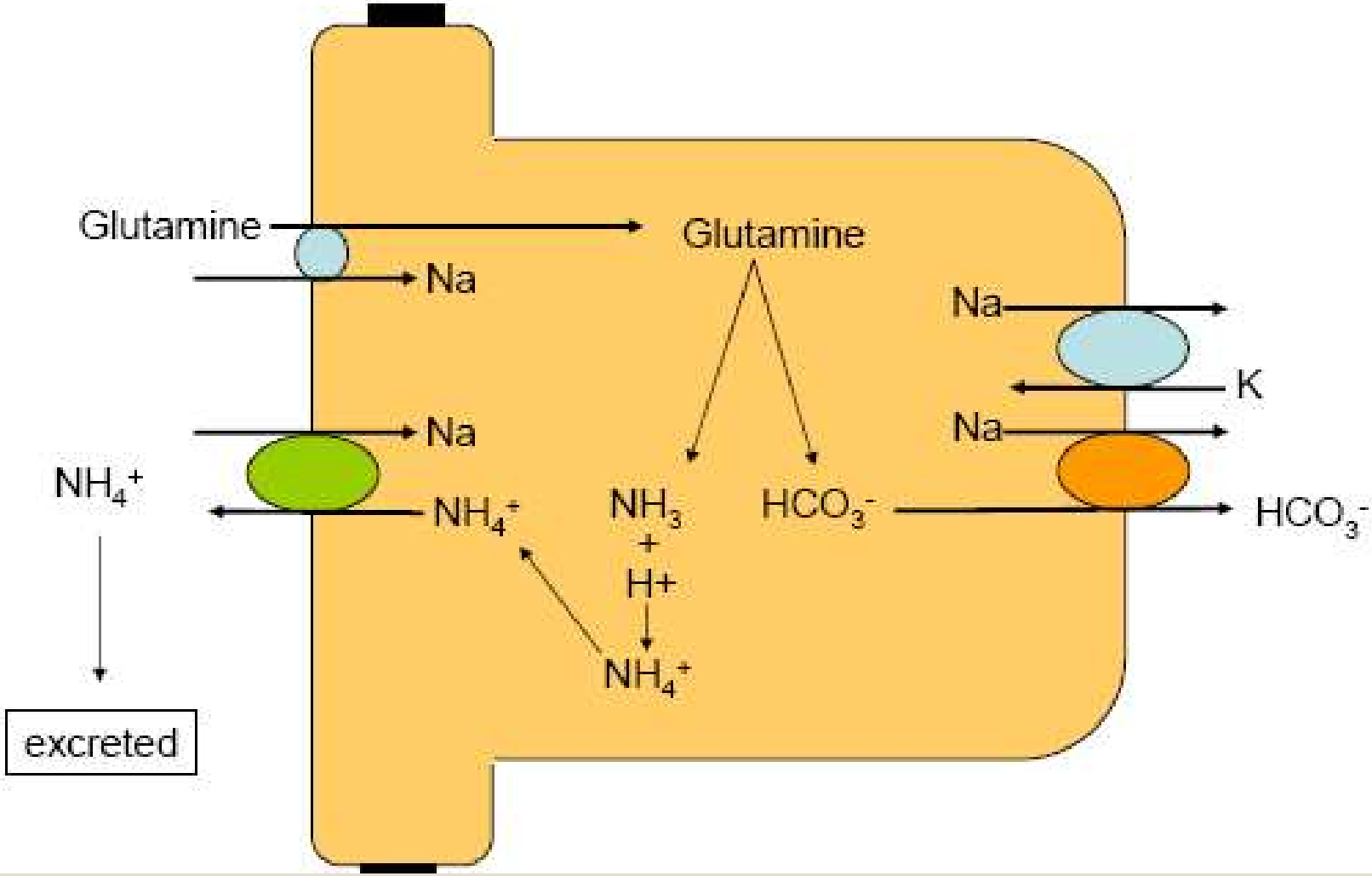
A third important buffer in the tubular fluid is the ***ammonia system***
• Also, works in the tubular fluid to buffer H^+ and allows for production of ***new HCO_3^-***

Renal HPO_4^{2-} handling and new HCO_3^-

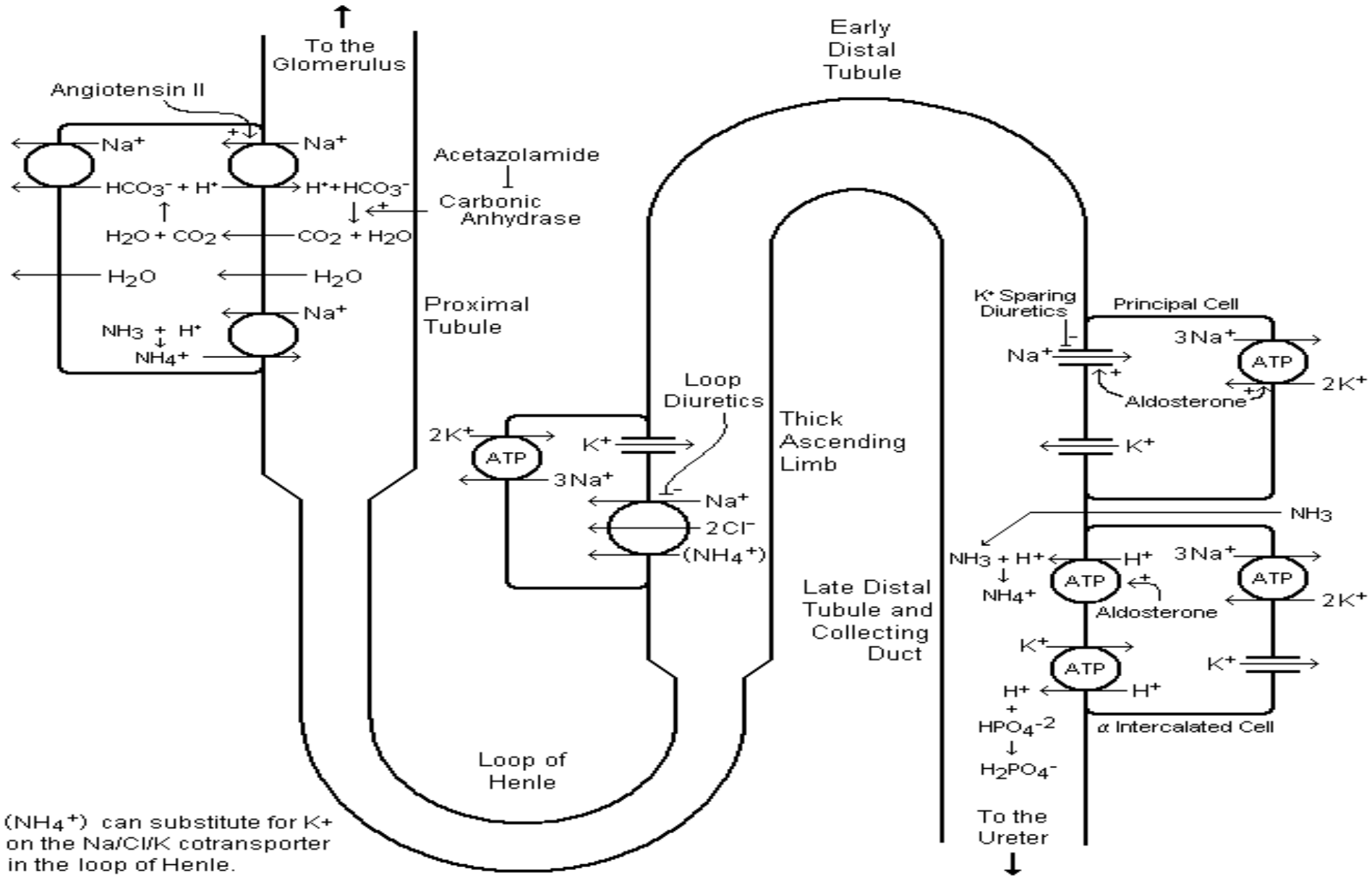
Almost all the HPO_4^{2-} in the plasma is filtered



Renal NH_4^+ handling and new HCO_3^-



Renal Regulation of Acid-Base



Bicarbonate buffers are important in the blood and extracellular fluids

• In the kidney:

– Bicarbonate allows for excretion of H+ as water and preservation of HCO3

– **Phosphate and ammonia serve as tubule** fluid specific buffers and they allow for production of 'new' HCO3-

Renal Response to Acid-Base Disturbance

1. Metabolic Acidosis

- Increase HCO3 reabsorption
- Increase H+ secretion
- Increase new HCO3 production

2. Metabolic Alkalosis

- decrease HCO3 reabsorption
- decrease H+ secretion

Responses to acid-base imbalance

1. Fast - Fluid buffering systems as outlined above

2. Moderate – Respiratory chemoreceptors sensitive to CO2 and [H+] regulate breathing and CO2 levels

3. Slow (days) Renal - adjust HCO3 and H+ handling and production of new HCO3

Practical Approach

1. Check the pH

If the pH < 7.35, acidemia (and at least 1 acidosis) is present.

If the pH > 7.45, alkalemia (and at least 1 alkalosis) is present.

Practical Approach

2. Check the pCO_2

pH < 7.35 and pCO_2 < 40 → metabolic acidosis
pH < 7.35 and pCO_2 > 40 → respiratory acidosis

pH > 7.45 and pCO_2 < 40 → respiratory alkalosis
pH > 7.45 and pCO_2 > 40 → metabolic acidosis

Practical Approach

Most prominent disorder	Compensation formula
Metabolic acidosis	$pCO_2 \approx 1.5\ [HCO_3^-] + 8$
Metabolic alkalosis	$pCO_2 \approx 0.9\ [HCO_3^-] + 16$
Respiratory acidosis	For every 10 Δ in pCO_2, pH decreases by: 0.08 (in acute resp. acidoses) 0.03 (in chronic resp. acidoses)
Respiratory alkalosis	For every 10 Δ in pCO_2, pH increases by: 0.08 (in acute resp. alkaloses) 0.03 (in chronic resp. alkaloses)

Anion "Gap"

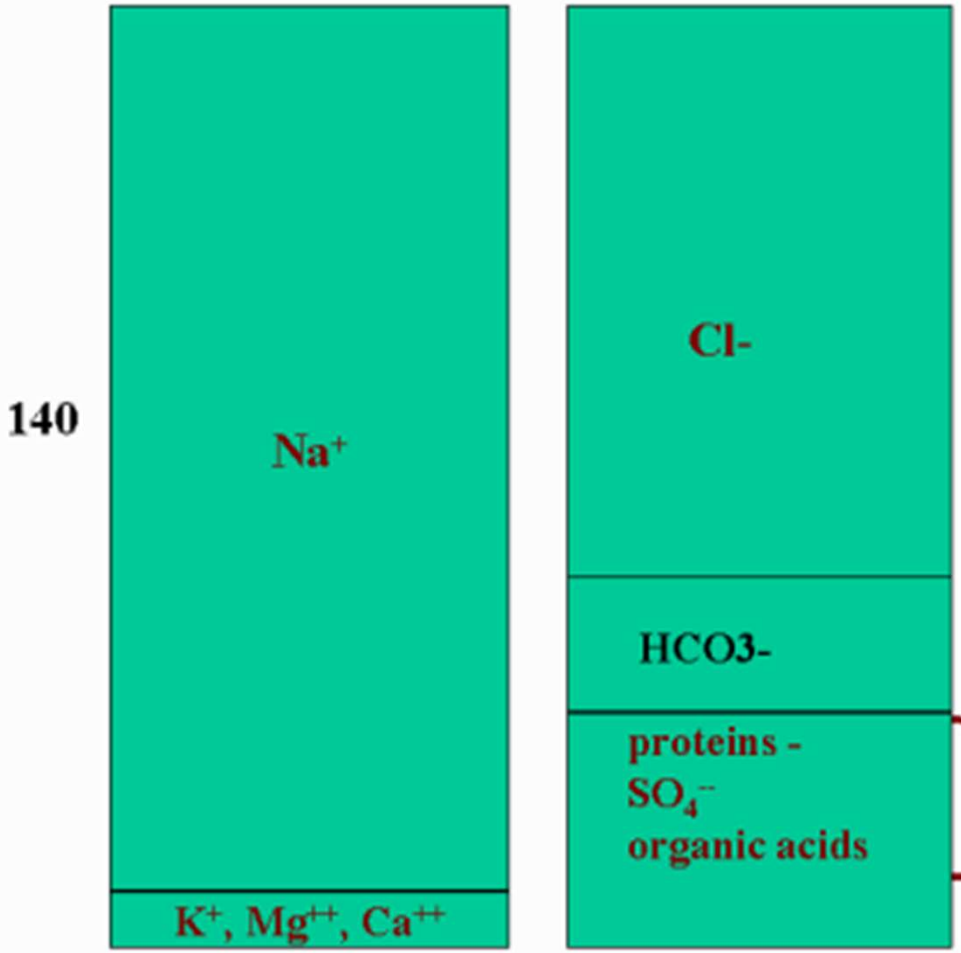
1. An "artefact" of how we measure blood electrolytes
2. Determined by:

Normal = 10

3. If the anion gap is normal with acidosis then Cl^- has increased to match $HCO3^-$ decline
4. If the anion gap is increased some other anion is involved

Anion Gap (AG)

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



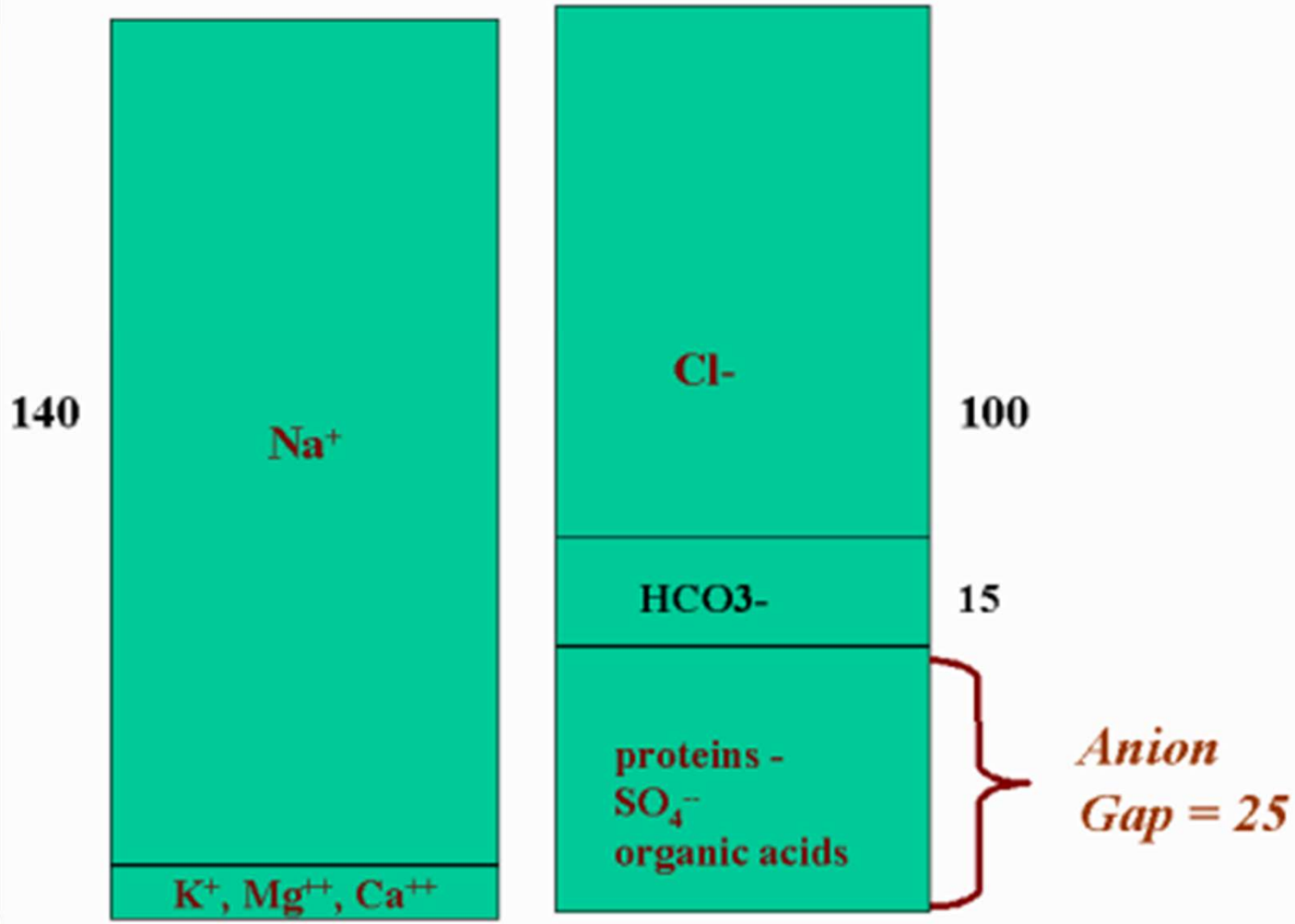
-Normal AG
10-14

-AG is primarily due to albumin

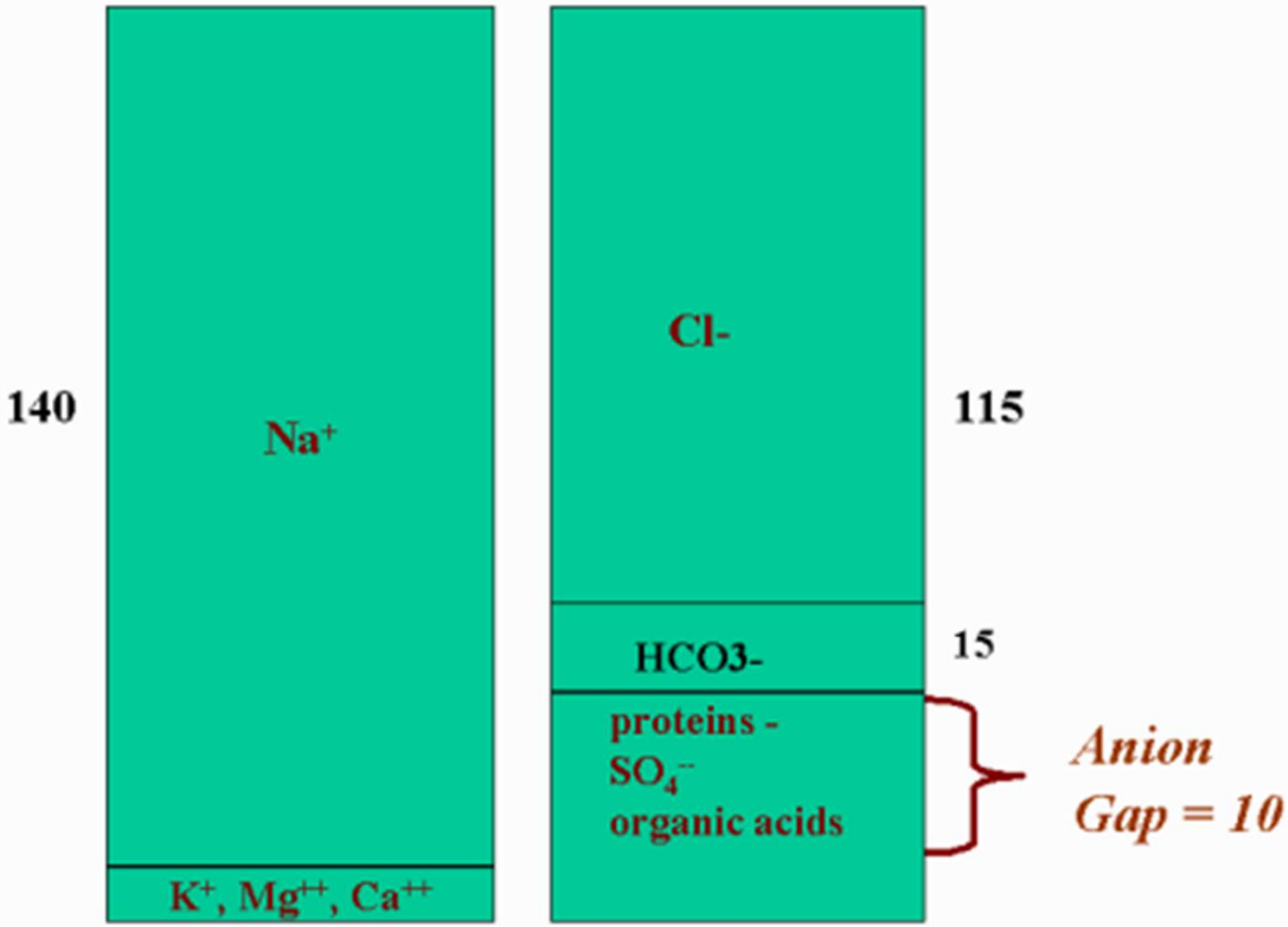
-Increased AG almost always due to a rise in unmeasured anions

Anion Gap = 10

Increased anion gap metabolic acidosis



Normal anion gap metabolic acidosis



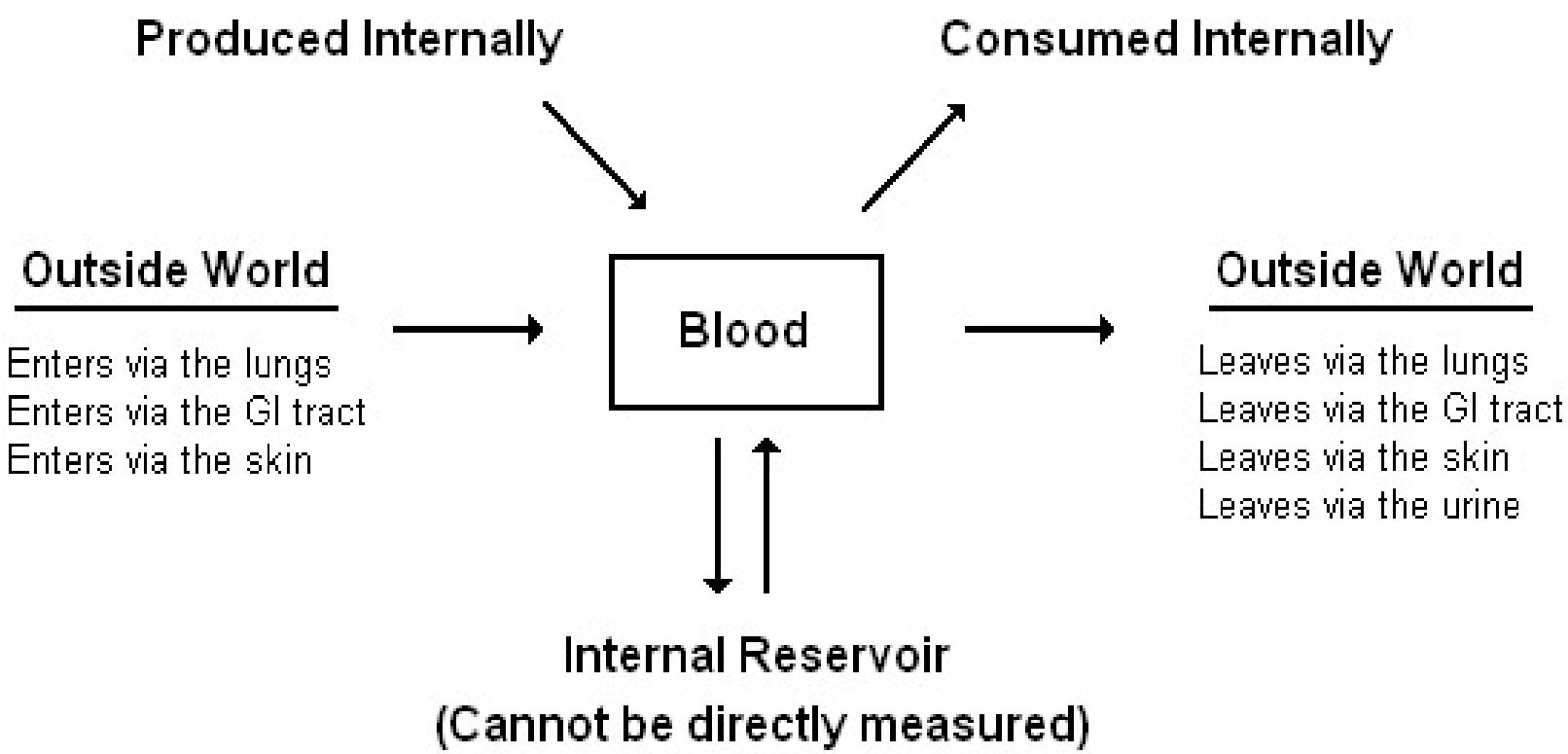
5. Calculate the anion gap

Anion gap = $[Na^+]$ – ($[Cl^-]$ + $[HCO_3^-]$)

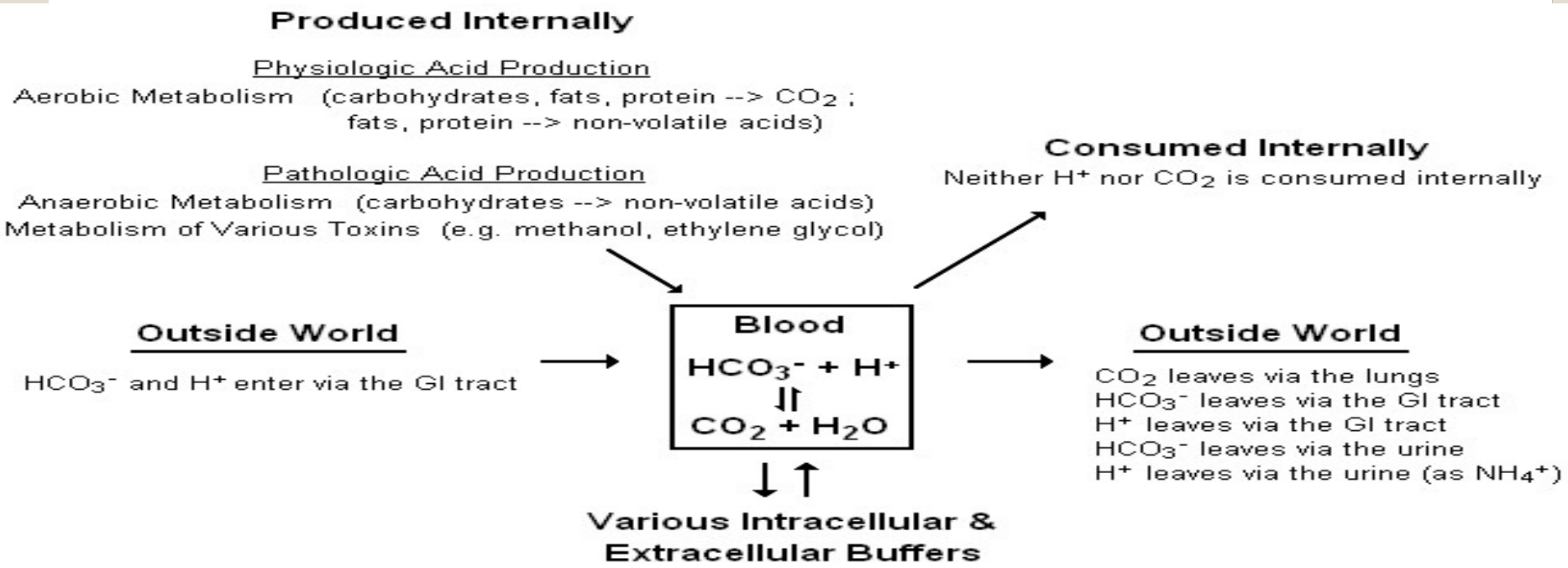
If the anion gap is elevated, an elevated gap metabolic acidosis is likely present.

Practical Approach

Overview of Biochemical Homeostasis



Differential Diagonsis for Acid-Base Disorders



Metabolic Acidosis
(Too much H^+ / Too little HCO_3^-)

Decreased intake of HCO_3^-
Increased intake of H^+
Increased aerobic metabolism
Production of pathologic acids (lactate, ketones)
Increased GI loss of HCO_3^-
Decreased GI loss of H^+
Increased urinary loss of HCO_3^-
Decreased urinary loss of H^+

Metabolic Alkalosis
(Too little H^+ / Too much HCO_3^-)

Decreased intake of H^+
Increased intake of HCO_3^-
Decreased aerobic metabolism
Decreased GI loss of HCO_3^-
Increased GI loss of H^+
Decreased urinary loss of HCO_3^-
Increased urinary loss of H^+

Respiratory Acidosis
(Too much CO_2)

Increased aerobic metabolism
Decreased CO_2 excretion via the lungs
(aka hypoventilation)

Respiratory Alkalosis
(Too little CO_2)

Decreased aerobic metabolism
Increased CO_2 excretion via the lungs
(aka hyperventilation)

- M ethanol
- U remia
- D iabetic Ketoacidosis, Ketoacidosis
- P araldehyde
- I ron, Isoniazid (INH)
- L actic Acidosis
- E thanol, Ethylene glycol
- S alicylates

Anion gap Acidosis

"MUDPILES"

- Drunk off their _____
- Hx of drug use
- Fruity breath
- Kussmaul's breathing
- tinnitus
- hypotension

Signs and Symptoms Gap Acidosis

Laboratory Workup

- Chemistries
  - BUN, Cr, glucose
- Lactate level
- Ketones
- Ethanol level
- Salicylate level
- Osmolal gap
- UA

- Uremic Acidosis
- Lactic Acidosis
- Ketoacidosis
- Salicylates

Osmolar Gap

Normal (< 25mOsm/kg)

- Ethylene Glycol
  - Look for Oxalate crystals in the Urine
- Methanol Intoxication
  - Visual Changes

Osmolar Gap

Increased (>25mOsm/kg)

Treatment

- Treat underlying condition
- Remember:
  - Methanol
  - Ethanol
  - Ethylene Glycol
  - Salicylates
- Can Be Removed via Dialysis

- H yperalimentation
- A cetazolamide, amphotericin
- R TA
- D iarrhea
- U reteral Diversions
- P ancreatic fistula
- S aline resucitation

Non gap Acidosis

"HARDUPS"

IF YES THINK About

- Ileostomy
- Diarrhea
- Enteric Fistula

Non Gap Acidosis

Is There Intestinal Fluid Loss?