Lecture 1C:
Fluid and Electrolyte Homeostasis
Saline Imbalance

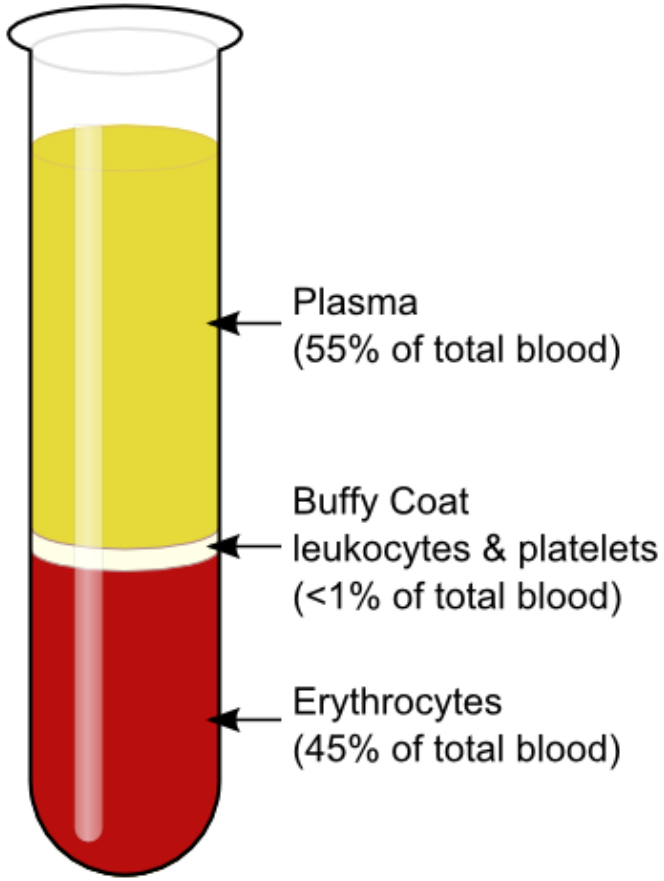
Fluid and Electrolyte Homeostasis

Overview: Blood Composition

- Blood is a connective tissue that occupies 4.5-5.5 L of body volume. Recall that all connective tissues contain both extracellular matrix and cells. A matrix contains ground substance and fibers.
  - **Plasma** is the matrix of blood. It has a liquid ground substance with various proteins and other substances dissolved in it. Plasma makes up about **55%** of the volume of whole blood.
  - **Formed elements** are the solid component of blood. The formed elements are cells, except for platelets. Formed elements make up about **45%** of whole blood.
    - **Erythrocytes** (red blood cells, or RBCs)
    - **Leukocytes** (white blood cells, or WBCs)
    - **Platelets** (cell fragments important in blood clotting)

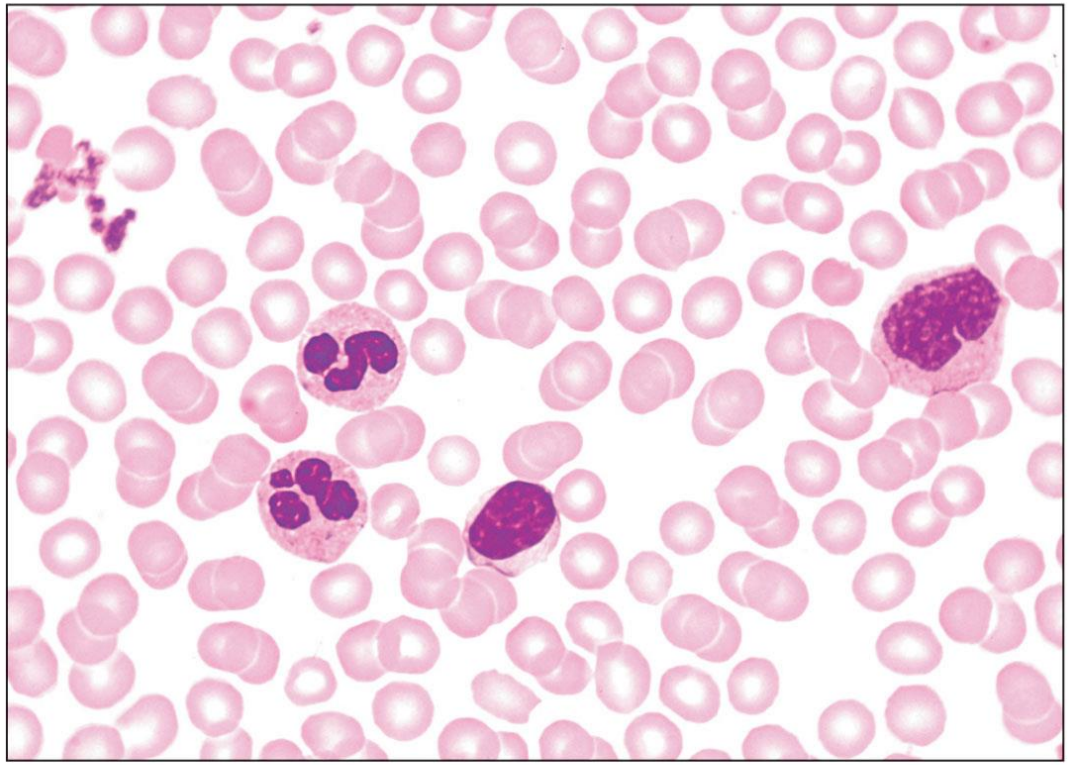
Fluid and Electrolyte Homeostasis 1

- Centrifuging (spinning blood tubes) causes blood to separate into three layers due to density differences among its components.
- **Red blood cells** settle to the bottom of the tube because they are the most dense component. **White blood cells and platelets** settle into the thin middle layer.
- **Plasma**, being the least dense component is located in the top layer of the tube.
- **Note the % of whole blood that each layer contains.**



Fluid and Electrolyte Homeostasis 2

Blood Smear
The small pink cells are RBCs. Platelets are the dark cell fragments in the upper left. Also shown, two neutrophils, a lymphocyte and an eosinophil.



Fluid and Electrolyte Homeostasis 3

Blood Plasma Components:

- **90% water**
- **Plasma proteins** cause plasma to be a pale yellow color. Types of plasma proteins include:
  - 60% **albumin** (The most important substance in determining the **osmotic pressure** of blood)
  - 36% **immunoglobulins** (antibodies)
  - 4% **fibrinogen** (inactive soluble **blood clotting protein**)
  - Trace amounts of various protein hormones, enzymes, and clotting factors other than fibrinogen, complement.
- **Nitrogenous by-products of metabolism**—urea, creatinine
- **Nutrients**—glucose, amino acids, fatty acids, glycerol, vitamins
- **Cholesterol and steroid hormones**

Fluid and Electrolyte Homeostasis 4

Blood Plasma Components, cont.

- **Electrolytes**—Na^+, K^+, Ca^{2+}, Cl^-, Mg^{2+}, bicarbonate, phosphate, etc.
- **Gases**—major gases in order of diminishing concentration: N_2, O_2, CO_2, (N_2 has no physiological significance.) (O_2 and CO_2 are called "respiratory gases".)

Blood Plasma and Other Body Fluids

- Some other body fluids are formed by the **filtration of blood plasma through capillary walls**: interstitial fluid, cerebrospinal fluid, renal filtrate (urine), aqueous humor of the eye.

Fluid and Electrolyte Homeostasis 5

Overview: Functions of Blood

Transport, cont.

- Blood absorbs O_2 from the lungs and nutrients from the digestive and transports them to body cells.
  - 98.5% of blood oxygen binds to **hemoglobin,** the protein inside RBCs.
- Blood absorbs CO2 and other metabolic wastes from body tissues and transports them to the lungs and kidneys for elimination.
- Blood transports hormones to their target organs.

- **Homeostasis**
  - Blood modulates body temperature by absorbing and distributing heat.
  - Blood modulates body fluid pH. It contains buffers.
  - Blood volume and composition are important in blood pressure homeostasis and fluid/electrolyte homeostasis.

Fluid and Electrolyte Homeostasis 6

Overview: Functions of Blood

- **Protection against:**
  - **Blood loss**
    - Plasma proteins and platelets participate in blood clot formation when a blood vessel wall is torn or punctured.
  - **Infection**
    - Antibodies (immune system proteins) are found in the plasma.
    - Complement proteins (immune system proteins) are found in the plasma.
    - WBCs (immune system cells) defend against foreign invaders.

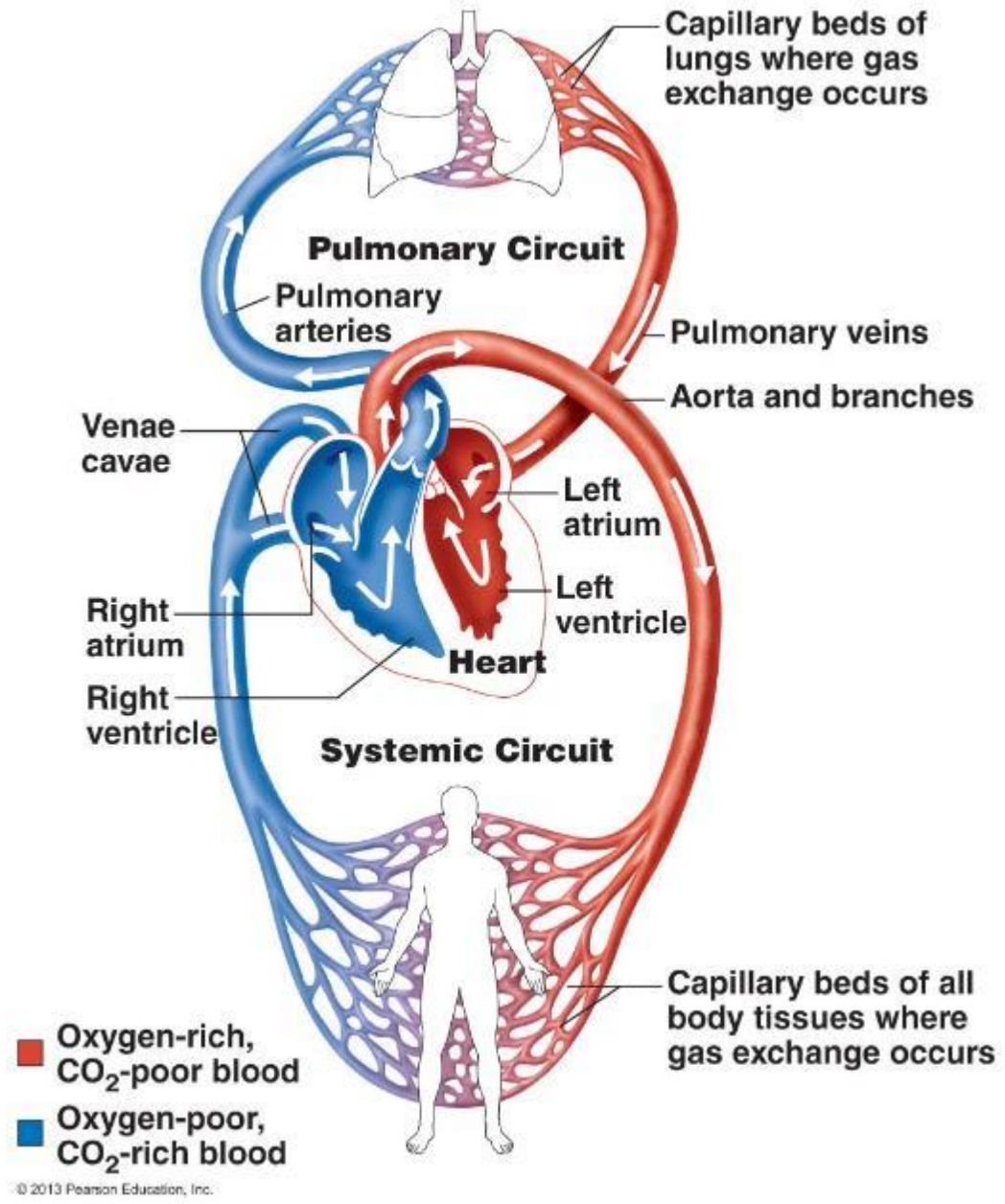
Fluid and Electrolyte Homeostasis 7

Blood Circuits

- **Arterial blood vessel**-a blood vessel that transports blood away from the heart toward a capillary bed; “A FOR AWAY”: aorta, artery, arteriole (in order of decreasing diameter)
- **Venous blood vessel**-a blood vessel that transports blood away from a capillary bed toward the heart: venule, vein, vena cava (in order of increasing diameter).
- The arterial system of vessels and the venous system of vessels are connected to each other by **capillary beds** that span the space between an arteriole and a venule. **Exchanges** of fluid, nutrients and respiratory gases between the blood and tissues occurs **ONLY** across the very thin walls of capillaries. The walls of the other vessel types are too thick to allow for such exchanges.

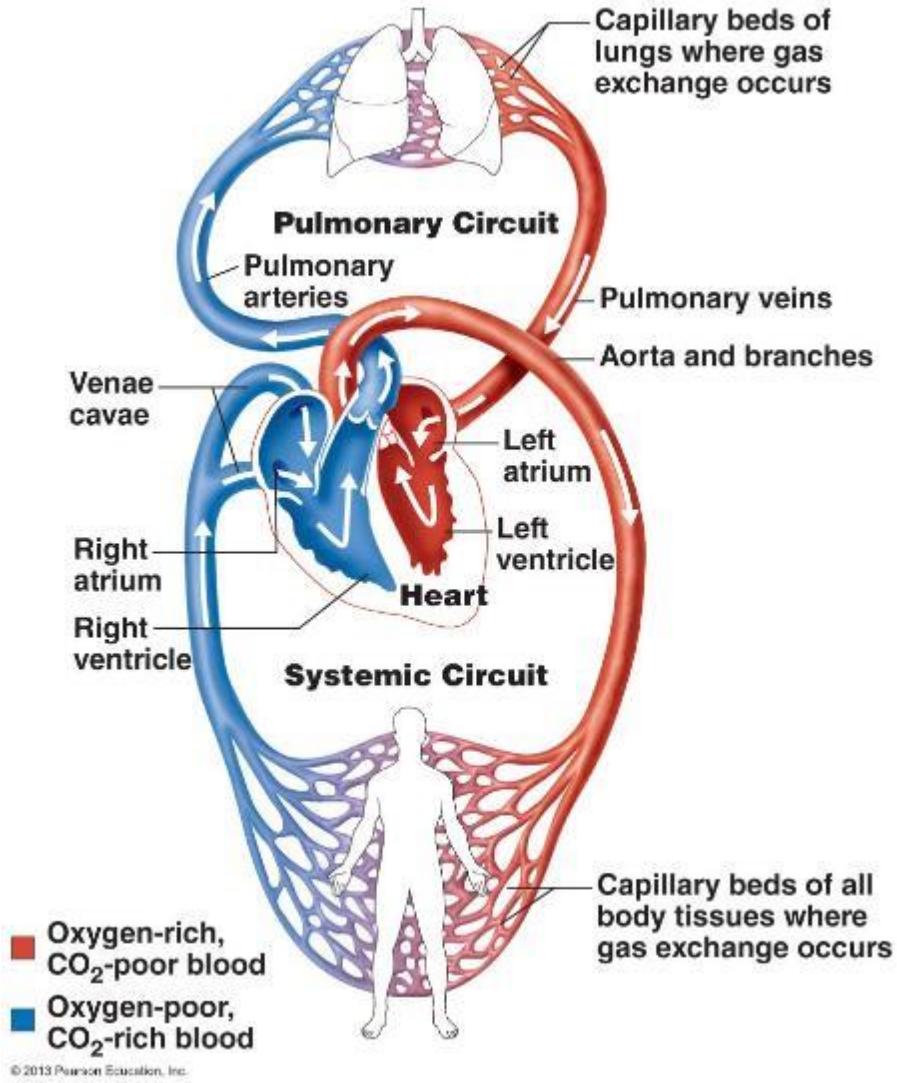
Blood Circuits

Blood uploads oxygen and downloads CO2 as it flows through **pulmonary capillary beds.**
Blood downloads oxygen and uploads CO2 as it flows through **systemic capillary beds.**



Blood Circuits 2

The pathway of blood starting in the right atrium:
Right Ventricle
Pulmonary arteries
Pulmonary arterioles
Pulmonary capillaries
Pulmonary venules
Pulmonary veins
Left Atrium
Left Ventricle
Aorta
Systemic arteries
Systemic arterioles
Systemic capillaries
Systemic venules
Systemic veins
Vena cava
Right Atrium



Fluid and Electrolyte Homeostasis 8

Body Water Content

- Adipose tissue (fat) is nonpolar and hydrophobic. It contains less water than other body tissues such as muscle or bone.
  - Infants: 73% or more water (low body fat, low bone mass)
  - Adult males: ~60% water (higher skeletal muscle mass, lower fat content)
  - Adult females: ~50% water (higher fat content, lower skeletal muscle mass)
- Water content declines to ~45% in old age!

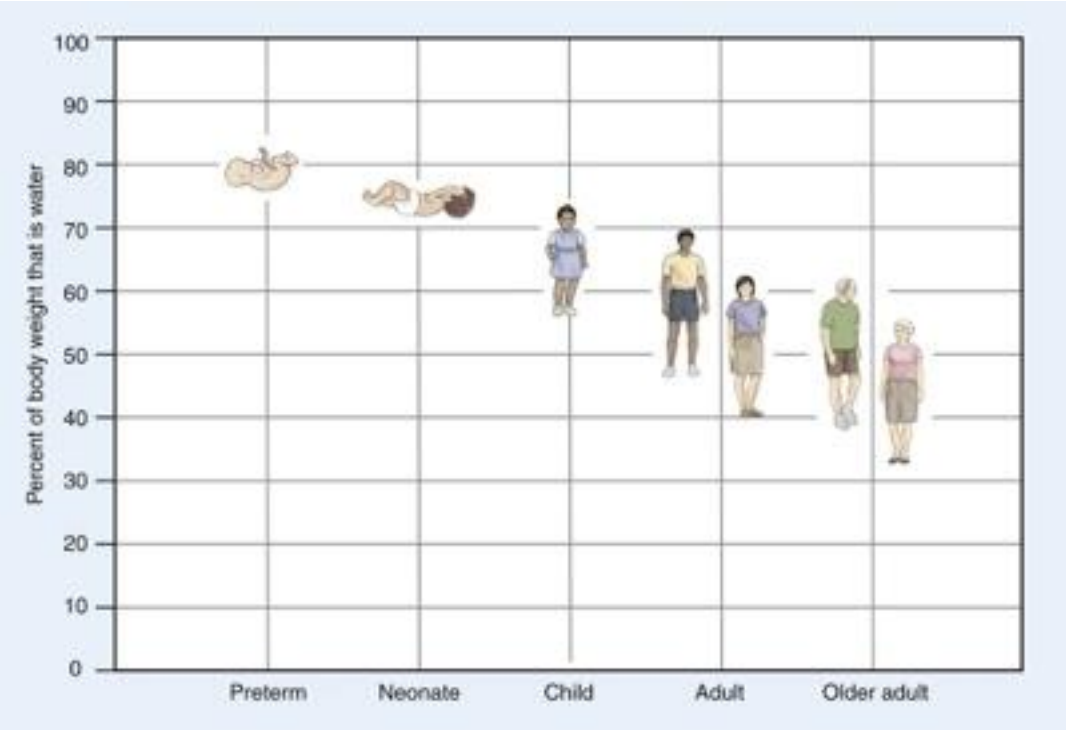
Location of Body Fluids

- Total body fluid = **40 L (adult)**
  - **Intracellular** (inside cells) fluid (ICF) compartment: ~2/3 of the total: **25 L**
  - **Extracellular** (outside cells) fluid (ECF) compartment: ~1/3 of the total: **15 L**
    - **Vascular Compartment (Blood Plasma): 3 L**
    - **Interstitial Compartment**: **12 L** in the spaces between cells
    - **Other minor ECF sources**: lymph, CSF, humors of the eye, synovial fluid, serous fluid, gastrointestinal secretions, alveolar fluid, kidney fluids

Fluid and Electrolyte Homeostasis 9

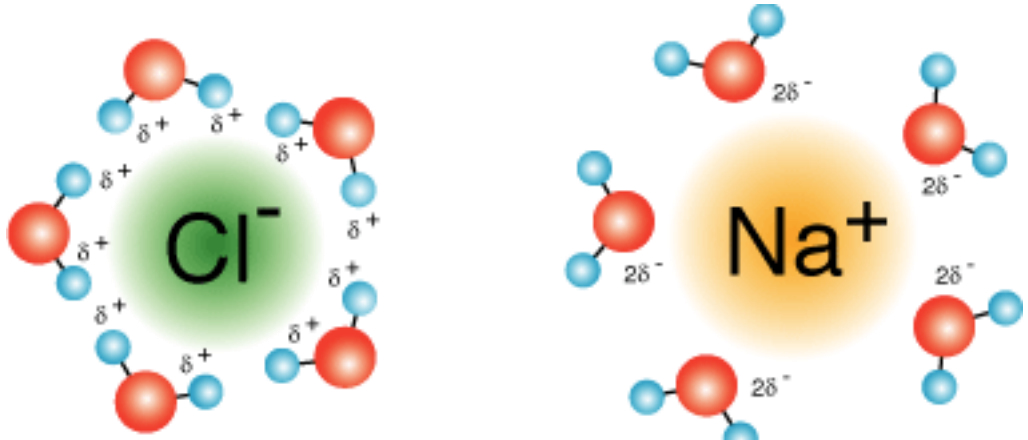
Total % Body Water Decreases With Age.

Total % Body Water Is Higher in Males Than in Females.



Fluid and Electrolyte Homeostasis 10

- Body fluids are **aqueous (water) solutions**. Water is the solvent for all of the **solute** molecules in the body.
- **Electrolytes** are solutions that conduct electricity because they contain ions. Ions are **charged** particles. An ion has unequal numbers of protons and electrons. Because water is **polar** it is an excellent solvent for ionic compounds like NaCl (Na+ Cl-) and many others in body fluids. It is also an excellent solvent for polar molecules. Recall that blood plasma is 90% water.
- **Cations** are positively charged ions, sodium (Na+) for example.
- **Anions** are negatively charged ions, chloride (Cl-) for example.



Slightly positive hydrogen are attracted to chlorine anions

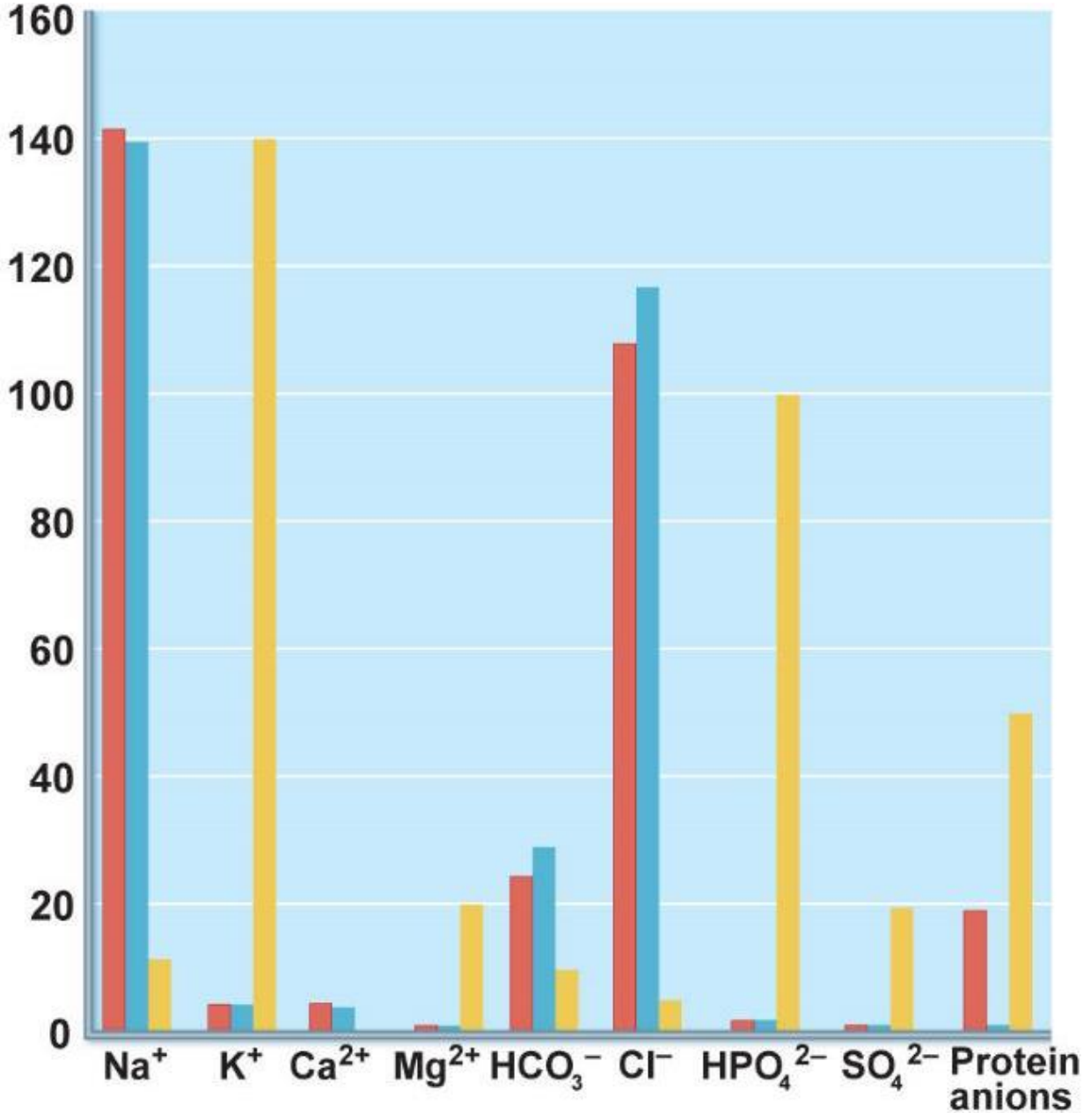
Slightly negative oxygen are attracted to sodium cations

Fluid and Electrolyte Homeostasis 11

- Each body fluid compartment has a distinctive pattern of ions. Study the chart on the following slide.
  - Note that **Na+, Ca2+ and Cl-** ion concentrations are higher in the extracellular fluids than intracellular fluids, while just the opposite is true for **K+ and Mg2+**. Ion concentration differences across plasma membranes play a major role in establishing the **resting membrane potentials** that are so important in the function of nerve cells and muscle cells, in particular.
  - **HCO_3^- ions (bicarbonate ions)** are higher in extracellular fluids than in intracellular fluids. While **HPO_4^{2-} (hydrogen phosphate ions)** are higher in intracellular fluids than in extracellular fluids. Both ions function as **buffers** to resist fluctuations in body fluid pH in their respective compartments. They are able to bind and release **H+ ions**.
  - **Protein** concentration is highest in intracellular fluid, followed by blood plasma. Because protein molecules are large they generally **do not cross either plasma membranes or capillary walls**. The protein concentration of the interstitial fluid is very low.
  - At normal body pH, there are many negatively charged R groups in proteins. Proteins are definitely **anions**! Protein concentration is major factor in the **osmotic** movement of water. And proteins are the **major pH buffers** in the blood. This includes the buffering power of hemoglobin inside RBCs.

Ions

Red- Intravascula (Blood)
Blue- Interstitial
Yellow- Intracellular



Fluid and Electrolyte Homeostasis 12

Movement of Fluid Between Compartments

- The barrier between the **intracellular and interstitial** fluid compartments consists of the semipermeable **plasma membranes** of cells.
  - Movement of **fluid (water)** across plasma membranes by osmosis from an area of lower solute concentration to an area of higher solute concentration.
    - Note, although plasma membranes are generally impermeable to polar molecules, water molecules are small enough to pass through the membrane easily.
  - Movement of **ions and polar molecules** (other than water) across plasma membranes requires membrane proteins. Protein pores for ion transport (ion channels) allow ions to **diffuse** across the plasma membrane **down(with)** their concentration gradients. **Active transport** is required to move ions or polar molecules **up (against)** their concentration gradients.
    - Maintaining concentration gradients for ions across a plasma membrane requires constant active transport (ion pumping).
  - Movement of **nonpolar substances (lipids and gases, including oxygen gas and carbon dioxide gas)** across plasma membranes is by **simple diffusion.**

Fluid and Electrolyte Homeostasis 13

Intracellular Ion Concentrations

Na+

K+

Ca2+

Mg2+

$HPO_4$2-

Cl-

Protein Anions-

Interstitial Ion Concentrations

Na+

K+

Ca2+

Mg2+

HPO42-

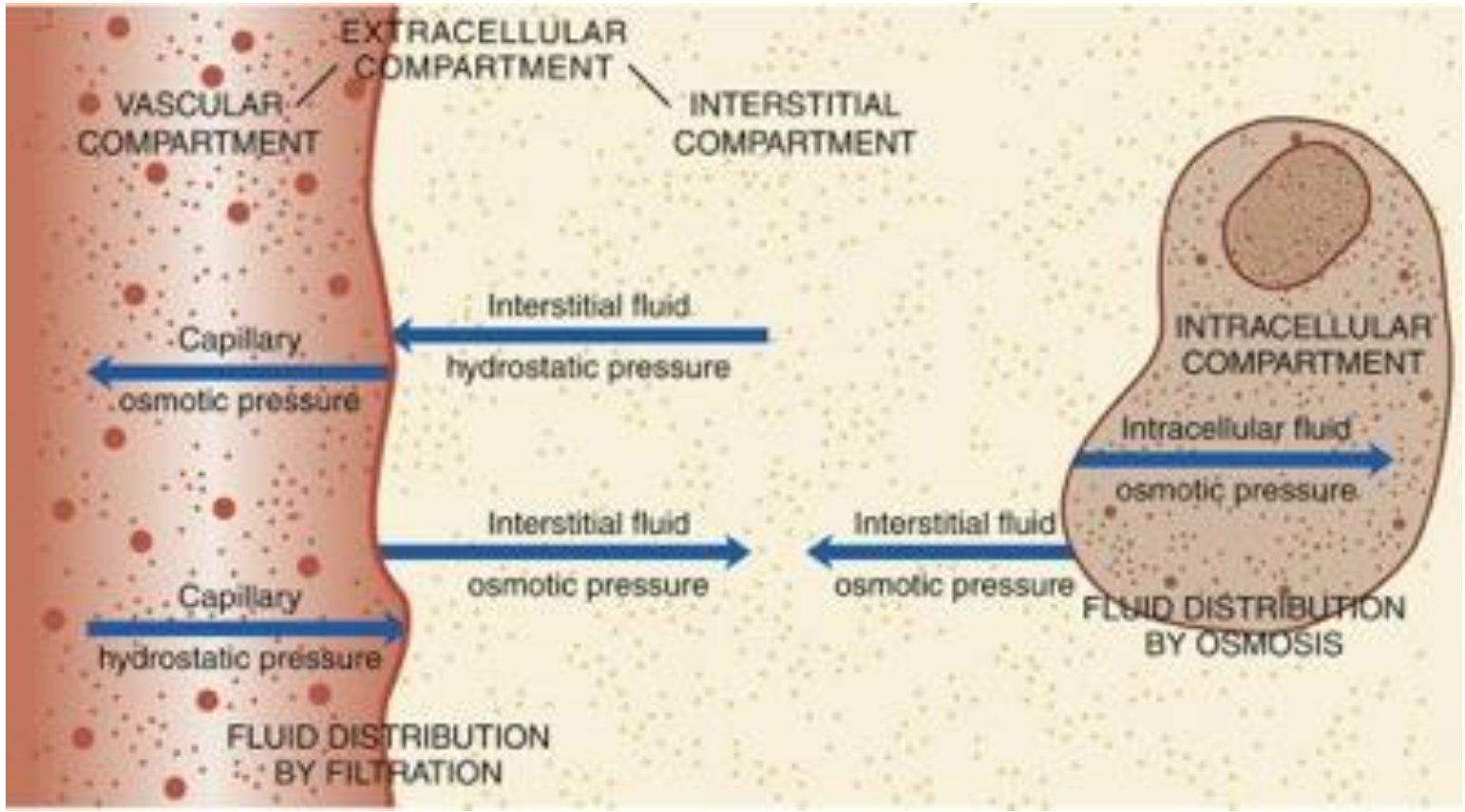
Cl-

Fluid and Electrolyte Homeostasis 14

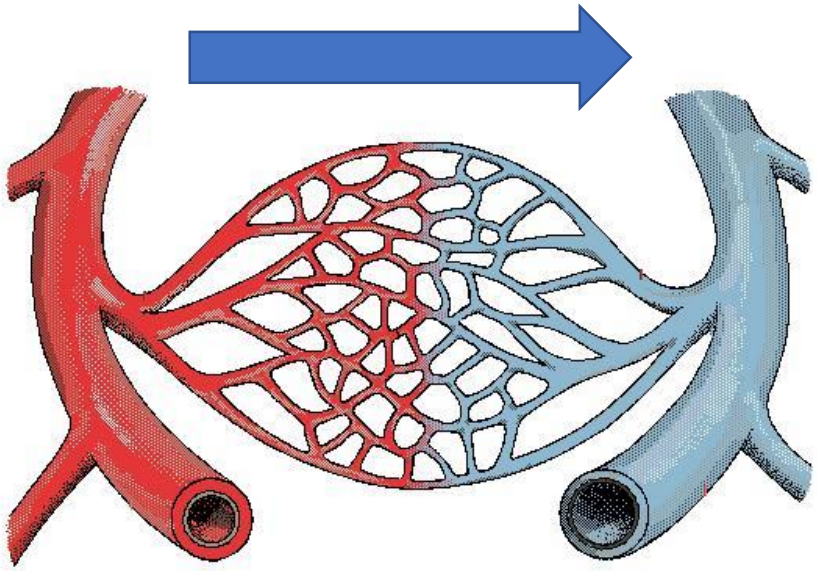
- The barrier between the **vascular and interstitial** sub-compartments of the extracellular fluid compartment are **capillary walls**. Capillary walls are constructed of tubular sheets of **simple squamous epithelial cells** having tiny gaps **BETWEEN** them to allow **fluid movement. Ions easily pass through the gaps between capillary wall cells because they are so tiny.** Note that this causes the ion concentrations in the blood and interstitial fluid to be very similar. Look back at the graph shown earlier!
- Movement of **fluid (water plus ions)** across capillary walls results from an interplay between **colloid osmotic pressure and hydrostatic pressure** of the blood plasma and the interstitial fluid.
  - The colloid osmotic pressure is the **pull** that proteins exert on water. Most proteins are too large to fit through the gaps between capillary wall cells so they stay put.
  - The hydrostatic pressure is the **push** that a fluid exerts on the walls of its container. Capillary walls are the container in this case.
  - Both the colloid osmotic pressure and hydrostatic pressure of interstitial fluid is normally **very low**.
  - Because blood contains plasma proteins the **colloid osmotic pressure** of blood is **relatively high** (about 25 mm Hg) and doesn't change as blood flows through a capillary.
  - The **hydrostatic pressure** of capillary blood **decreases** as blood flows through a capillary from about 35 mm Hg at the **arterial end** to about 18 mm Hg at the **venous end.**

Fluid and Electrolyte Homeostasis 15

SUMMARY:
Intracellular and Extracellular Fluid Compartments and Barriers Between Them
(Note the direction of the arrows.)

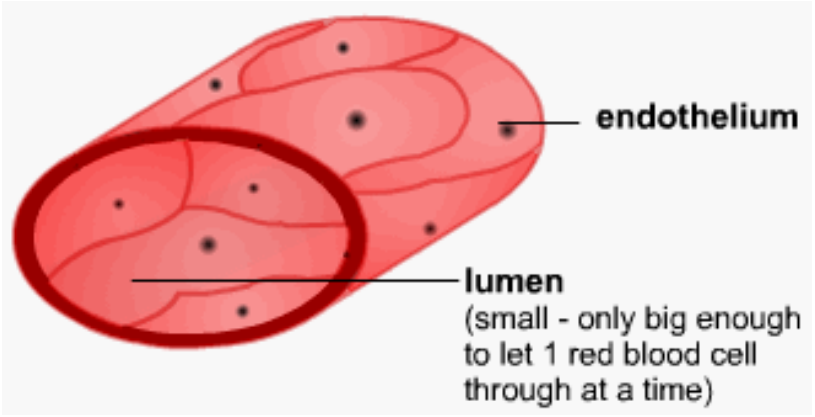


Fluid and Electrolyte Homeostasis 16



Capillary Bed

Blood flow is left to right.



Capillary Wall

Fluid and Electrolyte Homeostasis 17

Fluid Movement Across Capillary Walls:

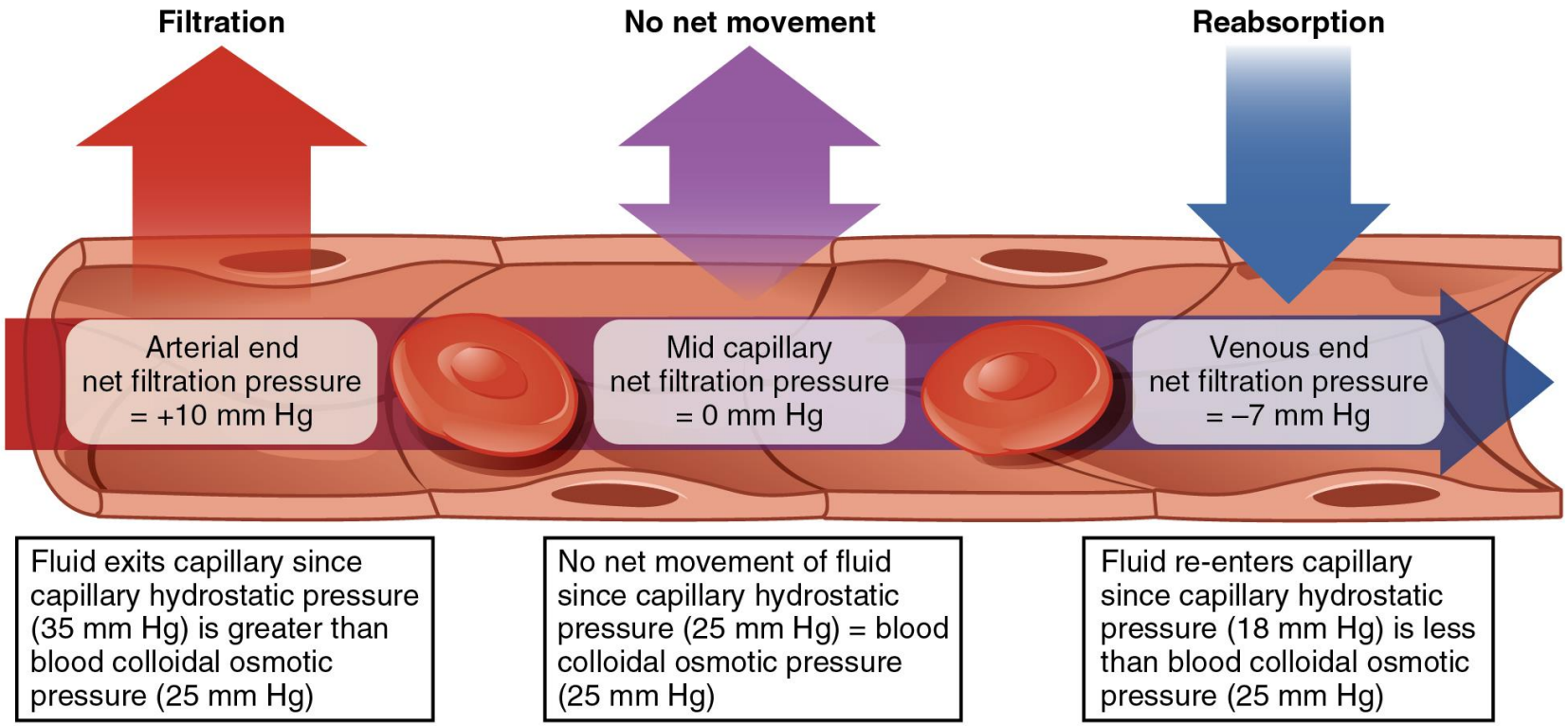
- **Filtration** is movement of fluid from the capillary blood across the capillary wall and into the interstitial space.
- **Reabsorption** is movement of fluid from the interstitial space across the capillary wall and into the capillary blood.
- The direction of flow and the amount of fluid that flows depends on the **net filtration pressure (NFP).** The NFP is the difference between the net hydrostatic pressure and the net colloid osmotic pressure.
  - **Net hydrostatic pressure** (the difference between the hydrostatic pressure of the blood and the hydrostatic pressure of the interstitial fluid)
  - **Net colloid osmotic pressure** (the difference between the colloid osmotic pressure of the blood and the colloid osmotic pressure of the interstitial fluid)

Fluid and Electrolyte Homeostasis 18

Net Filtration Pressures:

- At the **arterial end of a capillary** the **NFP is positive** because the net hydrostatic pressure is higher than the net colloid osmotic pressure. So **fluid leaves the blood** and enters the interstitial fluid.
- At the **venous end of a capillary** the **NFP is negative** because the net hydrostatic pressure is lower than the net colloid osmotic pressure. So **fluid leaves the interstitium** and enters the blood.
- The volume of fluid that exits the blood at the arterial end of the bed is greater than the volume of fluid that reenters the blood at the venous end of the bed. There is a **net fluid loss from the blood to the interstitial fluid of about 3 liters daily**. One of the functions of the **lymphatic system** is to return excess interstitial fluid to the blood.

Fluid and Electrolyte Homeostasis 19

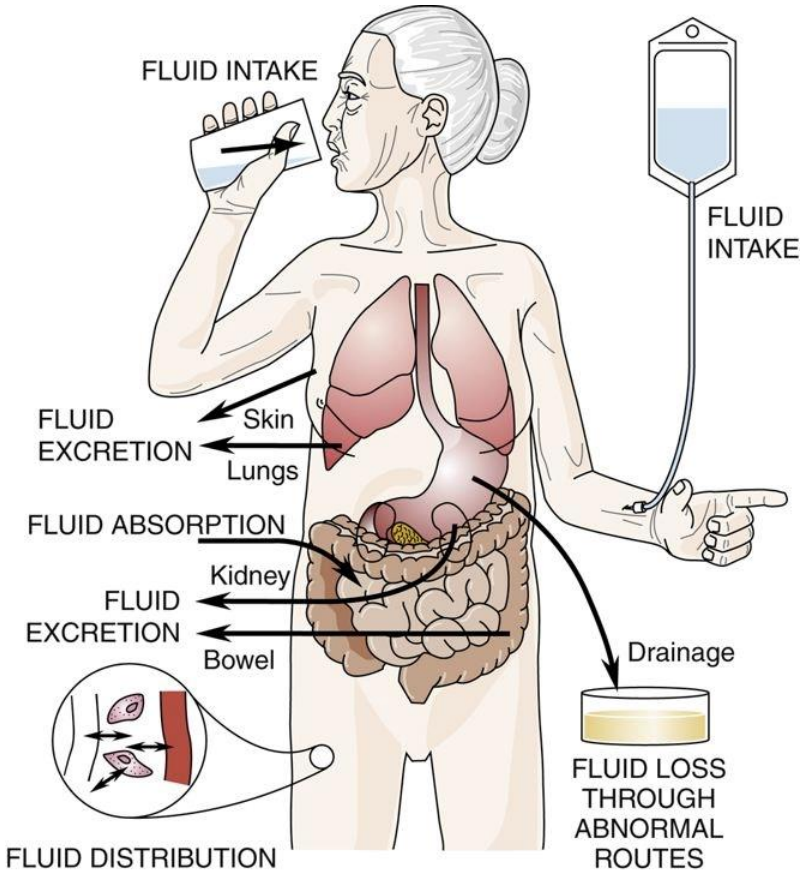


Fluid and Electrolyte Homeostasis 20

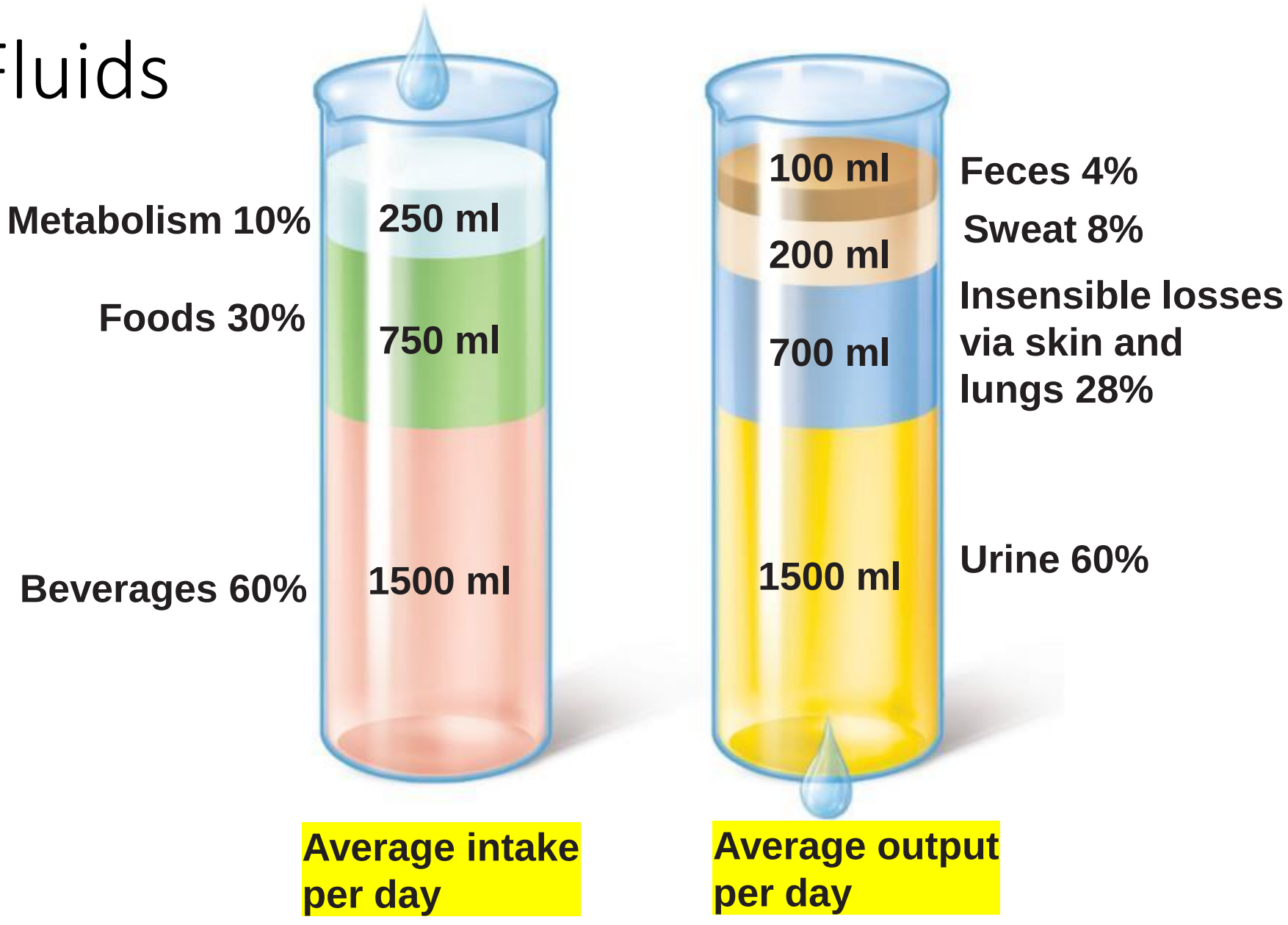
In a healthy body daily fluid intake roughly equals daily fluid output. About **2500 ml** of fluid moves each way each day.

Fluid intake: beverages, food, and metabolic water (produced mostly by cellular respiration, the electron transport chain)

Fluid output: urine, insensible water loss (evaporation from skin and lungs), perspiration, and feces



Body Fluids


Metabolism 10%
250 ml
Foods 30%
750 ml
Beverages 60%
1500 ml
Average intake per day
100 ml
Feces 4%
Sweat 8%
200 ml
Insensible losses via skin and lungs 28%
700 ml
1500 ml
Urine 60%
Average output per day

Fluid and Electrolyte Homeostasis 21

- Body fluid is taken in by drinking. Fluid intake is a function of the **thirst response** and good habits.
- Thirst is mostly mediated by the response of the **hypothalamus of the brain** to increased concentration of body fluid as detected by **osmoreceptors** in the brain.
- Thirst is quenched almost immediately after we begin drinking. So thirst is not always the best indicator of need. This is especially true of those participating in athletic events.
- Be aware that the thirst response is often depressed in elderly patients.
- Body fluid leaves the body chiefly by **excretion in the urine**. Fluid also **evaporates** from the skin and exhaled air contains water vapor.

Fluid and Electrolyte Homeostasis 22

- The **kidneys** play a major role in maintaining the concentration of nutrients, ions and water in the blood plasma. They are also responsible for removing toxic **nitrogenous (nitrogen-containing) wastes** from blood plasma.
- As blood flows through the **glomerular capillaries** of the kidneys blood plasma (except the plasma proteins) is filtered out of the blood and into a separate set of tubes in the kidneys. The substance that enters this set of tubes is called the **renal filtrate**.
- Through a process called **tubular reabsorption,** appropriate amounts of nutrients, ions and water leave the kidney tubules and move back into the blood by entering a separate set of kidney capillaries. Nitrogenous wastes as well as appropriate amounts of ions and water stay in the filtrate and become **urine**.
- The process of tubular reabsorption is regulated by various hormones as well as by the autonomic nervous system.

Fluid and Electrolyte Homeostasis 23

- The **hydrostatic pressure of the blood** in the glomerular capillaries is the major determinant of the rate of renal filtrate formation by the kidneys.
- Increased blood pressure increases the rate of renal filtrate formation. Decreased blood pressure decreases the rate of renal filtrate formation. Homeostatic mechanisms tightly regulate the rate of renal filtrate formation, the **GFR (glomerular filtration rate).**
- Renal homeostatic responses to blood pressure changes involve these hormones:
  - **Antidiuretic Hormone (ADH)** increases water reabsorption (water retention) without affecting sodium ion concentration. **Blood volume and blood pressure rise**. ADH is secreted by the hypothalamus in response to increased solute concentration of the blood. Diuresis means making urine. Antidiuretic means opposing diuresis.
  - **Aldosterone** increases both sodium ion reabsorption from the renal filtrate, and “water follows sodium”, so **blood volume and blood pressure rise**. Aldosterone also causes potassium ions to be secreted from the blood into the renal filtrate in exchange for the sodium ions. Aldosterone is secreted by the cortex of the adrenal gland in response to high blood potassium ions or low blood sodium ions. It is also secreted in response to the release of **renin** by kidney cells when they detect a decreased blood pressure in the arterioles that feed the glomeruli.

Fluid and Electrolyte Homeostasis 24

- **Atrial Natriuretic Peptide (ANP)** decreases water retention by decreasing sodium ion and water reabsorption from the renal filtrate. Water stays in the filtrate with the sodium ions. **Blood volume and blood pressure decrease.** ANP is secreted by the atria of the heart in response to elevated blood volume. When blood volume increases so does blood pressure. Natriuretic means “sodium in urine”. The Latin name for sodium is natrium (Na).

Fluid and Electrolyte Imbalances: Saline 1

- Pathological conditions of several types result in body fluid imbalances. Fluid imbalances fall into two general categories:

1. **Extracellular Fluid Volume (ECV) Imbalances**

   (aka "Saline Imbalances")

   - Note that **sodium (Na+) and chloride (Cl-)** are by far the most common ions in extracellular fluid. Thus, extracellular fluid is often referred to as **"saline" (salt) solution**.
   - ECV imbalances involve changes in the **volume** of extracellular fluid that do NOT involve changes in the concentration of the extracellular fluid. The **concentration** of the extracellular fluid is **NORMAL.**

2. **Body Fluid Concentration Imbalances**

   (aka "Water Imbalances" or "Electrolyte Imbalances")

   - Here the **concentration** of the extracellular fluid is **ABNORMAL.**

Fluid and Electrolyte Imbalances: Saline 2

- **ECV (Saline) Imbalance**- occurs in two forms:
  1. **Volume (Saline) Deficit**
  2. **Volume (Saline) Excess**
- **Volume (Saline) Deficit Etiology: two general causes:**
  1. **Too much extracellular fluid (sodium and water) leaves the body**
     a. Through the GI tract
        - Vomiting (emesis)
        - Diarrhea (including overuse of laxatives)
        - Gastric suction
     b. Through the urinary tract
        - Adrenal insufficiency (lack of aldosterone)
        - Overuse of diuretics (producing too much urine)

Fluid and Electrolyte Imbalances: Saline 3

c. Other means:
    - Hemorrhage
    - Massive diaphoresis (sweating)
    - Paracentesis-medical perforation and drainage of fluid

2. Too much extracellular fluid leaves the vascular compartment and/or interstitial compartment and enters a "third space" ("Third spacing" means the fluid is neither in the intracellular nor the extracellular compartment.)

a. Ascites-fluid accumulates in the peritoneal cavity

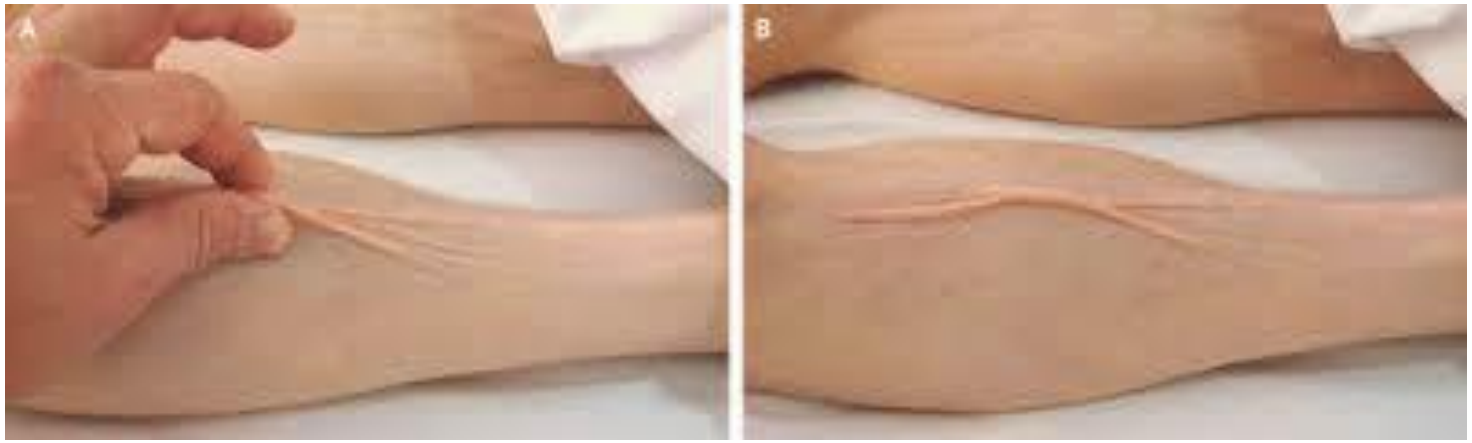
b. Fluid accumulation in the digestive tract as the result of intestinal **obstruction**

Fluid and Electrolyte Imbalances: Saline 4

- **Clinical Manifestations of Volume Deficit**
  - Sudden weight loss; one liter of saline weighs 1 kg (2.2 lb)
  - Decreased postural (when the patient moves from supine to standing) blood pressure with increased heart rate
  - Flat neck veins when patient is supine (lying down)
  - Lightheadedness, dizziness or fainting
  - Urine volume is decreased (oliguria).
  - If ECV deficit develops slowly the following may be observed:
    - Decreased turgor pressure of the skin causing “tenting” (Skin forms a tent when pinched .)
    - Dry oral mucosa between the cheek and gums and/or furrowed tongue
    - Hard stools
    - Sunken eyeballs
    - Lack of sweat and/or tears
  - In infants cranial fontanels are sunken. (Assessment of neck veins isn’t helpful.)

Fluid and Electrolyte Imbalances: Saline 5

Manifestations of Volume Deficit



Skin Tenting

Sunken Fontanel

Fluid and Electrolyte Imbalances: Saline 6

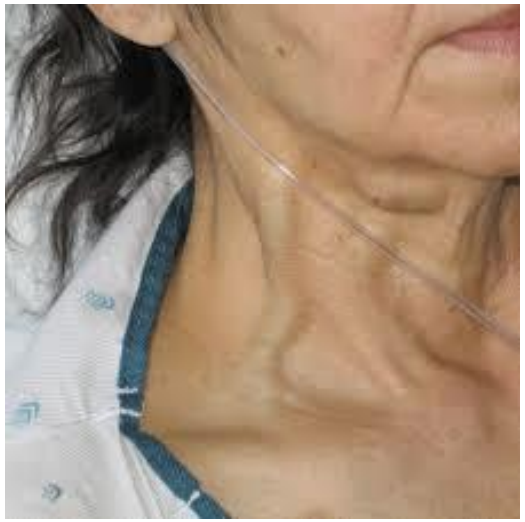
- **Volume (Saline) Excess Etiology: two major causes**
  1. **Extensive IV Infusion (with sodium-containing fluids)**
     - Normal saline
     - Ringer's solution
     - Lactated Ringer's solution
  2. **Renal Retention of BOTH Water and Sodium**
     - **Hyperaldosteronism** causes excessive renal reabsorption of sodium and water (usually due to an adrenal gland tumor).
     - **Chronic glomerulonephritis**: Glomerular inflammation causes decreased renal filtrate formation.
     - **Chronic heart failure-a** weak heart keeps blood from moving through the circulatory system properly. It tends to pool in the veins, so less blood flows to the kidneys.

Fluid and Electrolyte Imbalances: Saline 7

- **Volume (Saline) Excess Clinical Manifestations**
  - Sudden weight gain
  - **Generalized edema (Edema** means excess **interstitial fluid.)** Generalized (all over the body) edema occurs due to filtration of fluid out of both the pulmonary and systemic capillary beds.
  - Signs of circulatory overload (excessive blood volume):
    - **Bounding pulse**
    - **Bulging neck veins** in the standing position
    - **Crackles** (abnormal breathing sounds) in the dependent (where gravity effects the fluid) areas of the lungs
    - **Dyspnea**-difficulty breathing (due to extra fluid in pulmonary circuit)
    - **Orthopnea**-difficulty breathing when lying flat
  - In infants, **cranial fontanels bulge outward.**

Fluid and Electrolyte Imbalances: Saline 8

Manifestations of Volume Excess



Distended Neck Veins

Bulging Fontanel

Lecture 1D:
Water Imbalance
Specific Electrolyte Imbalances

Fluid and Electrolyte Imbalances: Water 1

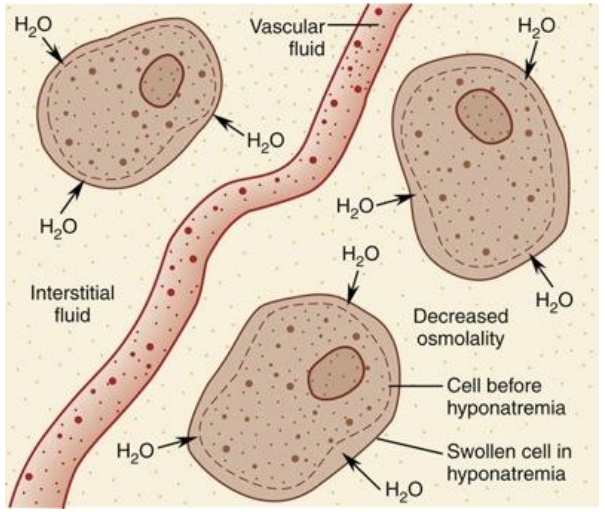
- **Body Fluid Concentration (Water) Imbalances**
  - Imbalances in body fluid **concentration** are recognized by **ABNORMAL serum sodium level**. Serum sodium ion concentration is a general measurement of the **osmolality (concentration) of the blood. (Serum is plasma minus clotting proteins.)**
  - Normally the serum sodium value is **135-145 mEq/L** (milliequivalents per liter).
  - Abnormal serum sodium level takes two forms:
    - **Hyponatremia**-abnormally low serum sodium, (Note: Natrium is the Latin word for sodium.) Extracellular fluid becomes **hypotonic** to intracellular fluid, so cells swell due to osmosis. Hyponatremia occurs due to:
      - Gain of relatively more water than salt
      - Loss of relatively more salt than water
    - **Hypernatremia**-abnormally high serum sodium. Extracellular fluid becomes **hypertonic** to intracellular fluid, so cells shrink due to osmosis. Hypernatremia occurs due to:
      - Gain of relatively more salt than water
      - Loss of relatively more water than salt

Fluid and Electrolyte Imbalances: Water 2

- **Etiology of Hyponatremia**
  - **Gain of Relatively More Water Than Salt**
    - Excessive ADH, a hormone that stimulates the reabsorption of water from the renal filtrate into the blood, but has no effect on sodium reabsorption.
    - Excessive D5W (5% dextrose in water) intravenous infusion
    - Hypotonic wound irrigating solutions
    - Tap water enemas
    - Psychogenic polydipsia (compulsive water drinking)
    - Forced excessive water ingestion (child abuse, hazing)
    - Excessive beer ingestion (beer potomania), 14+ beers per day
    - Near drowning in fresh water
  - **Loss of Relatively More Salt Than Water**
    - **Replacement of water, but not salt, after vomiting, diarrhea, gastric suction, diaphoresis or burns. (MOST COMMON CAUSE)**
    - Diuretics, especially thiazides (They block Na+ uptake from renal filtrate.)
    - Salt wasting renal disease; excess sodium is excreted in urine.
    - Hyperparathyroidism excessive uptake of calcium from the renal filtrate interferes with sodium and phosphate uptake from the renal filtrate.

Fluid and Electrolyte Imbalances: Water 3

- **Clinical Manifestations of Hyponatremia**
  - This is the **most common** electrolyte imbalance!
  - Sodium ions are crucial in the maintenance of resting membrane potentials and in action potential generation, particularly in neurons. Manifestations of hyponatremia are due to the **central nervous system** effects of **swollen** neurons and glial cells. The sodium gradient reverses creating an osmotic pressure that draws extracellular **water into the cells (hydropic swelling).** Swelling of the brain can cause damage to brain tissue.
    - Headache
    - Confusion
    - Lethargy
    - Seizure
    - Coma
    - Abnormal Heart Rhythm
    - Respiratory Arrest

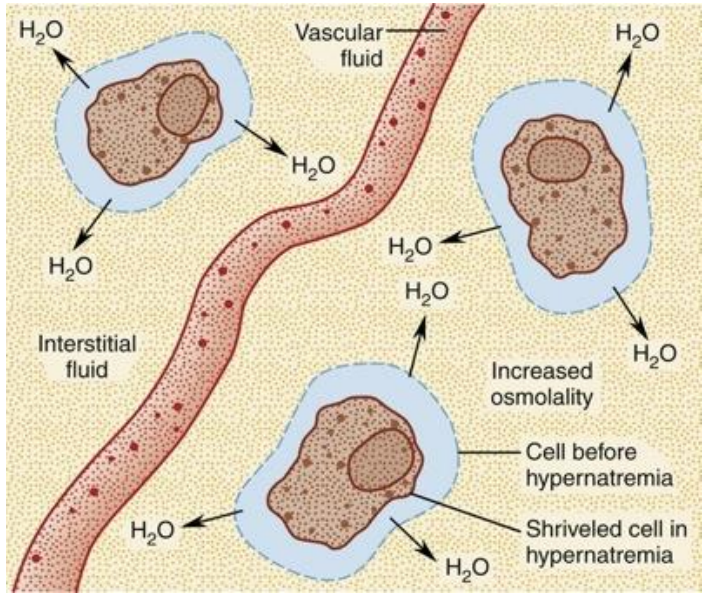


Fluid and Electrolyte Imbalances: Water 4

- **Etiology of Hypernatremia**
  - **Gain of Relatively More Salt Than Water**
    - **Tube feeding without enough water drinking (MOST COMMON CAUSE)**
    - Intravenous infusion with hypertonic solution
    - Near drowning in salt water
    - Overuse of salt tablets
    - Food intake with reduced water intake
    - Difficulty drinking (swallowing fluids)
    - No access to water
    - No thirst response, or depressed thirst response (common in elderly)
  - **Loss of Relatively More Water Than Salt**
    - **Prolonged emesis, diarrhea or diaphoresis without water replacement (MOST COMMON CAUSE)**
    - Diabetes insipidus (lack of ADH)
    - Osmotic diuresis (too much water in the urine); occurs in diabetes mellitus

Fluid and Electrolyte Imbalances: Water 5

- **Clinical Manifestations of Hypernatremia**
  - As in hyponatremia **manifestations of CNS dysfunction** occur. But in hypernatremia the symptoms are due to osmotic water loss from neurons and glial cells. Osmosis causes intracellular **water to move out of the cells**. Neurons and glial cells **shrink.** The brain may shrink.
    - Headache
    - Confusion
    - Lethargy
    - Seizure
    - Coma
    - Thirst
    - Nausea
    - Vomiting



Fluid and Electrolyte Imbalances: Water Clinical Dehydration

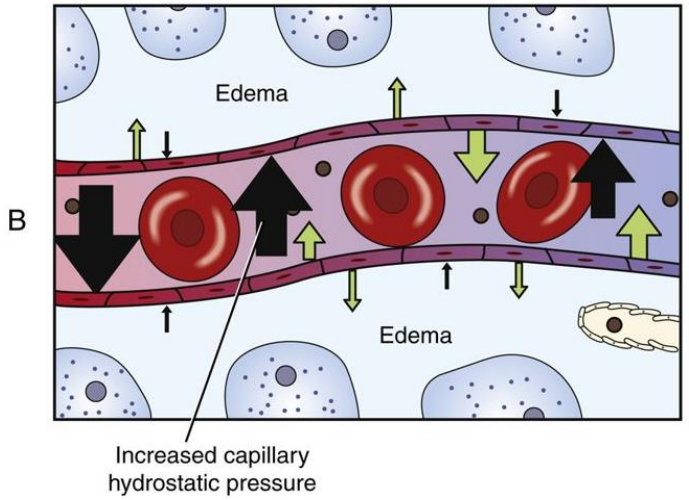
- **Clinical Dehydration-**a combination of ECV Deficit and Hypernatremia
- **Etiology of Clinical Dehydration-**Vomiting or diarrhea without replacement of water or salt is most often the cause.
- **Clinical Manifestations of Clinical Dehydration-**a combination of the manifestations of the two separate disorders: **ECV Deficit and Hypernatremia**
  - Sudden weight loss
  - Decreased postural blood pressure with increased heart rate
  - Flat neck veins when patient is supine
  - Dry oral mucosa between the cheek and gums
  - Swollen, furrowed tongue
  - Hard stools
  - Oliguria (low urine volume)
  - Sunken eyeballs
  - Lack of sweat and/or tears
  - In infants cranial fontanels are sunken
  - Increased serum sodium
  - Confusion, lethargy, coma
  - Hypovolemic shock due to very low blood pressure

Fluid and Electrolyte Imbalances: Edema 1

- **Edema** is caused by an increase in **interstitial fluid** volume. It may simply be a manifestation of ECV excess, or it may be caused by other mechanisms as listed below.
  1. **Increased capillary hydrostatic pressure.**
  2. **Increased interstitial fluid colloid osmotic pressure.**
  3. **Decreased drainage of interstitial fluid into the lymphatic system.**
  4. **Decreased capillary colloid osmotic pressure.**

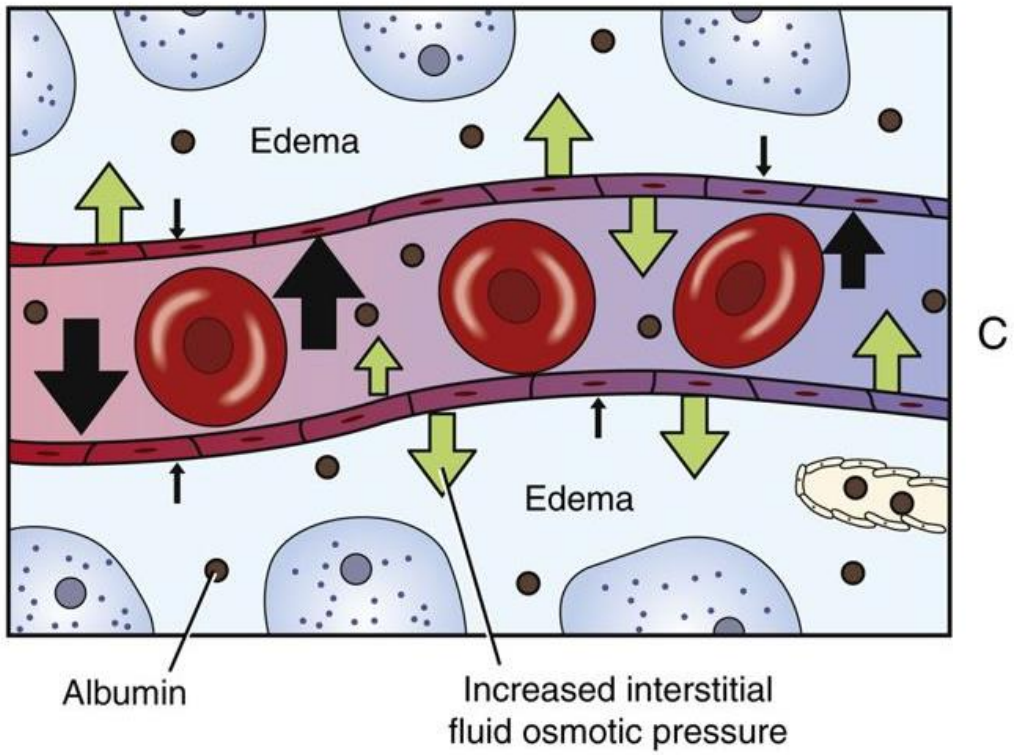
Fluid and Electrolyte Imbalances: Edema

- **Edema caused by increased capillary hydrostatic pressure, HPc (The large black arrows are larger than normal.):**
  - Due to ECV (saline) excess
  - Due to increased capillary bed perfusion (filling with blood) as in the inflammatory response
  - Due to venous congestion (Blood is not moving forward, so it pools in veins and capillary beds and leaks into the interstitium.)



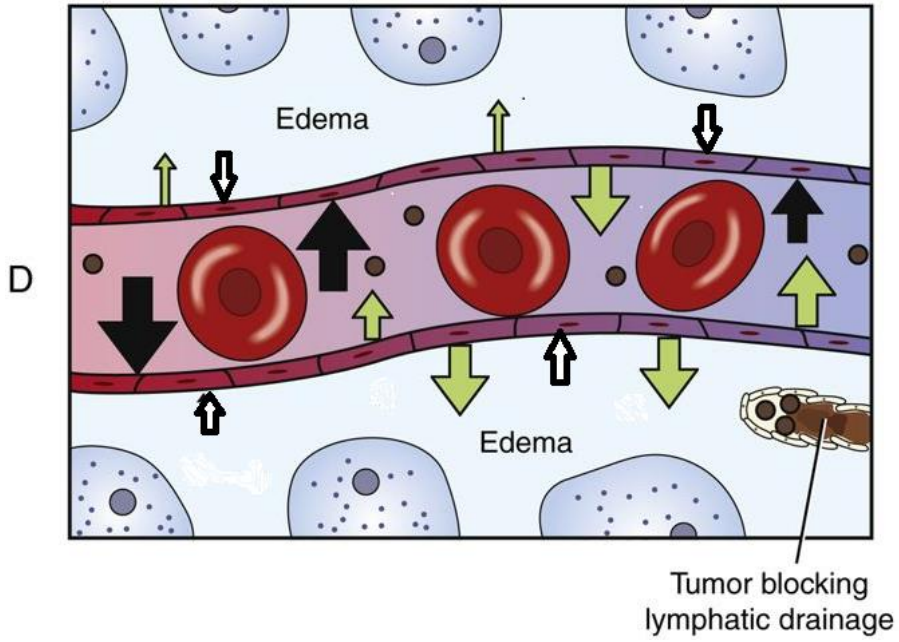
Fluid and Electrolyte Imbalances: Edema 2

- **Edema caused by increased interstitial fluid colloid osmotic pressure, OPif (Black dots in the interstitial space represent proteins.):**
  - Due to increased capillary permeability and the leakage of proteins from the plasma into the interstitial fluid as occurs in inflammation.



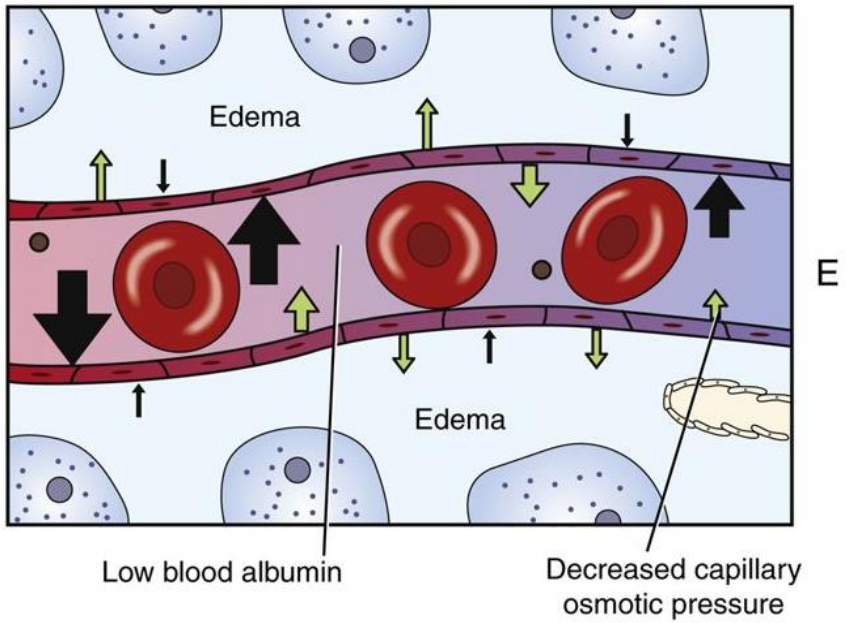
Fluid and Electrolyte Imbalances: Edema 3

- **Edema caused by blocked lymphatic drainage of interstitial fluid increases hydrostatic pressure of the interstitial fluid, HPif (See white arrows.):**
  - Due to tumors compressing or blocking lymph vessels
  - Due to blockage of lymph vessels by parasites (worms, especially)
  - Due to fibrosis resulting from radiation treatment
  - Due to surgical removal of lymph nodes or cutting lymph vessels during surgery



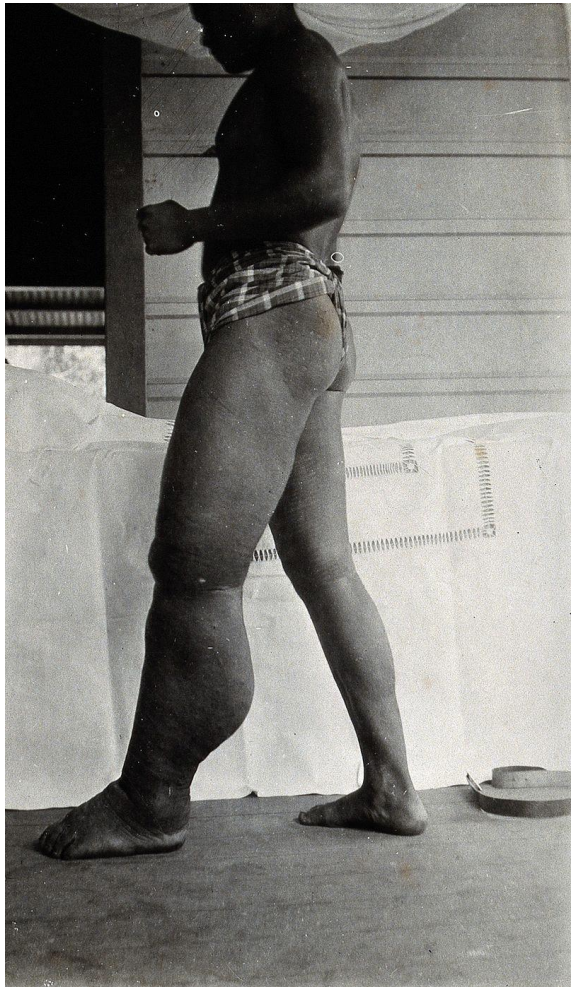
Fluid and Electrolyte Imbalances: Edema 4

- **Edema caused by decreased osmotic pressure of blood, OPc (There are fewer protein molecules in the blood plasma.):**
  - Since most plasma proteins are made by the liver, **liver disease** is the most common cause of reduced plasma protein level. Since albumin is the most common plasma protein, the decrease in plasma proteins is often called **hypoalbuminemia.**



Fluid and Electrolyte Imbalances: Edema 5

Elephantiasis is due to parasitic worm blockage of lymphatic drainage. Extreme edema results.



Electrolyte Homeostasis

- **Electrolyte Concentrations**
  - Serum electrolyte levels are clinically measured. BUT **electrolyte homeostasis** requires that electrolyte levels be normal in BOTH the blood and inside cells. There is **no way to measure** electrolyte concentrations inside cells.
  - Students, don't memorize these values.

Electrolyte	Normal Serum Concentration (Adult)
Calcium (total) Calcium (ionized)	4.5-5.5 mEq/L 2.0-2.5 mEq/L
Magnesium (total)	1.5-2.5 mEq/L
Phosphate	2.5-4.5 mEq/L
Bicarbonate	22-26 mEq/L
Potassium	3.5-5.0 mEq/L
Sodium	135-145 mEq/L

Electrolyte Homeostasis 1

- **Electrolyte Concentrations: What is a milliequivalent?**
- A milliequivalent is the number of electrical charges in a liter of fluid.
- To calculate the mEq/L of sodium or calcium, one would determine the normal concentration (mg/L) of these ions in the plasma, look up their atomic weights (mg/millimole) on the Periodic Table, and plug those values into these equations:

$$Na^+: \frac{3300\ mg/L}{23\ mg/mmol} \times 1 = 143\ mEq/L$$

$$Ca^{2+}: \frac{100\ mg/L}{40\ mg/mmol} \times 2 = 5\ mEq/L$$

  - (No, you will not be asked to do these calculations on assessments.)

Electrolyte Homeostasis 2

- **The serum concentration of an electrolyte represents the interplay among four factors:**
  - Electrolyte intake
  - Electrolytes absorption from the GI tract
  - Electrolyte distribution
  - Electrolyte excretion

Electrolyte Homeostasis 3

- **Electrolyte Intake and Absorption**
  - Normally electrolyte intake occurs by eating and drinking. Medications used at home also play a role, antacids, for example.
  - Electrolyte intake also occurs by various other routes:
    - Intravenous (IV)
    - Blood transfusion
    - Intramuscular (IM)
    - Nasogastric or gastrointestinal tubes
    - Burn treatments
    - Near drowning in salt water

Electrolyte Homeostasis 4

- Oral intake of electrolytes has no bearing on serum levels without **absorption** from the GI tract into the blood.
  - Absorption of **potassium ions** depends on a **concentration gradient**.
  - Absorption of **calcium ions** is dependent on membrane **transport proteins,** and the availability of the membrane transport proteins is dependent on **Vitamin D**.
  - Substances in the digestive tract may interfere with electrolyte absorption. For example, decreased absorption of fat from the intestine causes excretion of fat in feces. That fat binds **calcium and magnesium ions** decreasing their absorption.
  - **pH** of the digestive contents may alter the absorption of **calcium ions**.
  - Medications can alter electrolyte absorption.
  - Surgical removal of segments of the digestive tract decreases electrolyte absorption.

Keep these ions gradients in mind as you work through the next several slides.

Intracellular Ion Concentrations

Na+

K+

Ca2+

Mg2+

HPO_4^{2-}

Cl-

Protein Anions-

Interstitial Ion Concentrations

Na+

K+

Ca2+

Mg2+

HPO42-

Cl-

Electrolyte Homeostasis 5

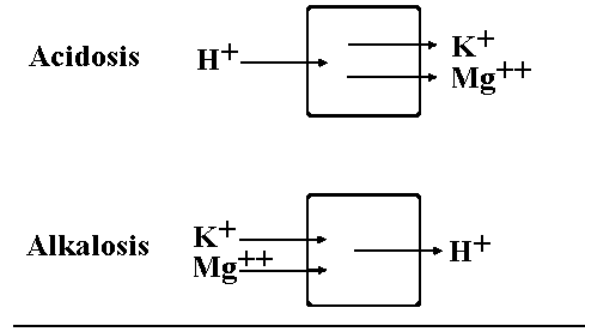
- **Electrolyte Distribution**
  - The **bones** serve as an **electrolyte pool** particularly for **calcium, phosphate, and magnesium ions**. Movement between the electrolyte pools (where ions are bound and have no charge) and the extracellular fluid (where ions are free and charged) is controlled primarily by **hormones**. Significant shifts between electrolyte pools and the extracellular fluid can occur quickly, within minutes.
  - **Hormone Effects**
    - **Stress hormones (epinephrine and cortisol)** increase renal **potassium** ion excretion, and thus decrease serum potassium.
    - **Aldosterone** increases renal reabsorption of **sodium** ions into the blood and renal excretion of **potassium** ions into the urine, and thus increases serum sodium and decreases serum potassium.
    - **Insulin** increases the uptake of **potassium and phosphate** by cells, and thus decreases serum potassium and phosphate.
    - **Parathyroid Hormone (PTH)**, moves **calcium** ions from bones to blood, and thus increases serum calcium.
    - **Calcitonin** moves calcium from blood to bones.
    - **Atrial Natriuretic Peptide (ANP)** increases renal excretion of sodium ions and decreases serum sodium

Electrolyte Homeostasis 6

- **Electrolyte Distribution**
  - The extracellular **pH** has a distinct effect on the distribution of **potassium ions and magnesium ions** due to **reciprocal shifts** between these ions and H+ ions across cell membranes in order to **maintain t**he electrical gradient.
    - **Acidosis** (High H+, Low pH) causes H+ ions to shift into cells. In turn, K+ and Mg 2+ ions shift out the cells and into the blood.
    - **Alkalosis** (Low H+, High pH) causes H+ ions to shift out of cells. In turn K+ and Mg2+ ions shift into the cells so their serum concentration decreases.

Students, you should know this diagram!

Table 7. Transcellular shifts at:



Electrolyte Homeostasis 7

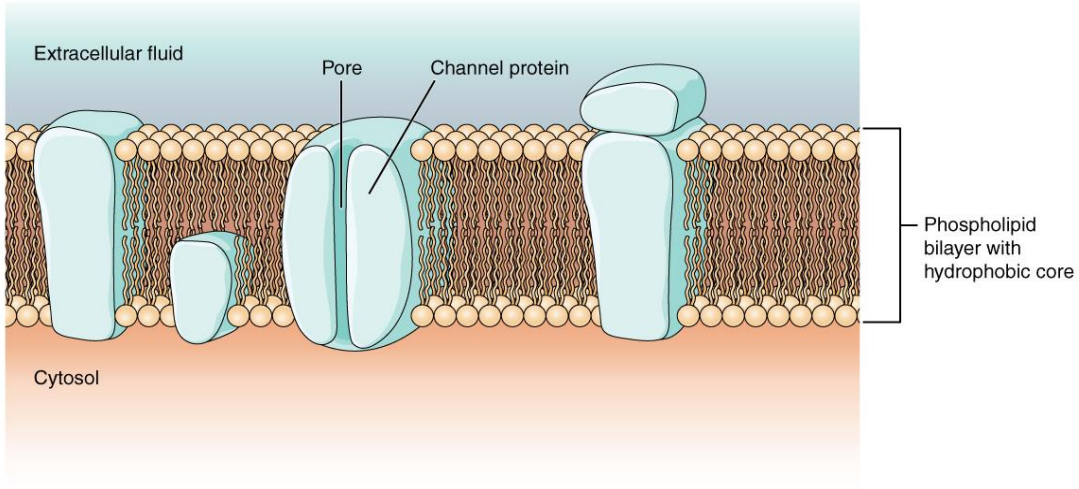
- **Electrolyte Excretion**
  - Electrolytes are normally excreted in feces, urine and sweat.
    - **Electrolytes in Urine**
      - Potassium-wasting diuretics increase K+ excretion and decrease serum K+**: furosemide (Lasix)**
      - Potassium-sparing diuretics decrease K+ excretion and increase serum K+**: spironolactone**
      - **Thiazide diuretics** increase Na+ and Cl- excretion and decrease Ca2+ excretion, so they decrease serum Na+ and Cl-, while increasing serum Ca2+.
    - **Electrolytes in Feces**
      - Fatty stools increase Mg2+ and Ca2+ excretion
- **Electrolyte Loss Through Abnormal Routes**
  - Emesis, nasogastric suction, paracentesis, hemodialysis, wound drainage, fistula drainage

Electrolytes in Neuromuscular Function

Types of Membrane Potentials

- Because of the differences in the distribution of ions and protein molecules in the extracellular and intracellular fluid there is a **charge difference (an electrical gradient, also known as a voltage)** across a plasma membrane as well as **chemical concentration gradients** for several ions. Thus each ion has an **electrochemical** gradient across the plasma membrane.
- The **inside of the cell is negative compared to the outside of the cell**. This is mostly due to the presence of intracellular proteins that carry negative charges at physiological pH. The difference in charge across a plasma membrane, called the **resting potential**, is about **–70 mV**, as measured from outside the membrane to inside the membrane.
- **Nerve cells and all three types of muscle cells** depend on changes in membrane potential, called actions potentials, for their function.
- An action potential can only occur if ion pores (aka ion channels) through the plasma membrane open to allow ions to flow through them. An action potential is generated at a certain voltage, the **threshold membrane potential**. The threshold membrane potential is higher (less negative) than the resting membrane potential. When positive ions enter the cell the membrane potential rises from the resting level toward the threshold level.

Electrolytes in Neuromuscular Function 1



Ion Channels

- Most ion channels are specific. For example, a sodium ion channel only allows sodium ions to pass through it.
- Ions diffuse through ion channels DOWN their concentration gradient (from the side of the membrane where the concentration of the ion is **higher** to the side of the membrane where the concentration of the ion is **lower**).
- So, when their ion channels are open, potassium, phosphate and magnesium ions will diffuse **out** of cells.
- Sodium and calcium ions will diffuse **into** cells.
- Moving ions across the plasma membrane UP their concentration gradients requires active transport (ATP required) also known as ion pumping.
- Ion gradients are maintained across the plasma membrane by ion pumping.

Electrolytes in Neuromuscular Function 2

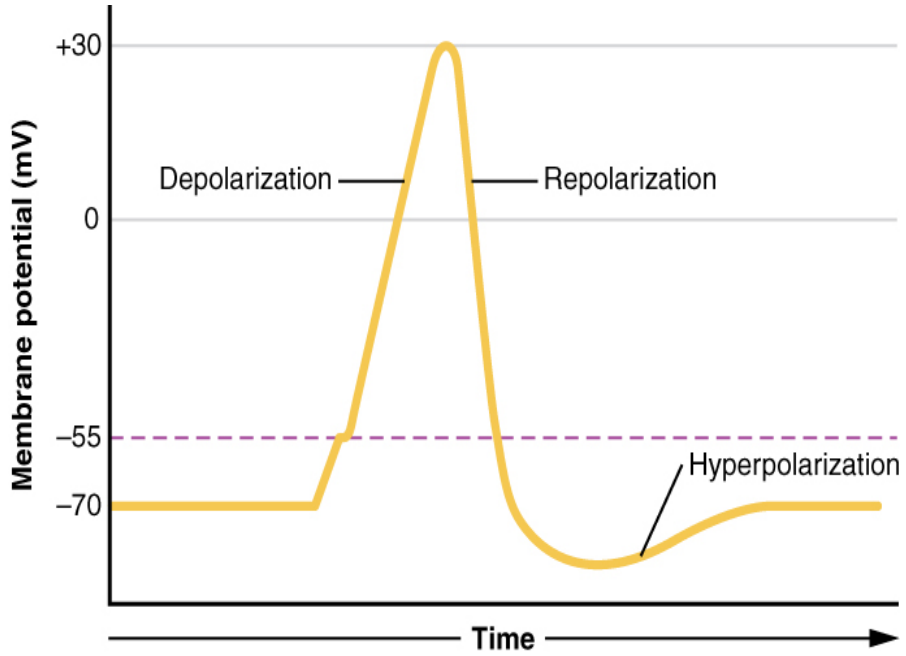
Action Potentials in Nerve Cells and Skeletal Muscle Cells

- **Sodium ions and potassium ions** are involved in the generation of action potentials in the plasma membranes of nerve and skeletal muscle cells. Here's what happens:
- A stimulus causes some **sodium ion channels** to open. Sodium ions (Na+) flow into the cell **down** their concentration gradient. That raises the membrane potential from **resting voltage (-70 mV)** toward the **threshold voltage (–55 mV)**.
- Above the threshold voltage, the **action potential** is triggered. The action potential causes a huge number of ion channels to open allowing positive Na+ ions to rapidly flow **into** the cell. The voltage across the membrane climbs past zero and well into the positive range.
- That voltage change causes sodium ion channels close and the **potassium ion channels** open. Potassium ions (K+) rapidly flow **out** of the cell **down** their concentration gradient causing the voltage across the membrane to drop into the negative range again.
- Following an action potential the **sodium potassium pumps** in the membrane bringing the membrane back to its resting potential.

Electrolytes in Neuromuscular Function 3

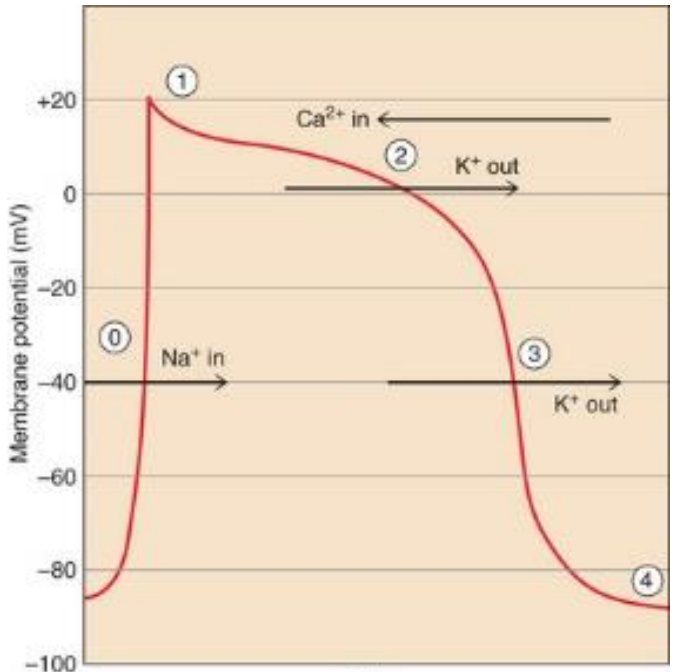
The graph of an action potential in a **nerve cell or skeletal muscle cell** has three parts:

- The **Depolarization Phase** begins just above the threshold potential when sodium ion channels open to allow **sodium ions to diffuse into** the cell.
- The **Repolarization and Hyperpolarization Phases** occur when, at about +30 mV, sodium ion channels close and potassium ion channels open to allow **potassium ions to diffuse out of** the cell. The membrane potential drops back toward resting. Note that hyperpolarization occurs when the voltage is lower than the resting membrane potential (-70 mV).



Electrolytes in Neuromuscular Function 4

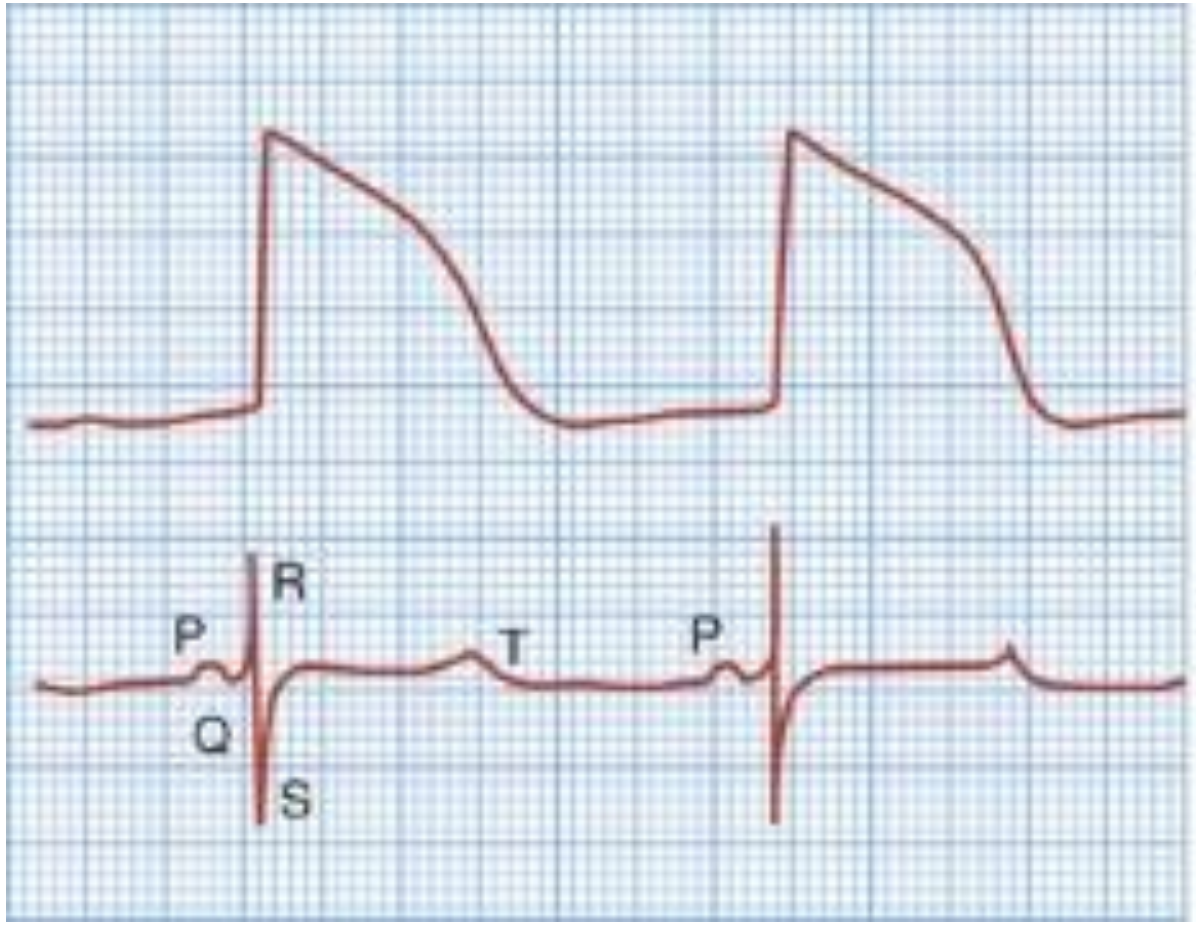
- **Cardiac Muscle Cell Action Potentials**
  - The graph of the cardiac muscle cell action potential differs from that of a nerve cell or skeletal muscle cell action potential both in shape and in the ion flows involved.
  - The **depolarization phase (area 0)** of the cardiac muscle cell action potential is due to sodium ion influx (sodium movement INTO the cell).
  - At about +20 mv the sodium ion channels close and the potassium ion channels open to produce **area 1** of the graph.
  - Shortly thereafter, the calcium ion channels open to produce the **plateau phase (area 2)** of the action potential. It is a period when both K+ efflux (potassium movement OUT OF the cell) and Ca2+ influx occur. The two ion flows oppose each other causing the membrane voltage to remain relatively constant.
  - The **repolarization phase** occurs when the Ca2+ channels close while the K+ channels remain open.



Electrolytes in Neuromuscular Function 5

- An **action potential graph** is the graph of the voltage changes across the membrane of a **single cell**.
- An **EKG is a graph** of the electrical changes that occur at the **surface of the body** due to the voltage changes occurring across the membranes of the **cardiac contractile cells**. (The patient must lie very still to prevent the electrical changes occurring in skeletal muscle cells from interfering with the EKG.)
- The EKG has 5 deflections: P, Q, R, S and T.
- Essentially all electrolyte imbalances can have an effect on the EKG, particularly if the imbalance is severe.

Electrolytes in Neuromuscular Function 6

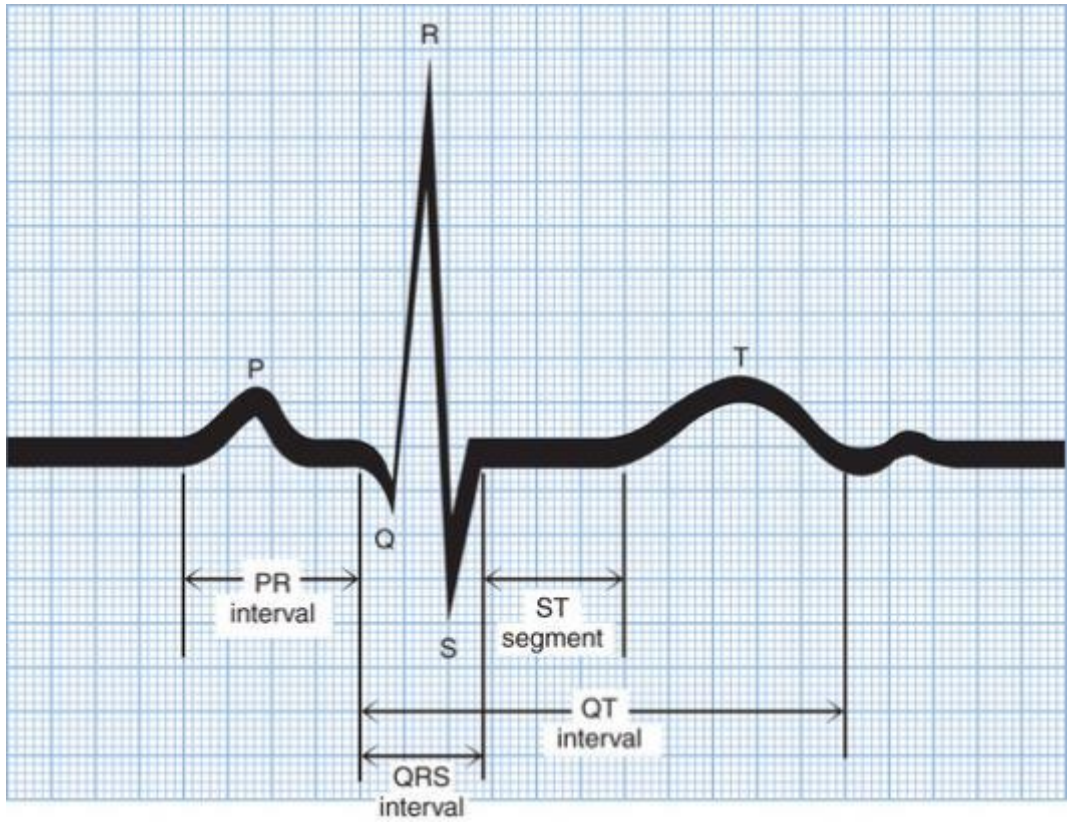


Action potential from a single ventricular muscle cell

ECG of potentials from the heart as a whole

Electrolytes in Neuromuscular Function 7

- The **P wave** occurs when the atria (upper heart chambers) depolarize.
- The **QRS complex** occurs when the ventricles (lower heart chambers) depolarize. The atria also repolarize during the QRS complex.
- The **T wave** occurs when the ventricles repolarize.



Fluid and Electrolyte Imbalances: Potassium

- **Specific Electrolyte Imbalances: Potassium (3.5-5.0 mEq/L is normal.)**
  - **Etiology of Hypokalemia (Deficit of Extracellular K+)**
    - Excess use of diuretics, especially K+-wasting diuretics like furosemide (Lasix), is the **most common cause.**
    - Emesis, diarrhea, GI suction=loss of K+ from the digestive tract
    - Alkalosis (high pH, low H+ in blood)
      - High pH (low extracellular H+) causes H+ to move out of cells and K+ to move into cells.
    - Decreased dietary K+ Intake
    - Excess aldosterone=hyperaldosteronism
    - Excess cortisol=Cushing's Syndrome or corticosteroid therapy
    - Excess insulin
    - Excess epinephrine or beta agonist meds
    - Excessive ingestion of black licorice (glycyrrhizin)!!

Fluid and Electrolyte Imbalances: Potassium 1

- **Pathogenesis of Hypokalemia**
  - Potassium ions are crucial in maintaining the resting membrane potential of nerve cells and muscle cells. There is a negative voltage across muscle cell membranes at rest (more negative on the inside of the membrane).
  - Most of the body's K+ (98%) is normally located inside cells, so there is a downward K+ gradient from the intracellular compartment to the extracellular compartment.
  - When K+ is deficient in the extracellular space, the K+ gradient becomes **steeper** and the **resting membrane potential** becomes **more negative**. The membrane is **HYPERPOLARIZED**.
  - The availability of active **sodium ion channels** increases under conditions of hyperpolarization, so the **threshold** for action potential generation also becomes more negative.
  - The resting potential and the threshold potential are **closer together** than when serum potassium ion is normal.
  - The membrane is thus **MORE EXCITABLE (more likely to produce action potentials)!**

Fluid and Electrolyte Imbalances: Potassium 2

- **Pathogenesis of Hypokalemia**
  - The voltage-gated K+ channels that are responsible for repolarization of the plasma membrane like to have a K+ ion sitting on their extracellular surface, if not, they tend to collapse.
  - So in hypokalemia many K+ channels are collapsed.
  - As a result the repolarization of the plasma membrane is prolonged

Fluid and Electrolyte Imbalances: Potassium 3

- **Clinical Manifestations of Hypokalemia**
  - **Cardiac Muscle Manifestations (greatest danger)**
    - Because the plasma membranes are at a higher level of excitability the risk of cardiac dysrhythmias increases.
    - EKG shows **round or flat T waves** due to prolonged ventricular repolarization.
    - Possible cardiac arrest
  - **Skeletal Muscle Manifestations**
    - Elevated membrane excitability causes muscle weakness due to **muscle fiber fatigue**.
    - Paralysis may occur.

Fluid and Electrolyte Imbalances: Potassium 4

- **Etiology of Hyperkalemia (Excess Extracellular K+): OFTEN IATROGENIC!**
  - Massive blood transfusions with stored blood. RBCs release K+ when they are stored.
  - Intravenous potassium chloride (KCl) that is excessive, too rapid or insufficiently mixed
  - Acidosis (low pH, high H+ in blood)
    - Low pH (high extracellular H+) causes H+ to move into cells and K+ move out of cells.
  - Crushing injury or massive cell death (releases K+ from cells).
  - Cytotoxic chemotherapy drugs (Lysis of tumor cells releases their K+.)
  - Deficit of hormones that stimulate sodium-potassium pumps: insulin, epinephrine and norepinephrine
  - Interference with the excretion of potassium in the urine:
    - Hypoaldosteronism (K+ stays in the blood rather than entering the urine.)
    - Use of ACE inhibitor diuretics (reduces aldosterone secretion)
    - Use of K+-sparing diuretics like spironolactone (K+ stays in the blood rather than entering the urine.)

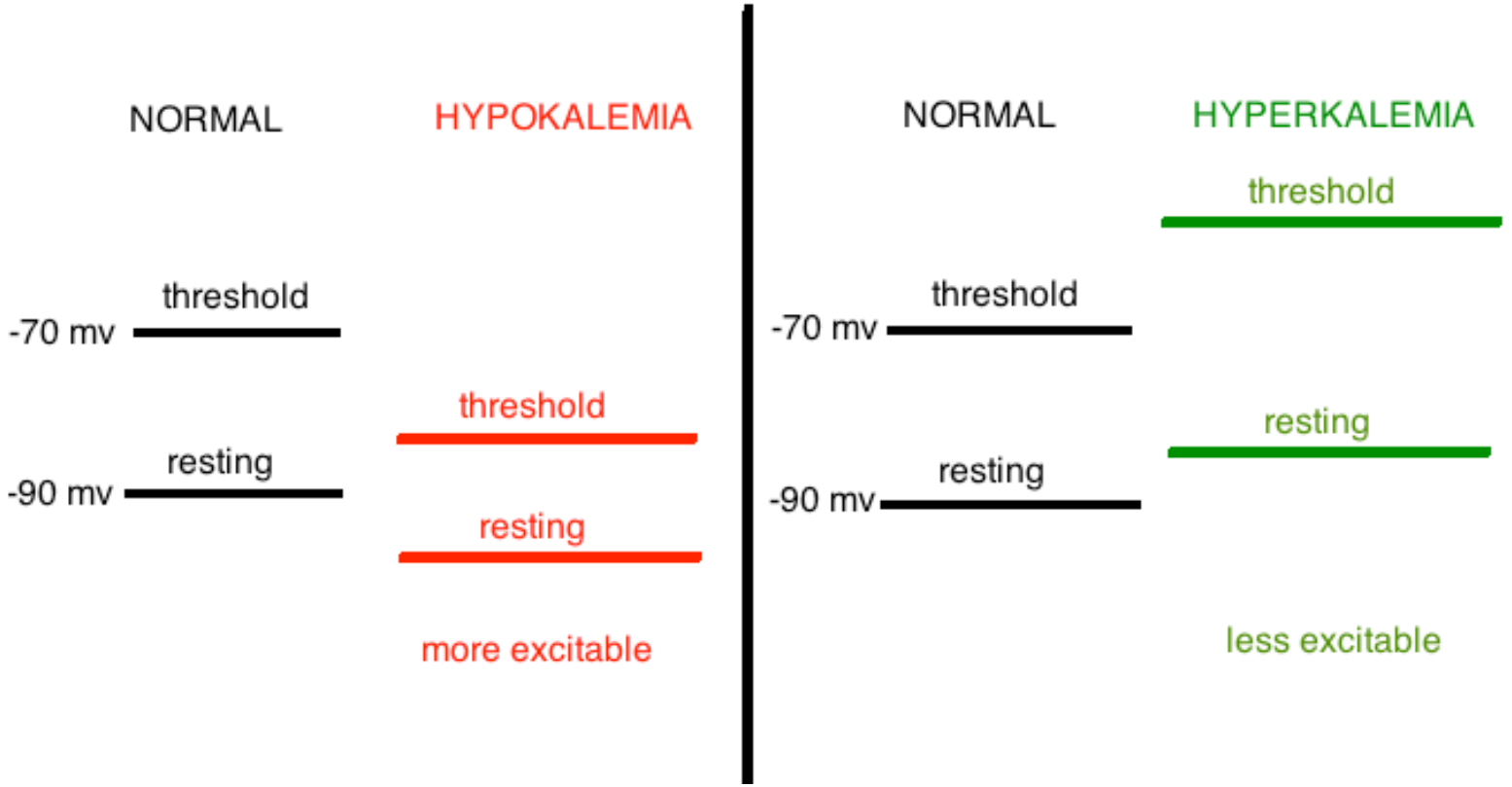
Fluid and Electrolyte Imbalances: Potassium 5

- **Pathogenesis of Hyperkalemia**
  - When K+ is excessive in the extracellular space, the K+ gradient becomes flatter, and the resting membrane potential becomes less negative. The membrane is **LESS POLARIZED** (more DEPOLARIZED), so the **resting potential is higher**. One would predict the membrane to be more excitable.
  - HOWEVER, the availability of active sodium ion channels decreases under conditions of higher depolarization, so the **threshold potential is higher.** The resting potential and the threshold potential are actually **father apart**. The membrane is actually **LESS EXCITABLE.**
  - Voltage-gated K+ channels stay open rather than collapsing because extracellular K+ is more available to sit on their extracellular surfaces.
  - Therefore, **repolarization** of the cardiac muscle cell membrane is rapid.

Fluid and Electrolyte Imbalances: Potassium 6

- **Clinical Manifestations of Hyperkalemia**
  - Hyperkalemia is **less likely** to be symptomatic than hypokalemia**.**
    - **Cardiac Muscle Manifestations (greatest danger)**
      - EKG shows **peaked T waves** due to shortened ventricular repolarization.
      - Possible cardiac arrest
    - **Skeletal Muscle Manifestations**
      - Muscle weakness due to poor action potential generation (less excitable membranes). Without action potentials muscles can’t contract.
      - If the diaphragm ceases to contract, respiratory arrest may occur.

Membrane Potentials in Hypokalemia and Hyperkalemia

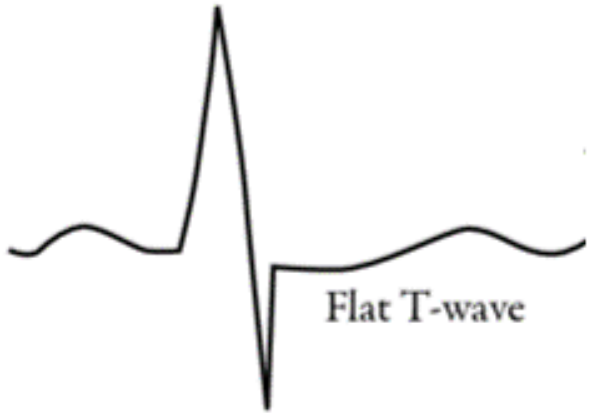


More Na+ ion channels available
More Excitable Membrane
Action Potentials Easier to Generate

Fewer Na+ ion channels available
Less Excitable Membrane
Action Potentials Harder to Generate

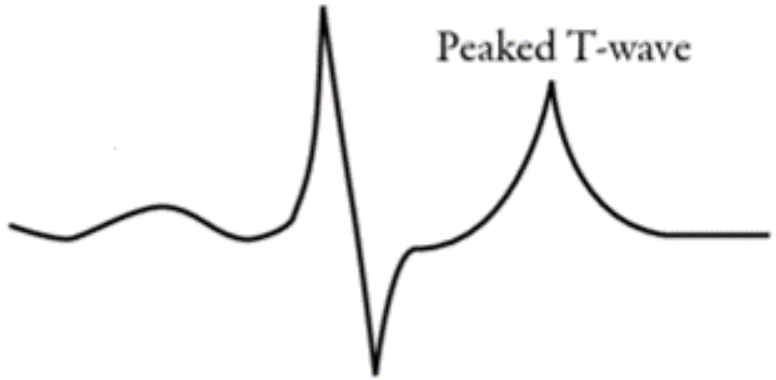
ECG Waves in Potassium Imbalance

Moderate hypokalemia



Lack of K+ external to the ion channel slows ventricular repolarization=flat T waves

Moderate hyperkalemia



Extra K+ external to the ion channel speeds ventricular repolarization=peaked T waves

Summary
Hypokalemia and Hyperkalemia

Hypokalemia	Hyperkalemia
Resting and threshold potentials closer together	Resting and threshold potentials farther apart
More excitable membrane	Less excitable membrane
K+ channels may collapse during repolarization	K+ channels stay fully open during repolarization
Prolonged repolarization phase	Rapid repolarization phase
Skeletal muscle weakness due to fatigue	Skeletal muscle weakness due to low AP generation
Flat T wave on ECG due to prolonged ventricular repolarization	Peaked T wave on ECG due to rapid ventricular repolarization

Fluid and Electrolyte Imbalances: Calcium

- **Specific Electrolyte Imbalances: Calcium (4.5-5.5 mEq/L is normal.)**
- NOTE: Two clinical measurements of calcium are available, **total** serum calcium (includes both calcium ions and bound calcium), and **ionized** serum calcium. Only free calcium ions are physiologically active and contribute to electrolyte imbalances.
  - **Etiology of Hypocalcemia**
    - **Diet deficient in calcium or Vitamin D**. Vitamin D stimulates intestinal absorption of calcium ions.
    - Deficient activated Vitamin D due to **kidney disease**. Vitamin D is activated by kidney cells.
    - **Chronic diarrhea**
    - **Steatorrhea** (Fatty stools bind Ca2+, so the ions are excreted.)
    - **Pancreatitis** (Reduced secretion of the enzyme, lipase, into the digestive tract contributes to steatorrhea.)
      - Lipase digests lipids (triglycerides). It is normally secreted into the GI tract by the pancreas. In pancreatitis lipase spills into the space around the pancreas, so very little lipase reaches the GI tract. Fat is not digested and absorbed, it is passed with feces.

Fluid and Electrolyte Imbalances: Calcium 1

- **Etiology of Hypocalcemia**
  - **Hypoparathyroidism** reduces serum calcium ion level. (Parathyroid hormone, PTH, causes calcium to move out of bones into the blood.)
  - **Hyperphosphatemia** (Phosphate ions bind up Ca2+ ions taking them out of solution.)
  - **Crohn disease**, a form of inflammatory bowel disease, impairs absorption of calcium from the intestine.
  - Infusion of **citrated** blood or blood plasma (Citrate ions bind up Ca2+)
  - Trapping of Ca2+ in **dead tissue** (pancreatitis, severe burns, etc.)
  - **Alkalosis:** H+ and Ca2+ compete for binding sites on serum albumin. If H+ is deficient, more Ca2+ will bind to albumin, (taking it out of solution and cancelling its charge.)

Fluid and Electrolyte Imbalances: Calcium 2

- **Clinical Manifestation of Hypocalcemia**
  - Normally, extracellular calcium ions **impede the diffusion of sodium ions** into the cell.
  - Hypocalcemia **lowers the threshold** (as in hypokalemia) for action potential generation by allowing more sodium ion channel activity. Nerve and muscle cell membranes are **more excitable**, more likely to produce action potentials.
  - Unlike potassium ion imbalances, calcium ion imbalances have **no effect on repolarization** of action potentials.
  - Tingling in fingers and lips
  - Muscle twitching, muscle cramping (spasm)
    - Positive **Trousseau** sign=carpal (wrist) spasm after restriction of arterial blood flow for about 3 minutes
    - Positive **Chvostek** sign=cheek spasm after tapping the facial nerve in front of the ear.
  - Seizure
  - Abnormal EKG, **prolonged QT interval (T wave is normal.)**
  - Impaired myocardial contractility leading to heart failure

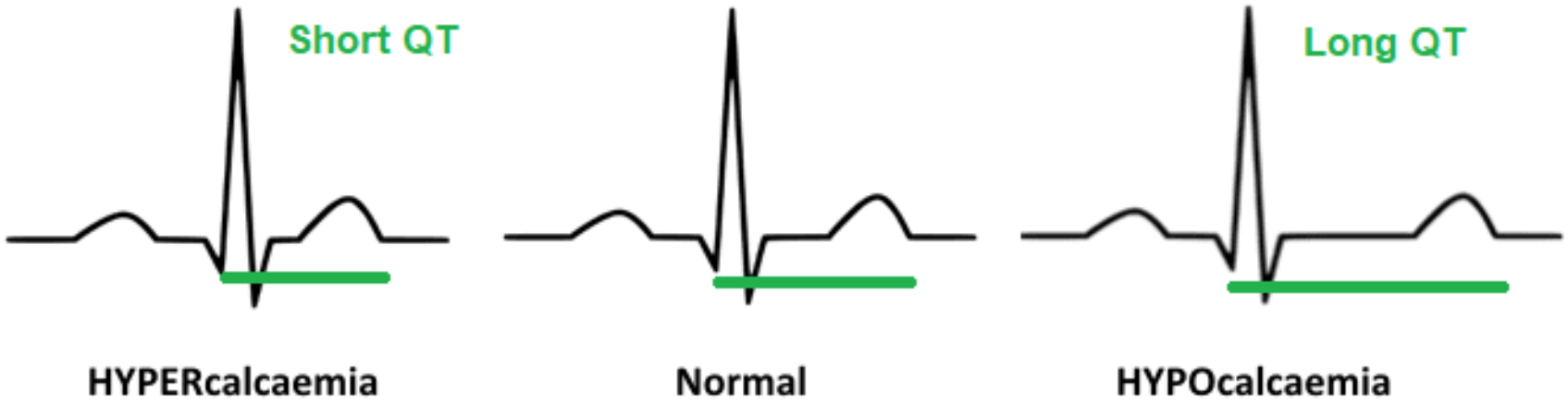
Fluid and Electrolyte Imbalances: Calcium 3

- **Etiology of Hypercalcemia**
  - **Hyperparathyrodism** (More calcium moves out of bone into the blood.)
  - **Cancer**- Many malignant tumors produce bone resorbing factors or factors that decrease excretion of Ca2+.
  - **Vitamin D overdose** causes too much Ca2+ absorption from intestines.
  - **Prolonged immobilization** reduces bone remodeling. Bone tissue does not take up calcium ions.
  - **Thiazide diuretics** increase calcium ion reabsorption from the renal filtrate into the blood
  - **Lithium** (treatment for bipolar disease) increases renal reabsorption of Ca2+ and also interferes with the negative feedback of Ca2+ on the secretion of PTH by the parathyroid glands.

Fluid and Electrolyte Imbalances: Calcium 4

- **Clinical Manifestations of Hypercalcemia**
  - Hypercalcemia causes an **increase in the threshold** for action potential generation (as in hyperkalemia) in nerve and muscle cells. Makes membranes **less excitable**. Action potentials are less likely. Clinical manifestations: "stones, bones, groans, thrones, psychiatric overtones"
    - Constipation, nausea, vomiting (abdominal groans)
    - Polyuria-increased urine volume due to osmotic effect of calcium in the urine (thrones)
    - Muscle weakness
    - Lethargy, fatigue, confusion, stupor, coma (psychiatric overtones)
    - Abnormal EKG, **shortened QT interval (T wave is normal.)**
    - Possible cardiac arrest
    - Bone pain due to calcium loss to blood (bones), especially if hyperparathyroidism is causative
    - Renal calculi (kidney stones) due to calcium in the urine

Fluid and Electrolyte Imbalances: Calcium 5



Fluid and Electrolyte Imbalances: Magnesium

- **Specific Electrolyte Imbalances: Magnesium (1.5-2.5 mEq/L is normal.)**
- NOTE: As is the case with calcium, magnesium in the blood is present in both bound and unbound (ionic) forms. Clinical measurement of ionized magnesium is not widely available.
- The effects of magnesium imbalances are similar to the effects of calcium imbalances.
  - **Etiology of Hypomagnesemia**
    - Chronic alcoholism causes increased urinary excretion of Mg^{2+} **(common cause)**
    - Steatorrhea-fat binds Mg^{2+}
    - Pancreatitis (enhances steatorrhea)
    - Alkalosis-Mg^{2+} shifts into cells
    - Excess use of diuretics
    - Chronic diarrhea

Fluid and Electrolyte Imbalances: Magnesium 1

- **Clinical Manifestations of Hypomagnesemia**
- If too few magnesium ions are present, too much acetylcholine (ACH) is released at neuromuscular junctions. (Mg^{2+} normally puts the brakes on ACH release!) This causes neuromuscular junction hyperexcitability.
- Symptoms are similar to hypocalcemia.
  - Positive Chvostek and Trousseau signs
  - Muscle twitching and cramping
  - Seizures

Fluid and Electrolyte Imbalances: Magnesium 2

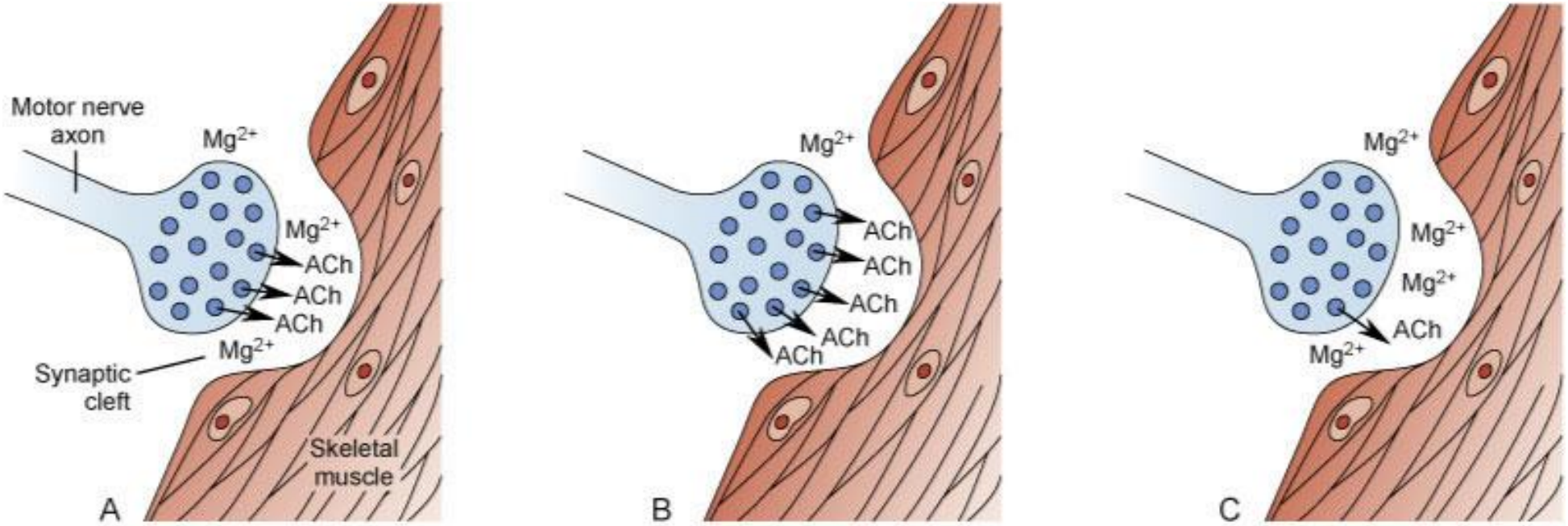
- **Etiology of Hypermagnesemia (RARE)**
  - Occurs in renal failure patients due to excessive intake of magnesium-containing laxatives or antacids (milk of magnesia).
  - Occurs in pregnant women due to excessive treatment with magnesium sulfate (treatment for pre-eclampsia or preterm labor).
- **Clinical Manifestations of Hypermagnesemia**
  - Due to decreased release of ACH at the neuromuscular junctions and abnormal Na+/K+ pump activity
    - Respiratory depression due to muscle weakness
    - Cardiac dysrhythmias
    - Possible cardiac arrest

Fluid and Electrolyte Imbalances: Magnesium

- Normal

Hypomagnesemia

Hypermagnesemia



Fluid and Electrolyte Imbalances: Phosphate

- **Specific Electrolyte Imbalances: Phosphate (2.5-4.5 mEq/L is normal.) These imbalances are relatively rare.**
- **Phosphate is an important in mineralizing bone and teeth. It is also required for forming ATP.**
- **NOTE: Calcium ions and phosphate ions form compounds with each other—then they are no longer ions!**
  - **Etiology of Hypophosphatemia**
    - **Hyperparathyroidism**-Excess PTH over-stimulates the reabsorption of calcium from the renal filtrate, but it interferes with the reabsorption of phosphate and sodium from the renal filtrate.
    - **Hypercalcemia-**calcium ions bind up phosphate ions to form compounds.
    - **Failure to absorb phosphate from the GI tract** occurs in malnutrition, alcoholism, chronic diarrhea and due to use of certain antacids (those that contain calcium).
    - **Refeeding** after starvation (Phosphate is sequestered by cells as they focus on restoring their ATP supply.)

Fluid and Electrolyte Imbalances: Phosphate 1

- **Clinical Manifestations of Hypophosphatemia**
  - Because it is often caused by **hypercalcemia** there is symptom overlap between the two imbalances.
  - Bone deformities
  - Muscle weakness including respiratory failure
  - Confusion, stupor, coma
  - Impaired cardiac contractility leading to congestive cardiomyopathy

Fluid and Electrolyte Imbalances: Phosphate 2

- **Etiology of Hyperphosphatemia**
  - Common in severe kidney disease when GFR and urine output are very low.
  - As with potassium, conditions that cause cells to break open (necrosis) will release intracellular phosphate into the extracellular compartment. Potassium and phosphate ions have higher intracellular concentrations than other ions.

- **Clinical Manifestations of Hyperphosphatemia**
  - Usually asymptomatic unless phosphate levels are quite high
  - Causes hypocalcemia by binding calcium ions and thus increases neuromuscular excitability and causes a prolonged QT interval on the EKG.
  - Calcium phosphate crystals may be deposited in soft tissues especially if kidney disease is causative.
    - Calcium phosphate deposits cause achy, stiff joints, itchy skin and conjunctivitis.

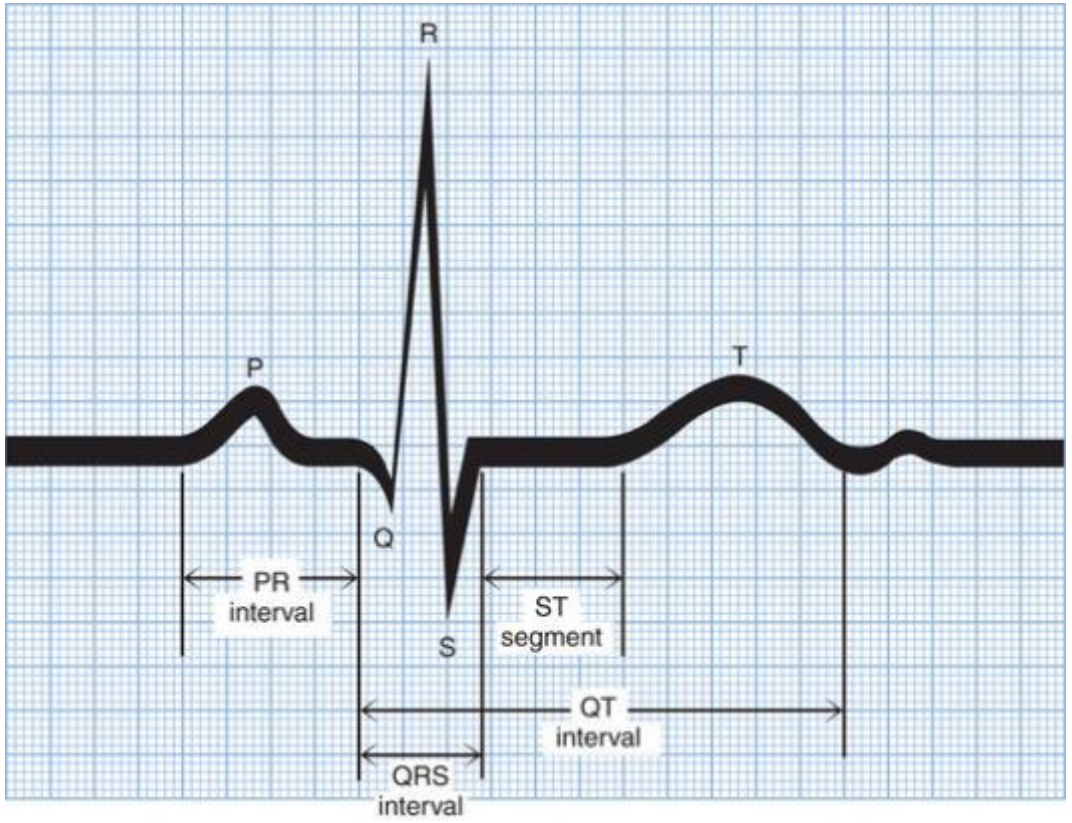
Fluid and Electrolyte Imbalances

The QT Interval is Prolonged in:

Hypocalcemia
Hypomagnesemia
Hyperphosphatemia

The QT Interval is Shortened in:

Hypercalcemia
Hypermagnesemia
Hypophosphatemia



Fluid and Electrolyte Imbalances: Summary

- It is important to note that most of the clinical manifestations of ion imbalances are associated with the effects of extracellular ion concentrations on action potential generation in nerve cells and/or muscle cells.
- As you review think about the roles of the various electrolytes in neuromuscular mechanisms.
- As you review think about the relationships between electrolyte concentrations and blood pH as well as the effects of hormones and diuretics on electrolyte concentrations.

QUIZ 1CD

- COMPLETE QUIZ 1CD.
- THEN PREPARE FOR EXAM 1.

EXAM 1

- COMPLETE EXAM 1.
- THEN GO ON TO MODULE 2AB PPT.