PART I: Introduction
A. Body Water Content
1. Total water content declines throughout life:
   a. Infants ~73% water; have low body fat, low bone mass
   b. Adults
      i. Healthy males ~60% water
      ii. Healthy females ~50% water
         1) Females have less water for two reasons:
         2) They maintain higher body fat
         3) They have less skeletal muscle
      iii. Elderly ~45% water

B. Fluid Compartments
1. Water occupies two main fluid compartments:
   a. Intracellular fluid (ICF): Inside cells; ~ 2/3 by volume
   b. Extracellular fluid (ECF): Outside of cells; about 1/3 by volume (2 major subdivisions):
      i. Plasma: Fluid portion of the blood
      ii. Interstitial fluid (IF): Fluid in spaces between cells
      iii. Other ECF: Lymph, cerebrospinal fluid, eye humors, synovial fluid, serous fluid, & g.i. secretions
   c. Movement: ICF ↔ ECF (driven largely by osmosis)

C. Composition of Body Fluids
   a. Water is the universal solvent
   b. Solutea are broadly classified into:
      i. Electrolytes inorganic salts, all acids and bases, and some proteins
      ii. Nonelectrolytes examples include glucose, lipids, creatinine, and urea
      iii. Water moves according to osmotic gradients

D. Extracellular and Intracellular Fluids
1. Each body fluid compartment has a unique mix of electrolytes
2. ECF are similar (except for the high protein content of plasma):
   a. Sodium (Na⁺) is the major cation
   b. Chloride (Cl⁻) is the major anion
3. Intracellular fluids have low sodium and chloride
   a. Potassium (K⁺) is the major cation
   b. Phosphate (HPO₄²⁻) is the major anion
4. Na⁺ and K⁺ concentrations in ECF and ICF are nearly opposites, reflecting activity of cellular ATP-dependent sodium-potassium pumps
5. Fluid Movement Among Compartments
   a. Compartmental exchange is regulated by osmotic & hydrostatic pressures
   b. Directionality:
      i. Water flow: Substantially two-way
      ii. Ion fluxes: Restricted; move selectively by active transport
      iii. Nutrients, respiratory gases, and wastes: Unidirectional
   c. Plasma: Only fluid that circulates throughout body & linking external & internal environments
PART II: WATER BALANCE

A. General Characteristics
1. To remain properly hydrated, water intake must equal water output
2. Water intake sources (~2500 ml/day):
   a. Ingested fluid  60%
   b. Preformed water (solid food)  30%
   c. Metabolic water (cellular metabolism)  10%
3. Water output sources (~2500 ml/day):
   a. Insensible water loss (cannot be controlled)
      i. Respiration, skin diffusion  28%
      ii. Feces  4%
      iii. Sweat  8% (some control)
   b. Sensible water loss (can be controlled): Urine  60% (not fully controlled)
4. Plasma osmolality remarkably constant: 285-300 mOsm/l
   a. A rise triggers thirst and release of ADH: water intake
   b. A decline inhibits thirst and release of ADH: water output
      i. Hypothalamic thirst center stimulated by two pathways:
         1) Increases in plasma osmolality of ~1-2%, detected by osmoreceptors
         2) Decreases in plasma volume of ~10%, detected by baroreceptors
5. Obligatory water loss includes:
   a. Insensible water loss cannot be controlled, including
      i. Respiration, skin diffusion
      ii. Feces
      iii. Sweat
   b. Sensible water loss a minimum of 500 ml in urine to eliminate solutes ingested with a normal diet and to flush toxic nitrogenous solutes

B. Regulation of Water Output
1. Antidiuretic hormone (ADH; a.k.a. vasopressin): Key role - Controlling amt of H₂O excreted in urine
   a. Secreted by hypothalamus
   b. Factors controlling release (same as for thirst!):
      i. Rise in plasma osmolality (hypertonicity): Hypothalamic osmoreceptors signal ADH release
      ii. Drop in plasma volume (hypovolemia) of ~10% detected by baroreceptors (→ ADH release)
   c. Primary target: Distal convoluted tubule (and collecting duct) epithelium
2. Disorders of Water Balance
   a. Dehydration
      i. Water loss exceeds water intake = Negative fluid balance
      ii. Causes: bad burns, vomiting/diarrhea, sweat, H₂O deprive
      iii. Symptoms: dry mouth, thirst (Result: weight loss/mental confuse [even hypovolemic shock])
   b. Hypotonic Hydration
      i. Renal insufficiency: Sudden increase in amount of water intake → cells overhydrates/swells
      ii. ECF is diluted: Na⁺ amt normal, but [ ] low due to excess water
   c. Edema
      i. Atypical accumulation of fluid in the interstitial space, leading to tissue swelling
      ii. Caused by anything that increases flow of fluids out of the bloodstream or hinders their return
   d. Factors that accelerate fluid loss include:
      i. Increased blood pressure, capillary permeability
      ii. Incompetent venous valves, localized blood vessel blockage
      iii. Congestive heart failure, hypertension, high blood volume
PART III: ELECTROLYTES

A. General Characteristics
1. Electrolytes: Salts, acids, bases, but electrolyte balance usually refers only to salts
2. Salts
   a. Important for: neuromuscular excitability, controlling fluid movements, etc.
   b. Enter body by ingestion & lost by perspiration, feces, & urine
   c. Sodium
      i. Primary solute in fluid & electrolyte balance:
      ii. 90-95% of all ECF solutes
      iii. Only significant cation osmotic pressure (controls water bal)
      iv. Renal acid-base ctrl mechanisms -> coupled to Na⁺ transport
      v. Imbalances:
         vi. Hyponatremia (deficit Na⁺ in ECF): causes dehydration
         vii. Hypernatremia (excess Na⁺ in ECF): causes brain swelling
         viii. Reabsorbed in kidney: Mostly in PCTs (some in loop of Henle)
            1) When levels of aldosterone, remaining Na⁺ is actively reabsorbed
            2) Water follows sodium if tubule permeability increased by ADH

B. Electrolyte Balance: Sodium
1. Sodium intake: Dietary (~ 6-18 g NaCl/day)
2. Sodium output: Usually 95% via urine; remainder via skin (sweating, etc.) & GI tract (substantial if diarrhea/vomiting)

INPUT (Ingest ~100-300 mEq/day) → Extracellular Fluid → OUTPUT (Skin, GI, Kidneys ~100-300 mEq/day)

3. Aldosterone (ALD) release
   a. Renin-angiotensin mech. (& K⁺): Primary cause of aldosterone release
      i. Mediated by juxtaglomerular apparatus - releases renin due to:
         1) SNS stimulation when there's a drop in filtrate osmolality or BP
      ii. Renin catalyzes production of angiotensin II, prompts aldosterone release
      iii. Elevated K⁺ levels in ECF; also stimulate adrenals to release aldosterone

4. Blood volume: Affects on sodium secretion
   a. Baroreceptors detect change in blood volume/BP (left atrium/main veins-arteries/kidney JGA)
      i. Result: Pressure diuresis: As BP/GFR change, Na⁺ & H₂O output changes to offset the volume/pressure change
   b. Atrial natriuretic peptide (ANP): Released by heart due to ↑BP - ↓BP & blood volume by vasoconstriction & Na⁺ excretion via lower ADH/renin/aldosterone supression

5. Effects of other hormones
   a. Estrogens (menstral cycle: Na⁺Cl⁻ & water retain & pregnancy: edema)
   b. Progesterone (↓Na⁺ reabsorb & is diuretic acting)
   c. Glucocorticoids (↓Na⁺ reabsorb → edema [puffy appearance])

C. Electrolyte Balance: Potassium
1. Relative K⁺ ICF-ECF [] affects cell's resting membrane potential
2. Imbalances:
   a. Hypokalemia (deficit K⁺ in ECF): skeletal weakness
   b. Hyperkalemia (excessive K⁺ in ECF): cardiac irregularities, even arrest (as in Dr. Kevorkian, a.k.a. "Dr. Death")
3. H⁺ shift in & out of cells: leads to corresponding shifts in K⁺ in opposite direction
   a. Acidosis (low pH with excessive H⁺): ECF K⁺ rises
   b. Alkalosis (high pH with reduced H⁺): ECF K⁺ drops
      ** K⁺ (excess) secreted while Na⁺ mostly reabsorbed **
D. Electrolyte Balance: Calcium
1. Used for: Blood clotting, cell membrane permeability
2. Imbalances:
   a. Hypocalcemia: Increased excitability (causes muscle tetany)
   b. Hypercalcemia: Inhibits neurons & muscle cells (heart arrhythmias)
3. Balance is carefully controlled by PTH & Calcitonin
4. PTH
   a. Causes Bones to increase osteoclast activity (degraded bone matrix releases Ca\(^+\) to ECF)
   b. Small intestine to absorb Ca\(^+\), Kidneys to reabsorb Ca\(^+\)
5. Calcitonin (Opposite of PTH)
   a. Released in response ↑blood calcium levels, ↑Ca\(^+\) reabsorption & ↑phosphate secretion
   b. Effect is very weak compared to PTH

E. Electrolyte Balance: Phosphate & Magnesium
1. Phosphate
   a. Filtrate Phosphate actively reabsorbed in PCT
   b. High or normal ECF calcium levels inhibit PTH secretion (More phosphate is retained)
2. Magnesium
   a. Activates coenzymes needed for carbohydrate & protein metabolism
   b. Important for neurotransmission, cardiac function, & neuromuscular activity

PART IV: ACID-BASE BALANCE
A. pH
1. Relative acidity or alkalinity of a solution ([ ] of free H\(^+\)); reflects only free H\(^+\) ions & not those bound to anions: 0 <= 7 => 14
   (more H\(^+\)) acid (less H\(^+\)) base
B. Definitions of Acids and Bases
1. Acids: proton (H\(^+\)) donors
   a. Strong acids: All H\(^+\) is dissociated (in water) very low pH (HCl)
   b. Weak acids: Partially dissociated (good at preventing pH change (e.g., carbonic & acetic acids)
2. Bases: Proton (H\(^+\)) acceptors
   a. Strong bases: Dissociate easily in water & quickly tie up H\(^+\) (e.g., hydroxides)
   b. Weak bases: Accept H\(^+\) more slowly (e.g., HCO\(_3^-\) and NH\(_3\))
3. Neutralization reaction: An acid reacts with a base to form a salt and water
   \[ \text{H}^+\text{Cl}^- + \text{Na}^+\text{OH}^- \rightarrow \text{Na}^+\text{Cl}^- + \text{H}_2\text{O} \]
C. Body Fluids
1. Normal pH of body fluids:
   a. Arterial blood is 7.4
   b. Venous blood and interstitial fluid is 7.35
   c. Intracellular fluid is 7.0
2. Alkalosis or alkalemia arterial blood pH rises above 7.45
3. Acidosis or acidemia arterial pH drops below 7.35 (physiological acidosis)
D. Sources of Hydrogen Ions
1. Sources of H\(^+\)
   a. Excess H\(^+\) mainly from cellular metabolism:
      i. Transporting CO\(_2\) as bicarbonate releases H\(^+\)
      ii. Incomplete Glucose metabolism (anaerobic respiration: lactic acid) or Fat metabolism (organic acids & ketone bodies)
      iii. Breakdown of dietary proteins:
E. Hydrogen Ion Regulation/Buffer Systems (These are physiological buffer systems)
1. Concentration of hydrogen ions is regulated sequentially by:
   a. Chemical buffer systems act within seconds
   b. Respiratory center in brain stem acts within 1-3 minutes
   c. Renal mechanisms require hours to days to effect pH changes
2. pH buffer: A substance that resists change in pH [H+] when either acid or base is added to a solution; it does not prevent a pH change

F. Chemical Buffer Systems: General Characteristics
1. Chemical buffer: A weak acid & its conjugate base (or vice-versa) resist pH changes when adding a Strong acid (weak base accepts excess H+) or Strong base (weak acid donates H+)
2. Chemical buffer systems work together:
   a. Phosphate buffer system (urine & ICF)
   b. Protein buffer system (STRONG: proteins have weak acids & base groups)
   c. Bicarbonate buffer system (Important in ECF!)
      - Strong acid/base converted to weak acid/base
      \[ \text{HCl} + \text{NaHCO}_3 \rightarrow \text{H}_2\text{CO}_3 + \text{NaCl} \]
      strong acid weak base weak acid salt
3. Any drifts in pH are resisted by the entire chemical buffering system (all buffering systems participate when acid or base is added)

G. Chemical Buffer Systems: Bicarbonate
1. Bicarbonate-CO₂ system is similar (respiratory buffer) & is primary buffer system in blood:
   \[
   \text{LUNGS} \quad \downarrow \quad \text{KIDNEYS} \\
   \text{CO}_2 + \text{H}_2\text{O} \rightarrow \text{H}_2\text{CO}_3 \rightarrow \text{H}^+ + \text{HCO}_3^- \\
   \]

   a. Acted on by Lungs & Kidneys: Physiological buffers (ECF)

H. Respiratory Buffer Systems
1. Reversible equilibrium
   a. When hypercapnia or rising plasma H⁺ occurs:
      i. Deeper and more rapid breathing expels more carbon dioxide
      ii. Hydrogen ion concentration is reduced and pH increases
      \[ \text{CO}_2 + \text{H}_2\text{O} \rightarrow \text{H}_2\text{CO}_3 \rightarrow \text{H}^+ + \text{HCO}_3^- \]

2. When hypocapnia or declining plasma H⁺ occurs:
   a. Shallower and slower breathing expels less carbon dioxide
   b. Hydrogen ion concentration increases and pH decreases
      \[ \text{CO}_2 + \text{H}_2\text{O} \rightarrow \text{H}_2\text{CO}_3 \rightarrow \text{H}^+ + \text{HCO}_3^- \]

3. Respiratory system impairment→ acid-base imbalance (respiratory acidosis or respiratory alkalosis)
   Reflexes associated w/ ↑ CO₂ (activated by peripheral & central chemoreceptors detecting ↑ H⁺ [ ])

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I. **Renal Mechanisms of Acid-Base Balance**
   1. Chemical buffers are temporary buffers (can't eliminate ions)
   2. Lungs can eliminate carbonic acid by eliminating $\text{CO}_2$
   3. Kidneys: Only way to rid body of metabolic acids (phosphoric, uric, and lactic acids and ketones) & prevent metabolic acidosis; hence, the kidneys are the ultimate acid-base regulatory organs
   4. Excess metabolic acid buffered to $\text{HCO}_3^-$, then Kidneys excrete H$^+$’s & replenish blood bicarbonate level [ Loosing a H$^+$ is same as gaining $\text{HCO}_3^-$ ]

J. **Respiratory Acidosis and Alkalosis**
   1. Result from failure of the respiratory system to balance pH
   2. $\text{PCO}_2$ is THE indicator of respiratory inadequacy
   3. Normal $\text{PCO}_2$ fluxes between **35 and 45 mm Hg**
      a. ABOVE 45 mm Hg = respiratory acidosis (most common cause of acid-base imbalance: usually when a person breathes too shallow or gas exchange hampered by diseases [e.g. pneumonia, cystic fibrosis, or emphysema])
      b. BELOW 35 mm Hg = respiratory alkalosis (common result of hyperventilation)

K. **Metabolic Acidosis and Alkalosis**
   1. All pH imbalances except those caused by abnormal blood $\text{CO}_2$ levels
   2. Normal $\text{HCO}_3^-$ fluctuate: 22-26 mEq/L
      a. BELOW 22 mEq/L = Metabolic acidosis
         - 2nd most common cause of acid-base imbalance: e.g. from too much alcohol beverage, excessive $\text{HCO}_3^-$ loss, accumulation of lactic acid, shock, starvation & kidney failure
      b. ABOVE 26 mEq/L = Metabolic alkalosis
         - Example: By vomiting the acid contents of the stomach, intake of excess base (e.g., from antacids) & constipation (excessive $\text{HCO}_3^-$ is reabsorbed)

L. **Respiratory and Metabolic Compensation**
   1. Acid-base imbalance: Result of inadequate physiological buffer systems (Inadequacy compensated for by other buffer systems)
      a. Respiratory system will attempt to correct metabolic acid-base imbalances
      b. Physiological buffer system (kidneys) will work to correct imbalances caused by inadequate respiratory buffering (e.g. respiratory disease)
   2. Respiratory compensation:
      a. Metabolic acidosis: Rate & depth of breathing become elevated
      b. Metabolic alkalosis: Compensation exhibits slow, shallow breathing (allows $\text{CO}_2$ to accumulate in blood & raise the pH)
   3. Metabolic compensation:
      a. Respiratory acidosis: Kidneys retain $\text{HCO}_3^-$ to offset the increased H$^+$ of acidosis
      b. Respiratory alkalosis: Kidneys eliminate $\text{HCO}_3^-$ from body by failing to reclaim it or actively secreting it
   4. Problem-solving:
      1st: Examine pH values to determine nature of disorder (acidosis, normal, alkalosis)
      2nd: Examine $\text{CO}_2$ and bicarbonate values to determine the cause(s) of the disorder (respiratory, metabolic)
      3rd: Examine the other values to determine whether compensation is taking place