Fluid and Electrolytes

Body Fluids

- Body water and dissolved substances
  - Cells need a stable environment to function

Body Fluids

- Body water content
  - Infants
    - 73% or more water
  - Adult males
    - ~60% water
  - Adult females
    - ~50% water
    - Higher fat content & less skeletal muscle mass
  - Water content declines with old age
    - ~45%

Fluid Compartments

- Total body water = 40 L
- Where is it all??
  1. Intracellular fluid (ICF) compartment
    - 2/3 (25 L)
  2. Extracellular fluid (ECF) compartment
    - 1/3 (15 L)
      a. Plasma: 3 L
      b. Interstitial fluid (IF): 12 L
      c. Other ECF
        - Lymph, CSF, humor of the eye, synovial fluid, serous fluid, gastrointestinal secretions

Fluid Compartments

- Intracellular fluid
  - Metabolic reactions
  - Homeostasis essential to health
**Fluid Compartments**

- **Extracellular fluid**
  - Examples?
  - Functions
    - Route in and out of cell
    - Osmosis is the primary force for movement
    - Lubricant
    - Solvent
    - Acid-base balance

**Composition of Body Fluids**

- ECF and ICF composition varies
  - ECF
    - All similar, except higher protein content in plasma
    - Major cation: Na
    - Major anion: Cl
  - ICF:
    - Low Na and Cl
    - Major cation: K
    - Major anions: proteins and HPO₄²⁻

**Composition of Body Fluids**

- **Electrolytes**
  - Dissociate into ions in water
  - Measure the number of electrical charges in a liter
    - Milliequivalents per liter (mEq/L)

**Water Balance**

- Water intake = water output = 2500 ml/day
  - Water intake
    - Gastrointestinal tract = 1,500 ml/day
    - Absorbed from food = 750 ml/day
    - Metabolism = 250 ml/day
  - Water output
    - Evaporation = 200 ml/day
    - Exhaled breath = 700 ml/day
    - Gastrointestinal tract = 100 ml/day
    - Urine = 1,500 ml/day
Figure 26.4

Regulation of Water Intake and Loss

- **Carefully regulated**
  - Influences blood pressure and cytoplasmic volume

Regulation of Water Intake and Loss

- **Obligatory water loss**
  - Expired air, perspiration, fecal moisture, urine output (minimum 400ml/day)
  - Independent of hydration status!

Regulation of Water Intake and Loss

- **Thirst mechanism**
  - Driving force for water intake
    - Response may be modified by behavior
    - Hypothalamic thirst center osmoreceptors stimulated by
      - Increased plasma osmolality of 2–3%
      - Substantial decrease in blood volume or pressure
    - Results in reduced salivary gland function
      - Dry mouth
      - Sensation of thirst

Regulation of Water Intake and Loss

- **Drinking water → inhibition of the thirst center**
- **Inhibitory feedback signals include**
  - Relief of dry mouth
  - Activation of stomach and intestinal stretch receptors

**Figure 26.5**

(*Minor stimulus*)

Granular cells in kidney

Dry mouth

Renin-angiotensin mechanism

Osmoreceptors in hypothalamus

Hypothalamic thirst center

Sensation of thirst; person takes a drink

Water absorbed from GI tract

Angiotensin II

Plasma osmolality

Blood pressure

Water moistens mouth, throat; stretches stomach, intestine

Plasma volume*
Regulation of Water Intake and Loss

- Endocrine function
  - ADH
    - Increases water reabsorption = reduces blood osmotic pressure
    - Hypothalamic osmoreceptors trigger or inhibit release
    - Released in response to:
      - Increases in blood osmolarity (primary trigger)
      - Large changes in blood volume or pressure
        - e.g. fever, sweating, vomiting, diarrhea, blood loss, burns

- Aldosterone
  - Increases reabsorption of sodium, chloride, and water
  - Increases blood volume = increases blood pressure
  - No change in blood osmotic pressure because water and sodium move together
  - Released in response to decreases in blood pressure

Regulation of ECF Movement

- Movement from capillaries mediated by hydrostatic and osmotic pressures
- Fluid distribution is a balance of forces
  - Capillary hydrostatic
  - Interstitial osmotic
  - Interstitial hydrostatic
  - Capillary osmotic

Fluid Shifts

- Extracellular fluid distribution is dynamic
- Interstitial fluid formation is continuous

Regulation of ECF Movement

- Net HP—Net OP
  - Positive pressure causes fluid to move out of the blood
  - Negative pressure causes fluid to move into the blood

Edema

- Atypical accumulation of interstitial fluid
  - Causes
    - Increased flow of fluid out of the blood or impaired lymphatic drainage
    - ↑ Blood pressure
    - ↑ Proteins in interstitial fluid
    - ↓ Plasma proteins
    - Lymphatic obstruction
Edema

- **↑ Blood pressure**
  - More tissue fluid at arteriolar end of capillary
  - Hypertension
- **↑ Proteins in interstitial fluid**
  - Decreases osmotic return of water into venous end of capillary
  - Inflammation
  - Allergic reaction

Edema

- **↓ Plasma proteins**
  - Decreases osmotic return of water into venous end of capillary
  - Liver disease
  - Kidney disease
  - Malnutrition
- **Lymphatic obstruction**
  - Parasites
    - Elephantiasis
  - Tumor

Dehydration

- **Fluid loss exceeds fluid intake**
  - Extracellular osmolarity exceeds intracellular osmolarity
  - Fluid moves into ECF compartment
    - Cell volume reduction = compromised function
- **Excessive loss of H₂O from ECF**
  - ECF osmotic pressure rises
  - Cells lose H₂O to ECF by osmosis; cells shrink

Dehydration

- **Fluid loss exceeds fluid intake**
  - Causes
    - Hemorrhage, severe burns, prolonged vomiting or diarrhea, profuse sweating, water deprivation, diuretic abuse
  - Symptoms
    - Thirst, dry flushed skin, oliguria
  - Consequences
    - May lead to weight loss, mental confusion, hypovolemic shock, and electrolyte imbalances

Hypotonic Hydration

- **A.K.A. Water intoxication**
  - Causes
    - Renal failure or rapid excessive water intake
Hypotonic Hydration

ECF is diluted
Hyponatremia
Net osmosis into tissue cells
Swelling, perhaps bursting of cells
Severe metabolic disturbances (nausea, vomiting, muscular cramping, cerebral edema)
Possible death

Electrolytes

- Salts, acids and bases
- Balance must be maintained between...
  - Ingestion to add materials
  - Excretion to remove materials
    - Kidneys play a key role

Electrolytes

- Importance of electrolytes
  - Controlling fluid movements
  - Excitability of cells
  - Membrane permeability

In addition to these general considerations, each electrolyte has its own specific physiological effects

Electrolytes

- Pica
  - Eating non-food substances, often due to mineral deficiency
  - Examples: Consumption of chalk, clay, match tips
Membrane Potential

- Polarized across resting membrane
  - Inside negative relative to outside
  - Nernst equation allows us to calculate the potential across the membrane for any single ion

60 mV

Membrane Potential

- Depolarization
  - Reduced membrane potential
  - Smaller stimulus needed to reach threshold
- Hyperpolarization
  - Increased membrane potential
  - Larger stimulus required to reach threshold

Membrane Potential

- Calcium and magnesium are normally non-diffusing
  - Changes in distribution do not directly affect membrane potential
- Changes in concentration influence sodium channel permeability

Membrane Potential

Hyperpolarized

<table>
<thead>
<tr>
<th>Hypernatremia</th>
<th>Hyponatremia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hyperkalemia</td>
<td>Hypokalemia</td>
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<tr>
<td>Hypocalcemia</td>
<td>Hypercalcemia</td>
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<tr>
<td>Hypomagnesemia</td>
<td>Hypermagnesemia</td>
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<tr>
<td>Hypochloremia</td>
<td>Hyperchloremia</td>
</tr>
</tbody>
</table>

Sodium

- Major extracellular cation
  - Normal: 135-145 mEq/L
  - $Na^+$ leaks into cells and is pumped out against its electrochemical gradient
- Primary roles
  - Necessary for impulse transmission
    - Nervous and muscle tissue
  - Primary regulator of ECF volume
Sodium

- Variations in Na⁺ can alter ECF volume
- Imbalances summary
  - Hypovolemic hyponatremia
    - Gain of water only (dilutes sodium)
  - Hypovolemic hypernatremia
    - Loss sodium first then water follows (more sodium lost)
  - Hypervolemic hypernatremia
    - Gain of sodium and water (more sodium gained)
  - Hypovolemic hyponatremia
    - Loss of sodium and water (more water lost)

- Hyponatremia
  - Hypovolemic
    - Replacing water (not electrolytes) after perspiration
    - Freshwater near-drowning
    - Syndrome of inappropriate ADH Secretion (SIADH)
    - Renal failure
  - Hypovolemic
    - GI disease (decreased intake, loss through vomiting and diarrhea)
    - Aldosterone deficiency (Addison’s)
    - Diuretics

- Hypernatremia
  - Not as common
  - Unconscious or confused patients higher risk
  - Hypervolemic
    - Saltwater near drowning
    - Excessive salt intake
    - Hyperaldosteronism
  - Hypovolemic hypernatremia
    - Decreased fluid intake
    - Excessive water loss (fever)

- Hyponatremia
  - Symptoms
    - Feeling of “impending doom”
    - Abdominal cramps
    - Nausea and vomiting
    - Anorexia
    - BP changes
    - Cellular swelling
    - Cerebral edema possible
      - Lethargy, confusion
      - Muscle twitching or convulsions

- Hypernatremia
  - Symptoms
    - Reduced interstitial fluid
    - Dry sticky mucous membranes, intense thirst, dry tongue
    - Reduced perspiration
    - Flushed skin
    - Cerebral cellular dehydration
      - Lethargy, muscle weakness, twitching, seizures
    - Severe cases: disorientation, delusions, hallucinations
    - Altered neuromuscular activity
      - Muscle weakness, twitching
    - Low blood volume
      - Hypotension, tachycardia

Potassium

- Major intracellular cation
  - Normal range 3.5-5.5 mEq/L
  - Normal kidney function required for balance
- Importance
  - Affects RMP in neurons and muscle cells
    - Especially cardiac muscle
  - Maintenance of cellular volume
  - pH regulation
Potassium

- Regulation
  - Aldosterone
    - Stimulates K⁺ secretion and Na⁺ reabsorption
  - Dietary sources
    - Very important since potassium is poorly stored in the body

- Acid-base balance
  - H⁺ shifts in and out of cells in response to pH
    - Leads to corresponding potassium shifts in the opposite direction to maintain cation balance
    - Shifts may cause changes in ECF potassium levels

Potassium

- Hypokalemia
  - Causes
    - GI losses
      - Intestinal fistula, NG suctioning, vomiting, diarrhea
    - Redistribution
      - Alkalosis, insulin administration
    - Medications
      - Diuretics, natural licorice (mimics aldosterone), steroids, certain drugs (amphotericin B is an antifungal)
    - Disorders
      - Hyperaldosteronism, Cushing’s, acute renal failure, alcoholism, liver disease

- Hypokalemia
  - Symptoms
    - Slowed smooth muscle contraction
      - Anorexia, constipation, GI distention
    - Slowed skeletal muscle contraction
      - Muscle weakness, cramping, paralysis
    - Decreased myocardial contraction
      - Dysrhythmias, hypotension, weak pulses

Potassium

- Hyperkalemia
  - Causes
    - Retention disorders
      - Renal failure (↓ GFR), Addison’s disease, hypoaldosteronism, transfusion with old RBCs (potassium is released as RBCs rupture)
    - Releases of intracellular potassium
      - Acidosis, trauma, severe burns, severe infection
    - Excessive administration
      - Oral or IV

- Hyperkalemia
  - Symptoms
    - GI effects
      - Nausea, explosive diarrhea, intestinal colic, cramping
    - Musculoskeletal effects
      - Paresthesia (“pins and needles” sensation), muscle weakness, muscle cramps, paralysis
    - Cardiac effects
      - Dysrhythmias (arrhythmias), hypotension, cardiac arrest, conduction abnormalities, ectopic foci
Calcium

- ECF levels closely regulated
  - 8.5-10.5 mg/dl
    - Nerve and muscle function
    - Blood clotting
    - Tissue development
    - Enzyme activation

Calcium

- Distribution
  - Most is stored in bone
  - Serum
    - Ionized form is active form (50%)
    - Plasma protein bound
  - pH determines equilibrium

Calcium

- PTH
  - Influences Ca\(^{2+}\) in bone, kidneys, and GI tract
  - Released when plasma Ca\(^{2+}\) concentration is low
    - Activates osteoclasts
      - Release calcium and phosphate from bone
    - Stimulates intestinal Ca\(^{2+}\) uptake
    - Increases renal tubule reabsorption
  - Calcitonin
    - Inhibits osteoclasts
    - Not as important in humans as PTH

Calcium

- Hypocalcemia
  - Causes
    - Inactive parathyroid glands
    - Removal of parathyroid glands
    - Low dietary calcium
    - Renal failure
    - Reduced intestinal absorption

Calcium

- Hypocalcemia
  - Symptoms
    - Increased nerve cell permeability and excitability
    - Tetany, carpopedal spasms, convulsions, seizures
    - Tingling in fingers, mouth and feet
    - Trousseau's sign
    - Cardiac arrhythmias
**Calcium**

- **Hypercalemia**
  - **Causes**
    - Overactive parathyroid gland
    - Excess vitamin D intake
    - Acidosis
    - Leukemia

- **Hypercalemia**
  - **Symptoms**
    - Decreased neuromuscular excitability
    - Muscle weakness
    - Poor coordination
    - Anorexia
    - Constipation
    - Renal calculi
    - Cardiac arrest

**Magnesium**

- **Second most abundant intracellular cation**
  - 1.5 – 2.5 mEq/liter
  - Activates many enzyme systems
  - Carbohydrate and protein metabolism
  - Important to neuromuscular function

- **Location**
  - Skeleton
  - Intracellularly
    - Heart, skeletal muscle, liver
  - Serum
    - Ionized and protein bound

- **Hypomagnesemia**
  - **Causes**
    - Critical illnesses
    - Alcohol withdrawal
    - Malnutrition followed by nourishment
    - Severe GI fluid losses

- **Hypomagnesemia**
  - **Symptoms**
    - Hyperexcitability with muscular weakness
    - Tremors
    - Athetoid movements
    - Tetany
    - Laryngeal stridor
    - Mood alterations
    - Cardiac arrhythmias

- **Hypermagnesemia**
  - **Causes**
    - Renal failure
    - Untreated DKA
    - Excessive administration
Magnesium

- **Hypermagnesemia**
  - Symptoms
    - Acute elevations
      - Depresses CNS
    - Mild elevation
      - Vasodilation → hypotension
    - Moderate to high elevations
      - Lethargy, dysarthria (unclear articulation of speech), drowsiness
      - Loss of deep tendon reflexes
      - Muscular weakness

Phosphate

- **Normal 2.5-4.5 mg/dl**
  - Phosphorus essential to mitochondrial function, RBCs, and nervous system function

Phosphate

- **Hypophosphatemia**
  - Causes
    - Hyperventilation
    - Alcohol withdrawal
    - Poor dietary intake
    - DKA
    - Major thermal burns
  - Symptoms
    - Neurologic symptoms
      - Irritability, apprehension, weakness, numbness, paresthesia, confusion, seizures, coma
    - Tissue anoxia
    - Infection
    - Muscle pain

Phosphate

- **Hyperphosphatemia**
  - Causes
    - Renal failure
    - Chemotherapy
    - Excessive dietary intake
    - Muscle necrosis
  - Symptoms
    - Altered mentation and cardiac abnormalities

Acid-Base Balance

- **Mechanisms that control acid-base homeostasis**
  - Acids and bases continually enter and leave body
  - Hydrogen ions also result from metabolic activity
Acid-Base Balance

- **Acids**
  - Hydrogen ion donors
  - Dissociation = $H^+$ and a conjugate base
- **Bases**
  - Hydrogen ion acceptors

  pH determined by hydrogen ion concentration

**Strong acids**
- Dissociate completely in water
- Can dramatically affect pH

**Weak acids**
- Dissociate partially in water
- Efficient at preventing pH changes

**Chemical buffer**
- System of two or more compounds that act to resist pH changes when acid or base is added
- Usually consist of a weak acid and its conjugate base

**Buffers**
- Sodium bicarbonate-carbonic acid
  - Mixture of $H_2CO_3$ (weak acid) and $NaHCO_3$
  - $NaHCO_3 \rightarrow Na^+ + HCO_3^-$ (conjugate base)
- Buffers ICF and ECF
- Present in all body fluids

---

(a) A strong acid such as HCl dissociates completely into its ions.
(b) A weak acid such as $H_2CO_3$ does not dissociate completely.
Acid-Base Balance

• Buffers
  – Sodium bicarbonate-carbonic acid
    • If acid is added:
      - $\text{HCO}_3^-$ ties up $\text{H}^+$ and forms $\text{H}_2\text{CO}_3$
      - Example: $\text{HCl} + \text{NaHCO}_3 \rightarrow \text{H}_2\text{CO}_3 + \text{NaCl}$
      - Prevents accumulation of $\text{H}^+$
      - pH decreases only slightly
      - $\text{H}_2\text{CO}_3$ is easily converted to $\text{CO}_2$ and $\text{H}_2\text{O}$
      - Removed by respiratory system

  • If base is added
    - Causes $\text{H}_2\text{CO}_3$ to dissociate and donate $\text{H}^+$
    - $\text{H}^+$ ties up the base (e.g., $\text{OH}^-$)
    - Example: $\text{NaOH} + \text{H}_2\text{CO}_3 \rightarrow \text{NaHCO}_3 + \text{H}_2\text{O}$
    - $\text{OH}^-$ does not accumulate
    - pH rises only slightly
    - $\text{H}_2\text{CO}_3$ supply is almost limitless from $\text{CO}_2$ produced by cellular respiration

• Normal body processes tend to acidify blood
  - More base is needed
  - Normal ratio is 20:1 (NaHCO$_3$:H$_2$CO$_3$)
  - Produces pH of 7.4

• Plasma bicarbonate highly regulated by kidneys
  • Plasma carbonic acid regulated by lungs

• Phosphate buffer system
  • Takes place in kidney tubular fluids and RBC’s
  • Action is nearly identical to the bicarbonate buffer

• Components are sodium salts of:
  - Dihydrogen phosphate ($\text{H}_2\text{PO}_4^-$) – Weak acid
  - Monohydrogen phosphate ($\text{HPO}_4^{2-}$) – Conjugate base
  • Effective buffer in urine and ICF (RBCs)
  • Where phosphate concentrations are high
Acid-Base Balance

- **Buffers**
  - Phosphate buffer system
    - Addition of acid
      - $\text{HCl} + \text{Na}_2\text{HPO}_4 \rightarrow \text{NaH}_2\text{PO}_4 + \text{NaCl}$
    - Addition of base
      - $\text{NaOH} + \text{NaH}_2\text{PO}_4 \rightarrow \text{Na}_2\text{HPO}_4 + \text{H}_2\text{O}$
  
  Both reactions prevent large changes in pH

Acid-Base Balance

- **Buffers**
  - Hemoglobin-oxyhemoglobin buffer system
    - Second buffer in RBCs
    - Don’t need to know any more details for our purposes

Acid-Base Balance

- **Buffers**
  - Protein buffer system
    - Most abundant buffer of the body
    - Active over wide pH range

  A single protein molecule may function as an acid or a base
  - Depends upon the pH in the solution

Acid-Base Balance

- **Respiratory and renal regulation**
  - Respiratory regulation
    - Regulates $\text{CO}_2$ and $\text{H}^+$
  - Renal regulation
    - Three actions
      1. Acidification of urine
      2. Reabsorption of bicarbonate
      3. Buffering effects of phosphate and ammonia in filtrate
Acid-Base Balance

• Respiratory acidosis
  – Carbonic acid excess, distinguished by CO2
  – Conditions which impair ventilation
    • Drug overdose (sedatives)
    • Chest or head injuries
    • Pulmonary edema
    • Sudden airway obstruction
    • COPD

  Compensation by kidneys
  – Work to reestablish 20:1 ratio of bicarbonate : carbonic acid
  – Kidneys increase formation of NaHCO3 and excretion of ammonium ion
  – Example
    \[ \text{pH} = 7.30 \quad \text{pCO}_2 = 55 \quad \text{HCO}_3^- = 27 \]

• Respiratory alkalosis
  – Carbonic acid deficit, characterized by fall in CO2
  – Causes of hyperventilation
    • Anxiety
    • Early COPD
    • Early aspirin toxicity
    • Excessive mechanical ventilation
    • High altitude

  Compensation involves
  – HCO3- excretion
  – H+ retention
  – Example
    \[ \text{pH} = 7.48 \quad \text{pCO}_2 = 30 \quad \text{HCO}_3^- = 20 \]

• Respiratory alkalosis
  – Temporary disturbance
    • Increased respiratory rate

  Signs and symptoms of respiratory alkalosis
  • Dilation of cerebral blood vessels
  • Cerebral edema and depressed CNS
  • Increased acid and ammonia in urine
  • Hyperkalemia
  • Arrhythmias

  Symptoms
  • Cerebral vasoconstriction
  • Lightheadedness
  • Lack of ability to concentrate
  • Tingling in hands and feet
  • Carpopedal spasms
  • Altered consciousness
Acid-Base Balance

• Metabolic acidosis
  • Loss of base
    – Kidney disease
    – Severe diarrhea or prolonged vomiting
  • Excess acid accumulation
    – Diabetes
    – Lactic acid
    – Impaired renal excretion
  • Respiratory compensation
    – Hyperventilation to blow of \( \text{CO}_2 \)
    – Kussmaul (deep, labored, fast) breathing
  • Renal compensation
    – If possible
      – Reabsorb \( \text{NaHCO}_3 \) and secrete \( \text{H}^+ \) and \( \text{NH}_4^+ \)

Example
\[ \text{pH} = 7.32 \quad \text{pCO}_2 = 29 \quad \text{HCO}_3^- = 17 \]

Acid-Base Balance

• Metabolic alkalosis
  • Excess accumulation of base
    – Increased consumption (antacid abuse)
  • Depletion of acid
    – Excessive vomiting, gastric suction, diuretics

• Compensation
  • Respiratory
    – Hypoventilation
    – Hypoxic drive of chemoreceptors limits this response
  • Kidneys
    – If possible
      – Secretes \( \text{NaHCO}_3 \) and retains \( \text{H}^+ \)

Example
\[ \text{pH} = 7.50 \quad \text{pCO}_2 = 50 \quad \text{HCO}_3^- = 32 \]

Acid-Base Balance

• Metabolic alkalosis
  • Signs and symptoms
    – Tingling of fingers and toes
    – Dizziness
    – Tetany
    – Carpopedal spasms

Signs mainly due to decreased ionized calcium and increased membrane permeability