L.1+2: HEMEOSTASIS OF ELECTROLYTES:

- ✓ Changes in extracellular K+ must not exceed ±0.3 mEq/L to avoid hypo- or hyperkalemia.
- ✓ Normal daily K+ intake is about 100 mEq. This intake must be balanced to maintain K+ homeostasis.

1. Exchange Between Compartments (First line regulation):

Redistribution: Fast transfer of K+ from ECF to ICF to lower blood K+ levels.

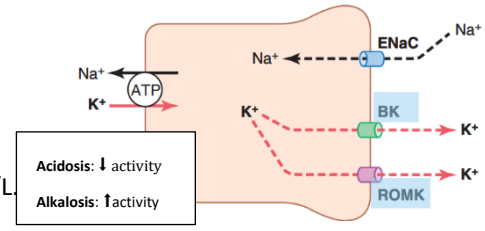
Factors That Shift K+ Into Cells (Decrease Extracellular [K+])	Factors That Shift K+ Out of Cells (Increase Extracellular [K+])
• **Alkalosis:** Stimulates Na+/K+ pump, moving more K+ intracellularly. • **Aldosterone**	• **Cell Lysis and Hyperosmolarity**: Lead to K+ leakage from cells. • **Strenuous Exercise and β-blockers**: Increase hyperkalemia risk. • **Acidosis**: Inhibits Na+/K+ pump, reducing K+ entry into cells.

2. Renal Control of Potassium:

- **PCT**: R. 65%
- **THICK.A LOH**: R. 27%
- **LDT & CD**: the end S. 12%

➢ Primary modulation occurs in the late distal tubules and collecting ducts**.**

principal cells: Secrete K+ in two steps: uptake by Na+/K+ pump and passive diffusion into tubular fluid.



⬆ k+ secretion: aldosterone**,** ⬆ Na+ delivery, ⬆ extracellular k+

- K+ secretion responds rapidly and significantly when levels exceed 4.1 mEq/L.
- even small ⬆ of extracellular K+➞ ⬆Aldosterone ➞⬆ k+ secretion➞ small changes in plasma k+ concentrations throughout the different intakes.
- **Aldosterone System blocked➞** extreme hypo- or hyperkalemia.
- **Flow Rate:** Higher flow rates increase K+ secretion, more significant with higher K+ intake.
- **Diuretics that⬇ Prox. Or ⬇Loop Na + Reabsorption:** ⬆ tubular fluid flow rate➞ ⬆ K+ secretion ➞ K+ depletion

➢ Sodium (Na+) Intake and Potassium (K+) Secretion:

Effects of Increased Na+ Intake:

- ⬆ GFR/⬇ Proximal Tubular Na+ Reabsorption: ⬆ tubular flow enhances K+ secretion.
- ⬇aldosterone: decreases K+ secretion.

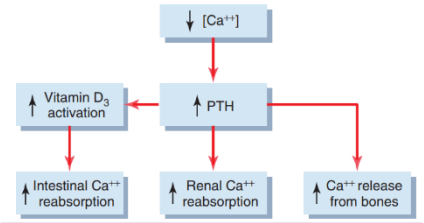
unchanged K+ excretion.

Condition	Effect on Na+/K+ ATPase	Effect on Intracellular K+	Effect on K+ Secretion	Result
Acute Acidosis	Inhibits	Decreases	Reduces	Leads to hyperkalemia
Chronic Acidosis	-	-	Stimulates (hyperkalemia remains mild due to compensatory mechanisms)	Increases tubular flow rate and inhibits proximal NaCl and water reabsorption
Alkalosis	Increases	Increases	Enhances	Leads to hypokalemia

- **Hyperkalemia** is caused by factors that reduce potassium excretion or increase potassium reabsorption, (renal failure, ⬇ distal nephron flow, ⬇ aldosterone or its effects, metabolic **acidosis**, diabetes, and removal of prostaglandins.)
- **Hypokalemia** from factors that increase potassium excretion or uptake into cells (very low potassium intake, GI losses, metabolic **alkalosis**, excess insulin, increased distal tubular flow, and excess aldosterone or other mineralocorticoids.)

➢ **Compensatory Responses to Decreased Plasma Ionized Calcium:**

- **<u>Proximal Tubular</u> Calcium Reabsorption:**
  1. Paracellular Pathway: Most of the calcium reabsorption here, calcium is dissolved in water and carried between cells.
  2. Transcellular Route: About 20% (diffuses down by **Ca++ ATPase** and **Ca++/Na+ countercurrent transporters**)



In Kidney Failure: the body compensates by increasing calcium release from bones➞ osteoporosis.

- **<u>Thick Ascending Limb and Distal Tubule</u>:** paracellular & transcellular (PTH effect)

○ **<u>Integration of Renal Mechanisms for Regulation of Body Fluids and Electrolytes:</u>**

Excretion = Filtration - Reabsorption + Secretion.

In a steady-state:

Fluid Excretion = Fluid Intake

Electrolyte Excretion = Electrolyte Intake

1. **Effect of Decreased GFR on Sodium**:
   - ⬇ GFR➞ ⬇ reabsorption ➞ excretion remains consistent. (+ balance)
2. **Maintenance of Sodium Balance after decrease reabsorption:**
   - ⬇ reabsorption ➞⬇ GFR ➞ excretion remains consistent. (– balance)

L.3+4: ACID-BASE BALANCE:

- Mechanisms of Hydrogen Ion Regulation:

⬆ $[H^+]$ ➞ ⬆acid➞ ⬇PH

⬇ $[H^+]$ ➞ ⬆base➞ ⬆PH

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

1. **Chemical Buffers (Rapid but Temporary):**

Temporarily reduce pH deviations until other systems can correct imbalances.

Buffer effectiveness depends on reactant concentrations and closeness of pH to buffer's pK.

Buffer System	Components	Location	Function
Bicarbonate most important buffer	CO2 and HCO3-	Extracellular fluid (ECF)	Regulates pH by adjusting CO2 and HCO3-. Carbonic anhydrase facilitates conversion. **Metabolic Alkalosis:** ⬆HCO3– in urine. **Acidosis:** ⬆ H+ relative to HCO3– in urine.
Phosphate	HPO_4^{2-} and H_2PO4^{1-}	Renal tubular fluid	Accepts or donates H+ ions to maintain pH stability.
Ammonia	NH3 and NH4+	Tubular fluid	Converts excess hydrogen to ammonium (NH4+) to reduce acidity, especially in chronic acidosis.
Proteins (Intracellular)	Intracellular proteins	Within cells	Intracellular buffering; follows extracellular pH deviations due to dynamic electrolyte movement.

- Kidneys and lungs regulate CO2, H+, and HCO3- levels, optimizing bicarbonate buffer effectiveness.

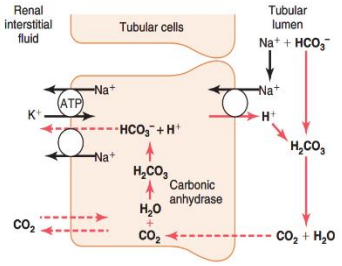
2. **Respiratory System (Lungs):**
   - Rapid response; eliminates CO_2
   - Not effective for non-volatile acids.

Acidosis Correction:	**Alkalosis Correction**:
• ⬆blood acidity (H+ concentration) triggers ⬆alveolar ventilation, ⬇ CO2. • ⬇CO2 shifts the equation to the left, promoting HCO3- combination with H+, ⬇ **H+ concentration**.	• ⬇ alveolar ventilation in alkalosis ⬇removal of CO2. • This shifts the equation towards **generating more H+,** counterbalancing alkalinity.

3. **Urinary System (Kidneys):** Slow but powerful; eliminates non-volatile acids.

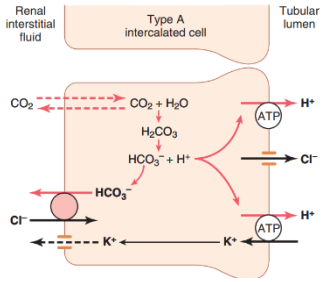
   Functions: secretes H^+, reabsorbs HCO_3^-, generates new HCO_3^-.

Proximal Tubule and Thick Loop of Henle: minimal PH 6.7



- **Na+/H+ exchanger** driven by Na+/K+ ATPase reabsorbs Na+ and **secretes H+.**
- H+ combines with filtered HCO3- to form H2CO3, which dissociates into H2O and CO2.
- CO2 re-enters cells to form more H+ and HCO3-, promoting **HCO3- reabsorption.**
- Each secreted H+ results in one HCO3- reabsorbed.

Late Distal and Collecting Tubules (Type A Intercalated Cells): minimal PH 4.5



- CO_2 combines with H_2O form HCO_3^- / H^+, HCO_3^- reabsorbed via HCO_3^-/Cl^- exchanger.
- **H+ ATPase pump** secretes H+ against a large gradient.
- **K+/H+ ATPase pump** secretes H+ and reabsorbs K+. (⬆ activity by hypokalemia)
  - Acidosis: ⬆ H+ secretion, HCO3- reabsorption, and new HCO3- production.
  - Alkalosis: ⬇ H+ secretion, decreased HCO3- reabsorption, and ⬆HCO3- excretion.

✓ Buffers like phosphate and ammonia neutralize excess H+.
✓ New HCO3- is produced when H+ is titrated by non-HCO3- buffers.

- **The kidneys must excrete at least 60 mmol of non-volatile acids daily. Without buffers, this would require excreting 2000 liters of urine daily, which is impractical.**

In acidosis, the kidneys manage excess H+ using HCO3-, phosphate, and ammonia buffers. When phosphate and ammonia titrate H+, new HCO3- is produced, adding extra bicarbonate to the extracellular fluid.

Phosphate Buffer: 6.8	**Ammonia Buffer**:
Mech: NaHPO4- combines with H+ to form NaH2PO4, titrating excess H+ and maintaining urine concentration. **Capacity**: Buffers about 30 mmol/day of H+. Not the major for C.acidosis	**Production**: Glutamine metabolism produces NH4+ and new HCO3-. **Mech**: NH3 combines with secreted H+ to form NH4+, which is then excreted, creating new HCO3-. Ammonia production increases in acidosis, providing a significant buffering capacity.

- **Total H+ Secretion**:

➢ HCO3- reabsorption: 4320 mmol/day+ Titratable acid: 30 mmol/day+ NH4+ excretion: 30 mmol/day= **Total**: 4380 mmol/day.

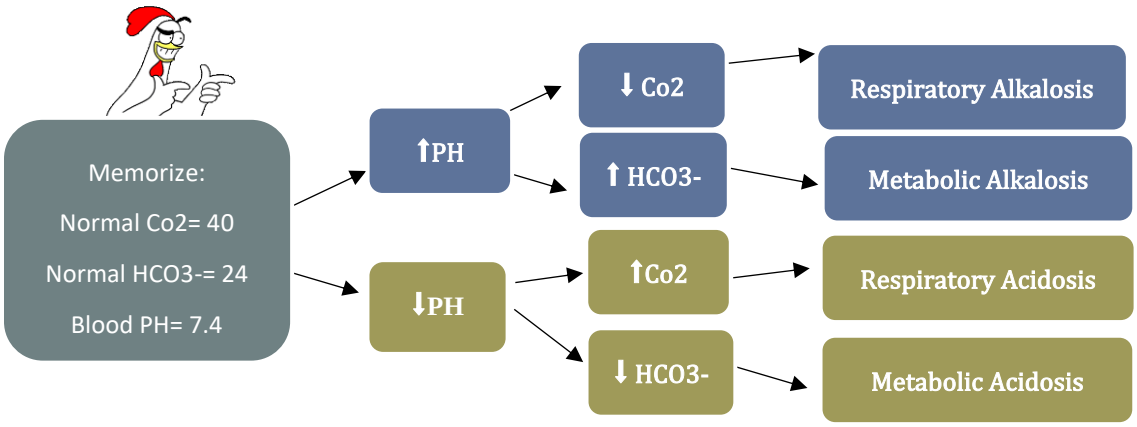
- **Net H+ Excretion**:

➢ Titratable acid: 30 mmol/day+ NH4+ excretion: 30 mmol/day- HCO3- excretion: 1 mmol/day= **Net Excretion**: 59 mmol/day.

SUMMARY OF ACID-BASE DISORDERS:

		Renal Responses	**Respiratory compensation**
Acidosis ⬇PH	**Respiratory Acidosis** ⬆ pCO2	• Complete HCO3- reabsorption+ generates new HCO3-. • ⬆ tubular H+ secretion➞ ⬆ buffers like NH4+ and NaHPO4-	
	Metabolic Acidosis ⬇ HCO3-	• Complete HCO3- reabsorption • ⬆secretion of H+ titrated by non-HCO3- buffers➞ generating new HCO3-	⬆ ventilation ➞ ⬇ **pCO2**
Alkalosis ⬆PH	**Respiratory Alkalosis** ⬇ pCO2	• ⬇ H+ secretion • ⬇ HCO3- reabsorption, leading to excess tubular HCO3- excretion	
	Metabolic Alkalosis ⬆ HCO3-	• ⬆HCO3- filtration • ⬇ H+ secretion, resulting in excess tubular HCO3- and increased excretion	⬇ventilation ➞ ⬆**pCO2**

NOTE: SOMETIMES WE MIGHT HAVE **MIXED ACISOSIS** OR **MIXED ALKILOSIS**



Anion Gap as a Diagnostic Tool

Anion Gap = Na+ - (Cl- + HCO3-)

Normal: 8-16 mEq/L

- helps differentiate **between types of metabolic acidosis** by revealing whether there is an accumulation of unmeasured anions or a simple loss of bicarbonate with a corresponding rise in chloride.
- **High Anion Gap Acidosis** suggests conditions like **diabetic ketoacidosis or lactic acidosis.**
- **Normal Anion Gap Acidosis** indicates conditions like **diarrhea or renal tubular acidosis**. (GI) hyperchloremia

↓ extracellular volume → ↑Ang2, aldosterone → ↓ K+↑ H+/ pump → ↑ H+ secretion → metabolic alkalosis

Overuse of Diuretics:

1. ↑aldosterone
2. K+ depletion

→ Increases tubular H+ secretion. → metabolic alkalosis

Done by: Mariam Qussay

Corrected by: Rama Alameer