Chapter 27: Water, Electrolytes, and Acid-Base Balance

Body Fluid

--Body Fluid: all the water and dissolved solutes in the body’s fluid compartments
--Mechanisms regulate:
   a. total volume
   b. distribution
   c. concentration of solutes and pH
--Intracellular: all fluids inside cells of body (cytoplasm, nucleoplasm, etc.)
   *about 40% of total body weight
--Extracellular: all fluids outside cells
   *about 20% of total body weight
*Subcompartments
   a. interstitial fluid (largest, 80%)
   b. plasma (20%)
   c. CSF
   d. Synovial fluid
--2 places for exchange b/w compartments:
   a. cell membranes: separate intracellular from interstitial fluid
   b. Capillaries: have walls thin enough for exchange b/w plasma and interstitial fluids
--Body Water Gain and Loss
*45-75% body weight: declines with age since fat contains almost no water
*gain from ingestion and metabolic water formed during aerobic respiration and dehydration synthesis reactions (2500mL/day)
*normally loss equals gain (urine, feces, sweat, breathe)
--Water Content Regulation
*Content regulated so total volume of water in body remains constant
*kidneys are primary regulator of water excretion
*Regulation processes
   a. Osmosis
   b. osmolarity
   c. baroreceptors
   d. Learned behavior
*sources of water
   a. ingestion
   b. cellular metabolism
*routes of water loss
   a. urine
   b. evaporation: perspiration and respiratory passages
   c. feces
--Regulation of Water Gain
a. Formation of metabolic water is not regulated (function of the need for ATP)
b. Main regulator of water gain is intake regulation: thirst
c. Stimulators of thirst center in hypothalamus:
   * dry mouth, osmoreceptors in hypothalamus
   * decreased blood volume causes drop in BP
   * increased angiotensin II
d. drinking occurs: body water levels return to normal
e. dehydration stimulates thirst: regulation of fluid gain is regulation of thirst

--Regulation of Water and Solute Less
a. Elimination of excess water or solutes occurs through urination
b. consumption of very salty meal demonstrates function of hormones
c. Major hormones: RAA, ADH, ANP
d. Demonstrates how water follows salt, excrete Na and water will follow and decrease blood volume

--Hormone Effects on Solute
a. Angiotensin II and aldosterone promote reabsorption of Na and Cl and an increase in fluid volume
b. Increased fluid volume stretches atria and promotes release of ANP
c. ANP
   * slows release of rennin and formation of angiotensin II
   * increases filtration rate
   * reduces water and Na reabsorption
   * decreases secretion of aldosterone slowing reabsorption of Na and Cl in collecting ducts
   * promotes natriuresis or the increased excretion of Na and Cl which decreases blood volume

--Hormone Regulation of Water Balance
a. Antidiuretic hormone (ADH) from posterior pituitary
   * stimulates thirst
   * increases permeability of principal cells of collecting ducts to assist in water reabsorption
   * concentrated urine is formed
b. ADH secretion shuts off after intake of water
c. ADH secretion is increased when there is:
   * large decrease in blood volume
   * severe dehydration and drop in blood pressure
   * vomiting, diarrhea, heavy sweating or burns

--Regulation of ECF Volume
* Mechanisms:
  a. Neural
  b. Hormonal: RAA, ANP, ADH
* Increased ECF results in:
a. decreased aldosterone secretion  
b. increased AHP secretion  
c. decreased ADH secretion  
d. decreased sympathetic stimulation  

*Decreased ECF results in:
  a. increased aldosterone secretion  
b. decreased ANP secretion  
c. increased ADH secretion  
d. increased sympathetic stimulation  

--Movement of Water  
*Intracellular and interstitial fluids normally have the same osmolarity, so cells neither swell nor shrink  
*Swollen cells (water intoxication) because Na conc. of plasma falls below normal  
a. drink plain water faster than kidneys can excrete it  
b. replace water lost from diarrhea or vomiting with plain water  
c. may cause convulsions, coma, and death unless oral rehydration includes small amount salt in water intake  

--Edema and Fluid Balance:  
*Introduction of a solution into the bowel to stimulate activity and evacuate feces  
*Increase risk of fluid and electrolyte imbalance unless isotonic solution is used  

--Extracellular Fluid Osmolarity  
*Osmolarity: adding or removing water from a solution changes osmolarity  
*Increased osmolarity: triggers thirst and ADH secretion  
*Decreased osmolarity: inhibits thirst and ADH secretion  

**Electrolytes**  

--Concentrations of Electrolytes  
*functions of Electrolytes  
  a. control osmosis b/w fluid compartments  
b. help maintain acid-base balance  
c. carry electric current  
d. cofactors needed for enzymatic activity  
*Conc. expressed in mEq/liter or milliquivalents per liter for plasma, interstitial fluid and intracellular fluid  

--Comparison between Fluid Components  
*Plasma contains many proteins, but interstitial fluid does not (producing blood colloid osmotic pressure)
*Extracellular fluid contains Na and Cl
*Intracellular fluid contains K and phosphates

--Regulation of Electrolytes in ECF

*Electrolytes
  a. molecules or ions with an electrical charge (water ingestion adds electrolytes to body; kidneys, liver, skin, lungs remove from body)
  b. Concentration changes only when growing (gaining or losing weight)

*Na\(^+\) Ions
  a. dominant ECF cations
  b. Responsible for 90-95% of cations in ECF

*Regulation of Na Ions
  a. Kidneys major route of excretion
  b. Small quantities lost in sweat

**Sodium**

--Most abundant extracellular ion: accounts for ½ of osmolarity of ECF
--Average daily intake exceeds normal requirements
--Hormonal controls
  a. aldosterone causes increased reabsorption of Ha
  b. ADH release ceases if Na levels too low—dilute urine lost until Na levels rise
  c. ANP increases Na and water excretion if Na levels are too high

--Edema, Hypovolemia, and Na Imbalance
  *Sodium retention causes water retention: edema is abnormal accumulation of interstitial fluid
  *Causes of sodium retention: renal failure, hyperaldosterone
  *Excessive loss of sodium causes excessive loss of water (low blood volume—due to inadequate secretion of aldosterone, too many diuretics)

--Abnormal Plasma Levels of Sodium Ions
  a. Hyponatremia
    *Cause: high dietary sodium rarely causes symptoms
    *Symptoms: thirst, fever, dry mucous membranes, restlessness
  b. Hyponatremia
    *Cause: inadequate dietary intake of sodium rarely causes symptoms
    *Symptoms: lethargy, confusion, apprehension, seizures, and coma

**Chloride, Potassium, Magnesium Ions**

--Regulation of Chloride, Potassium, Magnesium Ions
  *Chloride ions: predominate anions in ECF
*Magnesium ions: capacity of kidney to reabsorb is limited, excess lost in urine, decreased extracellular magnesium results in greater degree of reabsorption
*Potassium ions: maintained in narrow range, affect resting membrane potentials, aldosterone increases amount secreted
*Terms:
  a. Hyperkalemia: acidosis
  - Symptoms (mild): increased neuromuscular irritability, restlessness, taller T waves and shortened QT intervals, partial depolarization of plasma membranes
  - Symptoms (severe): hamper AP conduction, muscle weakness, loss of muscle tone, depressed ST segment, prolonged PR intervals, wide QRS complex, arrhythmias, cardiac arrest
  b. Hypokalemia: alkalosis
  - Symptoms: hyperpolarization of membranes, dec. neuromuscular excitability, skeletal muscle weakness, decreased tone in smooth muscle, cardiac muscle delayed ventricle

--Chloride
*most prevalent extracellular anion
*moves easily between compartments due to Cl leakage channels
*helps balance anions in different compartments
*Regulation:
  a. passively follows Na so it is regulated indirectly by aldosterone levels
  b. ADH helps regulate Cl in body fluids b/c it controls water loss in urine
*chloride shift and hydrochloric acid of gastric juice

--Potassium
*most abundant cation in intracellular fluid
*helps establish resting membrane potential and repolarize nerve and muscle tissue
*exchanged for H to help regulate pH in intracellular fluid
*Control is mainly by aldosterone which stimulates principal cells to increase K secretion into the urine (abnormal plasma K levels adversely affect cardiac and neuromuscular function)
*K is reabsorbed (intercalated cells) and secreted (principal cells)

--Physiological Role of intracellular K:
  a. Cell volume maintenance:
    - Net loss of K: cell crenation
    - Net gain of K: cell swelling
  b. pH regulation
- Net loss of K: cell acidosis
- Net gain of K: cell alkalosis

c. Enzyme function
-- Physiological Role in Transmembrane [K] ratio
   * RMP: reduced $K_{in}/K_{out}$ membrane depolarization
     increased $K_{in}/K_{out}$ membrane hyperpolarization

-- Role of plasma [K]
  a. Neuromuscular activity:
     * low plasma K: muscle weakness, paralysis, intestinal indigestion,
       peripheral vasodilation, respiratory failure
     * high plasma K: increased muscle excitability, later muscle weakness
      and paralysis
  b. Cardiac Activity
     * low plasma K: slowed pacemaker activity, arrhythmias
     * high plasma K: conduction disturbances, ventricular arrhythmias,
       ventricular fibrillation
  c. Vascular resistance
     * low plasma K: vasoconstriction
     * high plasma K: vasodilation

-- Magnesium
   * found in bone matrix and as ions in body fluids (intracellular cofactor for
     metabolic enzymes, heart, muscle, and nerve function)
   * urinary excretion increased in hypercalcemia, hypermagnesemia, increased
     extracellular fluid volume, decreases in parathyroid hormone and
     acidosis

**Bicarbonate**

-- common extracellular anion
-- major buffer in plasma
-- conc. increases as blood flows through systemic capillaries due to $CO_2$ released
  from metabolically active cells
-- concentration decreases as blood flows through pulmonary capillaries and $CO_2$ is
  exhaled
-- kidneys are main regulator of plasma levels
  * intercalated cells form more if levels are too low
  * excrete excess in the urine

**Calcium**

-- most abundant mineral in body (skeleton and teeth)
-- abundant extracellular cation in body fluids
-- important role in blood clotting, NT release, muscle tone, and nerve and muscle
  function
Regulated by parathyroid hormone
* stimulates osteoclasts to release calcium from bone
* increases production of calcitriol (Ca\(^{2+}\) absorption from GI tract and reabsorption from glomerular filtrate)

Regulation of Calcium Ions
a. regulated within a narrow range
   * elevated extracellular levels prevent membrane depolarization
   * decreased levels lead to spontaneous AP generation
b. PTH increases Ca extracellular levels and decreases extracellular phosphate levels
c. Vitamin D stimulates Ca uptake in intestines
d. Calcitonin decreases extracellular Ca levels

Terms
a. hypocalcemia
b. hypercalcemia

Phosphate
-- present as calcium phosphate in bones and teeth and in phospholipids, ATP, DNA and RNA
-- HPO\(_{4}^{2-}\) is important intracellular anion and acts as buffer of H in body fluids and in urine (mono and dihydrogen phosphate act as buffers in the blood)
-- Plasma levels are regulated by PTH and calcitriol
   * resorption of bone releases phosphate
   * in the kidney, PTH increase phosphate excretion
   * calcitriol increases GI absorption of phosphate
-- Regulation of Phosphate Ions
   * under normal conditions, reabsorption of phosphate occurs at maximum rate in the nephron
   * an increase in plasma phosphate increases amount of phosphate in nephron beyond that which can be reabsorbed; excess is lost in urine

Acids and Bases and Buffers
-- Acids: release H into solution
-- Bases: remove H from solution
-- Acids and Bases: grouped as strong or weak
-- pH: 1-14 scale
   * pH 7 is neutral
*change of 1 pH unit is a 1-fold change in proton concentration

*Henderson-Hasselbalch equation: \( \text{pH} = \text{pK}_a + \log \left( \frac{[\text{base}]}{[\text{acid}]} \right) \)

*measurement of pH: \( -\log[H^+] = \log \frac{1}{[H^+]} \)

--3 Major Mechanisms to Regulate pH

a. Buffer systems: fastest way, temporary (does not remove/add net H\(^+\) to solution
b. Exhalation of CO\(_2\): respiratory system, fast (within minutes), removes ‘volatile acid’, not just buffering
c. Kidney excretion of H\(^+\): urinary system, slowest the only way to eliminate non-volatile acid (acid other than carbonic)

--Buffers: resist changes in pH

*when H added, buffer removes and when H removed, buffer replaces

--Actions of Buffer Systems

a. prevent rapid, drastic changes in pH
b. change either strong acid or base into weaker one
c. work in fractions of a second
d. found in fluids of the body

--Types of buffer systems:

a. carbonic acid/bicarbonate

*Acts as extracellular and intracellular (RBC) buffer system

  - Bicarbonate ion can act as a weak base (holds excess H)
  - carbonic acid can act as weak acid (dissociates into H ions)

*At a pH of 7.4, HCO\(_3^\) conc. is about 20x that of H\(_2\)CO\(_3\)

*can NOT protect against pH changes due to respiratory problems (low or high CO\(_2\) levels) b/c CO\(_2\) combines with water to form carbonic acid

b. protein buffer system:

*the most abundant buffer system in intracellular fluids and in plasma (hemoglobin very good at buffering H in RBCs, albumin is main plasma protein buffer)

*amino acids contain at least 1 carboxyl group (acts like an acid and releases H) and at least one amino group (acts like a base and combines with H), some side chains can buffer H\(^+\)

*hemoglobin acts as a buffer in blood by picking up CO\(_2\) or H\(^+\)

c. phosphate

*most important intracellular, but also acts to buffer acids in the urine

*dihydrogen phosphate ion acts as a weak acid that can buffer a strong base

*monohydrogen phosphate acts a weak base by buffering the H released by a strong acid

--Acid-Base Balance

*homeostasis of H conc. is vital (proteins 3-D structure sensitive to pH changes, normal plasma pH must be maintained b/w 7.35 and 7.45, diet
high in proteins tends to acidify the blood

--Respiratory Regulation of Acid-Base Balance
  *respiratory regulation of pH is achieved through carbonic acid/bicarbonate buffer system
  a. CO₂ increase, pH decreases
  b. CO₂ decrease, pH increases
  *hypoventilation: increases blood carbon dioxide levels: a ¼ reduction in respiration decreases plasma pH by 0.4 units (4x)
  *hyperventilation: decreases blood carbon dioxide levels: doubling ventilation rate increases plasma pH by 0.23 units

--Exhalation of Carbon Dioxide
  *breathing plays a role in the homeostasis of pH
  *pH modified by changing rate and depth of breathing:
    a. faster breathing rate, blood pH rises
    b. slow breathing rate, blood pH drops
  *H⁺ detected by chemoreceptors in medulla oblongata, carotid and aortic bodies
  *respiratory centers inhibited or stimulated by changes in pH

--Kidney Excretion of H⁺
  *metabolic reactions produce 1mEq/liter of nonvolatile acid for every kilogram of body weight
  *metabolic acidosis/alkalosis
  *elimination of non-volatile acid
  *excretion of H in the urine is the only way to eliminate huge acid excess
  *kidneys synthesize new bicarbonate and save filtered bicarbonate
  *renal failure can cause death rapidly due to its role in pH balance

--Renal regulation of Acid-Base Balance
  *Secretion of H into filtrate (in PCT and collecting ducts) inc. plasma pH
  *Reabsorption of HCO₃ in filtrate into ECF inc. plasma pH
  *Rate of H secretion inc. as body fluid pH dec. or as aldosterone levels inc.
  *Secretion of H inhibited when urine pH falls below 4.5 (H conc. gradient too high to pump against it)

--Secretion of H and Absorption of Bicarbonate by Intercalated Cells
  *proton pumps on apical mem. of intercalated cells secrete H into tubular fluid (can secrete against a conc. gradient so urine can be 1000 times more acidic than blood)
  *Cl/HCO₃ antiporters on basolateral side move bicarbonate ions from carbonic acid into the blood (this HCO₃ is new; thus blood leaving the kidney may have higher HCO₃ level than blood entering the kidney)
  *Other type of intercalated cells have Cl/HCO₃ antiporters on the apical side and proton pumps on the basolateral side (thus kidney can excrete HCO₃
when pH is too high)

*Mechanism of excretion of H as non-titratable acid = NH$_4^+$
  a. in PCT: NH$_3$ is produced from glutamine in the renal cells; NH$_4^+$ is secreted by the Na/H exchanger
  b. In collecting ducts: NH$_3$ diffuses from the medullary interstitium into the lumen, combines with secreted H in the lumen and is excreted as NH$_4^+$

**Acidosis and Alkalosis**

--Acidosis: pH body fluids below 7.35
  *Causes: depression of CNS (coma and death)
  *Respiratory: caused by inadequate ventilation
  *Metabolic: results form all conditions other than respiratory that dec. pH

--Alkalosis: pH body fluids above 7.45
  *Causes: excitability of CNS (spasms, convulsions, death)
  *Respiratory: caused by hyperventilation
  *Metabolic: results form all conditions other than respiratory that inc. pH

**Respiratory Acidosis**
  *cause is elevation of pCO$_2$ of blood
  *due to lack of removal of CO$_2$ form blood (emphysema, pulmonary edema, injury to the brainstem and respiratory centers)
  *Treatment:
    a. IV administration of bicarbonate
    b. ventilation therapy to increase exhalation of CO$_2$

**Respiratory Alkalosis**
  *arterial blood pCO$_2$ is too low
  *hyperventilation caused by: high altitude, pulmonary disease, stroke, anxiety
  *renal compensation involves: decrease in excretion of H and decrease reabsorption of bicarbonate
  *Treatment:
    a. breath into a paper bag

**Metabolic Acidosis**
  *blood bicarbonate ion concentration too low due to:
    a. loss of ion through diarrhea or kidney dysfunction
    b. accumulation of acid other than carbonic acid (ketosis)
    c. kidney failing to remove H form protein metabolism
  *respiratory compensation by hyperventilation
  *Treatment:
    a. IV administration of sodium bicarbonate
    b. correct the cause
--Metabolic Alkalosis

* Blood bicarbonate levels are too high
* Cause is nonrespiratory loss of acid (vomiting, gastric suctioning, use of diuretics, dehydration, excessive intake of alkaline drugs)
* Respiratory compensation is hypoventilation
* Treatment
  a. fluid and electrolyte therapy, correct the cause

--Diagnosis of Acid-Base Imbalances

* Evaluate:
  a. systemic arterial blood pH: acidosis/alkalosis
  b. identify the cause of acidosis or alkalosis
  c. if conc. of bicarbonate is too low or too high
  d. if $P_{co2}$ is too low or too high
  e. look at values that do not correspond with observed pH change

* Solution:
  a. if respiratory: the pC$_2$ will not be normal
  b. if problem is metabolic, the bicarbonate level will not be normal

--Homeostasis in Infants

* high surface to volume ratio

--Impaired Homeostasis in Elderly

* decreased volume of intracellular fluid
* decreased total body K due to loss of muscle tissue or potassium-depleting diuretics for treatment of hypertension or heart disease
* decreased respiratory and renal function