Chapter 24 Water, Electrolyte and Acid-Base Balance

- Total body water for 150 lb. male = 40L
  - 65% ICF
  - 35% ECF
    - 25% tissue fluid
    - 8% blood plasma, lymph
    - 2% transcellular fluid (CSF, synovial fluid)
Water Movement in Fluid Compartments

- Electrolytes play principle role in water distribution and total water content
Water Gain

• Metabolic water
  – from aerobic metabolism
  – from dehydration synthesis

• Preformed water
  – ingested in food and drink
Water Loss

• Routes of loss
  – urine, feces, expired breath, sweat, cutaneous transpiration

• Loss varies greatly with environment and activity
  – respiratory loss ↑: with cold, dry air or heavy work
  – perspiration loss ↑: with hot, humid air or heavy work

• Insensible water loss
  – breath and cutaneous transpiration

• Obligatory water loss
  – breath, cutaneous transpiration, sweat, feces, minimum urine output (400 ml/day)
Fluid Balance

Intake: 2,500 mL/day
- Metabolic water: 200 mL
- Food: 700 mL
- Drink: 1,600 mL

Output: 2,500 mL/day
- Feces: 200 mL
- Expired air: 300 mL
- Cutaneous transpiration: 400 mL
- Sweat: 100 mL
- Urine: 1,500 mL
Regulation of Fluid Intake

• Dehydration
  – ↓ blood volume and pressure
  – ↑ blood osmolarity

• Thirst mechanisms
  – stimulation of thirst center (in hypothalamus)
    • angiotensin II: produced in response to ↓ BP
    • ADH: produced in response to ↑ blood osmolarity
    • hypothalamic osmoreceptors: signal in response to ↑ ECF osmolarity
  – inhibition of salivation
    • thirst center sends sympathetic signals to salivary glands
Satiation Mechanisms

• Short term (30 to 45 min), fast acting
  – cooling and moistening of mouth
  – distension of stomach and intestine

• Long term inhibition of thirst
  – rehydration of blood (↓ blood osmolarity)
    • stops osmoreceptor response, ↑ capillary filtration, ↑ saliva
Dehydration & Rehydration

Dehydration
- Increased blood osmolarity
- Antidiuretic hormone
- Stimulates thirst center

Reduced blood pressure
- Renin
- Angiotensin II
- Stimulates thirst center

Reduces salivation
- Dry mouth
- Sense of thirst

Ingestion of water
- Cools and moistens mouth
- Distends stomach and intestines
- Rehydrates blood
- Short-term inhibition of thirst
- Long-term inhibition of thirst
Regulation of Output

• Only control over water output is through variations in urine volume

• By controlling $\text{Na}^+$ reabsorption (*changes volume*)
  – as $\text{Na}^+$ is reabsorbed or excreted, water follows it

• By action of ADH (*changes concentration of urine*)
  – ADH secretion (*as well as thirst center*) stimulated by hypothalamic osmoreceptors in response to dehydration
  – aquaporins synthesized in response to ADH
    • by cells of kidney collecting ducts, as membrane proteins to channel water back into renal medulla, $\text{Na}^+$ is still excreted
  – Effects: slows ↓ in water volume and ↑ osmolarity
Action of Antidiuretic Hormone

Dehydration
\[ \uparrow H_2O \quad \downarrow H_2O \quad \uparrow Na^+ \quad \downarrow Na^+ \]

Elevates blood osmolarity

Stimulates hypothalamic osmoreceptors

Stimulates posterior pituitary to release ADH

Stimulates distal convoluted tubule and collecting duct

Increases water reabsorption

Increases ratio of Na\(^+\): H\(_2\)O in urine

Reduces urine volume

Negative feedback loop

Water ingestion

Thirst

Negative feedback loop
Disorders of Water Balance

• Fluid deficiency
  – volume depletion (hypovolemia)
    • total body water ↓, osmolarity normal
    • hemorrhage, severe burns, chronic vomiting or diarrhea
  – dehydration
    • total body water ↓, osmolarity rises
    • lack of drinking water, diabetes, profuse sweating, diuretics
    • infants more vulnerable
      – high metabolic rate demands high urine excretion, kidneys cannot concentrate urine effectively, greater ratio of body surface to mass
    • affects all fluid compartments
  – most serious effects: circulatory shock, neurological dysfunction, infant mortality
Water Loss & Fluid Balance

1) profuse sweating
2) produced by capillary filtration
3) blood volume and pressure drop, osmolarity rises
4) blood absorbs tissue fluid to replace loss
5) fluid pulled from ICF
Fluid Excess

- **Volume excess**
  - both Na$^+$ and water retained, ECF *isotonic*
  - aldosterone hypersecretion

- **Hypotonic hydration**
  - more water than Na$^+$ retained or ingested, ECF *hypotonic* - can cause cellular swelling

- **Most serious effects are pulmonary and cerebral edema**
Kidneys compensate very well for excessive fluid intake, but not for inadequate intake.
Fluid Sequestration

• Excess fluid in a particular location
• Most common form: edema
  – accumulation in the interstitial spaces
• Hematomas
  – hemorrhage into tissues; blood is lost to circulation
• Pleural effusions
  – several liters of fluid may accumulate in some lung infections
Electrolytes

- Chemically reactive in metabolism, determine cell membrane potentials, osmolarity of body fluids, water content and distribution
- Major cations
  - Na\(^+\), K\(^+\), Ca\(^{2+}\), H\(^+\)
- Major anions
  - Cl\(^-\), HCO\(_3\)^-, PO\(_4\)^{3-}\)
- Normal concentrations
  - see table 24.2
Sodium - Functions

- Membrane potentials
- Accounts for 90 - 95% of osmolarity of ECF
- $\text{Na}^+-\text{K}^+$ pump
  - (exchanges intracellular $\text{Na}^+$ for extracellular $\text{K}^+$)
  - cotransport of other solutes (glucose)
  - generates heat
- $\text{NaHCO}_3$ has major role in buffering pH
Sodium - Homeostasis

• Deficiency rare
  – 0.5 g/day needed, typical diet has 3 to 7 g/day

• Aldosterone - “salt retaining hormone”
  – primary effects: ↓ NaCl and ↑ K⁺ excreted in urine

• **ADH** - ↑ blood Na⁺ levels stimulate ADH release
  – kidneys reabsorb more water (without retaining more Na⁺)

• Others - estrogen retains water during pregnancy
  – progesterone has diuretic effect
Sodium - Imbalances

• Hypernatremia
  – plasma sodium $> 145$ mEq/L
    • from IV saline
  – water retension, hypertension and edema

• Hyponatremia
  – plasma sodium $< 130$ mEq/L
  – result of excess body water, quickly corrected by excretion of excess water
Potassium - Functions

• Most abundant cation of ICF
• Determines intracellular osmolarity
• Membrane potentials (with sodium)
• Na\(^+\)-K\(^+\) pump
Potassium - Homeostasis

• 90% of K⁺ in glomerular filtrate is reabsorbed by the PCT
• DCT and cortical portion of collecting duct secrete K⁺ in response to blood levels
• Aldosterone stimulates renal secretion of K⁺
Aldosterone

Hypotension $\downarrow$ H$_2$O

↓H$_2$O

Renin

Angiotensin

Hyponatremia $\downarrow$ Na$^+$

Hyperkalemia $\uparrow$ K$^+$

Stimulates adrenal cortex

Secretes aldosterone

Stimulates renal tubules

Increases Na$^+$ reabsorption

Less Na$^+$ and H$_2$O in urine

Supports existing fluid volume and Na$^+$ concentration pending oral intake

Increases K$^+$ secretion

More K$^+$ in urine

↓K$^+$

Negative feedback loop
Potassium - Imbalances

• Most dangerous imbalances of electrolytes

• Hyperkalemia - effects depend on rate of imbalance
  – if concentration rises quickly, (crush injury) the sudden increase in extracellular K⁺ makes nerve and muscle cells abnormally excitable
  – slow onset, inactivates voltage-gated Na⁺ channels, nerve and muscle cells become less excitable

• Hypokalemia
  – sweating, chronic vomiting or diarrhea, laxatives
  – nerve and muscle cells less excitable
    • muscle weakness, loss of muscle tone, ↓ reflexes, arrhythmias
Potassium & Membrane Potentials

- **K+ concentrations in equilibrium**: Equal diffusion into and out of cell.
- **Normal resting membrane potential (RMP)**

Hyponatremia

- **Elevated extracellular K+ concentration**
- **Less diffusion of K+ out of cell**
- **Elevated RMP (cells partially depolarized)**

- **Cells more excitable**

Hypernatremia

- **Reduced extracellular K+ concentration**
- **Greater diffusion of K+ out of cell**
- **Reduced RMP (cells hyperpolarized)**

- **Cells less excitable**
Chloride - Functions

• ECF osmolarity
  – most abundant anions in ECF

• Stomach acid
  – required in formation of HCl

• Chloride shift
  – CO₂ loading and unloading in RBC’s

• pH
  – major role in regulating pH
Chloride - Homeostasis

- Strong attraction to Na\(^+\), K\(^+\) and Ca\(^{2+}\), which it passively follows
- Primary homeostasis achieved as an effect of Na\(^+\) homeostasis
Chloride - Imbalances

• Hyperchloremia
  – result of dietary excess or IV saline

• Hypochloremia
  – result of hyponatremia

• Primary effects
  – pH imbalance
Calcium - Functions

- Skeletal mineralization
- Muscle contraction
- Second messenger
- Exocytosis
- Blood clotting
Calcium - Homeostasis

• PTH
• Calcitriol (vitamin D)
• Calcitonin (in children)
  – these hormones affect bone deposition and resorption, intestinal absorption and urinary excretion
• Cells maintain very low intracellular Ca^{2+} levels
  – to prevent calcium phosphate crystal precipitation
    • phosphate levels are high in the ICF
Calcium - Imbalances

• Hypercalcemia
  – alkalosis, hyperparathyroidism, hypothyroidism
  – ↓ membrane Na$^+$ permeability, inhibits depolarization
  – concentrations $> 12$ mEq/L causes muscular weakness, depressed reflexes, cardiac arrhythmias

• Hypocalcemia
  – vitamin D ↓, diarrhea, pregnancy, acidosis, lactation, hypoparathyroidism, hyperthyroidism
  – ↑ membrane Na$^+$ permeability, causing nervous and muscular systems to be abnormally excitable
  – very low levels result in tetanus, laryngospasm, death
Phosphates - Functions

• Concentrated in ICF as
  – phosphate ($\text{PO}_4^{3-}$), monohydrogen phosphate ($\text{HPO}_4^{2-}$), and dihydrogen phosphate ($\text{H}_2\text{PO}_4^-$)

• Components of nucleic acids, phospholipids, ATP, GTP, cAMP

• Activates metabolic pathways by phosphorylating enzymes

• Buffers pH
Phosphates - Homeostasis

- **Renal control**
  - if plasma concentration drops, renal tubules reabsorb all filtered phosphate

- **Parathyroid hormone**
  - ↑ excretion of phosphate

- **Imbalances not as critical**
  - body can tolerate broad variations in concentration of phosphate
Acid-Base Balance

• Important part of homeostasis
  – metabolism depends on enzymes, and enzymes are sensitive to pH
• Normal pH range of ECF is 7.35 to 7.45
• Challenges to acid-base balance
  – metabolism produces lactic acids, phosphoric acids, fatty acids, ketones and carbonic acids
Acids and Bases

• Acids
  – strong acids ionize freely, markedly lower pH
  – weak acids ionize only slightly

• Bases
  – strong bases ionize freely, markedly raise pH
  – weak bases ionize only slightly
Buffers

• Resist changes in pH
  – convert strong acids or bases to weak ones

• Physiological buffer
  – system that controls output of acids, bases or CO₂
  – urinary system buffers greatest quantity, takes several hours
  – respiratory system buffers within minutes

• Chemical buffer systems
  – restore normal pH in fractions of a second
  – bicarbonate, phosphate and protein systems
Bicarbonate Buffer System

- Solution of carbonic acid and bicarbonate ions
  \[ \text{CO}_2 + \text{H}_2\text{O} \leftrightarrow \text{H}_2\text{CO}_3 \leftrightarrow \text{HCO}_3^- + \text{H}^+ \]

- Reversible reaction important in ECF
  \[ \text{CO}_2 + \text{H}_2\text{O} \rightarrow \text{H}_2\text{CO}_3 \rightarrow \text{HCO}_3^- + \text{H}^+ \]
  - lowers pH by releasing \( \text{H}^+ \)
  \[ \text{CO}_2 + \text{H}_2\text{O} \leftarrow \text{H}_2\text{CO}_3 \leftarrow \text{HCO}_3^- + \text{H}^+ \]
  - raises pH by binding \( \text{H}^+ \)

- Functions with respiratory and urinary systems
  - to lower pH, kidneys excrete \( \text{HCO}_3^- \)
  - to raise pH, kidneys and lungs excrete \( \text{CO}_2 \)
**Phosphate Buffer System**

- $\text{H}_2\text{PO}_4^- \leftrightarrow \text{HPO}_4^{2-} + \text{H}^+$
  - as in the bicarbonate system, reactions that proceed to the right release $\text{H}^+$ and ↓pH, and those to the left ↑pH

- Important in the ICF and renal tubules
  - where phosphates are more concentrated and function closer to their optimum pH of 6.8
    - constant production of metabolic acids creates pH values from 4.5 to 7.4 in the ICF, avg. 7.0
Protein Buffer System

• More concentrated than bicarbonate or phosphate systems especially in the ICF
• Acidic side groups can release H⁺
• Amino side groups can bind H⁺
Respiratory Control of pH

• Neutralizes 2 to 3 times as much acid as chemical buffers can

• Collaborates with bicarbonate system
  – $\text{CO}_2 + \text{H}_2\text{O} \rightarrow \text{H}_2\text{CO}_3 \rightarrow \text{HCO}_3^- + \text{H}^+$
    • lowers pH by releasing $\text{H}^+$
  – $\text{CO}_2(\text{expired}) + \text{H}_2\text{O} \leftarrow \text{H}_2\text{CO}_3 \leftarrow \text{HCO}_3^- + \text{H}^+$
    • raises pH by binding $\text{H}^+$

• $\uparrow \text{CO}_2$ and $\downarrow$ pH stimulate pulmonary ventilation, while an $\uparrow$ pH inhibits pulmonary ventilation
Renal Control of pH

• Most powerful buffer system (but slow response)
• Renal tubules secrete $H^+$ into tubular fluid, then excreted in urine
H⁺ Secretion and Excretion in Kidney
Limiting pH

• Tubular secretion of $H^+$ (step 7)
  – continues only with a concentration gradient of $H^+$ between tubule cells and tubular fluid
  – if $H^+$ concentration ↑ in tubular fluid, lowering pH to 4.5, secretion of $H^+$ stops

• This is prevented by buffers in tubular fluid
  – bicarbonate system
  – $Na_2HPO_4$ (dibasic sodium phosphate) + $H^+$ $\rightarrow$ $NaH_2PO_4$ (monobasic sodium phosphate) + $Na^+$
  – ammonia ($NH_3$), from amino acid catabolism, reacts with $H^+$ and $Cl^-$ $\rightarrow$ $NH_4Cl$ (ammonium chloride)
Buffering Mechanisms in Urine
Acid-Base Balance
Acid-Base & Potassium Imbalances

• Acidosis
  – H⁺ diffuses into cells and drives out K⁺, elevating K⁺ concentration in ECF
  – H⁺ buffered by protein in ICF, causing membrane hyperpolarization, nerve and muscle cells are harder to stimulate, CNS depression from confusion to death
Acid-Base & Potassium Imbalances

• Alkalosis
  – $H^+$ diffuses out of cells and $K^+$ diffuses in, membranes depolarized, nerves overstimulate muscles causing spasms, tetany, convulsions, respiratory paralysis
Disorders of Acid-Base Balances

• Respiratory acidosis
  – rate of alveolar ventilation falls behind CO₂ production

• Respiratory alkalosis (hyperventilation)
  – CO₂ eliminated faster than it is produced

• Metabolic acidosis
  – ↑ production of organic acids (lactic acid, ketones), alcoholism, diabetes, acidic drugs (aspirin), loss of base (chronic diarrhea, laxative overuse)

• Metabolic alkalosis (rare)
  – overuse of bicarbonates (antacids), loss of acid (chronic vomiting)
Compensation for Imbalances

• Respiratory system adjusts ventilation (fast, limited compensation)
  – hypercapnia (↑ CO₂) stimulates pulmonary ventilation
  – hypocapnia reduces it

• Renal compensation (slow, powerful compensation)
  – effective for imbalances of a few days or longer
  – acidosis causes ↑ in H⁺ secretion
  – alkalosis causes bicarbonate and pH concentration in urine to rise