Body Water Content

- Infants: 73% or more water (low body fat, low bone mass)
- Adult males: ~60% water
- Adult females: ~50% water (higher fat content, less skeletal muscle mass)
  - Adipose tissue least hydrated of all
- Water content declines to ~45% in old age

Fluid Compartments

- Total body water = 40 L
- Two main fluid compartments
  - Intracellular fluid (ICF) compartment: 2/3 in cells
  - Extracellular fluid (ECF) compartment: 1/3 outside cells
    - Plasma: 3 L
    - Interstitial fluid (IF): 12 L in spaces between cells
      - Usually considered part of IF: lymph, CSF, humors of the eye, synovial fluid, serous fluid, and gastrointestinal secretions

Electrolyte Concentration

- Expressed in milliequivalents per liter (mEq/L), measure of number of electrical charges per liter of solution
  \[
  \text{mEq/L} = \frac{\text{ion concentration (mg/L)}}{\text{atomic weight of ion (mg/mmol)}} \times \text{no. of electrical charges on one ion}
  \]

Electrolyte Concentration

- For single charged ions (e.g. Na\(^+\)), 1 mEq = 1 mOsm
- For bivalent ions (e.g. Ca\(^{2+}\)), 1 mEq = 1/2 mOsm
- 1 mEq of either provides same amount of charge
Extracellular and Intracellular Fluids

- Each fluid compartment has distinctive pattern of electrolytes
- ECF
  - All similar
    - Major cation: Na⁺
    - Major anion: Cl⁻
  - Except: higher protein, lower Cl⁻ content of plasma

ICF:
- Low Na⁺ and Cl⁻
- Major cation: K⁺
- Major anion HPO₄²⁻
- More soluble proteins than in plasma

Water Balance and ECF Osmolality

- Water intake must = water output = ~ 2500 ml/day
- Water intake: beverages, food, and metabolic water
- Water output: urine (60%), insensible water loss (lost through skin and lungs), perspiration, and feces
Maintenance of Body fluid Osmolality

- Osmolality maintained at ~ 280 – 300 mOsm
- Rise in osmolality →
  - Stimulates thirst
  - ADH release
- Decrease in osmolality →
  - Thirst inhibition
  - ADH inhibition

Regulation of Water Output: Influence of ADH

- Other factors may trigger ADH release
  - Large changes in blood volume or pressure
    - E.g., ↓ BP → ↑ ADH release due to blood vessel baroreceptors and renin-angiotensin-aldosterone mechanism
    - Factors lowering blood volume: intense sweating, vomiting, or diarrhea; severe blood loss; traumatic burns; and prolonged fever

Disorders of Water Balance

- Principal abnormalities of water balance
  - Dehydration
  - Hypotonic hydration
  - Edema

Disorders of Water Balance: Hypotonic Hydration

- Cellular overhydration, or water intoxication
- Occurs with renal insufficiency or rapid excess water ingestion
- ECF osmolality ↓ → hyponatremia → net osmosis into tissue cells → swelling of cells → severe metabolic disturbances (nausea, vomiting, muscular cramping, cerebral edema) → possible death
- Treated with hypertonic saline
Disorders of Water Balance: Edema

- Atypical accumulation of IF → tissue swelling (not cell swelling)
- Result of ↑ fluid out of blood or ↓ fluid into blood
- ↑ fluid out of blood caused by
  - Increased capillary hydrostatic pressure or permeability
    - Capillary hydrostatic pressure increased by incompetent venous valves, localized blood vessel blockage, congestive heart failure, ↑ blood volume
    - Capillary permeability increased by ongoing inflammatory response

Edema

- ↓ fluid returning to blood result of
  - Imbalance in colloid osmotic pressures, e.g., hypoproteinemia (↓ plasma protein levels → low colloid osmotic pressure)
    - Fluids fail to return at venous ends of capillary beds
    - Results from protein malnutrition, liver disease, or glomerulonephritis

Electrolyte Balance

- Electrolytes are salts, acids, bases, some proteins
- Electrolyte balance usually refers only to salt balance
- Salts control fluid movements; provide minerals for excitability, secretory activity, membrane permeability
- Salts enter body by ingestion and metabolism; lost via perspiration, feces, urine, vomit

Central Role of Sodium

- Most abundant cation in ECF
  - Sodium salts in ECF contribute 280 mOsm of total 300 mOsm ECF solute concentration
- Only cation exerting significant osmotic pressure
  - Controls ECF volume and water distribution
  - Changes in Na⁺ levels affects plasma volume, blood pressure, and ECF and IF volumes
Regulation of Sodium Balance: Aldosterone

- Regardless of aldosterone presence
  - 65% Na\(^+\) reabsorbed in proximal tubules; 25% reclaimed in nephron loops
  - Na\(^+\) never secreted into filtrate
- Water in filtrate follows Na\(^+\) if ADH is present
  - ↑ Na\(^+\) in urine → ↑ water loss

Aldosterone

- Aldosterone → decreased urinary output; increased blood volume
  - By active reabsorption of remaining Na\(^+\) in distal convoluted tubule and collecting duct
- Also causes increased K\(^+\) secretion

Regulation of Sodium Balance: Aldosterone

- Renin-angiotensin-aldosterone mechanism main trigger for aldosterone release
  - Granular cells of JGC secrete renin in response to
    - Sympathetic nervous system stimulation
    - ↓ filtrate NaCl concentration
    - ↓ stretch (due to ↓ blood pressure) of granular cells

Regulation of Sodium Balance: Aldosterone

- Renin catalyzes production of angiotensin II
  - Prompts aldosterone release from adrenal cortex
  - ↑ Na\(^+\) reabsorption by kidney tubules
- Aldosterone release also triggered by elevated K\(^+\) levels in ECF
- Aldosterone brings about its effects slowly (hours to days)
Influence of other Hormones

- Female sex hormones
  - Estrogens: $\uparrow$ NaCl reabsorption (like aldosterone)
    • $\rightarrow H_2O$ retention during menstrual cycles and pregnancy
  - Progesterone: $\downarrow Na^+$ reabsorption (blocks aldosterone)
    • Promotes Na$^+$ and H$2O$ loss
- Glucocorticoids: $\uparrow Na^+$ reabsorption and promote edema

Regulation of Potassium Balance

- Importance of potassium
  - Affects RMP in neurons and muscle cells (especially cardiac muscle)
    • $\uparrow$ ECF [K$^+$] $\rightarrow$ RMP $\rightarrow$ depolarization $\rightarrow$ reduced excitability
    • $\downarrow$ ECF [K$^+$] $\rightarrow$ hyperpolarization and nonresponsiveness

Regulation of Potassium Balance

- Hyperkalemia - too much K$^+$
- Hypokalemia - too little K$^+$
  • Both disrupt electrical conduction in heart $\rightarrow$
    – Sudden death

Regulation of Potassium Balance

- K$^+$ part of body’s buffer system
- H$^+$ shifts in and out of cells in opposite direction of K$^+$ to maintain cation balance, so
  – ECF K$^+$ levels rise with acidosis
  – ECF K$^+$ levels fall with alkalosis
    • Interferes with activity of excitable cells

Influence of Plasma Potassium Concentration

- Most important factor affecting K$^+$ secretion is its concentration in ECF
- High K$^+$ diet $\rightarrow$ $\uparrow$ K$^+$ content of ECF $\rightarrow$ K$^+$ entry into principal cells $\rightarrow$ K$^+$ secretion
- Low K$^+$ diet or accelerated K$^+$ loss reduces its secretion
Regulation of Potassium Balance

- Influence of aldosterone
  - Stimulates K⁺ secretion (and Na⁺ reabsorption) by principal cells
  - Adrenal cortical cells directly sensitive to K⁺ content of ECF
    - Increased K⁺ in adrenal cortex causes
      - Release of aldosterone → K⁺ secretion
  - Abnormal aldosterone levels severely influence K⁺ levels

Regulation of Calcium

- 99% of body’s calcium in bones
  - Calcium phosphate salts
- Ca²⁺ in ECF important for
  - Blood clotting
  - Cell membrane permeability
  - Secretory activities
  - Neuromuscular excitability - most important

Regulation of Calcium

- Hypocalcemia → ↑ excitability and muscle tetany
- Hypercalcemia → inhibits neurons and muscle cells, may cause heart arrhythmias
- Calcium balance controlled by parathyroid hormone (PTH) from parathyroid gland
  - Rarely deviates from normal limits

Influence of PTH

- PTH promotes increase in calcium levels by targeting
  - Bones – osteoclasts break down matrix, releasing calcium and phosphate to blood
  - Kidneys – increases calcium reabsorption; decreases phosphate ion reabsorption
  - Small intestine – increases calcium absorption (indirectly through stimulation of kidney to activate vitamin D precursor)

Influence of PTH

- 98% filtered calcium reabsorbed due to PTH
- If ECF calcium levels normal PTH secretion inhibited
- 75% of filtered phosphates reabsorbed in PCT
  - PTH inhibits this by decreasing the Tₘ
- Phosphate reabsorption also affected by insulin (increases it) and glucagon (decreases it)
Regulation of Anions

- **Cl⁻** is major anion in ECF
  - Helps maintain osmotic pressure of blood
  - 99% of **Cl⁻** is reabsorbed under normal pH conditions
- When acidosis occurs, fewer chloride ions are reabsorbed
- Other anions have transport maximums and excesses are excreted in urine

Acid-base Balance

- pH affects all functional proteins and biochemical reactions, so closely regulated
- Normal pH of body fluids
  - Arterial blood: pH 7.4
  - Venous blood and IF fluid: pH 7.35
  - ICF: pH 7.0
- **Alkalosis** or alkalemia: arterial pH > 7.45
- **Acidosis** or acidemia: arterial pH < 7.35

Acid-base Balance: Chemical Buffer Systems

- Most **H⁺** produced by metabolism
  - Phosphorus-containing protein breakdown releases *phosphoric acid* into ECF
  - *Lactic acid* from anaerobic respiration of glucose
  - *Fatty acids and ketone bodies* from fat metabolism
  - **H⁺** liberated when CO₂ converted to HCO₃⁻ in blood

Acid-base Balance

- Concentration of hydrogen ions regulated sequentially by
  - Chemical buffer systems: rapid; first line of defense
  - Brain stem respiratory centers: act within 1–3 min
  - Renal mechanisms: most potent, but require hours to days to effect pH changes
Chemical Buffer Systems

- Chemical buffer: system of one or more compounds that act to resist pH changes when strong acid or base is added
  - Bind H⁺ if pH drops; release H⁺ if pH rises
1. Bicarbonate buffer system
2. Phosphate buffer system
3. Protein buffer system

Phosphate Buffer System

- Action nearly identical to bicarbonate buffer
- Components are sodium salts of:
  - Dihydrogen phosphate (H₂PO₄⁻), a weak acid
  - Monohydrogen phosphate (HPO₄²⁻), a weak base
- Unimportant in buffering plasma
- Effective buffer in urine and ICF, where phosphate concentrations are high

Respiratory Regulation of H⁺

- **Hypercapnia** activates medullary chemoreceptors
  - → Increased respiratory rate and depth
- Rising plasma H⁺ activates peripheral chemoreceptors
  - → Increased respiratory rate and depth
  - More CO₂ is removed from the blood
  - H⁺ concentration is reduced

Respiratory Regulation of H⁺

- Alkalosis depresses respiratory center
  - Respiratory rate and depth decrease
  - H⁺ concentration increases
- Respiratory system impairment causes acid-base imbalances
  - Hypoventilation → respiratory acidosis
  - Hyperventilation → respiratory alkalosis

Renal Mechanisms of Acid-Base Balance

- Most important renal mechanisms
  - Conserving (reabsorbing) or generating new HCO₃⁻
  - Excreting HCO₃⁻
- Generating or reabsorbing one HCO₃⁻ same as losing one H⁺
- Excreting one HCO₃⁻ same as gaining one H⁺

Renal Mechanisms of Acid-base Balance

- Renal regulation of acid-base balance depends on kidney's ability to secrete H⁺
- H⁺ secretion occurs in PCT and collecting duct type A intercalated cells:
  - The H⁺ comes from H₂CO₃ produced in reactions catalyzed by carbonic anhydrase inside cells
  - As H⁺ secreted, Na⁺ reabsorbed
  - See Steps 1 and 2 of following figure
Renal Mechanisms of Acid-base Balance

- Rate of H⁺ secretion changes with ECF CO₂ levels
  - ↑ CO₂ in peritubular capillary blood → ↑ rate of H⁺ secretion
  - System responds to both rising and falling H⁺ concentrations

Ammonium Ion Excretion

- More important mechanism for excreting acid
- Involves metabolism of glutamine in PCT cells
- Each glutamine produces 2 NH₄⁺ and 2 "new" HCO₃⁻
- HCO₃⁻ moves to blood and NH₄⁺ is excreted in urine
- Replenishes alkaline reserve of blood

Bicarbonate Ion Secretion

- When body in alkalosis, type B intercalated cells
  - Secrete HCO₃⁻
  - Reclaim H⁺ to acidify blood
Bicarbonate Ion Secretion

- Mechanism is opposite of bicarbonate ion reabsorption process by type A intercalated cells
- Even during alkalosis, nephrons and collecting ducts conserve more $\text{HCO}_3^-$ than they excrete

Respiratory Acidosis and Alkalosis

- Most important indicator of adequacy of respiratory function is $P_{\text{CO}_2}$ level (normally 35–45 mm Hg)
  - $P_{\text{CO}_2}$ above 45 mm Hg $\Rightarrow$ respiratory acidosis
    - Common cause of acid-base imbalances
    - Due to decrease in ventilation or gas exchange
    - $\text{CO}_2$ accumulates in blood
    - Characterized by falling blood pH and rising $P_{\text{CO}_2}$

- Most important indicator of adequacy of respiratory function is $P_{\text{CO}_2}$ level (normally 35–45 mm Hg)
  - $P_{\text{CO}_2}$ below 35 mm Hg $\Rightarrow$ respiratory alkalosis
    - Common result of hyperventilation often due to stress or pain
    - $\text{CO}_2$ eliminated faster than produced

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Metabolic Acidosis and Alkalosis

- Metabolic acidosis much less common than metabolic acidosis
  - Indicated by rising blood pH and $\text{HCO}_3^-$
  - Causes include vomiting of acid contents of stomach or by intake of excess base (e.g., antacids)

- Metabolic acidosis $\Rightarrow$ low blood pH and $\text{HCO}_3^-$
  - Causes
    - Ingestion of too much alcohol ($\rightarrow$ acetic acid)
    - Excessive loss of $\text{HCO}_3^-$ (e.g., persistent diarrhea)
    - Accumulation of lactic acid (exercise or shock), ketosis in diabetic crisis, starvation, and kidney failure

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Respiratory Compensation

- Changes in respiratory rate and depth
- In metabolic acidosis
  - High $\text{H}^+$ levels stimulate respiratory centers
  - Rate and depth of breathing elevated
  - Blood pH is below 7.35 and $\text{HCO}_3^-$ level is low
  - As $\text{CO}_2$ eliminated by respiratory system, $P_{\text{CO}_2}$ falls below normal