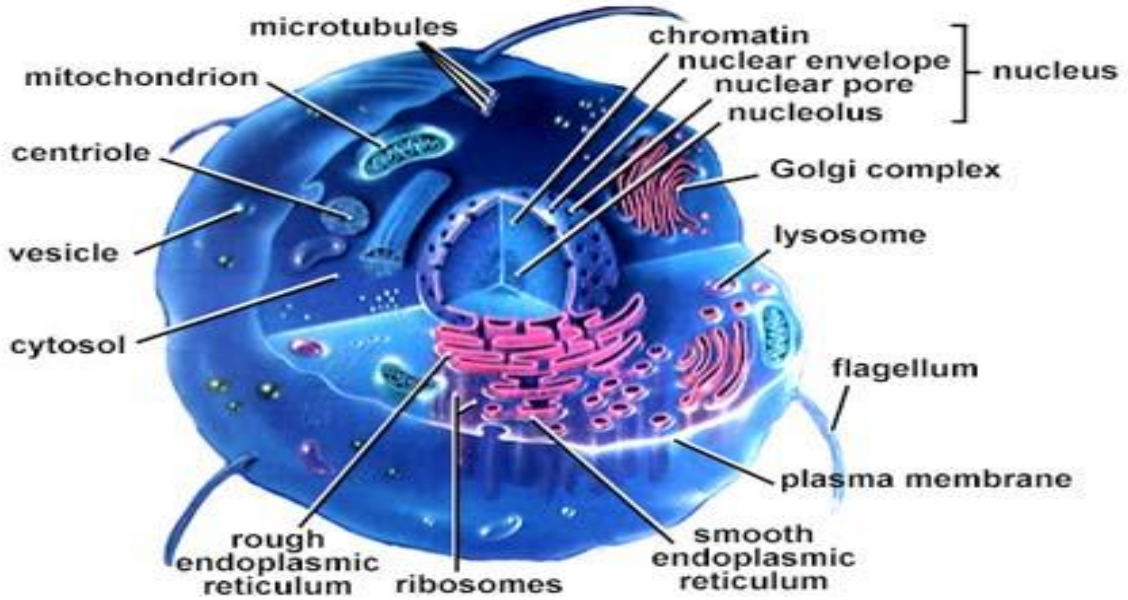
Cell physiology

Cell Structure and Function

Cells are the microscopic fundamental units of all living things.

An adult human body is composed of about 100 billion cells. Each cell has basic requirements to sustain it, and the body's organ systems are largely built around providing the many trillions of cells with those basic needs (such as oxygen, food, and waste removal).

- There are about 200 different kinds of specialized cells in the human body.
- Many identical cells are organized together in tissue.
- Various tissues organized together for a common purpose are called organs .



Specialized Cells of the Human Body

Within the body, all cells have similarities in their structural organization and metabolic needs , but some of the different types specialized within the human body as :

Nerve Cells: specialized in function to process and transmit information. use chemical and electrical synapses to relay signals throughout the body.

Epithelial cells: specialized functions of epithelial cells include secretion, absorption, protection, transcellular transport, sensation detection, and selective permeability.

Exocrine cells: secrete products through ducts, such as mucus, sweat, or digestive enzymes. The products of these cells go directly to the target organ by ducts.

Endocrine cells: secrete their products directly into the bloodstream . The products of the endocrine cells go throughout the body in the blood stream but act on specific organs by receptors on the cells of the target organs.

Blood Cells: as: (RBC). collect oxygen in the lungs and deliver it through the blood to the body tissues. various types of (WBC). help the body to fight infectious disease and foreign objects in the immune system.

Proteins and Cholesterol of cell membrane

Proteins and cholesterol in CM are:

- **Peripheral proteins :attach loosely to the inner or outer surface of the plasma membrane.**
- **Integral proteins :lie across the membrane, extending from inside to outside.**
- **A variety of other proteins : are scattered throughout the flexible matrix of phospholipid molecules in a *fluid mosaic model* of the cell membrane.**
- **The phospholipid bilayer: is selectively permeable. Only small, uncharged polar molecules can pass freely across the membrane. Some of these molecules are H_2O and CO_2, nonpolar molecules like O_2, and lipid soluble molecules such as hydrocarbons.**

Other molecules need the help of a membrane protein to get across.

Types of membrane proteins that serve various functions:

1- **Channel proteins**: Proteins that provide passageways through the membranes for certain hydrophilic or water-soluble substances such as polar and charged molecules. No energy is used during transport, hence this type of movement by **Channel proteins** is called facilitated diffusion.

2- **Transport proteins:** Proteins that spend energy (ATP) to transfer materials across the membrane by the process is called active transport.

3-**Recognition proteins:** Proteins that distinguish the identity of neighboring cells. These proteins have oligosaccharide or short polysaccharide chains extending out from their cell surface.

4-**Adhesion proteins:** Proteins that attach cells to neighboring cells or provide anchors for the internal filaments and tubules that give stability to the cell.

5-**Receptor proteins:** Proteins that initiate specific cell responses for hormones or other trigger molecules bind to them.

6- **Electron transfer proteins:** Proteins that are involved in moving electrons from one molecule to another during chemical reactions.

Transport across cell membrane/ Three modes utilized for transport:

1st :Passive Transport Across the Cell Membrane

1-Passive transport :describes the movement of substances down a concentration gradient and does not require energy use.

2-Bulk flow :is the collective movement of substances in the same direction in response to a force such as pressure. Blood moving through a vessel is an example of bulk flow.

3-Simple diffusion or diffusion: is the net movement of substances from an area of higher concentration to an area of lower concentration. This movement occurs as a result of the random and constant motion characteristic of all molecules, (atoms or ions) and is independent from the motion of other molecules. Since, at any one time, some molecules may be moving against the gradient and some molecules may be moving down the gradient, although the motion is random, the word "net" is used to indicate the overall, eventual end result of the movement.

4-Facilitated diffusion :is the diffusion of solutes through channel proteins in the plasma membrane with out use of energy.

5-Osmosis : is the diffusion of water molecules across a selectively permeable membrane. When water moves into a body by osmosis, hydrostatic pressure or osmotic pressure may build up inside the body.

6-Dialysis : is the diffusion of solutes across a selectively permeable membrane.

2nd :Active Transport Across the Cell Membrane

Active transport is the movement of solutes against a gradient and requires use of energy, usually in the form of ATP. Active transport is achieved through one of these two mechanisms:

1-Protein Pumps

Transport proteins in the plasma membrane transfer solutes such as small ions (Na^+, K^+, Cl^-, H^+), amino acids, and monosaccharides. The proteins involved with active transport are also known as ion pumps.

The protein binds to a molecule of the substance to be transported on one side of the membrane, then it uses the released energy (ATP) to change its shape, and releases it on the other side.

The protein pumps are specific, there is a different pump for each molecule to be transported. Protein pumps are catalysts in the splitting of ATP → ADP + phosphate, so they are called ATPase enzymes.

2-The sodium-potassium pump (also called the Na^+/K^+-ATPase enzyme) actively moves sodium to out of the cell and potassium into the cell. These pumps are found in the membrane of virtually every cell, and are essential in transmission of nerve impulses and in muscular contractions.

3rd : Vesicular Transport

Is transport as vesicles in the cytoplasm that move macromolecules or large particles across the plasma membrane. Types of vesicular transport include:

1-Exocytosis: which describes the process of vesicles fusing with the plasma membrane and releasing their contents to the outside of the cell. This process is common when a cell produces substances for export.

2-Endocytosis: which describes the capture of a substance outside the cell when the plasma membrane merges to engulf it. The substance subsequently enters the cytoplasm enclosed in a vesicle.

There are three kinds of endocytosis:

1 Phagocytosis or cellular eating, in Phagocytosis, the plasma membrane engulfs the solid material, forming a phagocytic vesicle.

2 Pinocytosis or cellular drinking occurs when the plasma membrane folds inward to form a channel allowing dissolved substances to enter the cell. When the channel is closed, the liquid is encircled within a pinocytic vesicle.

3 Receptor-mediated endocytosis : Occurs when specific molecules in the fluid surrounding the cell bind to specialized receptors in the plasma membrane. As in pinocytosis, the plasma membrane folds inward and the vesicle formed in side the cell.

Cytoskeleton

Are threadlike proteins in side cells that make the cytoskeleton.

Functions

1- It helps cells to maintain their shape and allows cells and their contents to move.

2-The cytoskeleton allows certain cells such as neutrophils and macrophages to make amoeboid movements.

is composed of microtubules and microfilaments.

Microtubules :

They are long hollow cylinders, composed of protein subunits, called tubulin.

Microtubules form mitotic spindles, the machinery that partitions chromosomes between two cells in the process of cell division.

Mts. function as the framework along which organelles and vesicles move within a cell. They are the thickest of the cytoskeleton structures.

Microfilaments:Microfilaments provide mechanical support for the cell, determine the cell shape, and in some cases enable cell movements. They have an arrow-like appearance. They are found in almost every cell, but are predominant in muscle cells and in the cells that move by changing shape, such as phagocytes .

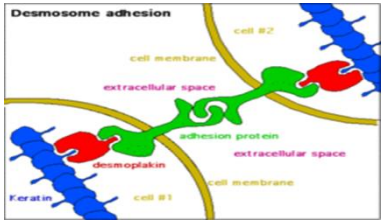
Cell Junctions

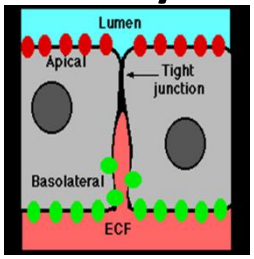
The plasma membranes of adjacent cells are usually separated by extracellular fluids that allow transport of nutrients and wastes to and from the bloodstream. In certain tissues, however, the membranes of adjacent cells may join and form a junction. Three kinds of cell junctions are recognized:

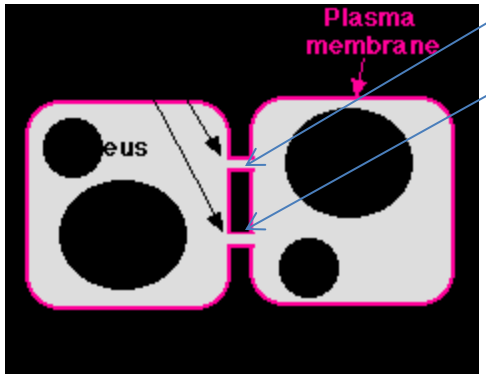
1-Desmosomes :Are protein attachments between adjacent cells. Inside the plasma membrane, a desmosome bears a disk shaped structure from which protein fibers extend into the cytoplasm. Desmosomes hold together tissues that undergo considerable stress, such as skin or heart muscle.

2-Tight junctions : Tight junctions are specialized structures at the plasma membrane that link adjacent epithelial cells, preventing the movement of material between the cell. Tight junctions are characteristic of cells lining the digestive tract, where materials are required to pass through cells, rather than intercellular spaces, to penetrate the bloodstream.

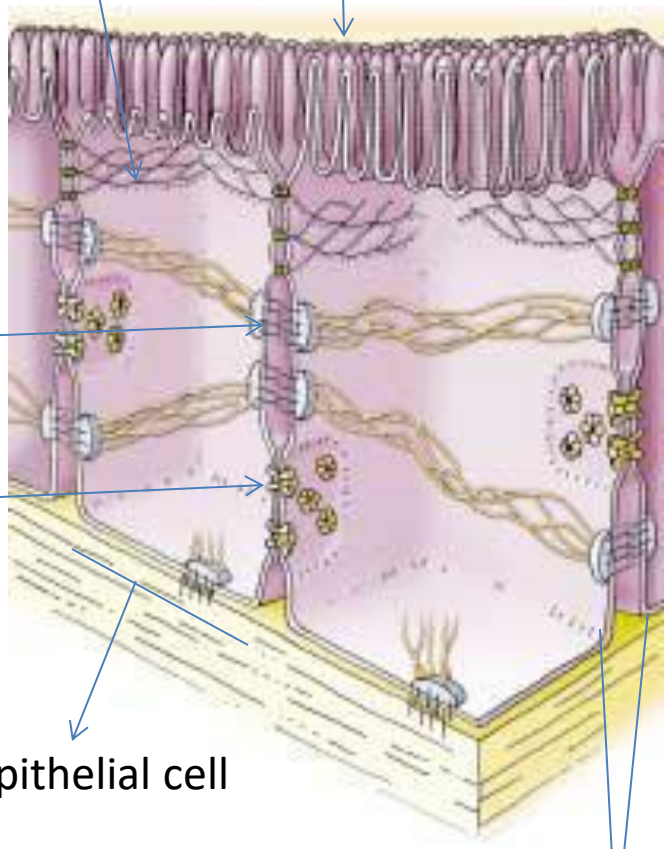
3-Gap junctions: Are narrow tunnels between cells that consist of proteins called connexons. The proteins allow only the passage of ions and small molecules.







Desmosomes



10

Energy Rich Molecules

Adenosine Triphosphate (ATP)

ATP is the currency of the cell. When the cell needs to use energy such as when it needs to move substances across the cell membrane via the active transport system, it "pays" with molecules of ATP. The total quantity of ATP in the human body at any one time is about 0.1 Mole. The energy used by human cells requires the hydrolysis of 200 to 300 moles of ATP daily. This means that each ATP molecule is recycled 2000 to 3000 times during a single day. ATP cannot be stored, hence its consumption must closely follow its synthesis. On a per-hour basis, 1 kilogram of ATP is created, processed and then recycled in the body. Looking at it another way, a single cell uses about 10 million ATP molecules per second to meet its metabolic needs, and recycles all of its ATP molecules about every 20-30 seconds.

Flavin Adenine Dinucleotide (FAD)

When two hydrogen atoms are bonded, FAD is reduced to $FADH_2$ and is turned into an energy-carrying molecule. FAD accommodates two equivalents of Hydrogen; both the hydride and the proton ions. This is used by organisms to carry out energy requiring processes. FAD is reduced in the citric acid cycle during aerobic respiration

Nicotinamide Adenine Dinucleotide (NADH)

Nicotinamide adenine dinucleotide (NAD^+) and nicotinamide adenine dinucleotide phosphate (NADP) are two important cofactors found in cells. NADH is the reduced form of NAD^+, and NAD^+ is the oxidized form of NADH. It forms NADP with the addition of a phosphate group to the 2' position of the adenosyl nucleotide through an ester linkage.

q1

Count different types of specialized cells within the human body.

Q2

Differntiaten between Recognition proteins & Adhesion proteins

Q3

Define :

Receptor-mediated endocytosis

Microfilaments

Digestion physiology -

Mechanical Digestion, Chemical Digestion

Digestion in the Mouth and Pharynx

major components of saliva & control

Gastric glands

Small intestine , Liver functions, Gall Bladder , Pancreas

Fat digestion , Carbohydrate digestion , DNA and RNA digestion , Digestion of protein

Absorption of nutrients

Stages in the Digestive Process

Regulation of appetite

Control of Digestion,

Digestive hormones,

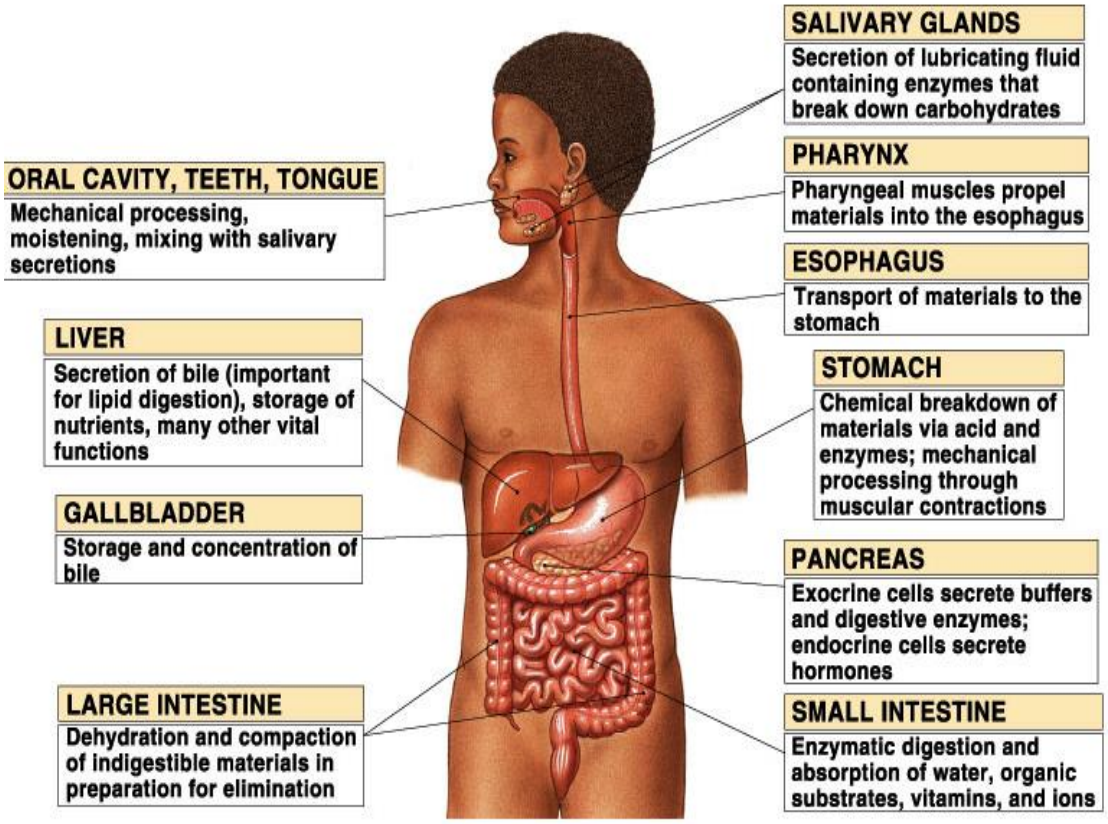
Digestive Disorders

Chapter 2 Physiology of the Digestion

Objectives

1. Describe the structure and general function of each digestive organ and the liver.
2. Describe the structure of the wall of the alimentary canal.
3. Explain how the contents of the alimentary canal are mixed and moved.
4. Describe the mechanisms of Digestion, Absorption , Control, Abnormal Functions.

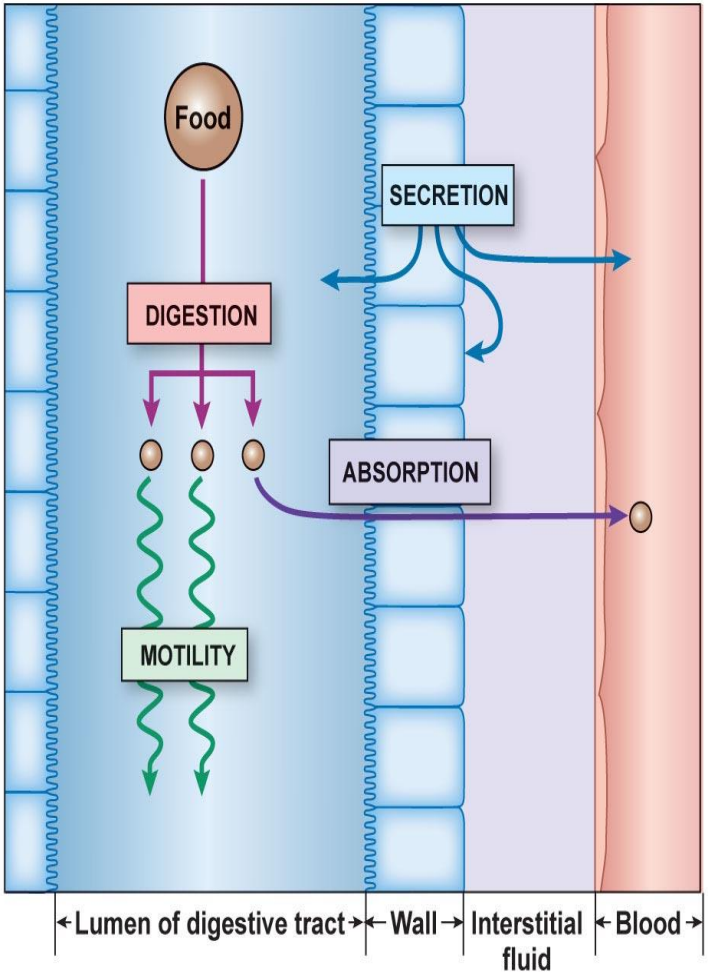
Digestive System Anatomy



- Digestive tract
  - Alimentary tract or canal – GI tract:
- Accessory organs
  - Primarily glands –
- Regions
  - Mouth or oral cavity –
  - Pharynx –
  - Esophagus –
  - Stomach –
  - Small intestine –
  - Large intestine –
  - Anus –

Basic GI Functions

- Primary function
  - Movement of nutrient molecules from the external environment to the internal environment
- Secondary functions
  - Mass balance
    - Ensuring daily fluid input and output are equal
  - Protection
    - GI tract provides a huge external surface for pathogens to gain entrance into the internal environment



Steps of food processing

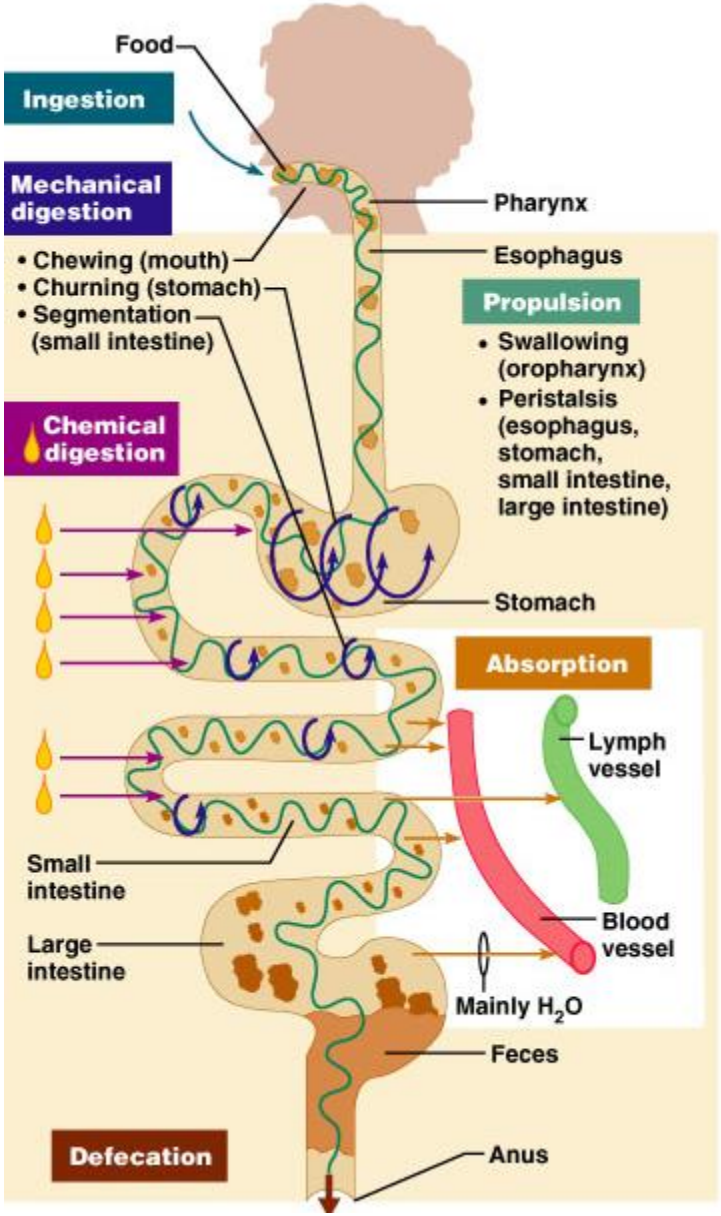
Animals process food in four stages which are : ingestion , digestion , absorption , elimination

During digestion, two main processes occur at the same time;

Mechanical Digestion: larger pieces of food get broken down into smaller pieces while being prepared for chemical digestion. Mechanical digestion starts in the mouth and continues into the stomach.

Chemical Digestion: starts in the mouth and continues into the intestines. Several different enzymes break down macromolecules into smaller molecules that can be absorbed.

The Digestive Process



- **Ingestion**
  - Taking in food through the mouth
- **Propulsion** (movement of food)
  - Swallowing
  - Peristalsis – propulsion by alternate contraction &relaxation
- **Mechanical digestion**
  - Chewing
  - Churning in stomach
  - Mixing by segmentation
- **Chemical digestion**
  - By secreted enzymes: see later
- **Absorption**
  - Transport of digested end products into blood and lymph in wall of canal
- **Defecation**
  - Elimination of indigestible substances from body as feces

Digestion in the Mouth and Pharynx

Mechanical breakdown begins in the mouth by chewing with teeth and actions of the tongue. Chemical breakdown of starch start by production of salivary amylase from the salivary glands, salivary amylase, begins the breakdown of starch .

Salivary glands are: Parotid gland, submandibular gland, sublingual gland , these are exocrine glands that produces saliva which begins the process of digestion with amylase, Salivary glands also produce an estimated three liters of saliva per day.

control of salivation:

Secretion:

ingestion of foodstuffs → activate chemoreceptors and pressoreceptors → salivatory nuclei (pons & medulla) → parasympathetic nerve activation → stimulates secretion by salivary Facial (VII) and Glassopharyngeal (IX) nerves → glands.

Stop secretion

sympathetic nerve activation → decreased salivation.

Tongue

The tongue is a fleshy and muscular sensory organ, and the very first sensory information is received via the taste buds on its surface.

If the taste is agreeable the tongue will go into action, manipulating the food in the mouth which stimulates the secretion of saliva from the salivary glands.

Taste is a form of chemoreception that takes place in the specialized receptors of taste cells, contained in structures called taste buds in the mouth. Taste buds are mainly on the upper surface (dorsum) of the tongue. Taste perception is vital to help prevent harmful or rotten foods from being consumed. The taste buds are innervated by a branch of the facial nerve the chorda tympani, and the glossopharyngeal nerve.

Taste messages are sent via these cranial nerves to the brain. The brain can distinguish between the chemical qualities of the food.

The five basic tastes are referred to as those of : saltiness, sourness, bitterness and sweetness, and the most recent addition of a certain savouriness termed umami. The detection of saltiness and sourness enables the control of salt and acid balance. The detection of bitterness warns of poisons

Epiglottis

The epiglottis is a flap that is made of elastic cartilage and attached to the entrance of the larynx. The epiglottis functions to guard the entrance of the glottis, the opening between the vocal folds. It is normally pointed upward during breathing with its underside functioning as part of the pharynx, but during swallowing, the epiglottis folds down to a more horizontal position, with its upper side functioning as part of the pharynx. In this manner it prevents food from going into the trachea and instead directs it to the esophagus, which is posterior. During swallowing, the backward motion of the tongue forces the epiglottis over the glottis' opening to prevent any food that is being swallowed from entering the larynx which leads to the lungs; the larynx is also pulled upwards to assist this process. Stimulation of the larynx by ingested matter produces a strong cough reflex in order to protect the lungs.

STOMACH

(The wall of the stomach is stronger than all regions of the tract , and is lined with million of *gastric glands* which secrete about 400 --- 800 mL. of gastric juice at each meal).

Gastric glands : Three type of secretary cells found in each gland:

A-Parietal cells , B-chief cells , C-mucus cells .

Parietal cells (oxyntic cells): Secrete gastric Hcl.

Function of gastric Hcl

1-It has a role in digestion .

2-Making the medium of the stomach acidic (pH-2) .

3-Stimulate pancreatic and bile secretion where it enter intestine

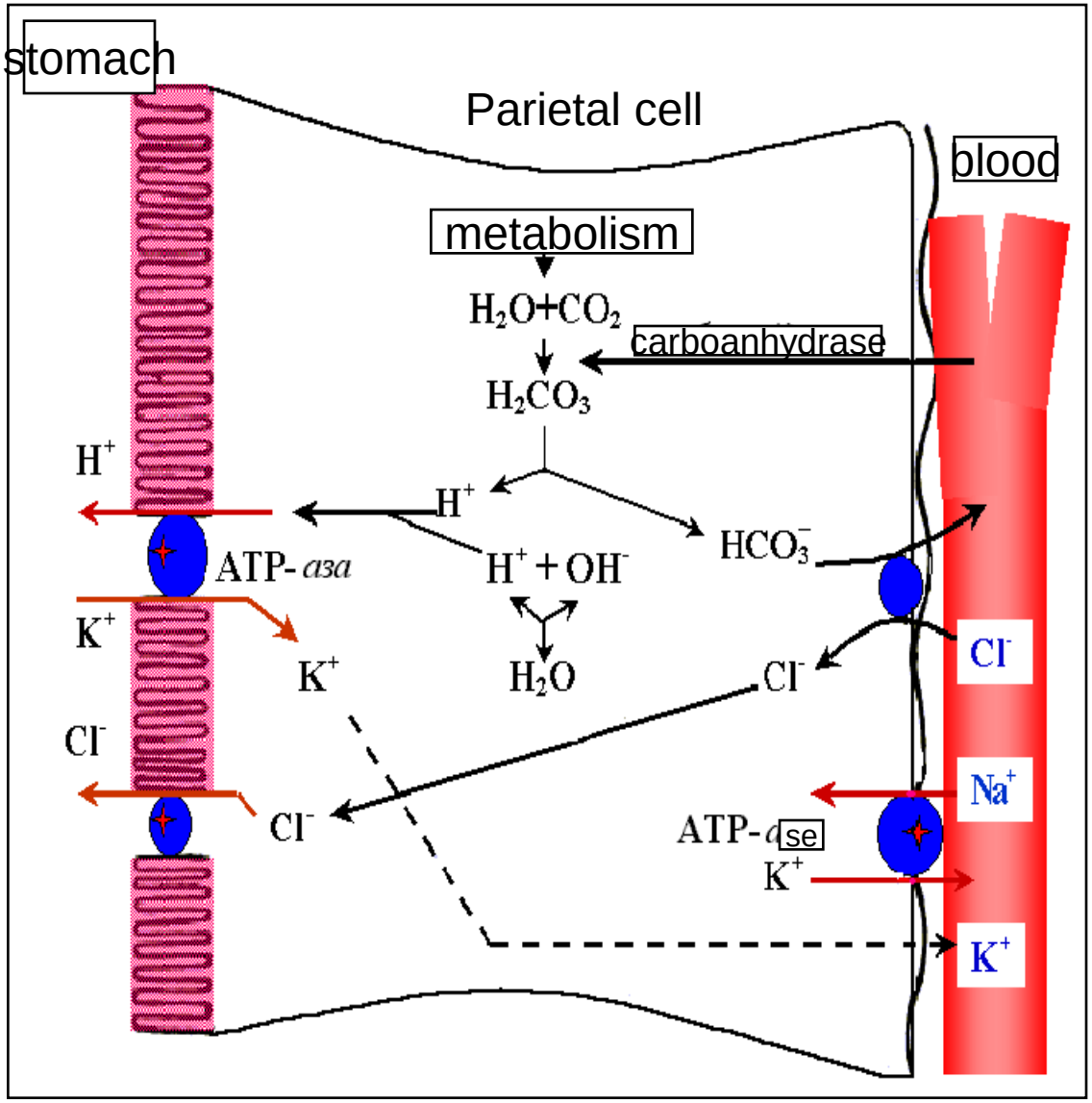
4- Kills much of bacteria that may be ingested along with food

5-Stops activity of salivary amylase, but promotes pepsin activity.

Chief cells

It synthesize and secrete in active pepsinogen which activated by gastric Hcl into active pepsin that digest proteins by cleaving peptide bonds and breaks long polypeptide chains into shorter ones .

Food in the stomach is in semi-liquid form, which upon completion is known as chyme.


stomach
Parietal cell
blood
metabolism
H_2O+CO_2
carboanhydrase
H_2CO_3
H^+
H^+
HCO_3^-
ATP-аза
$H^+ + OH^-$
K^+
K^+
H_2O
Cl^-
Cl^-
Cl^-
Cl^-
Na^+
ATP-аза
K^+
K^+

Small intestine :

Two ducts enter the duodenum which are:

1-Common duct which is composed from liver duct and bile duct –it draining the gall bladder and liver secretions into duodenum .

2-Pancreatic duct which draining the exocrine product from pancreas into duodenum .

Liver functions:

1. detoxify blood - remove and metabolize poisonous substances.

2. destroy old RBC - hemoglobin converted to bile -- bile stored in gall bladder and used in digestion of fats.

3. stores glucose as glycogen - converts glycogen to glucose to keep blood sugar concentration in blood constant

4. production of urea from amino groups and ammonia.

5-synthesis of blood proteins.

Small Intestine Secretions

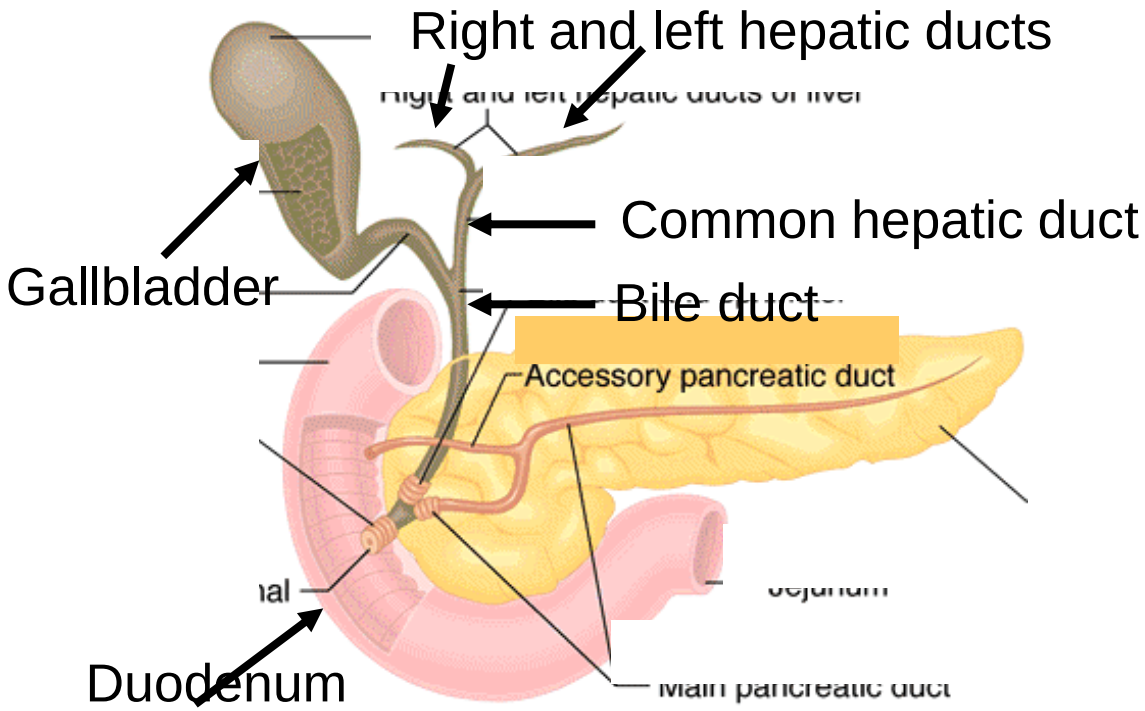
- Mucus
  - Protects against digestive enzymes and stomach acids
- Digestive enzymes
  - Disaccharidases: Break down disaccharides to monosaccharides
  - Peptidases: Hydrolyze peptide bonds
  - Nucleases: Break down nucleic acids

Bile Release into Small Intestine

The liver is stimulated by the hormones “secretin” and “cholecystokinin” (CCK) to produce bile. The bile enters the right and left hepatic ducts and travels to the common hepatic duct. The bile is stored in the gallbladder. The gallbladder is stimulated to release the bile by the vagal nerve and CCK. The bile enters the duodenum via the bile duct.

Function of bile juice

Emulsification of ingested fat by breaking large fat droplets into smaller &changing fast from insoluble material into water soluble that could digested by lipase . Also bile juice helps in absorption of fat soluble vitamins (E,D,A,K).



The role of bile

1. Neutralize the stomach acid;
2. Inhibit the act of stomach proteases;
3. Increase the activity of pancreatic lipase;
4. Emulsificates the lipids by help of bile acids actions;
5. Bile acids help stabilizing of emulsion;
6. Increase the absorption of fatty acids, carrotin, vitamins K, D, E;
7. Increase tone and motor function of intestines (more duodenum and large intestine);
8. Decrease the activity of intestine micro flora;
9. Take place of enzymes fixation on the intestines surface.

Pancreas : Is an gland has two type of secretion

First

Endocrine secretions from islets of langerhans , which are following hormone
insuline , glucagune , somatostatin

Second

Exocrine secretion whose drain in to duodenum and called pancreatic juice
its pH (8) and contain
1-sodium bicarbonate – neutralize the acidity of gastric Hcl in duodenum
2-Ions of Cl^- , $So4^-$, Hpo4, K^+ , Ca^+ , Mg
3-Many digestive enzymes that are

- **A- Pancreatic amylase** — **hydrolyze starch**
- **B- pancreatic lipase** — **hydrolyze fats**
- **C- trypsin** — **hydrolyze proteins**
- **D- chemotrypsin** — **hydrolyze proteins**
- **E- Elastase** — **hydrolyze proteins**
- **F- Carboxypeptidase** — **hydrolyze polypeptides**
- **G- nuclease** — **hydrolyze nucleic acids**

Regulation of Pancreatic Secretion

1. **parasympathetic:** causes release of pancreatic exocrine secretion during cephalic and gastric phases of gastric secretion
2. **secretin** - hormone that causes release of "bicarbonate-rich" pancreatic juices in response to the presence of HCl.
3. **cholecystokinin** - hormone that causes release of "enzyme-rich" pancreatic juice in response to the presence of proteins and fats

Phases of gastric secretion

1-Cephalic phase - This phase occurs before food enters the stomach and involves preparation of the body for eating and digestion.

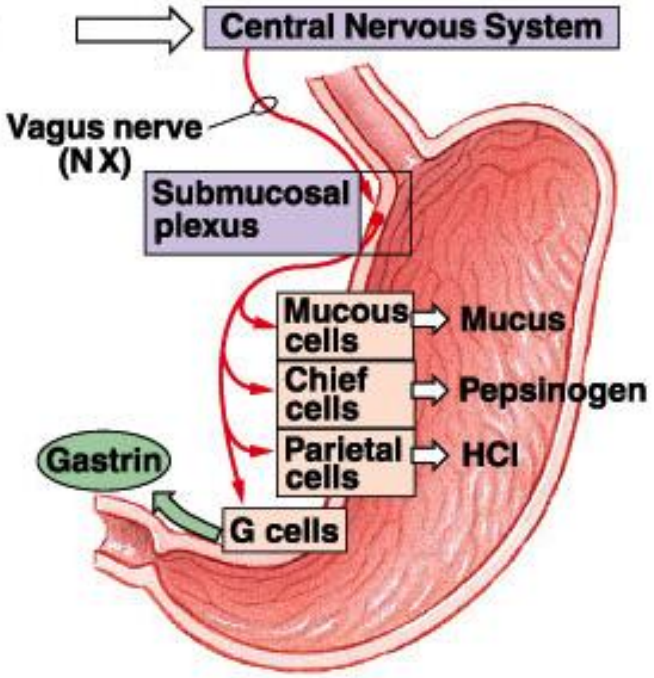
The Cephalic Phase Sight, smell, taste, or thoughts of food

Function:
Prepare stomach for arrival of food

Duration:
Short (minutes)

Mechanism:
Neural, via preganglionic fibers in vagus nerve and synapses in submucosal plexus

Actions:
Primary: increased volume of gastric juice by stimulating mucus, enzyme, and acid production
Secondary: stimulation of gastrin release by G cells



2-Gastric phase - This phase takes 3 to 4 hours. It is stimulated by distension of the stomach, presence of food in stomach and decrease in pH. (Distention activates long and myenteric reflexes.

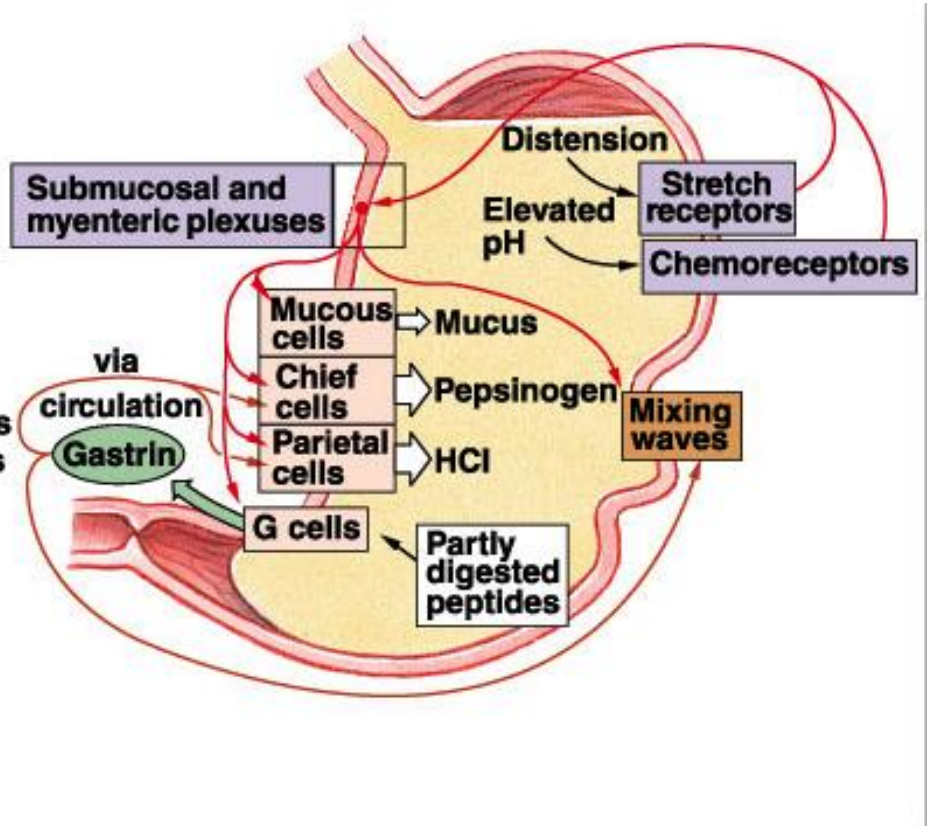
The Gastric Phase

Functions:
- Enhance secretion started in cephalic stage; homogenize and acidify chyme; initiate digestion of proteins by pepsin

Duration:
- Long (3–4 hours)

Mechanisms:
- *Neural:* short reflexes triggered by
  - (1)stimulation of stretch receptors as stomach fills
  - (2)stimulation of chemoreceptors as pH increases
- *Hormonal:* stimulation of gastrin release by G cells by parasympathetic activity and presence of peptides and amino acids in chyme
- *Local:* release of histamine by mast cells as stomach fills (not shown)

Actions:
- Increased acid and pepsinogen production; increased motility and initiation of mixing waves



3-Intestinal phase -

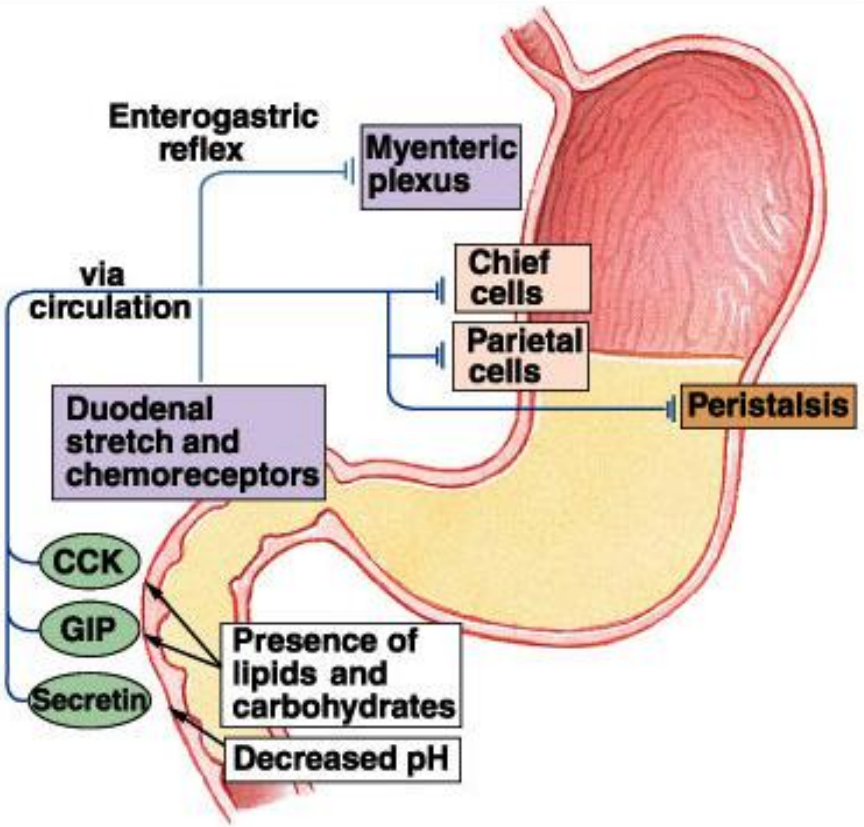
The Intestinal Phase

Function:
- Control rate of chyme entry into duodenum

Duration:
- Long (hours)

Mechanisms:
- *Neural:* short reflexes (enterogastric reflex) triggered by distension of duodenum
- *Hormonal:*
  - Primary: stimulation of cholecystokinin (CCK), gastric inhibitory peptide (GIP), and secretin release by presence of acid, carbohydrates, and lipids
  - Secondary: release of gastrin stimulated by presence of undigested proteins and peptides (not shown)

Actions:
- Feedback inhibition of gastric acid and pepsinogen production; reduction of gastric motility



Fat digestion

All fats ingested digested into three type of molecules which are :

Glycerol,

Triglycerides, ➢

Fatty acids

These products are absorbed into intestinal lymphatic circulation not into the blood circulation .And then thy pass to the fat deposts of the body either in the abdomen or under the skin .

The presence of fat in the small intestine produces hormones which stimulate the release of pancreatic lipase from the pancreas and bile from the liver for breakdown of fats into fatty acids

Carbohydrate digestion

Starches are broken down into sugars (glucose and fructose) by amylase and hydrochloric acid in the stomach.

DNA and RNA digestion

DNA and RNA are broken down into mononucleotides by the nucleases deoxyribonuclease and ribonuclease (DNase and RNase) from the pancreas.

Digestion of protein

Ingested proteins broken down into amino acids by enzymatic activity :

Food protein —**pepsin**→ **long chain peptides**

↓

trypsin

↓

short chain peptides

↓

erepsin

↓

amino acids

All amino acids absorbed by active transport in the presence of Na ion .

Absorption of Nutrients

General Features

Transepithelial transport - nutrients must transported by pass across the membrane of the epithelial lining of the small intestine, mostly using ATP of the cells.

Carbohydrate Absorption

by facilitated diffusion - glucose and galactose (coupled with active transport of Na^+)

"carrier molecule" has binding sites for both sugar and Na^+; relies on Na^+ gradient.

Protein (Amino Acid) Absorption

by facilitated diffusion - amino acids and small peptides (coupled with Na+ active transport), "carrier molecule" has binding sites for both amino acid and Na+; relies on Na+ gradient

Lipid Absorption

micelles - tiny balls of fats that result from bile salt emulsification and "lecithin" 1.

contain cholesterol and fat-soluble vitamins , diffuse through lipid bilayer of membrane

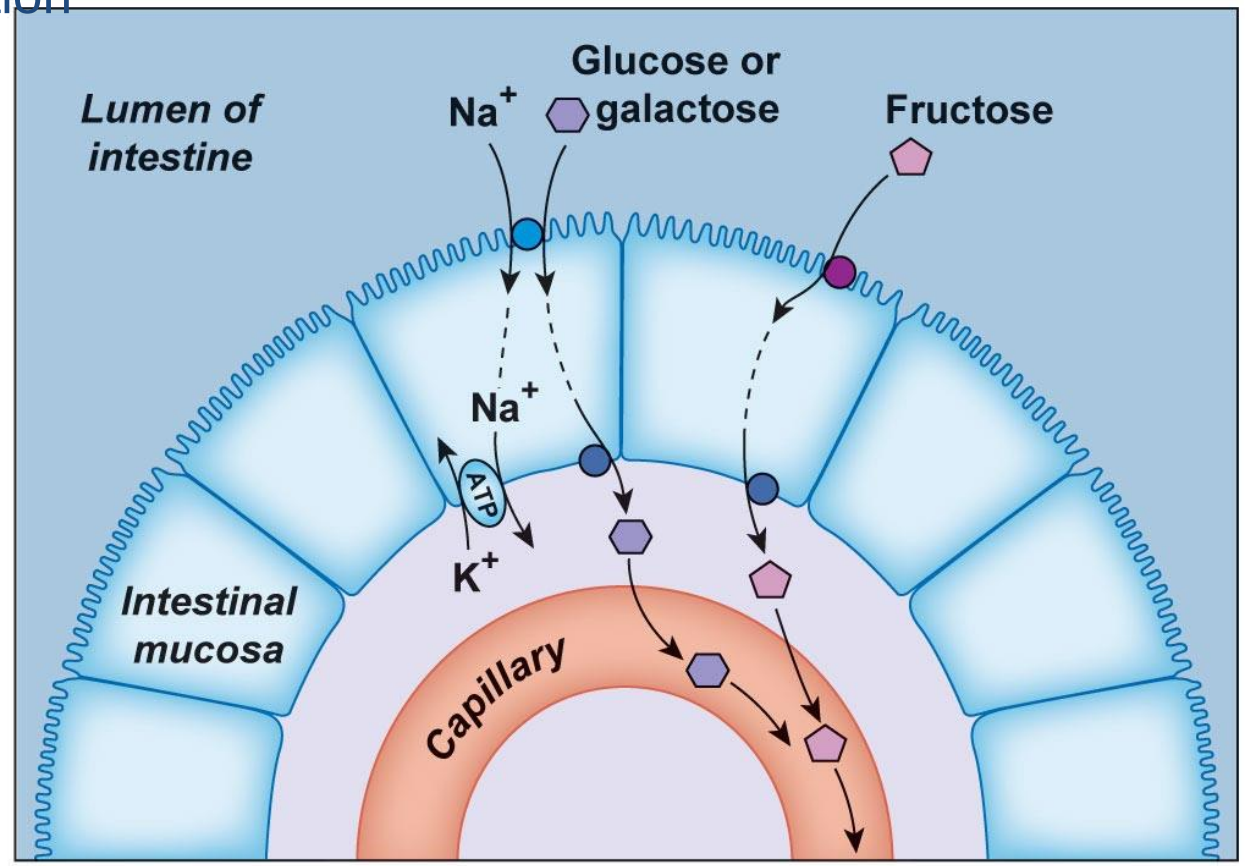
chylomicrons - micelles combined with associated proteins within the cell; enter the lacteals of the lymphatic system c.

Nucleic Acid Absorption

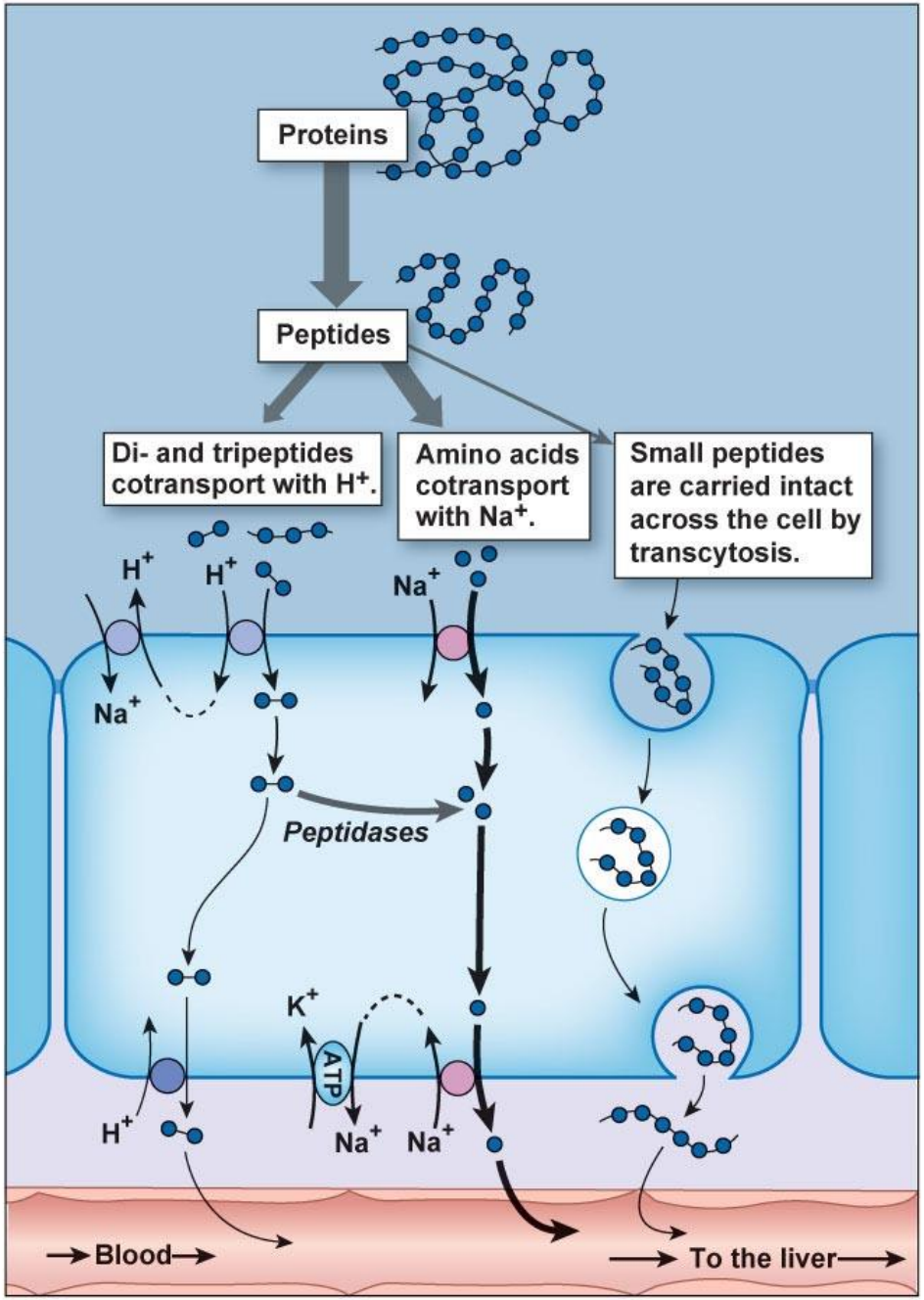
pentoses, nitrogen bases, phosphates - absorbed by similar processes as sugars and amino acids

Absorption

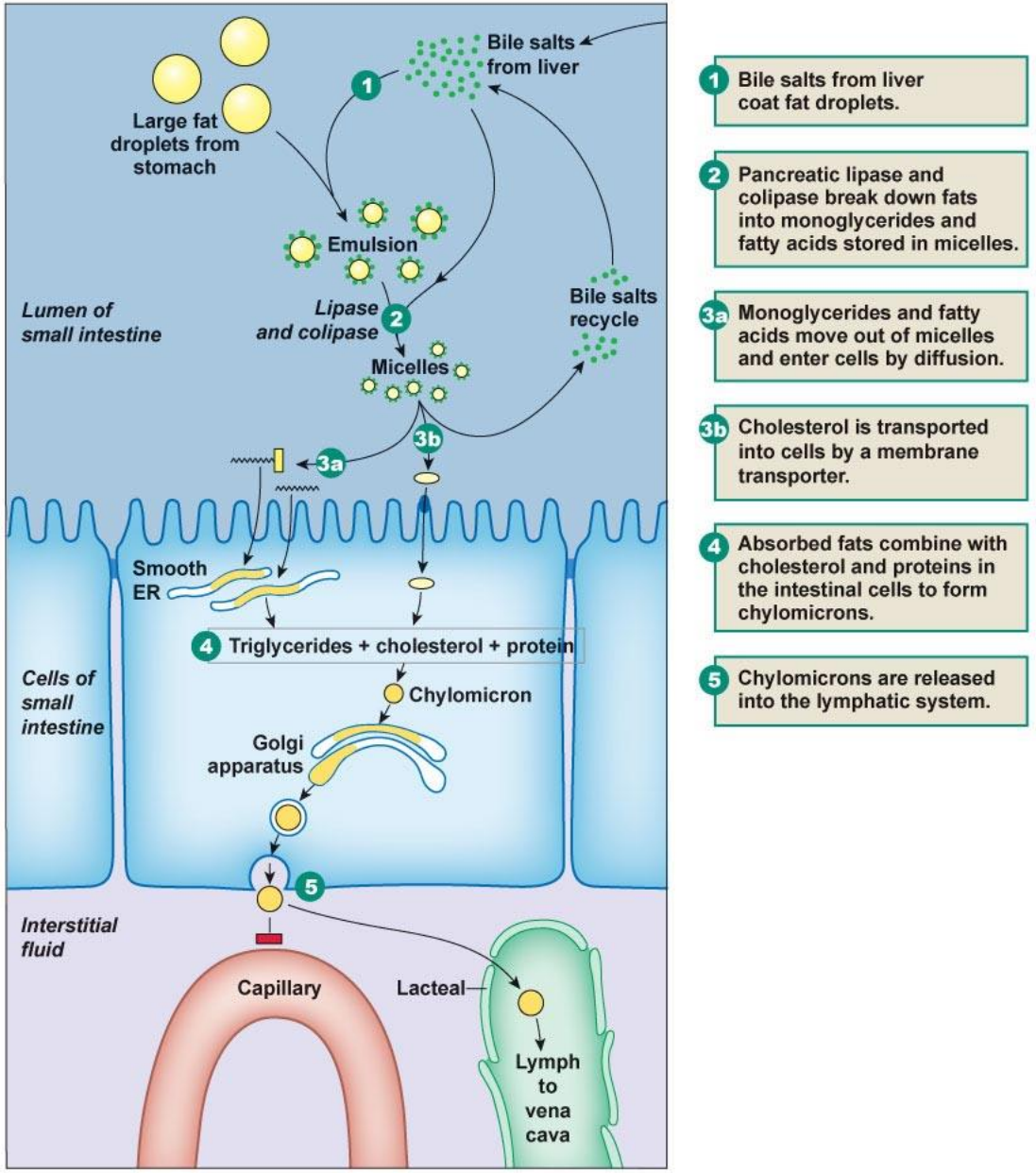
- Carbohydrate absorption



- Protein absorption



Lipid digestion & absorption

- 

Vitamin Absorption

1-fat soluble - Vitamins A, D, E, K are absorbed by epithelial cells along with lipid micelles by aids of bile juice.

2- water soluble - Vitamins B & C absorbed by diffusion.

3. Vitamin B_{12} - large and electrically charged, must bind with "intrinsic factor" before being taken into the cell by endocytosis.

Electrolyte Absorption

1. Fe and Ca - primarily absorbed in small intestine
2. Na - exchanged for sugars and amino acids
3. Cl - absorbed into cells and exchanged for HCO_3^-
4. K - absorbed into cells due to osmotic gradients

Water Absorption

1. small intestine - 95% of water absorbed by small intestine following transport of solutes
2. large intestine - absorbs remaining water before moving the chyme on to the rectum

Control of Digestion

1- by Nervous *System:* Two Phases controlled by N. system:

1-Cephalic Phase - Triggered by the site, smell, and taste of food. This stimulates the stomach to prepare for the entry of food.

2-Gastric Phase - Stomach distension by food stimulates the release of gastric juices.

2- by Hormons

1-Gastrin - Produced by the stomach; stimulates the release of gastric juices.

2-Secretin - Produced by the small intestine; stimulates the pancreas and gall bladder to release pancreatic juices and bile.

3-Cholecystokinin (CCK) - Produced by the small intestine; stimulates the pancreas and gall bladder to release pancreatic juices and bile.

Regulation of appetite

Neural control

The hypothalamus in the brain has two centers controlling hunger.

1-Appetite center stimulate ingestion, 2- the satiety center inhibit ingestion.

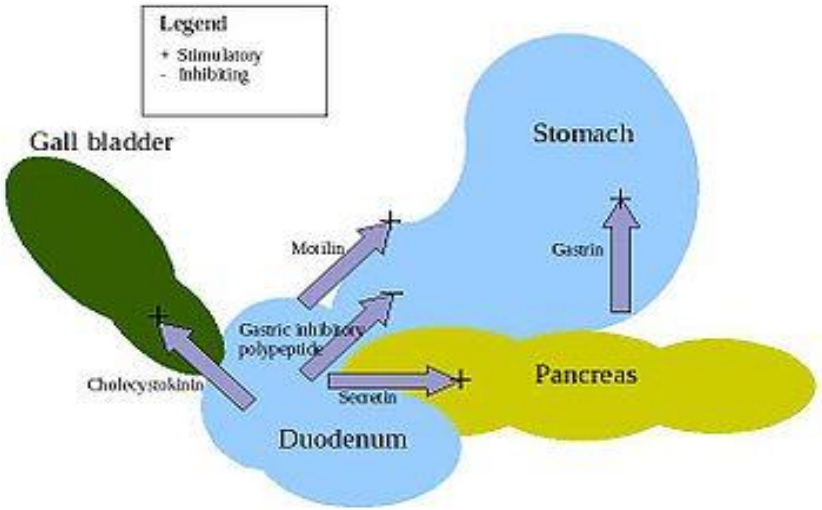
Hormonal control

Gastrin, secretin, and cholecystokinin are hormones that regulate stages of digestion.

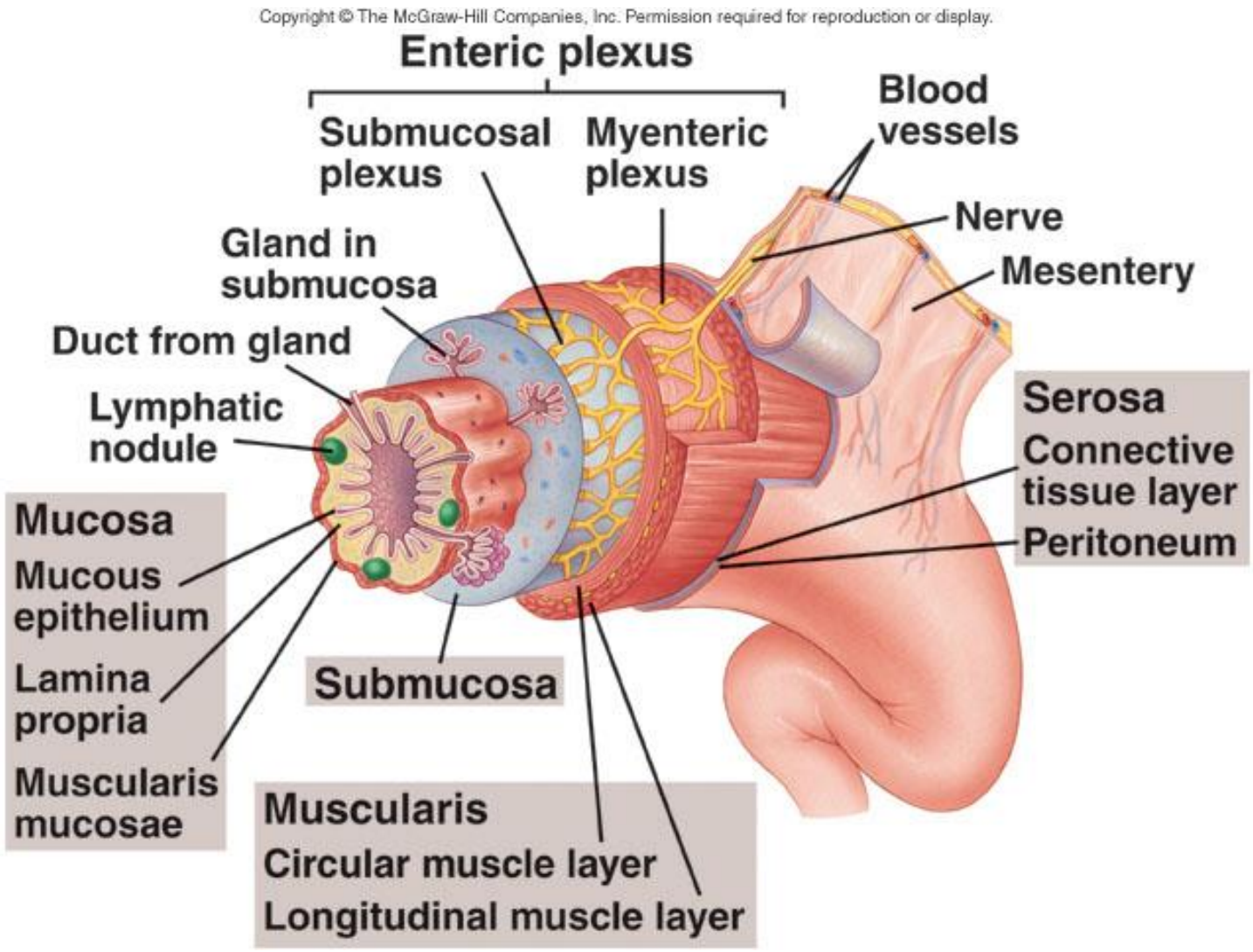
***A-Protein in the stomach stimulates secretion of gastrin, which causes increased stomach acid secretion and mobility of the digestive tract to move food.**

B- Food passing into the duodenum causes the production of secretin, which in turn promotes release of alkaline secretions from the pancreas, stops further passage of food into the intestine until the acid is neutralized.

C- Cholecystokinin (CCK) is released from intestinal epithelium in response to fats, and causes the release of bile from the gall bladder and lipase (a fat digesting enzyme) from the pancreas.



Digestive Tract Histology



Digestive Enzymes

Location	Enzyme	Targets
Salivary Glands	**Amylase** **Lipase**	**Starch** **Triglycerides**
Stomach	**Pepsin** **Lipase**	**Proteins** **Triglycerides**
Pancreas	**Amylase** **Lipase and Colipase** **Phospholipase** **Trypsin** **Chymotrypsin**	**Starch** **Triglycerides** **Phospholipids** **Peptides** **Peptides**
Intestine	**Enterokinase** **Disaccharidases** **Peptidases**	**Activates trypsin** **Complex sugars** **peptides**

Questions about digestion physiology

Q1: Count the functions of the followings :

1-Gastric glands

2-Pancreas

3- Gastrin

4-Chemical Digestion

5-Chief cells

6-filter feeder

Q2- Count the Liver functions:

Q3: Complete the following blanks with correct words or paragraphs:

1-Three type of secretary cells found in each gland: A-…. , B-…. , C-…..

2-Parietal cells (oxyntic cells) function is : ……., while Chief cells function is…… which activated by …… into …… that digest ……by .

3-Cephalic phase of gastric secretion stimulated by, a…. b….. , where as Gastric phase is stimulated by……. and ……..

4-Absorptive eaters live in a digestive system of another animal and absorb nutrients from that animal directly through their body wall. such as tapeworms, while the fluid feeders pierce …….. such as ……. .

Q4: Complete the following blanks with correct words or paragraphs:

1-The bile is stored in the gallbladder, the gallbladder is stimulated to release the bile by …… .

2- Secretin –hormone causes release of …… .

3-The liver is stimulated by the hormones ……. And…… to produce ….. . The bile is stored in the…….,which is stimulated to release the bile by ……..

4-The fat digestion end products are absorbed into …… and then thy pass to the ……. either in the ……..

Q 5: Define the following terms:

1-Chemical Digestion

2-Transepithelial transport

3-micelles

4-Cholecystokinin

5-Emulsification

Q6: Explains the control of salivation:

Q7:Wirte the mechanism of the absorption of :glucose, fatty acids , amino acids, Vit E, Drugs .

Q8: By diagram only explain the pathway of protein digestion.

Complete

1-Cephalic phase of gastric secretion stimulated by, a…. b….. , where as Gastric phase is stimulated by……. and …….. 1-Three type of secretary cells found in each gland: A-…. , B-…. , C-…..
2-Parietal cells (oxyntic cells) function is : ……., while Chief cells function is…… which activated by …… into …… that digest ……by .

Define
1-Transepithelial transport
2-Emulsification

physiology of Circulation

Functions of the Circulatory System

Type of circulatory systems, opne and closed types.

Evolution of Circulatory Systems, Cardiac cycle , Cardiac out put

Vertebrate Cardiovascular System , Layers of the heart ,

Exchanges Between Blood and Cells , Heart valves, Plasma Proteins,

Hematopoiesis: the formation of blood cells, Growth and differentiation inducers (cytokines, hormones), Erythropoietin, B12 Vitamin & Folic acid,

Blood Pressure, Factors changes BP, Regulation of Blood Pressure by Hormones, Cardiac Muscle Contraction, Heart beats, Heart conducting system , ECG (Electrocardiogram), **The Lymphatic System, Cardiovascular Disease , Intrinsic Control of heartbeat, Extrinsic Control of Heartbeat**

Prof. Dr. Ismail Kakey

Physiology of Circulation

Type of circulatory systems

1-**open circulatory system:** Blood is pumped by a heart through artery into the body cavities (hemocoel) where tissues are surrounded by the blood that come in contact tissues directly , then return into heart. (evolved in insects, mollusks and other invertebrates)

2- **Closed circulatory systems** : blood is pumped by a heart through vessels, and does not normally fill body cavities but blood closed at all times within vessels of different size and wall thickness and not directly contact with tissues . (evolved in echinoderms and vertebrates) .

3-Absence of circulatory system

Circulatory systems are absent in some animals, including flatwormssystems are absent in some animals,
including flatworms (phylumPlatyhelminthessystems are absent in some animals, including flatworms (phylumPlatyhelminthes). Their body cavitysystems are absent in some animals,
including flatworms (phylumPlatyhelminthes). Their body cavity has no lining or enclosed fluid. Instead a muscular pharynxsystems are absent in some animals, including flatworms (phylumPlatyhelminthes). Their body cavity has no lining or enclosed fluid. Instead a muscular pharynx leads to an

Evolution of Circulatory Systems

Living things must be capable of transporting nutrients, wastes and gases to and from cells there for specialized systems developed in different levels for this function.

1- Single-celled organisms

use their cell surface as a point of exchange with the outside environment.

2-Multicellular organisms

have developed transport and circulatory systems to deliver O2 and food and remove Co2 and metabolic wastes. Sponges are the simplest animals, yet even they have a transport system. Seawater is the medium of transport and is propelled in and out of the sponge by ciliary action.

Simple animals, such as the hydra and planaria , lack specialized organs such as hearts and blood vessels, instead using their skin as an exchange point for materials.

As the size of the animals became larger they need more complex and specialized organs.

Cardiac cycle :

is sequence of events occur in the heart during single heart beat .

Cardiac cycle are of 4 stages :

1-Late diastole

2-Atrial systole

3-Ventricle systole

4-Ventricle diastole

Heart beats (spread of impulse)

Heart beat originate from area called *pacemaker* at sinoatrial node (SA) node then passed to atria and then to *atrioventricular* node (AV) node and then to bundle of *His* after that to its branches called *purkinje* fibers on ventricle wall .

Cardiac out put

The volume of blood pumped by each ventricle in are minute . The volume of blood pumped from each ventricle with each systole is called *stroke volume .*

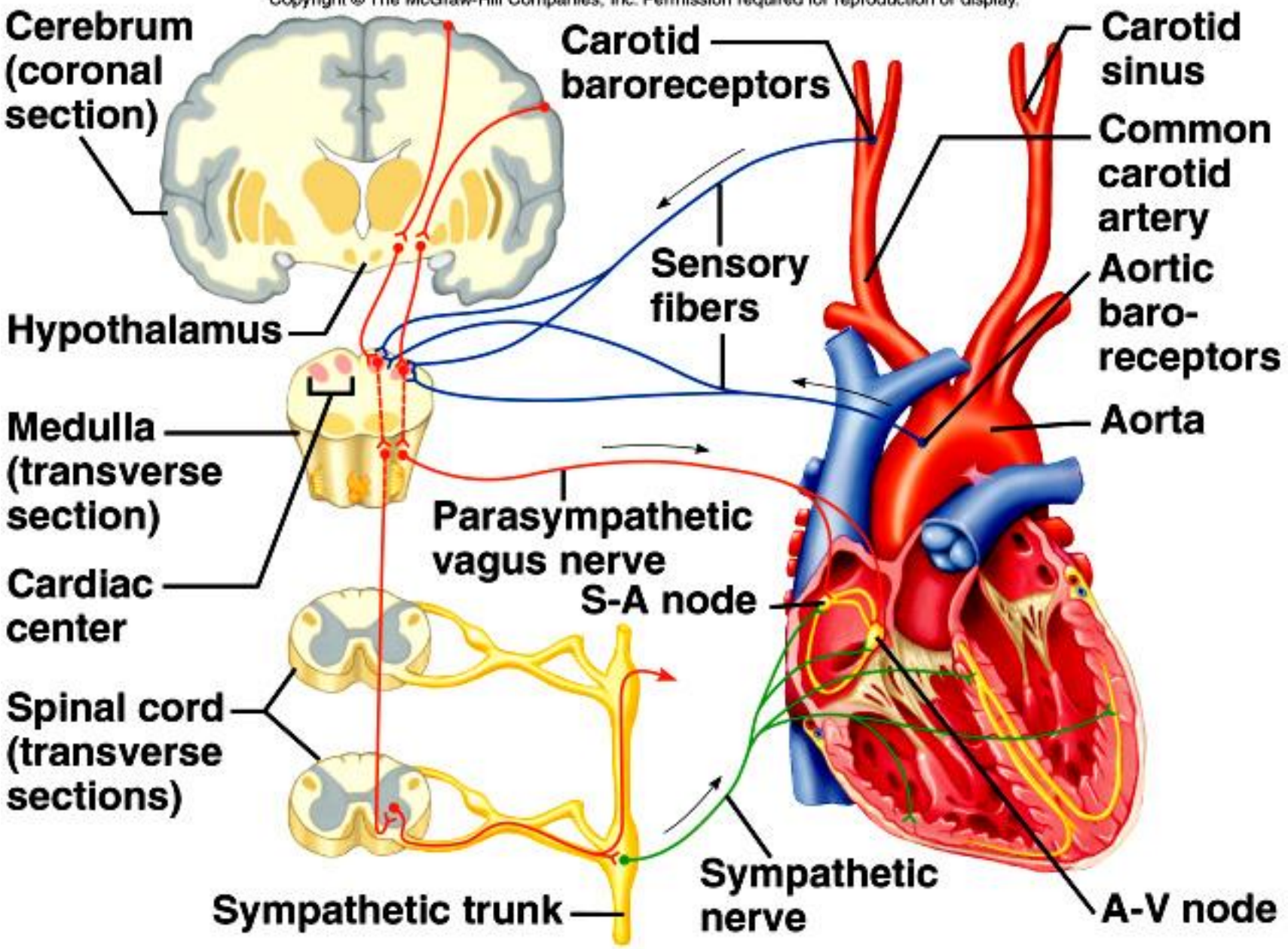
Cardiac out put = stroke volume x Rate of heart beat .

***Regulation of the cardiac cycle**
Sympathetic and parasympathetic nervous systems
Parasympathetic: from medulla oblongata (vagus nerve)
Nerve branches to S-A and A-V nodes, and secretes acetylcholine (slows rate)
Parasympathetic activity can increase (slow heart rate) or decrease (increase heart rate)

***Sympathetic nervous system**
through celiac plexus to heart
secretes norepinephrine
increases force of contractions

Cardiac control center in medulla oblongata maintains balance between the two

Normally both sympathetic and parasympathetic function at a steady background level



Vertebrate Cardiovascular System

1-Heart

-Is a muscular pump that contracts to propel blood out to the body through blood vessels.

- **The heart for the average human will contract about 3 billion times; never resting, never stopping to take a break except for a fraction of a second between beats. At 80 years of age, a person's heart will continue to beat an average of 100,000 times a day. There are an estimated 60,000 miles of vessels throughout an adult body.**

- **The upper chamber of the heart, (atrium The upper chamber of the heart, (atrium) receives the blood from body parts. Then through a valve, blood enters the lower chamber(ventricle The upper chamber of the heart, (atrium) receives the blood from body parts. Then through a valve, blood enters the lower chamber(ventricle). Contraction of the ventricle forces blood from the heart through an artery. Arterial walls are able to expand and contract. Arteries have three layers of thick walls. Smooth muscle fibers contract, another layer of connective tissue is quite elastic, allowing the arteries to carry blood under high pressure.**

Layers of the heart

Myocardium

is the muscular tissue of the heart. The myocardium is composed of specialized cardiac muscle cells.

Pericardium

The pericardium is the thick, membranous sac that surrounds the heart. It protects and lubricates the heart. There are two layers to the pericardium: the fibrous pericardium and the serous pericardium.

Epicardium

This is the innermost layer and consists of connective tissue.

2-aorta : is the main artery leaving the heart.

3-pulmonary artery : is the only artery that carries oxygen-poor blood (deoxygenated blood) to the lungs. Were gas exchange occurs.

4- Arterioles are small arteries that connect larger arteries with capillaries. all arterioles branch into collections of capillaries known as capillary beds. Capillaries, are thin-walled blood vessels in which gas exchange occurs. In the capillary, the wall is only one cell layer thick.

capillary beds. Some capillaries have small pores between the cells of the capillary wall, allowing materials to flow in and out of capillaries as well as the passage of white blood cells. Nutrients, wastes, and hormones are exchanged across the thin walls of capillaries.
Capillaries are the points of exchange between the blood and surrounding tissues.
Blood leaving the capillary beds flows into a progressively larger series of venules that in turn join to form veins.

5-Veins carry blood from capillaries to the heart.

6-Venules are smaller veins that gather blood from capillary beds into veins. Pressure in veins is low, so veins depend on nearby muscular contractions to move blood along. The veins have valves that prevent back-flow of blood.

Functions of the Circulatory System

Transport: the delivery of O2, nutrient molecules, and hormones for cells , and the removal of CO2, ammonia and other metabolic wastes from cells

Regulation:Carry hormones to target tissues to produce their effects.

Temperature:Divert blood to cool or warm the body.

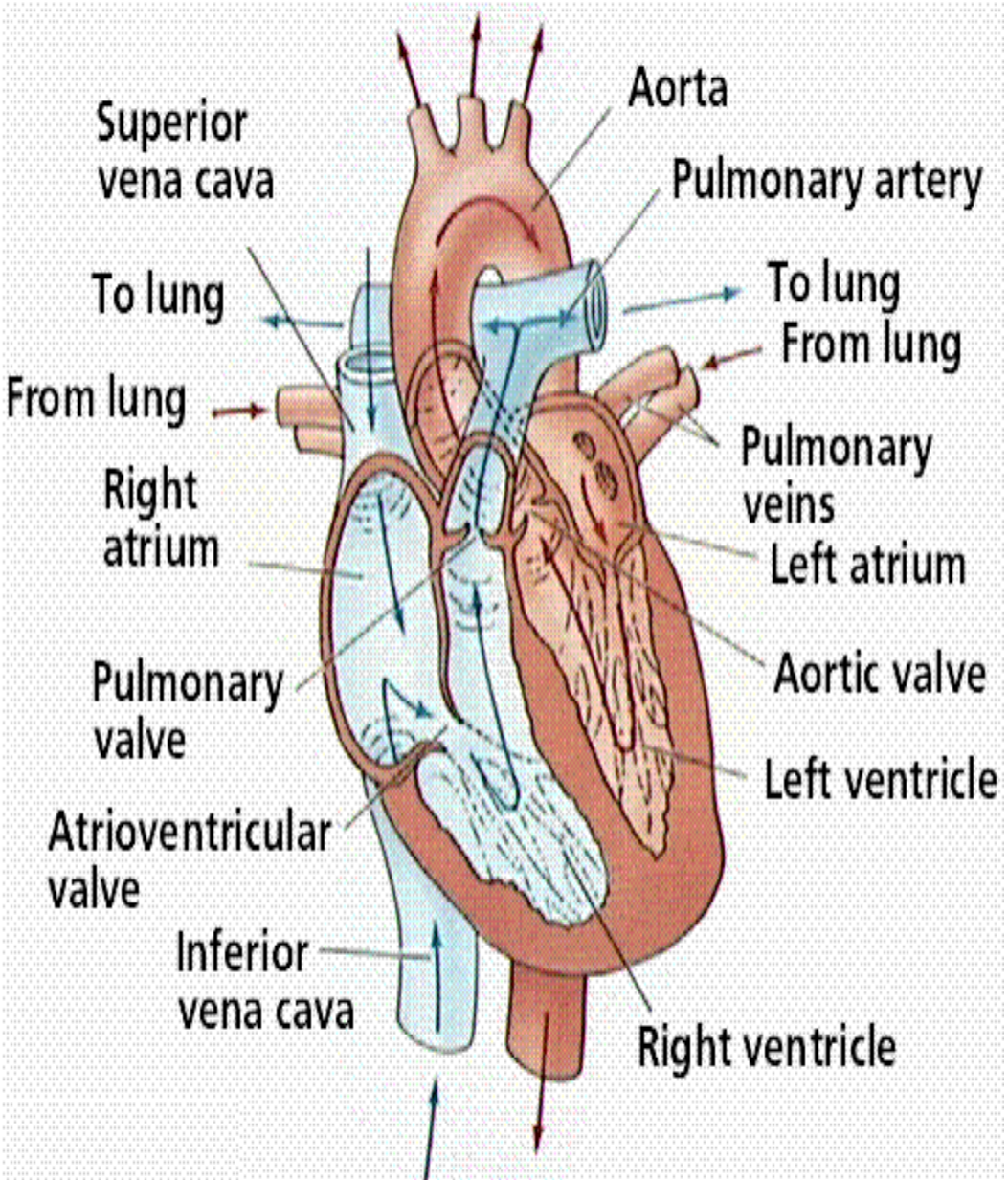
Protection: Blood clotting.

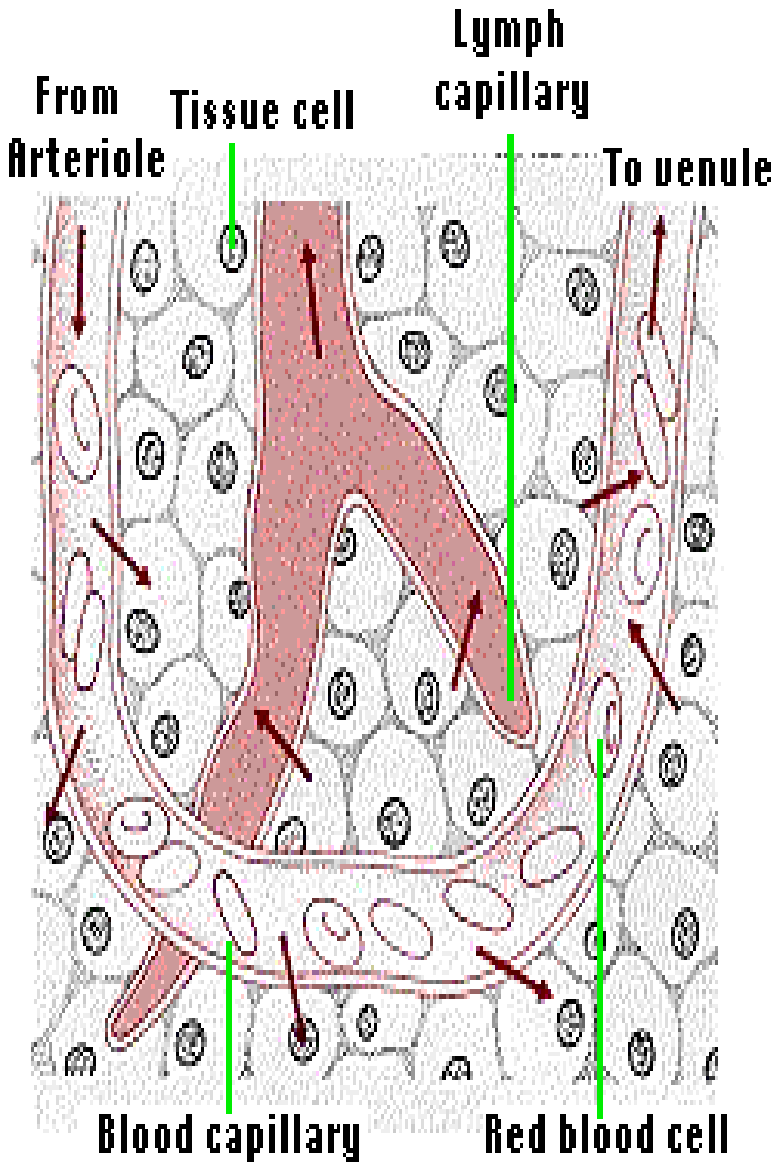
Immune: Leukocytes,cytokines and complement act against pathogens.

Exchanges Between Blood and Cells

About 98.5% of the oxygen in arterial blood in a healthy human is transported chemically combined with hemoglobin molecules. About 1.5% is transported physically dissolved in the other blood liquids.

With rare exceptions, our blood does not come into direct contact with the cells it nourishes. As blood enters the capillaries surrounding a tissue space, a large fraction of it is filtered into the tissue space. It is this interstitial or extracellular fluid (ECF), it can enter the cells by diffusion or active transport. Substances, like carbon dioxide, can diffuse out of cells and into the interstitial fluid. all of their requirements and takes away their products.


Superior vena cava
Aorta
Pulmonary artery
To lung
To lung
From lung
From lung
Pulmonary veins
Right atrium
Left atrium
Aortic valve
Pulmonary valve
Left ventricle
Atrioventricular valve
Inferior vena cava
Right ventricle


From Arteriole
Tissue cell
Lymph capillary
To venule
Blood capillary
Red blood cell

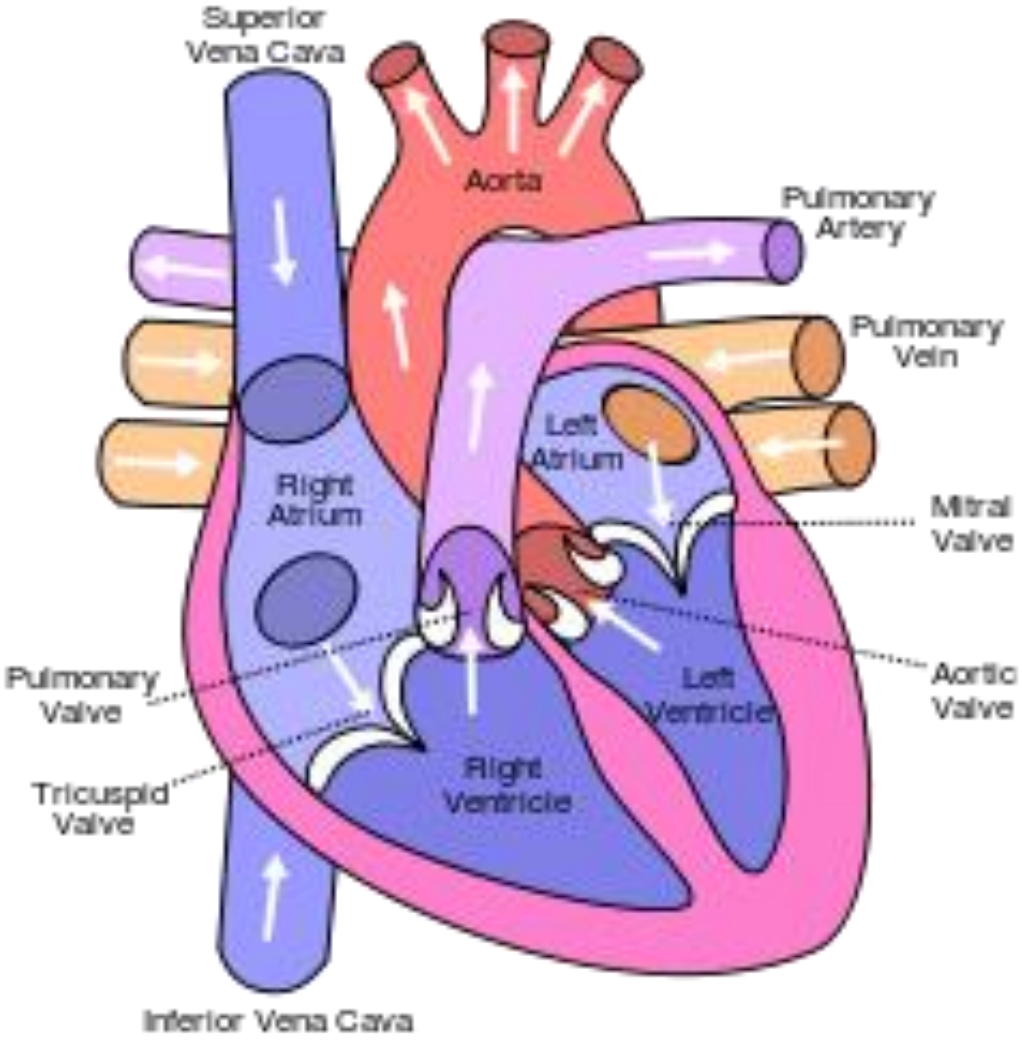
Heart valves : 2 types

1-Atrioventricular (AV) are called the tricuspid valve because it has three flaps, are one-way valves that ensure blood flows from the atria to the ventricle when the heart is relaxed during diastole. It is located between the atrium and the ventricle.

2-Semilunar (SL) called the bicuspid valve because it has two flaps valves are present in the arteries leaving the heart; they prevent blood return.

a-The pulmonary semilunar valve: lies between the right ventricle and the pulmonary trunk.

b-The aortic semilunar valve: is located between the left ventricle and the aorta .


Superior
Vena Cava
Aorta
Pulmonary
Artery
Pulmonary
Vein
Left
Atrium
Right
Atrium
Mitral
Valve
Pulmonary
Valve
Aortic
Valve
Left
Ventricle
Right
Ventricle
Tricuspid
Valve
Inferior Vena Cava

***Plasma Proteins**

Albumin , globulin , and fibrinogen .

Essentially all the albumin and fibrinogen of the plasma proteins, as well as 50 -80 % of the globulins, are formed in the liver (30 g/day). The remainder of the globulins (mainly the gamma globulins) are formed in the lymphoid tissue.

Conditions that cause rapid loss of plasma proteins as :*severe burns*; severe renal disease; *cirrhosis of the liver,* causing a reduction in their ability to synthesize plasma proteins this leads to decreased plasma colloid osmotic pressure, which causes generalized edema.

Plasm**a Proteins as a Source of Amino Acids for the Tissues.**

Protein tissues depletion cause plasmatic proteins pinocytosis by Macrophages intracell split into amino acids that are transported back into the blood (plasma proteins function as a labile protein storage medium)

*Hematopoiesis: the formation of blood cells

Hematopoiesis is the process that generates blood cells of all line ages.

Calculations based on the blood volume and the level and half-life of each type of blood cell in the circulation indicate that each day an adult produces ~ 200 billion erythrocytes, 100 billion leukocytes, and 100 billion platelets. These rates can increase by a factor of 10 or more when the demand for blood cells increases .

Stages:

- embryonic: up to 2 months – yolk sac
- fetal: 2-7 months – liver, spleen, lymph nodes
- after birth: exclusively in the bone marrow
- up to 5 years: bone marrows of essentially all bones
- after 20 years: bone marrows of the membranous bones (vertebrae, sternum, ribs, ilia); proximal portions of the humeri and tibiae

***Hematopoiesis:**

-are produced in the bone marrow, arise from a single type of cell called a *pluripotential hematopoietic stem cell (PHSC)*

- the path that is taken, to a *committed stem cell, is regulated by the* need for more of a certain type of blood cell which is, in turn, controlled by grows inducers (cytokines: IL-3, IL-7, IL-11, etc.)
- committed cells colony forming units (CFU):
CFU erythrocytes (E)/ granulocytes & monocytes (GM)/ megakaryocytes (M)

- differentiation inducers then act on CFUs final adult blood cells
-hypoxia, infectious diseases: control grows & differentiation inducers.

Pluripotential hematopoietic stem cell
- attached (probably by adherens junctions) to osteoblasts lining the inner surface of bone cavities; - produce, by mitosis, two kinds of progeny:
1) more stem cells
2) cells that begin to differentiate along the paths leading to the various kinds of blood cells.
- their number decrease with age;

***Growth and differentiation inducers (cytokines, hormones) for the formation of blood cells**

Interleukin-3 (IL-3) promotes growth of most of the different types of stem cells
Interleukin-7 (IL-7) - major cytokine in stimulating bone marrow stem cells to start down the path leading to the various lymphocytes (mostly B cells and T cells).
Erythropoietin (EPO), produced by the kidneys, enhances the production of red blood cells
Thrombopoietin (TPO/ megakaryocyte growth and development factor), assisted by Interleukin-11 (IL-11), stimulates the production of megakaryocytes.
Their fragmentation produces platelets.

Granulocyte-monocyte colony-stimulating factor (GM-CSF), as its name suggests, sends cells down the path leading to both those cell types. In due course, one path or the other is taken.
- Under the influence of granulocyte colony-stimulating factor (GCSF), they differentiate into neutrophils.
- Further stimulated by interleukin-5 (IL-5) they develop into eosinophils.
- Stimulated by macrophage colony-stimulating factor (M-CSF) the granulocyte/macrophage progenitor cells differentiate into monocytes, the precursors of macrophages.

***Erythropoietin**

Glycoprotein, MW = 34.000, T1/2 = 6 - 9 hours

Mechanism of action:

↑ the committment of stem cells to proerythroblasts

↑ the differentiation of erythroblastic stages

Synthesized - 90% kidneys (renal *tubular* epithelial cells?),*
the rest of 10% formed mainly in the liver

Regulation of erythropoietin control mechanism…

Therapeutically used: 50 – 300 U / kg, 3 times / week
in kidneys diseases, transplant, anemia,
pulmonary diseases, blood loss…

***B12 Vitamin & Folic acid**

Act on the final maturation of RBC.

Both are essential for DNA synthesis through the formation of an essential DNA building block, thymidine triphosphat

B12 Vitamin:

- the body uses 1-3 µg/day of B12 vitamin
- hepatic stores amounts 1000-3000 µg

(enough for 3-4 years…)

- intrinsic factor needed for absorption …

Vit. B12 & folic acid deficiency □ proliferation & maturation failure:

- pernicious anemia □ macrocytes (large, oval, fragile)□ short life
- causes:

atrophic gastric mucosa□ intrinsic factor deficiency□ no B12 absorption

Blood Pressure

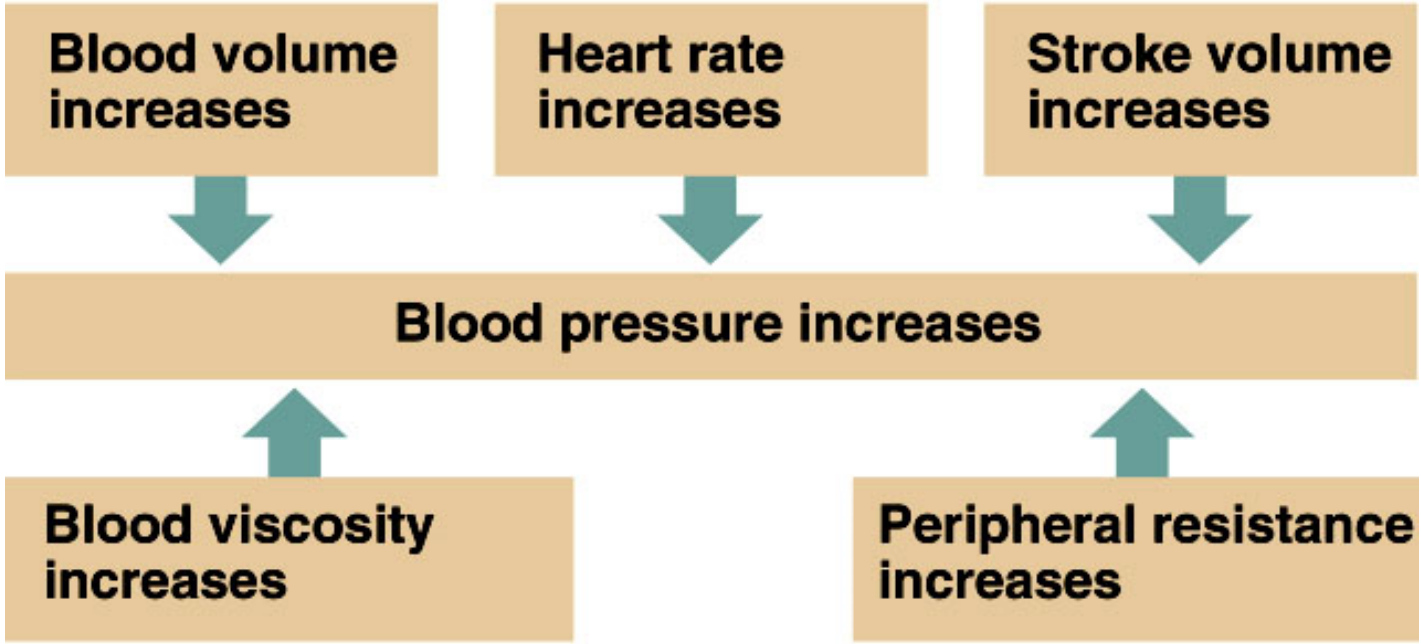
Blood pressure is the pressure exerted by the blood on the walls of the blood vessels. BP refers to systemic arterial blood pressure. BP values are universally stated in millimeters of mercury (mmHg).

The systolic pressure is defined as the peak pressure in the arteries during the contraction phase of the cardiac cycle;

the diastolic pressure is the lowest pressure (at the resting relaxation phase of the cardiac cycle). Typical values for a resting, healthy adult are approximately 120 mmHg systolic and 80mm Hg diastolic (written as 120/80 mmHg), with individual variations.

Factors changes BP

The measures of BP are not static, but undergo natural variations from one heartbeat to another, and throughout the day; they also change in response to stress, nutritional factors, drugs, or disease.



Regulation of Blood Pressure by Hormones

The Kidney : One of the functions of the kidney is to monitor blood pressure .The kidney does this by secreting **Renin**

acts on

angiotensinogen, a plasma peptide, splitting off a fragment containing 10 amino acids called angiotensin I

angiotensin I is cleaved by a peptidase angiotensin converting enzyme secreted by blood vessels called ACE — producing

angiotensin II, which contains 8 amino acids

angiotensin II constricts the walls of arterioles closing down capillary beds; stimulates the proximal tubules in the kidney to reabsorb sodium ions; stimulates the adrenal cortex to release **Aldosterone**

Aldosterone causes the kidneys to reclaim still more sodium and thus water increases the strength of the heartbeat; stimulates the pituitary to release

Vasopressin

*All of these actions, which are mediated by its binding to G-protein-coupled receptors on the target cells, lead to an increase in blood pressure.

*blood pressure = the systemic arterial pressure of large vessels of the body (mm Hg)

C. Resistance to Flow (Peripheral Resistance) - the FORCE resisting the flow of blood through a vessel (usually from friction)

1. viscosity - a measure of the "thickness" or "stickiness" of a fluid flowing through a pipe

a. V water < V blood < V toothpaste

b. water flows easier than blood

2. tube length - the longer the vessel, the greater the drop in pressure due to friction

3. tube diameter - smaller diameter = greater friction

Relation Between Blood Flow, Pressure, Resistance

$$\text{Blood Flow (F)} = \frac{\text{difference in blood pressure } (\Delta P)}{\text{peripheral resistance (R)}}$$

a. increased P -> increased flow

b. decreased P -> decreased flow

c. increased R (vasoconstriction) -> DECREASED flow

d. decreased R (vasodilation) -> INCREASED flow

Cardiac Muscle Contraction

1-The contraction is due to an increase in the cytoplasmic concentration of Ca+ ions.

2-the release of Ca+ ions from the sarcoplasmic reticulum binds to troponin which allows actin to bind with myosin.

3-The difference between skeletal muscle and cardiac muscle is that when the action potential opens voltage gated calcium ion channels in the T-tubules. The increase in cytosolic calcium causes calcium ions to bind to receptors on the surface of the sarcoplasmic reticulum.

4-The binding of calcium ions to these receptors causes the opening of more calcium ion channels in the SR membrane.

5-Calcium ions then rush out of the SR and bind to troponin and allow the myosin and actin to bind together which causes contraction.

6-This sequence is called calcium-induced calcium release.

7-Contraction ends when the level of cytosolic calcium returns to normal resting levels.

Heart beats

hear beats as electrical activity begins in the pacemaker portion of the heart and spreads from cell to cell through membrane junctions over the rest of the heart.

A pacemaker is an excitable group of cells that create these rhythmical impulses **spontaneously and rhythmically.**

In vertebrates, the pacemaker is the sinoatrial (SA) node, It contains contractile specialized muscle cells that do not require constant stimulation.

These muscle cells are considered to be myogenic not neurogenic . All of these cells have an unstable resting potential and can therefore steadily depolarize to its threshold voltage, at which time an action potential is generated and the muscle contracts.

In invertebrates, it is not always clear whether an animal's heart is myogenic or neurogenic. The hearts of decapod crustaceans are neurogenic and the pacemaker within their hearts is called the cardiac ganglion. If the ganglion is removed from the heart, it ceases to beat but does show some activity.

Heart conducting system

Human heartbeats originate from

1-the sinoatrial node (SA node - (pacemaker)) near the right atrium.

2-sending a signal to the atrioventricular node (AV node).

3-which conducts the normal electrical impulse from the atria to the ventricles.

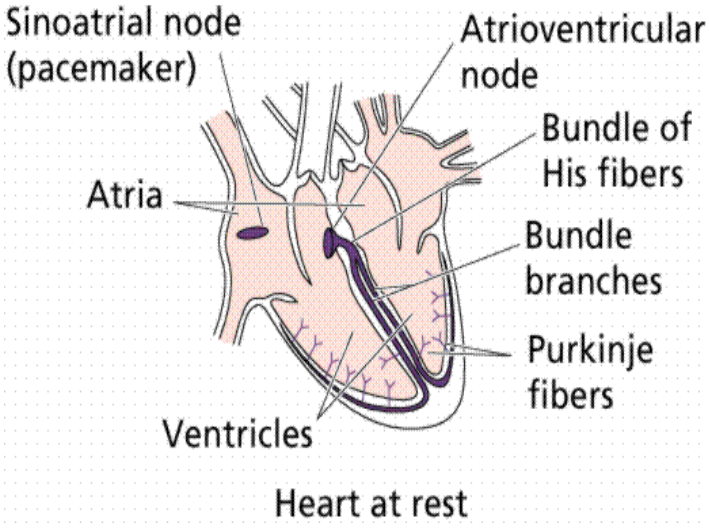
4-Signals carried from the AV node, slightly delayed,

through bundle of His fibers and Purkinjie fibers is

a collection of heart muscle cells specialized

for electrical conduction that transmits the

electrical impulses from the AV node



ECG (Electrocardiogram)

is a reflection of the electrical activity of the heart. The changes in the duration of the **action potential** and the rates of depolarization and repolarization of the heart are recorded as an electrocardiogram.

All of these electrically-generated controls of the heart can be recorded in an electrocardiogram. Each of the peaks on an electrocardiogram is given one or more initials.

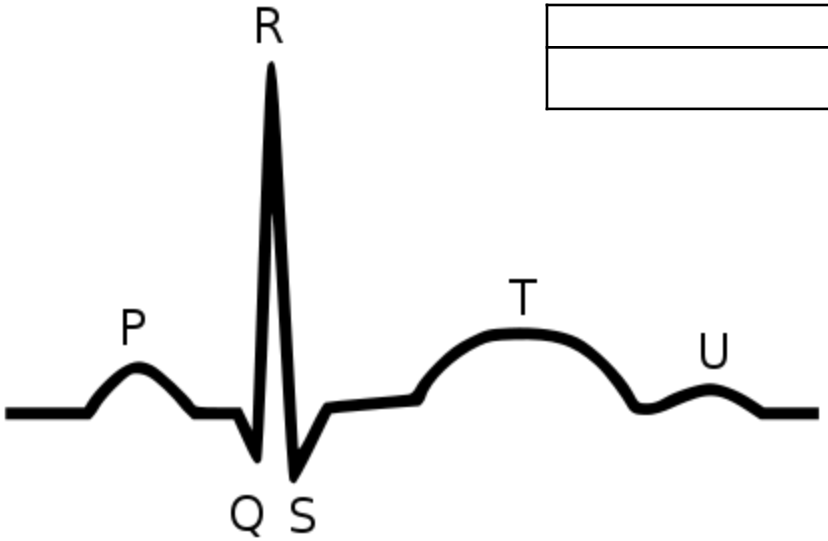
-The first wave is the P wave, which represents atrial depolarization. It is a small wave that is slow to rise and fall.

-The QRS complex comes next and is the summation of two waves, ventricular depolarization and atrial repolarization.

-The T wave comes after the QRS complex and represents ventricular repolarization.

-The P-R interval is the time between the beginning of the P wave and the beginning of the R wave.

-ECGs are useful in diagnosing heart abnormalities.



EKG Waveform	

P wave- indicates the slow wave of atria depolarized to pump blood into the ventricles.

QRS is the summation of two waves, ventricular depolarization and atrial repolarization) to pump blood out.

ST segment- indicates the amount of time from the end of the contraction of the ventricles to the beginning of the T wave.

T wave- indicates the recovery period (repolarization) of the ventricles.

U wave- rarely seen, and thought to possibly be the repolarization of the papillary muscles

The Lymphatic System

Water and plasma are forced from the capillaries into intracellular spaces. This interstitial fluid transports materials between cells. Most of this fluid is collected in the capillaries of a secondary circulatory system, the lymphatic system. Fluid in this system is known as lymph.

Lymph flows from small lymph capillaries into lymph vessels that are similar to veins in having valves that prevent backflow. Lymph vessels connect to lymph nodes, lymph organs, or to the cardiovascular system at the thoracic duct and right lymphatic duct.

Lymph nodes are small irregularly shaped masses through which lymph vessels flow. Clusters of nodes occur in the armpits, groin, and neck. Cells of the immune system line channels through the nodes and attack bacteria and viruses traveling in the lymph.

*Cardiovascular Disease

Cardiovascular disease refers to the class of diseases that involve the heart and/or blood vessels:

Hypertension

Hypertension or high blood pressure is a medical condition wherein the blood pressure is chronically elevated. Persistent hypertension is one of the risk factors for strokes, heart attacks, heart failure and arterial aneurysm, and is a leading cause of chronic renal failure

Atherosclerosis

is a disease affecting the arterial blood vessel. It is commonly referred to as a "hardening“ of the arteries. It is caused by the formation of multiple plaques within the arteries. Arteriosclerosis results from a deposition of tough, rigid collagen inside the vessel wall and around the atheroma.

Plaque

Plaque Atheroma or commonly known as plaque is an abnormal inflammatory accumulation of macrophage white blood cells within the walls of arteries.

Circulatory Shock

is a severe condition that results from reduced blood circulation .

Thrombus

A thrombus, or blood clot, is the final product of the blood coagulation step in hemostasis. It is achieved via the aggregation of platelets that form a platelet plug, and the activation of the humoral coagulation system (i.e. clotting factors.

Embolism

An embolism occurs when an object (the embolus) migrates from one part of the body (through circulation) and causes a blockage of a blood vessel in another part of the body.

Stroke

A stroke, also known as cerebrovascular accident (CVA), is an acute neurological injury whereby the blood supply to a part of the brain is interrupted.

Angina Pectoris

Angina Pectoris is chest pain due to ischemia (a lack of blood and hence oxygen supply) of the heart muscle, generally due to obstruction or spasm of the coronary arteries

Congestive Heart Failure

Congestive heart failure (CHF), also called congestive cardiac failure (CCF) or just heart failure, is a condition that can result from any structural or functional cardiac disorder that impairs the ability of the heart to fill with or pump a sufficient amount of blood throughout the body.

*Intrinsic Control of heartbeat

- **SA node (located in the right atrium near the entrance of the superior vena cava)**
- **AV node (located at the base of right atrium)**
- **AV bundle (located in the intraventricular septum between the two ventricles that go in two directions right and left bundle branches that leave the septum to enter the walls of both ventricle)**
  - **Bundle Branches (the branching off the septum to the walls of the ventricles that run into the purkinje fibers that then make contact with ventricular myocardial cells to spread the impulse to the rest of the ventricles)**

*Extrinsic Control of Heartbeat

Autonomic system with two subdivisions: the sympathetic division and the parasympathetic division. Hormonal control of blood pressure

Epinephrine

Norepinephrine

ANP : Atrial natriuretic peptide

ADH: Antidiuretic hormone

Renin-Angiotension system

physiology of Excretion & Body fluid (Two Weeks)

Functions, waste production-excretion cycle,
Regulation of Extracellular Fluids, Water balance ,
Nitrogenous wastes , Osmoregulation ,
Problems of osmoregulations in animals
Osmoregulatory organs in animals
Key functions of most excretory systems
Human Human excretory system,
Nephron , Homeostatic functions of the kidney
The nephron functions to produce urine ,
Hormonal Control of Water and Salt balance
Renin-angiotensin-aldosterone axis , Kidney Stones ,
Disruption of Kidney Function ,
Diseases of the Kidney
Dialysis and Kidney Transplant

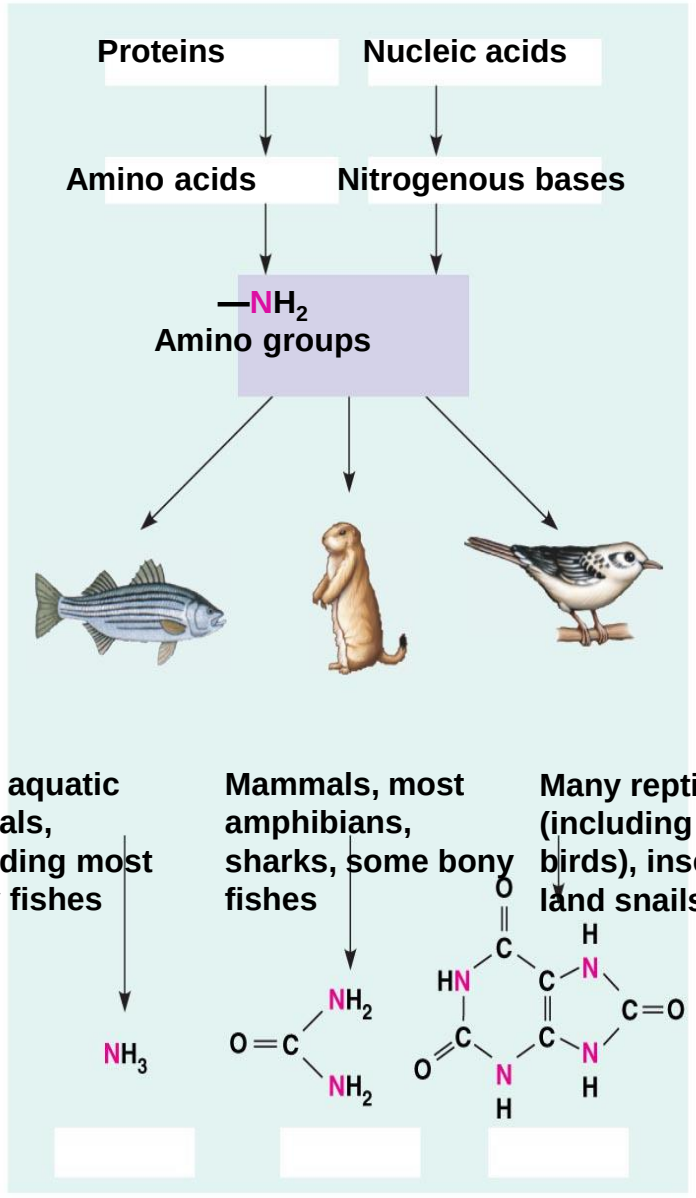
Objective

Body fluid homeostasis
Excretory functions
Brief review of renal anatomy
Explanation of kidney function
The 3 basic renal processes for urine formation
Renal stone formation
Renal dysfunctions

THE EXCRETORY SYSTEM

functions:

1-Regulation of plasma ionic composition
2-Regulation of plasma osmolarity
3-Regulation of plasma volume
4-Regulation of plasma hydrogen ion concentration pH
5-Removal of metabolic waste products
6-Secretion of Hormones



THE EXCRETORY SYSTEM (waste production-excretion cycle)

Sugars,fats,proteins In cells

metabolism

H2O + Co2 + metab.wastes
(nitro., sulfur, phosphorous)

diffuse out of cells into the extrace. fluid

Single-celled organisms

Diffuse in environment direct.

Multicellular

Interstitial fluid

Blood

Excr. Organs

Excreted out side

Regulation of Extracellular Fluids

Homeostatic mechanisms protect an animal's internal environment from harmful fluctuations. Since aqueous solutions are the chief environment for metabolic reactions they are also the target of homeostatic mechanisms.

Internal body fluids are compartmentalized and may be found as:

Blood, interstitial fluid & cytoplasmic fluid

Excretory systems regulate the chemical composition of body fluids by removing metabolic wastes and retaining the proper amounts of water, salts, and nutrients.

Water balance

Is a balance between water gain & water lost activities.

Water gained by:

1- drinking , 2- eating , 3-a byproduct of oxidation of food in mitochondria (metabolic water).

Water lost by :

1- breathing , 2- sweating ,3- defecation , 4- most importantly by urination.

Nitrogenous wastes

different organisms produce different nitrogenous wastes as a result nitrogen-containing molecules metabolized.

1. ammonia NH_3

highly toxic & highly soluble in water , produced by marine invertebrates and freshwater fishes & called ammonotilic animals

2. uric acid

not very toxic and poorly soluble in water, produced insects, birds, and reptiles in liver and transported to kidney by the blood.

& called uricotilic animals.

3. urea

In marine fishes and mammals ,liver converts ammonia to urea -- passed out in urine.

Osmoregulation

Is regulates of solute concentrations and balances the gain and loss of water by excretory system ,According to osmoregulatory ability animals divided into:

1 – Osmoconformers : animals have internal salt concen. Very like to that of surrounding water as crabs.(not regulate salt conc.)

2- Osmoregulators: animals have internal concentrations of salt that are about one-third of the surrounding seawater as Marine vertebrates , these animals face two problems:

a-prevention of water loss from the body

b- prevention of salts diffusing into the body.

- Most animals are stenohaline; they cannot tolerate fluctuation in environmental salt conc. But live within narrow range of osmolarity.
- Euryhaline animals can survive within large fluctuations in external osmolarity

Problems of osmoregulations in animals :

Different organisms face different problems when it comes to regulating ionic &water concentrations(osmoregulation):

I. Freshwater fishes : live in environment hypotonic to body fluids, the problem is loss of salts by diffusion and water loading by osmosis; - solutions:

A. don't drink water -- swallow food only.

B. gills remove salts from water against concentration gradient by active transport.

C. kidney reabsorbs salts by active transport.

D. large quantities of hypotonic urine are produced.

II. Marine fishes - reverse problem , body fluids hypotonic to environment , problem is water loss (dehydration) and salt loading – the solutions for their problem are :

A. drink sea water to replace water loss through osmosis.

B. salt put back into water by active transport in gills.

C. produce small quantities of isotonic urine.

111-Terrestrial Animals : the main problem is water loss, solutions are : Adaptations for survival on dry land include:

1-Surface coverings that prevent water loss as :

- the exoskeleton of insects are coated with wax effectively holds in water
- the scales of reptiles, feathers of birds, and hair of mammals insulate and trap moisture.
- the oily, keratinized skin composed of numerous layers of dead cells acts as a barrier

2-Behavioral adaptations

- nocturnal activity when heat is reduced
- drinking and eating food which contains water

3-Kidneys

- by increasing the length of the loop of Henle

Osmoregulatory organs in animals :

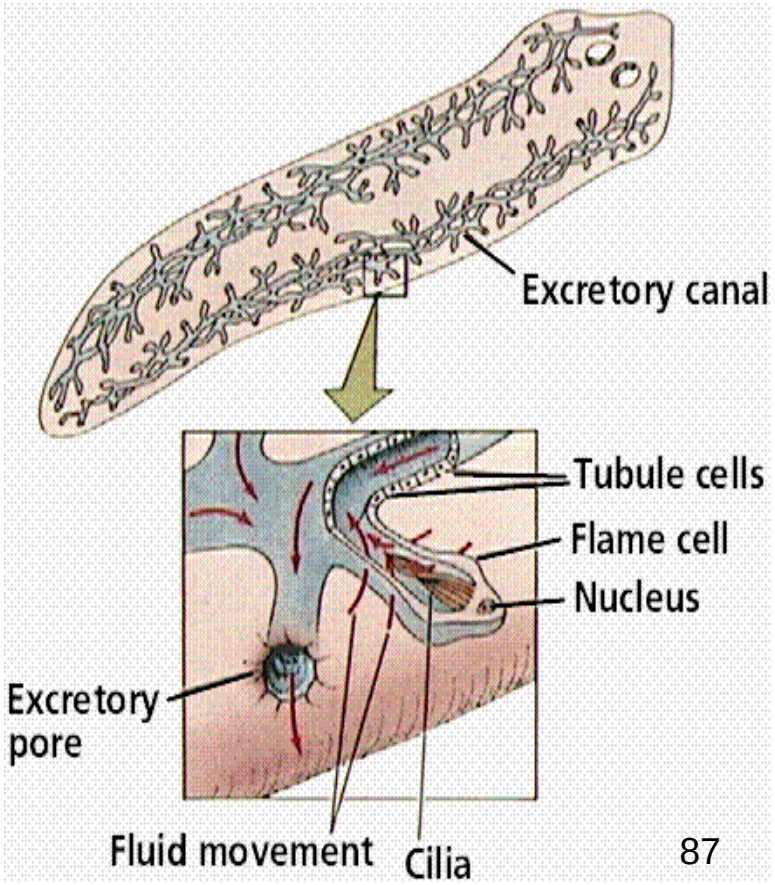
- **Protonephridia** - is a network of dead-end tubules lacking internal openings ,The smallest branches of the network are capped by a cellular unit called a flame drawing in the body fluids, processing them and excreting a dilute nitrogen waste through openings called nephridiopores.

Tubules empty their contents

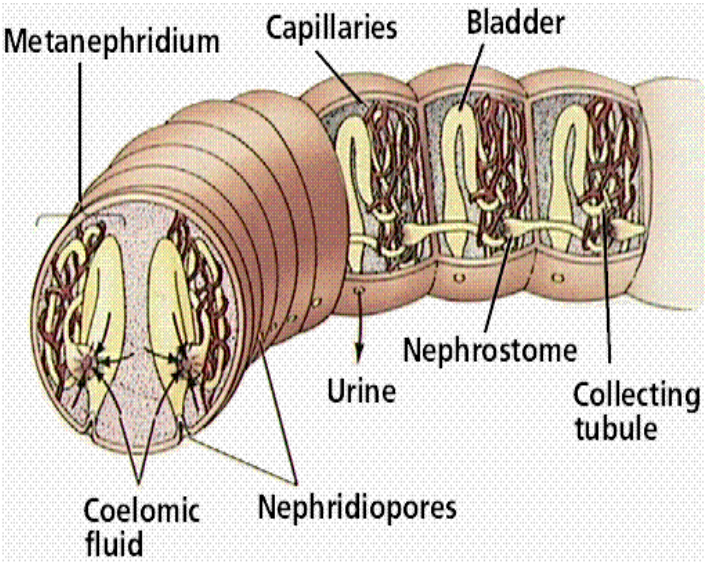
(nitrogenous wastes) into

the anterior portion of the hindgut.

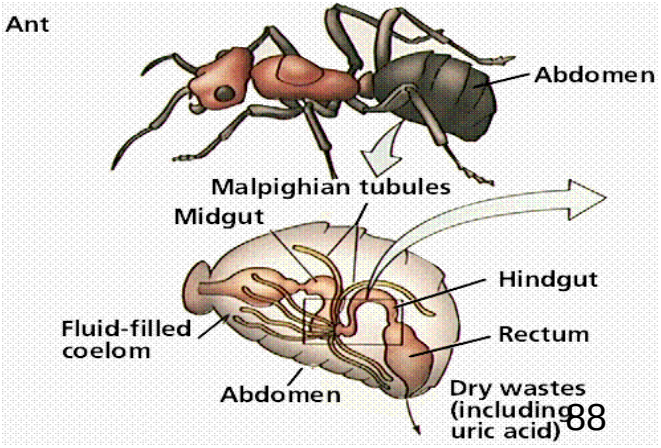
Examp: flatworms



Metanephridia - A tubular excretory system surrounded by closed circulatory system, the excretory tubing within each segment. The formation of dilute urine allows copious amounts of water to leave the worm through an opening called a nephridiopore. This water loss helps compensate for the earthworm's respiratory system which takes in large amounts o oxygen saturated water through its moist skin. Examp. Earthworms



Malpighian Tubules :
The tubular osmoregulatory system of insects is unique. These tubes absorb nitrogen wastes from the hemolymph.



Key functions of most excretory systems:

1-Filtration: pressure-filtering of body fluids.

2-Reabsorption: returning of valuable solutes after filtration.

3-Secretion: adding toxins and other solutes from the body fluids to the filtrate.

4-Excretion: removing the filtrate from the system to the out side.

Human excretory system:

1. kidneys -- paired organs lying at back of abdominal cavity.
2. renal arteries - supply kidneys with blood - come off aorta.
3. renal veins - take blood way from kidneys -- empty into inferior vena cava.
4. ureter - tube carrying urine away from each kidney to the urinary bladder.
5. urinary bladder - urine reservoir.
6. urethra - tube leading from urinary bladder to the outside.

Function of kidney

Eliminate METABOLIC WASTE PRODUCTS

- **Eliminate FOREIGN COMPOUNDS**
- **Regulate BODY FLUID OSMOLALITY**
- **Regulate plasma IONIC COMPOSITION**
- **Regulate EXTRACELLULAR FLUID VOLUME**
- **Help regulate ARTERIAL PRESSURE**
- **Help maintain ACID-BASE BALANCE**
- **Synthesize GLUCOSE**
- **Metabolize/degrade POLYPEPTIDE HORMONES**
- **Act as an ENDOCRINE organ:**

–Erythropoietin

–1,25-(OH)2vitamin D3

–Renin

The Nephron

Is tiny tubules that are the functional unit of kidney,each kidney contains about 1 million nephrons , part of nephron lies in cortex, part in medulla.The nephron is, responsible for the actual purification and filtration of the blood

Components of The Nephron

1-**Glomerulus**: mechanically filters blood .

2-**Bowman's Capsule**: site of Glomerulus location.

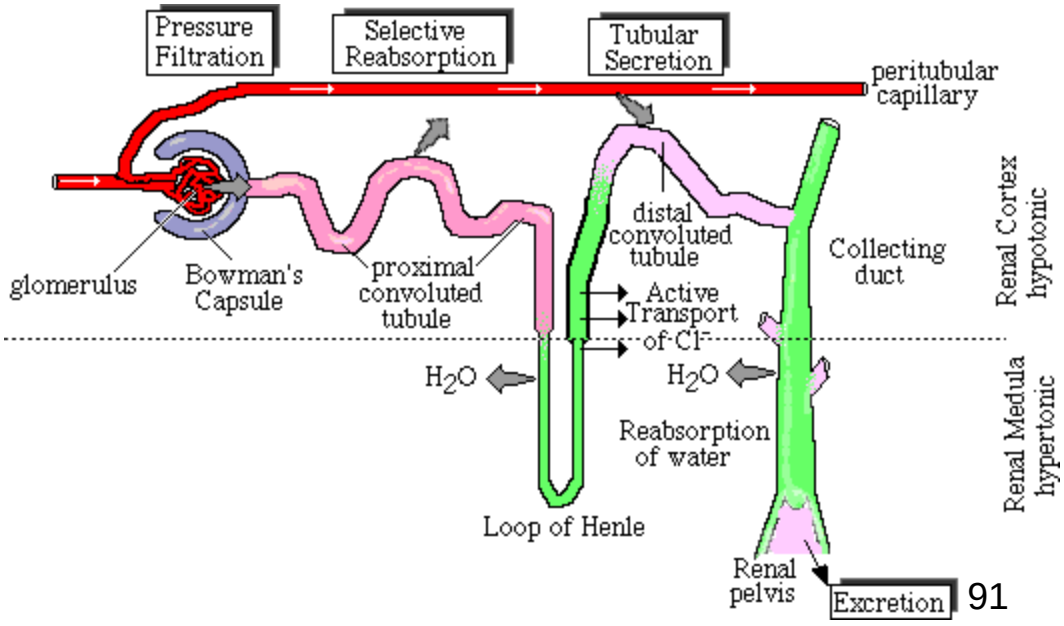
3-**Proximal Convoluted Tubule**: Reabsorbs 75% of the water, salts, glucose, and amino acids

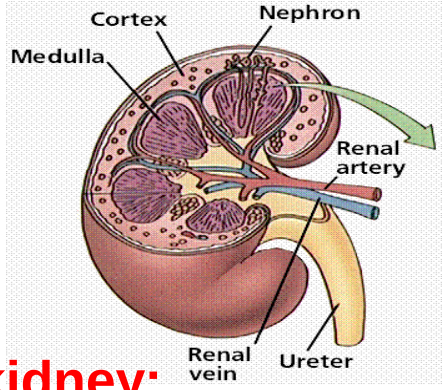
4-**Loop of Henle**: Countercurrent exchange, which maintains the concentration gradient.

5-**Distal Convoluted Tubule**:

Tubular secretion of H ions, potassium, and certain drugs.

6- each distal convoluted tubule empties into a **collecting duct,** which leads and empties into the renal pelvis





q Homeostatic functions of the kidney:

1-Maintain volume of extracellular fluid

2-Maintain ionic balance in extracellular fluid

3-Maintain pH and osmotic concentration of the extracellular fluid.

4-Excrete toxic metabolic by-products such as urea, ammonia, and uric acid.

Urine formation

Average urine production in adult humans is about 1-2 litres (L) per day, depending on state of hydration, activity level, environmental factors, weight, and the individual's health. Producing too much or too little urine requires medical attention. Polyuria is a condition of excessive urine production (> 2.5 L/day).Oliguria when < 400 mL (millilitres) are produced, and anuria one of < 100 mL per day.

The nephron has three functions to produce urine (*Pathway of the Filtrate)*

1-Glomerular filtration: The glomerulus is the main filter of the nephron. It resembles a twisted mass of tiny tubes through which the blood passes from afferent arteriole .The glomerulus is semipermeable, allowing wastes (molecules include water, glucose, amino acids, salts, and urea.) to pass through and be excreted out of the Bowman's capsule under blood pressure into proximal tubules as urine,

2-Selective reabsorbtion - Diffusion and active transport return molecules to blood at the proximal convoluted tubule. Molecules rapidly returned to the blood include water, glucose, amino acids, and various salt ions.

3-Tubular secretion - Active transport moves molecules from blood into the distal convoluted tubule or collecting duct. This steps helps to rid the blood of such wastes as uric acid, creatine, hydrogen ions, ammonia, and various foreign molecules such as penicillin.

4- Reabsorption of water - Along the length of the nephron and notably at the loop of Henle, water returns by osmosis following active transport of salt.

5-Excretion - Urine formation rids the body of metabolic wastes such as excess water, salts, urea, uric acid, ammonium, and creatine.

Nephrons filter 125 ml of body fluid per minute; filtering the entire body fluid component 16 times each day. In a 24 hour period nephrons produce 180 liters of filtrate, of which 178.5 liters are reabsorbed. The remaining 1.5 liters forms urine.

The amount of filtrate produced every minute is called the glomerular filtration rate or GFR and amounts to 180 litres per day. About 99% of this filtrate is reabsorbed as it passes through the nephron and the remaining 1% becomes urine.

Regulation of concentration and volume

The urinary system is under influence of circulatory system, nervous system and endocrine system.

Aldosterone plays a central role regulating blood pressure through its effects on the kidney. It acts on the distal tubules and collecting ducts of the nephron and increases reabsorption of sodium from the glomerular filtrate. Reabsorption of sodium results in retention of water, which increases blood pressure and blood volume. Antidiuretic hormone (ADH), is aneurohypophysial hormone found in most mammals. Its two primary functions are to retain water in the body and to constrict blood vessels. Vasopressin regulates the body's retention of water by increasing water reabsorption in the collecting ducts of the kidney nephron. Vasopressin increases water permeability of the kidney's collecting duct and distal convoluted tubule by inducing translocation of aquaporin-CD water channels in the kidney nephron collecting duct plasma membrane.

Hormonal Control of Water and Salt balance:

1-(ADH) ADH is released from the pituitary gland .

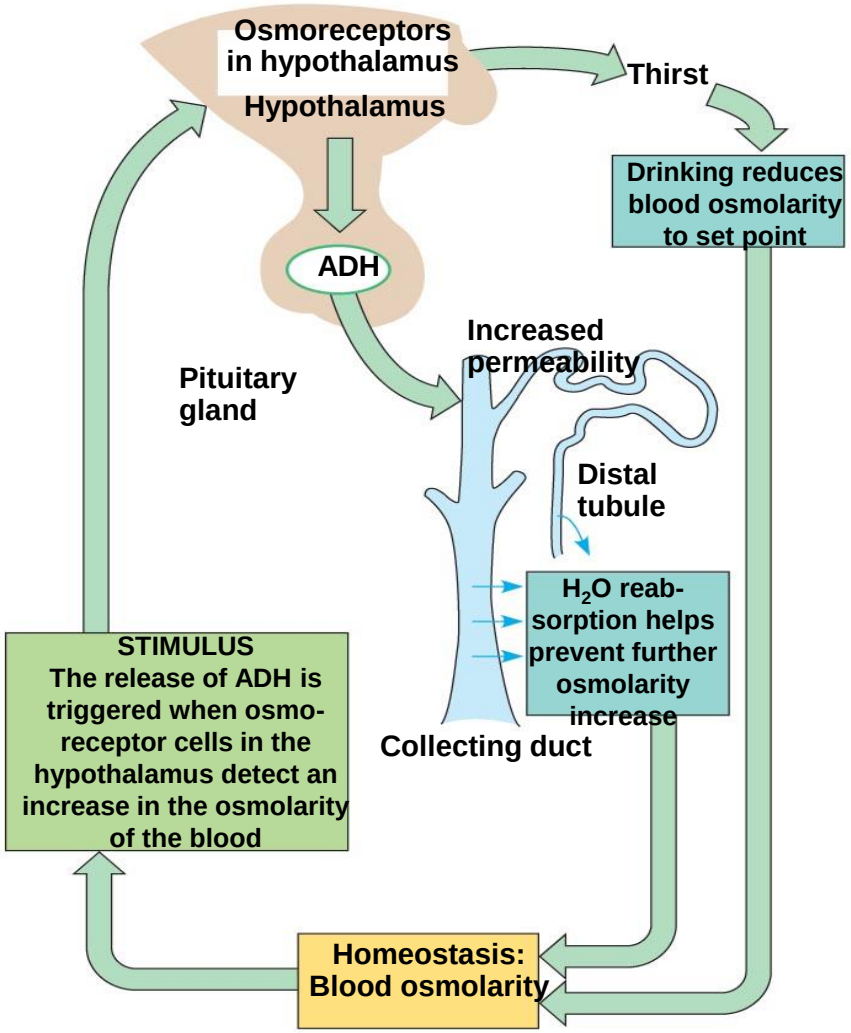
Dropping levels of fluid in the blood signal the hypothalamus to stimulate pituitary to release ADH, that acts to increase water absorption in the kidneys leading to raising levels of fluid in the blood by puts more water back in the blood, increasing the concentration of the urine.

When too much fluid is present in the blood, sensors in the heart signal the hypothalamus to reduce amounts of ADH in the blood. This decreases the amount of water absorbed by the kidneys, producing large quantities of a more dilute urine.

2-Aldosterone, a hormone secreted by the adrenal , regulates the transfer of sodium from the nephron to the blood. When sodium levels in the blood fall, aldosterone is released into the blood, causing more sodium to pass from the nephron to the blood. Renin is released into the blood to control aldosterone.

Urination

Urination is the ejection of urine from the urinary bladder through the urethra to the outside of the body. In healthy humans (and many other animals), the process of urination is under voluntary control. In infants, some elderly individuals, and those with neurological injury, urination may occur as an involuntary reflex. Physiologically, micturition involves coordination between the central, autonomic, and somatic nervous systems. Brain centers that regulate urination include the pontine micturition center, periaqueductal gray, and the cerebral cortex.



(a)

Kidney Stones

In some cases, excess wastes crystallize as kidney stones. They grow and can become a painful irritant that may require surgery or ultrasound treatments. Some stones are small enough to be forced into the urethra, others are the size of huge, massive boulders

(or so I am told).

Disruption of Kidney Function

Infection, environmental toxins such as mercury, and genetic disease can have devastating results by causing disruption of kidney function. Many kidney problems can be treated by dialysis, where a machine acts as a kidney. Kidney transplants are an alternative to dialysis.

Diseases of the Kidney

Diabetic nephropathy : is a progressive kidney disease caused by angiopathy of capillaries in the kidney glomeruli. It is characterized by nodular glomerulosclerosis. It is due to longstanding diabetes mellitus.

Hematuria : is the presence of blood in the urine. It is a sign of a large number of diseases of the kidneys and the urinary tract.

Kidney stones: or renal calculi: are solid accretions (crystals) of dissolved minerals in urine found inside the kidneys or ureters.

- **Urinary tract infections (UTI's)**

The second most common type of bacterial infections seen by health care providers is UTI's. Out of all the bacterias that colonize and cause urinary tract infections the big gun is *Escherichia coli*.

- ***Pyelonephritis :When an infection of the renal pelvis and calices, called pyelitis, spreads to involve the rest of the kidney as well, the result is pyelonephritis.**

- ***glomerulonephritis Inflammation of the glomerular can be caused by immunologic abnormalities, drugs or toxins, vascular disorders, and systemic diseases. Glomerulonephritis can be acute, chronic or progressive.**

- ***Renal Failure Uremia is a syndrome of renal failure and includes elevated blood urea and creatinine levels.**
- ***Diabetes Insipidus**

This is caused by the deficiency of or decrease of ADH. The person with (DI) has the inability to concentrate their urine in water restriction, in turn they will void up 3 to 20 liters/day. There are two forms of (DI), neurogenic, and nephrogenic. In nephrogenic (DI) the kidneys do not respond to ADH. Usually the nephrogenic (DI) is characterized by the impairment of the urine concentrating capability of the kidney along with concentration of water.

Dialysis and Kidney Transplant

Generally, humans can live normally with just one kidney. Only when the amount of functioning kidney tissue is greatly diminished will renal failure develop. If renal function is impaired, various forms of medications are used, while others are contraindicated. Provided that treatment is begun early, it may be possible to reverse chronic kidney failure due to diabetes or high blood pressure. If creatinine clearance (a measure of renal function) has fallen very low ("end-stage renal failure"), or if the renal dysfunction leads to severe symptoms, dialysis is commenced. Dialysis is a medical procedure, performed in various different forms, where the blood is filtered outside of the body.

Kidney transplantation is the only cure for end stage renal failure; dialysis, is a supportive treatment; a form of "buying time" to bridge the inevitable wait for a suitable organ.

Neurophysiology

Function of the Nervous System

Mechanism to perform the functions

Cellular Basis of the Nervous System

Functionally three types of neurons found, Neuron characters , The Nerve Impulse, Resting potential , action potential , Steps in an Action Potential, Synapse physiology , Types of synapses (functional classification or Types of comnications),

Inhibitory synapses

Excitatory synapses

Convergence and divergence, Impulse transduction , Neurotransmitters,

Turning Synapses Off

Drugs and Synapses , Synapses blocking pain signals,

Evolution of Nervous System

The Sensory-Somatic Nervous System

peripheral nervous system (PNS)

The Autonomic Nervous System

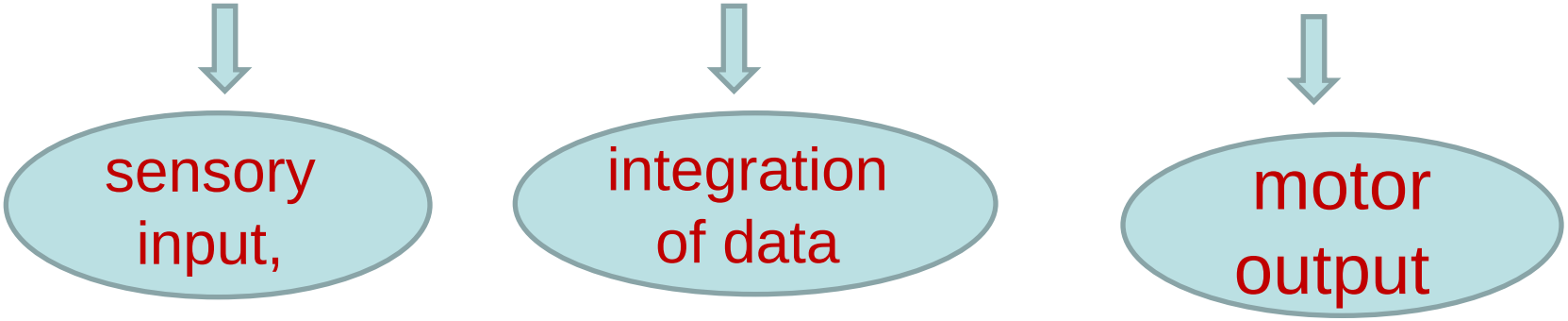
Central Nervous System

Objective

1- Students will be able to explain the three stages of information processing in the nervous system and relate them to the major anatomical divisions of the vertebrate nervous system.
2. Students will be able to describe how neural reflexes control physiological variables and mediate simple behaviors.
3. Students will be able to explain the ionic basis of the resting membrane potential, action potentials, synaptic and receptor potentials, and describe how the three types of gated ion channels produce these signals.
4. Students will know the structure of the neuron and be able to describe how electrical signals are generated and propagated in it.
5. Students will understand the role that myelination plays in nervous system function.

Neurophysiology: Function of the Nervous System:

The nervous system has three main functions:



Mechanism to perform the functions

1-Receive sensory input from internal and external environments & Integrate the input.

2-provides communication &coordination between all organs .

3-establishes homeostasis by monitoring the internal environment of the organism

4- works in close association with the endocrine system.

5-Respond to stimuli

Cellular Basis of the Nervous System

Nervous tissue is composed of two main cell types: neurons and glial cells. Neurons transmit nerve messages. Glial cells are in direct contact with neurons and often surround them give support to the tissue.

Neuron

Is the functional unit of the nervous system. Humans have about 100 billion neurons in their brain alone. While variable in size and shape, all neurons have three parts.

1-Dendrites receive information from another cell and transmit the message to the cell body.

2-cell body contains the nucleus, mitochondria and other organelles of eukaryotic cells.

3-axon conducts messages away from the cell body.

Functionally three types of neurons found

1-Sensory neurons typically have a long dendrite and short axon, and carry messages from sensory receptors to the central nervous system.

2-Motor neurons have a long axon and short dendrites and transmit messages from the central nervous system to the muscles (or to glands).

3- Interneurons are found only in the central nervous system where they connect neuron to neuron.

Some axons are wrapped in a myelin sheath formed from the plasma membranes of specialized glial cells known as Schwann cells.

Schwann cells serve as supportive, nutritive, and service facilities for neurons.

The gap between Schwann cells is known as the node of Ranvier, and serves as points along the neuron for generating a signal.

Signals jumping from node to node travel hundreds of times faster than signals traveling along the surface of the axon.

Neuron characters

- The plasma membrane of neurons, like all other cells, has an unequal distribution of ions between the two sides.

- The outside has a positive charge(sodium and potassium), inside has a negative charge (protein, nucleic acids). This charge difference is a (resting potential) and is measured in millivolts. is -65mV at rest .

- Sodium ions are more concentrated outside , while potassium ions are more concentrated inside the membrane, this called polarization of membrane

- This imbalance is maintained by the active transport of ions to reset the membrane known as the sodium potassium pump. The sodium-potassium pump maintains this unequal concentration by actively transporting ions against their concentration gradients.

The Nerve Impulse

When a nerve is stimulated ,Na ion channels open , changing the resting potential. The rapid change in polarity that moves along the nerve fiber is called the "ACTION POTENTIAL." This moving change in polarity has several stages:

Depolarization : is caused when (Na+) suddenly rush through open Na gates into a nerve cell .The membrane potential undergoes a localized change from-65 millivolts to 0 in a limited area. As additional Na rushes in, the membrane potential actually reverses its polarity so that the outside is negative relative to the inside. During this change of polarity the membrane actually develops a positive value for a moment(+40 millivolts).

Repolarization :

is caused by the closing of Na ion channels and the opening of K+ ion channels. Release of (K+) from the nerve cell . This expulsion acts to restore the localized negative membrane potential of the cell (about -65 σρϑ-70 mV is typical for nerves).

Refractory phase

- is a short period of time after the depolarization stage. Shortly after the sodium gates open they close and go into an inactive conformation. The sodium gates cannot be opened again until the membrane is repolarized to its normal resting potential. The sodium-potassium pump returns sodium ions to the outside and potassium ions to the inside.
- During the refractory phase this particular area of the nerve cell membrane cannot be depolarized.
- This area of depolarization/repolarization/recovery moves along a nerve fiber like a very fast wave.
- In myelinated fibers, conduction is hundreds of times faster because the action potential only occurs at the nodes of Ranvier by jumping from node to node. This is called "saltatory" conduction.
- Damage to the myelin sheath by the disease can cause severe impairment of nerve cell function. Some poisons and drugs interfere with nerve impulses by blocking sodium channels in nerves.

Resting Potential

is the electrical potential across the plasma membrane of a cell that is not conducting an impulse.

Resting potential is maintained by active transport (antiport):

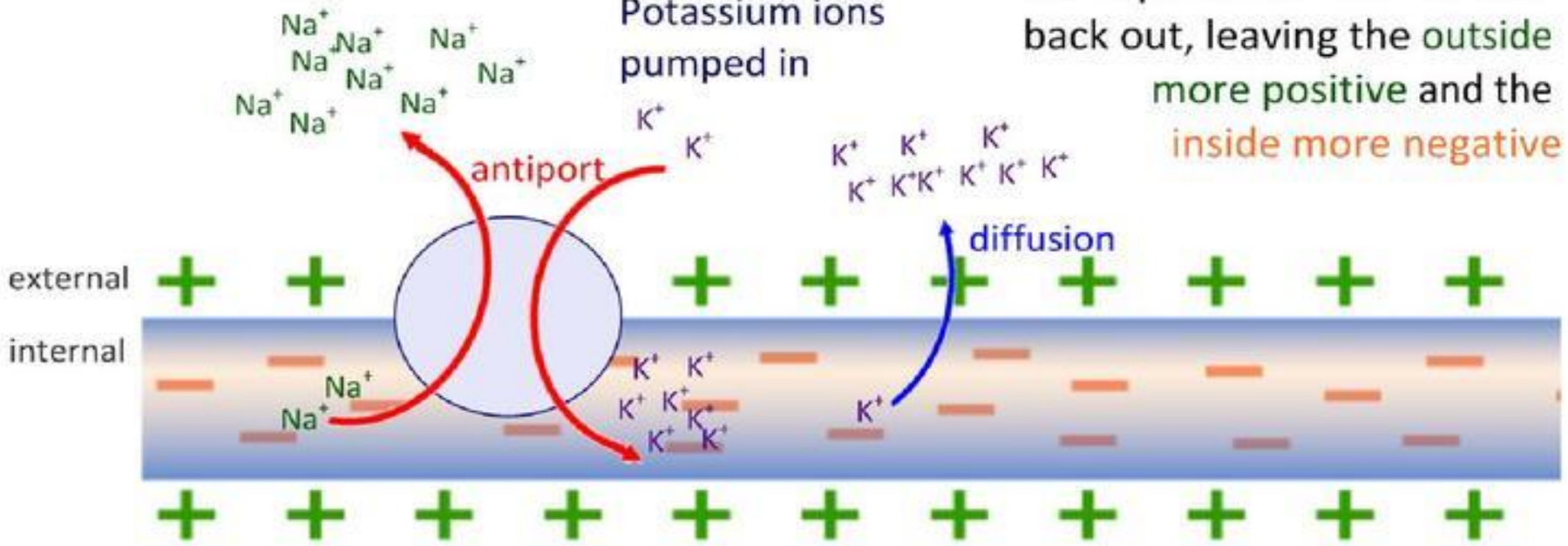
Why is RP negative?

http://lessons.harveyproject.org/development/nervous_system/cell_neuro/synapses/xmtrs.html

Sodium ions pumped out

Potassium ions pumped in

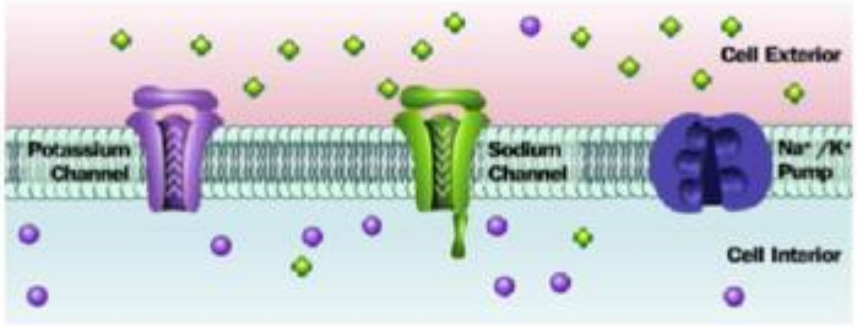
Some potassium ions diffuse back out, leaving the outside more positive and the inside more negative

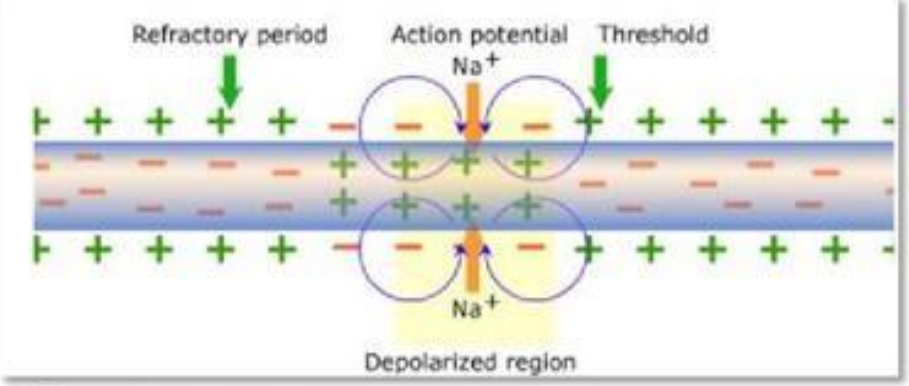


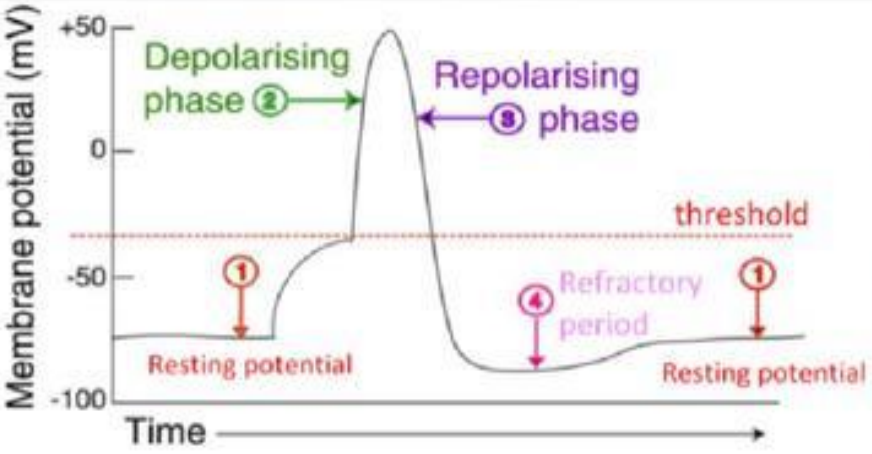
Adapted from http://www.blackwellpublishing.com/matthews/actionp.html

Action Potential

is the the reversal (depolarisation) and restoration (repolarisation) of the electrical potential across a plasma membrane as a nerve impulse passes along a neuron.







1. Resting potential is maintained by active transport: Na^+/K^+ pump pumps Na^+ out and K^+ in.

2. Arrival of an Action Potential (AP) causes depolarisation of adjacent sections of the neuron.
   - This causes local Na^+ diffusion and a current.
   - If the current is enough to rise above the threshold, voltage-gated Na^+ channels open and Na^+ rushes in. Internal potential is reversed - it is more positive than the outside (depolarisation).

3. K^+ channels are opened and K^+ diffuses out. Internal charge is negative again (repolarisation)

4. Refractory period is when the channels rest between openings. This ensures one-way impulse flow.
   Resting potential is then returned by active transport.

http://lessons.harveyproject.org/development/nervous_system/cell_neuro/synapses/xmtrs.html

http://scienceblogs.com/clock/upload/2006/06/ActionPotential.jpg

http://www.blackwellpublishing.com/matthews/actionp.html

Steps in an Action Potential

1-At rest the outside of the membrane is more positive than the inside.

2-Sodium moves inside the cell causing an action potential, the influx of sodium ions makes the inside of the membrane more positive than the outside.

3-Potassium ions flow out of the cell, restoring the resting potential net charges.

4-Sodium ions are pumped out of the cell and potassium ions are pumped into the cell, restoring the original distribution of ions.

Synapses physiology

The junction between a nerve cell and another cell is called a synapse .

The CNS contains more than 100 billion neurons.

Incoming signals enter the neuron through synapses located mostly on the neuronal dendrites, but also on the cell body.

For different types of neurons, there may be only a few hundred or as many as 200,000 such synaptic connections from input fibers.

Conversely, the output signal travels by way of a single axon leaving the neuron.

Anatomical Types of Synapses

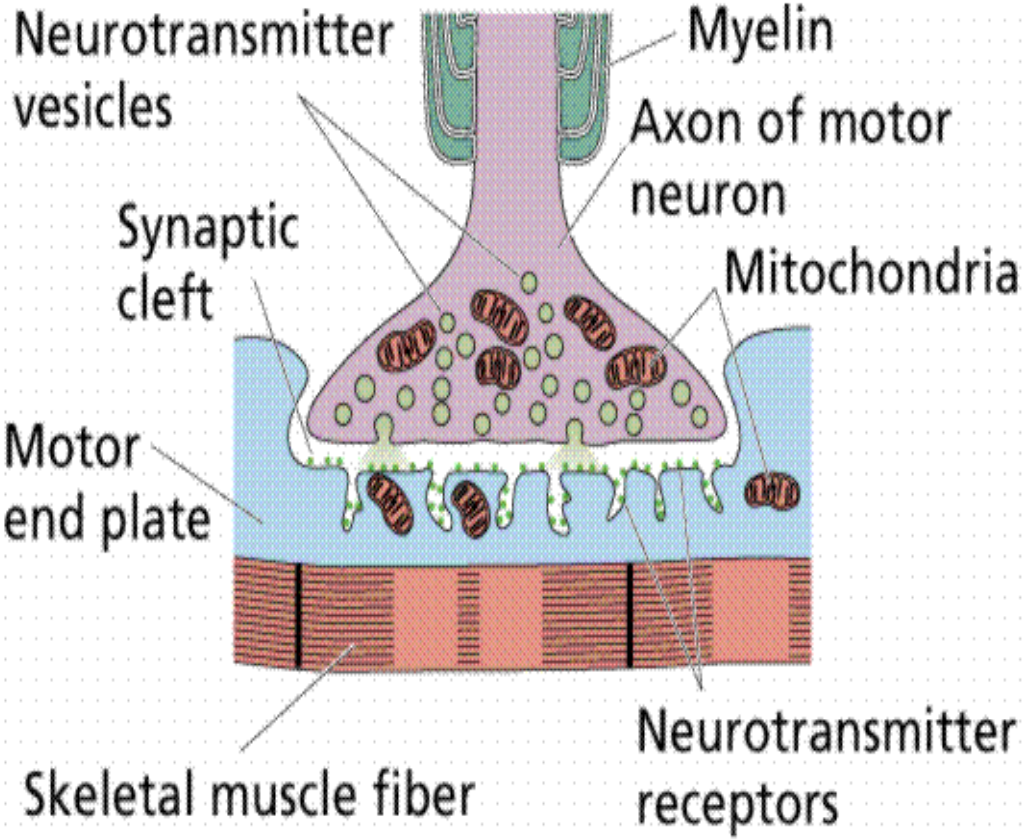
- Axodendritic – synapses between the axon of one neuron and the dendrite of another
- Axosomatic – synapses between the axon of one neuron and the soma of another
- Other types of synapses include:
  - Axoaxonic (axon to axon)
  - Dendrodendritic (dendrite to dendrite)
  - Dendrosomatic (dendrites to soma)

-Messages travel within the neuron as an electrical action potential.

-The space between two cells is known as the synaptic cleft.

-To cross the synaptic cleft requires the actions of neurotransmitters.

- Neurotransmitters are stored in small synaptic vessicles clustered at the tip of the axon.



Types of synapses (functional classification or Types of comnications)

A.Chemical synapse

Almost all synapses used for signal transmission in the CNS of human being are chemical synapses.

i.e. first neuron secretes a chemical substance called neurotransmitter at the synapse to act on receptor on the next neuron to excite it, inhibit or modify its sensitivity.

B. Electrical Synapses

Membranes of the pre- and post-synaptic neurons come close together and gap junctions forms → low membrane borders which allow passage of ions.

- **Are less common than chemical synapses**
- **Correspond to gap junctions found in other cell types**
- **Are important in the CNS in:**
  - **Arousal from sleep**
  - **Mental attention**
  - **Emotions and memory**
  - **Ion and water homeostasis**

C.Conjoint synapse

Both electrical and chemical.

Examples for 2,3 → neurons in lateral vestibular nucleus.

Convergence and divergence

Convergence
When many pre-synaptic neurones converge on any single post-synaptic neuron.

Divergence
Axons of most pre-synaptic neurons divide into many branches that diverge to end on many post-synaptic neuron.

Impulse transduction

-Arrival of the action potential along neuron causes some of the vesicles to move to the end of the axon and discharge their contents into the synaptic cleft.

-Released neurotransmitters diffuse across the cleft, and bind to receptors on the other cell's membrane,

-causing ion channels on that cell to open. Some neurotransmitters cause an action potential, others are inhibitory.

Neurotransmitters

⟹ are small molecules released by special vesicles at end of axons cross the cleft, binding to receptor molecules on the next cell, prompting transmission of the message along that cell's membrane , The time for neurotransmitter action is between 0,5 and 1 millisecond.

⟹ Neurotransmitters are either destroyed by specific enzymes in the synaptic cleft, diffuse out of the cleft, or are reabsorbed by the cell.

⟹ Most important once are :

1-Acetylcholine is commonly secreted at neuromuscular junctions, to stimulates muscle contraction.

2- norepinephrine, is neurotransmitter mostly between neurons of the CNS.

3-Gamma aminobutyric acid is neurotransmitter among neurons of the brain.

Type of synapses

1-Excitatory synapses

The neurotransmitter as(acetylcholine (ACh)) at excitatory synapses depolarizes the postsynaptic membrane at binding to its receptors on the postsynaptic cell opens up ligand-gated sodium channels. These allow an influx of Na^+ ions, reducing the membrane potential. This reduced membrane potential is called an excitatory postsynaptic potential or EPSP. If depolarization of the postsynaptic membrane reaches threshold, an action potential is generated in the postsynaptic cell.

2- Inhibitory synapses

The neurotransmitter as (gamma aminobutyric acid (GABA)) at inhibitory synapses hyperpolarizes the postsynaptic membrane at binding to the receptors increases the influx of chloride (Cl^-) ions into the postsynaptic cell raising membrane potential and inhibiting it. This increased membrane potential is called an inhibitory postsynaptic potential (IPSP) because it counteracts any excitatory signals that may arrive at that neuron. This is a fast response taking only about 1 millisecond.

Turning Synapses Off

Once its job is done, the neurotransmitter must be removed from the synaptic cleft to prepare the synapse for the arrival of the next action potential. Two methods are used:

Reuptake. The neurotransmitter is taken back into the synaptic knob of the presynaptic neuron by active transport. All the neurotransmitters except acetylcholine use this method.

Acetylcholine is removed from the synapse by enzymatic breakdown into inactive fragments. The enzyme used is acetylcholinesterase.

***Nerve gases used in warfare (e.g., sarin) and the organophosphate insecticides (e.g., parathion) achieve their effects by inhibiting acetylcholinesterase thus allowing ACh to remain active. Atropine is used as an antidote because it blocks ACh muscarinic receptors.**

Drugs and Synapses

Many drugs that alter mental state achieve at least some of their effects by acting at synapses.

* Synapses blocking pain signals

The two **enkephalins** are released at synapses on neurons involved in transmitting pain signals back to the brain. The enkephalins **hyperpolarize** the postsynaptic membrane thus inhibiting it from transmitting these pain signals.

The ability to perceive pain is vital. However, faced with massive, chronic, intractable pain, it makes sense to have a system that decreases its own sensitivity. Enkephalin synapses provide this intrinsic pain-suppressing system.

Opiates such as heroin ,morphine ,codeine ,methadone

bind these same receptors. This makes them excellent pain killers.

However, they are also highly **addictive**.

By binding to enkephalin receptors, they enhance the pain-killing effects of the enkephalins.

A homeostatic reduction in the sensitivity of these synapses compensates for continued exposure to opiates.

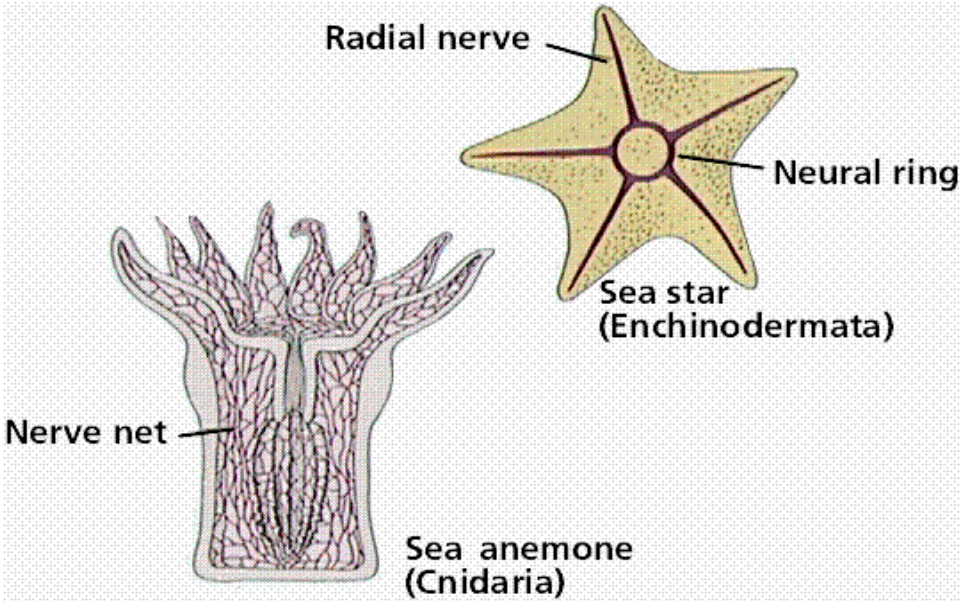
This produces **tolerance**, the need for higher doses to achieve the prior effect.

If use of the drug ceases, the now relatively insensitive synapses respond less well to the soothing effects of the enkephalins, and the painful symptoms of **withdrawal** are produced.

Evolution of Nervous System

Not all animals have highly specialized nervous systems. the evolution of nervous systems must have been an important adaptation in the evolution of body size and mobility.

Coelenterates, cnidarians, and echinoderms have their neurons organized into a nerve net. These creatures have radial symmetry and lack a head. Although lacking a brain or either nervous system (CNS or PNS) nerve nets are capable of some complex behavior.

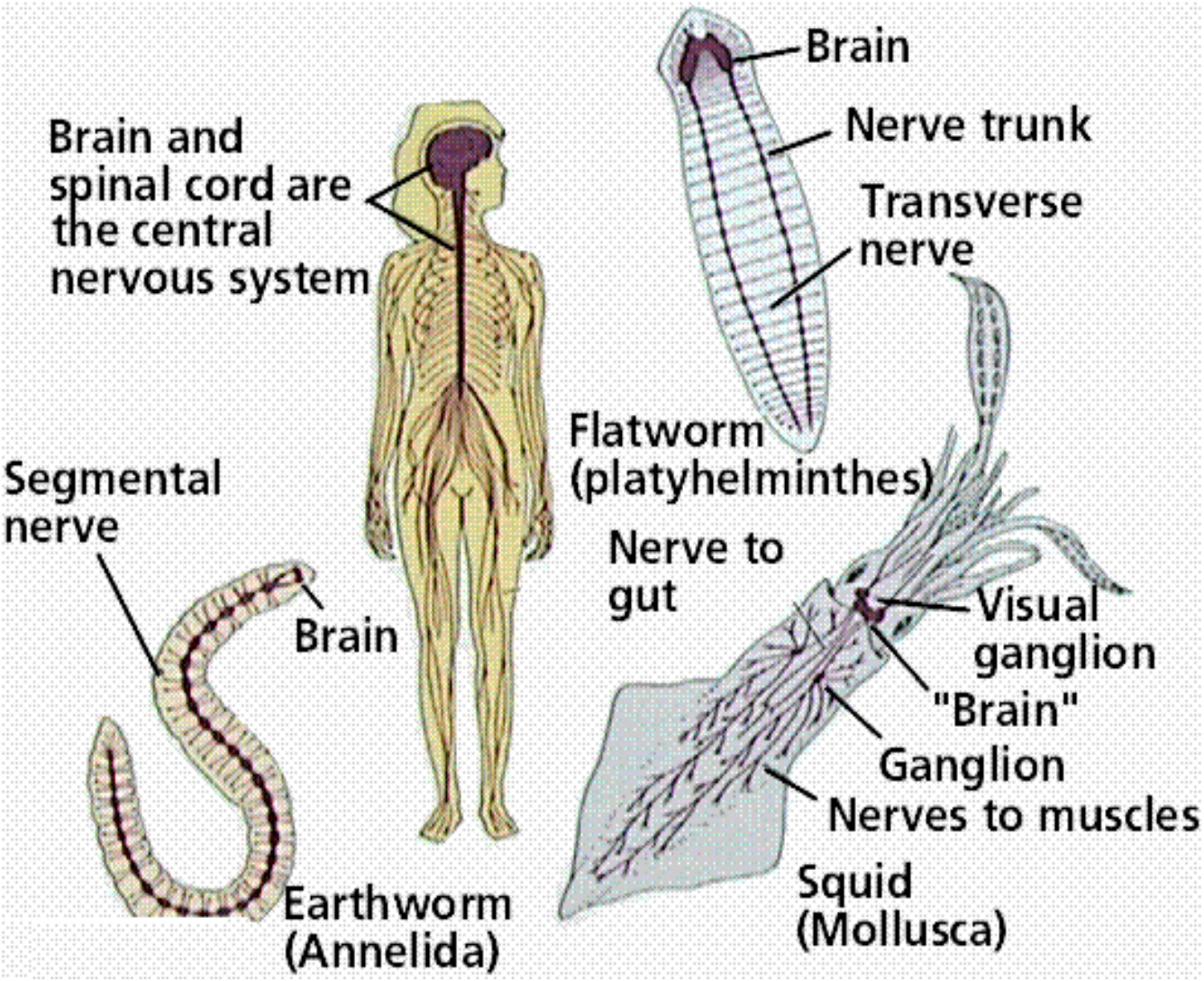


Bilaterally symmetrical animals have a body plan that includes a defined head and a tail region. Development of bilateral symmetry is associated with cephalization,

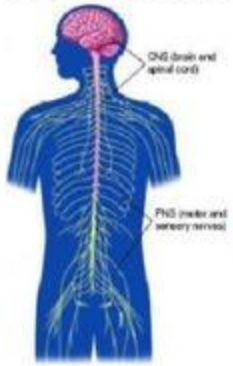
the development of a head with the accumulation of sensory organs at the front end of the organism.

Flatworms have neurons associated into clusters known as ganglia, which in turn form a small brain.

Vertebrates have a spinal cord in addition to a more developed brain.


Brain and spinal cord are the central nervous system
Segmental nerve
Brain
Earthworm (Annelida)
Brain
Nerve trunk
Transverse nerve
Flatworm (platyhelminthes)
Nerve to gut
Visual ganglion
"Brain"
Ganglion
Nerves to muscles
Squid (Mollusca)

The nervous system consists of the central nervous system and peripheral nerves



Nervous System

Central Nervous System

Brain

Spinal Cord

Peripheral Nervous System

Autonomic NS

homeostasis

involuntary control

Sympathetic

"fight or flight"

Parasympathetic

"rest and digest"

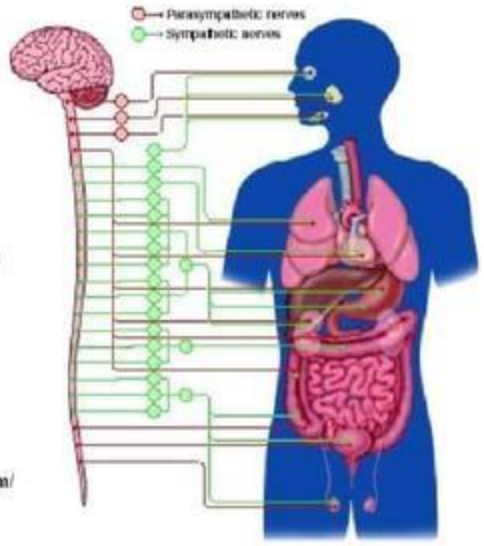
Enteric

controls digestive system

Somatic NS

-receives external stimuli

-voluntary control of muscle



Brain:
http://faculty.washington.edu/chudler/gif/brainwig.gif

CNS/ANS:
http://www.biologyreference.com/images/biol_03_img0336.jpg

Chordates have a dorsal rather than ventral nervous system.Several evolutionary trends occur in chordates:

1 -spinal cord, 2-continuation of cephalization in the form of larger and more complex brains, 3- and development of a more elaborate nervous system.

The vertebrate nervous system is divided into a number of parts. CNS includes brain and spinal cord.

The peripheral nervous system consists of all body nerves. Motor neuron pathways are of two types: somatic (skeletal) and autonomic (smooth muscle, cardiac muscle, and glands).

The autonomic system is subdivided into the sympathetic and parasympathetic systems.

peripheral nervous system (PNS)

Two main components of the PNS:

1- sensory (afferent) pathways that provide input from the body into the CNS.

2- motor (efferent) pathways that carry signals to muscles and glands (effectors) from CNS .

The peripheral nervous system is subdivided into the :

sensory-somatic nervous system and the autonomic nervous system

The Sensory-Somatic Nervous System

consists of nerve fibers originate from brain and spinal cord that are : 12 pairs of cranial nerves and 31 pairs of spinal nerves.

The cranial nerves some of them are sensory others motor and mixed:

The Autonomic Nervous System

is that part of PNS consisting of motor neurons that control internal organs. It has two subsystems.

Sympathetic Nervous System is involved in the fight or flight response.

Parasympathetic Nervous System is involved in relaxation.

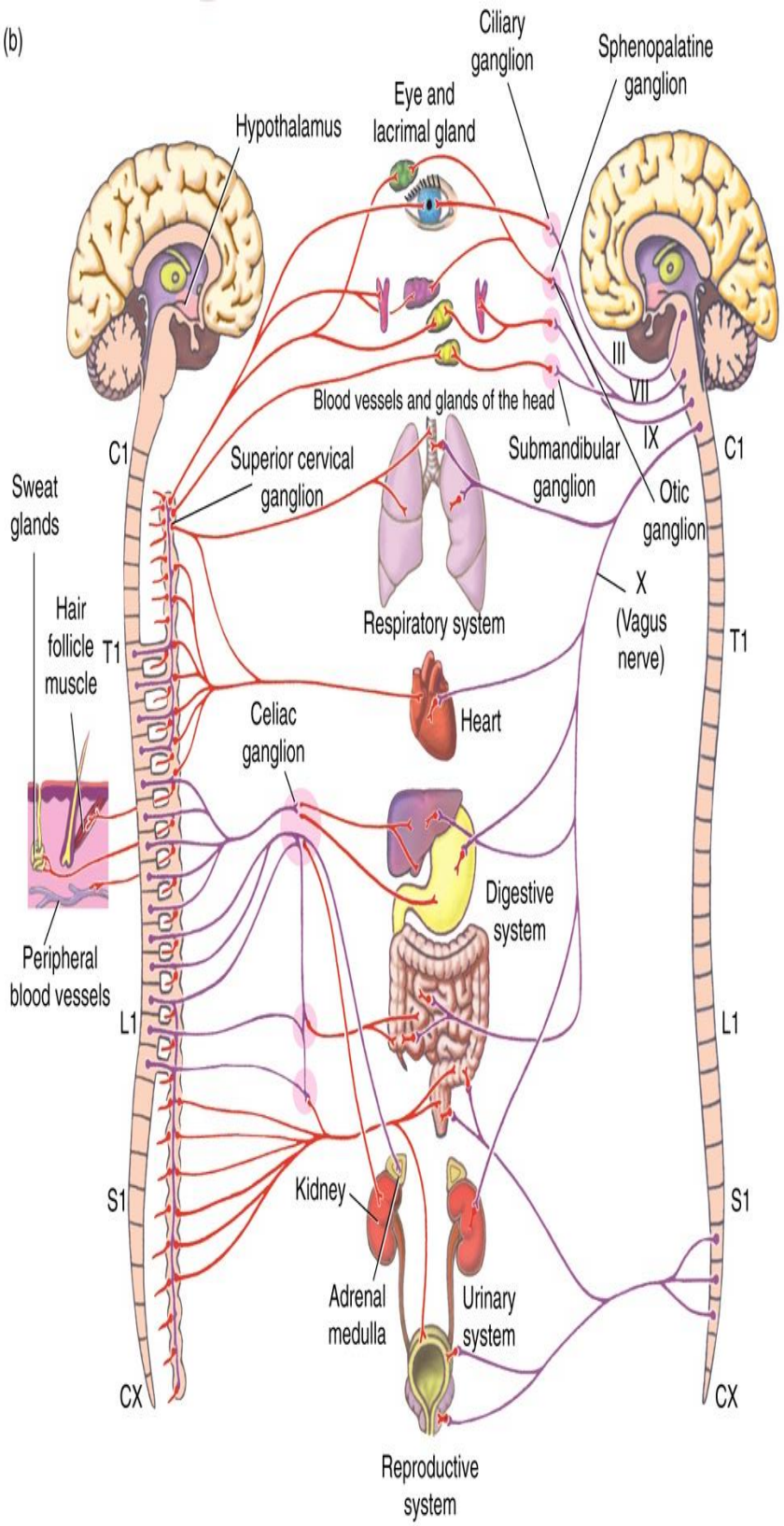
Each of these subsystems operates in the reverse of the other (antagonism). Both systems innervate the same organs , that called dual innervations and each nerve act in opposition to the other in order to maintain homeostasis.

The autonomic nervous system consists of sensory neurons and motor neurons that run between the central nervous system and various internal organs such as the: heart ,lungs ,viscera ,glands.

The actions of the autonomic nervous system are largely involuntary.

- **The Sympathetic Nervous System**
- Act on following organs causing :
- stimulates heartbeat
- raises blood pressure
- dilates the pupils
- dilates the trachea and bronchi
- stimulates the conversion of liver glycogen into glucose
- shunts blood away from the skin and viscera to the skeletal muscles, brain, and heart
- inhibits peristalsis in the gastrointestinal (GI) tract
- inhibits contraction of the bladder and rectum
- In short, stimulation of the sympathetic branch of the autonomic nervous system prepares the body for emergencies: for "fight or flight" (and, perhaps, enhances the memory of the event that triggered the response).

- In short**The Parasympathetic Nervous System**: Parasympathetic stimulation causes
- slowing down of the heartbeat ,
- lowering of blood pressure ,
- constriction of the pupils
- increased blood flow to the skin and viscera , peristalsis of the GI tract
- , the parasympathetic system returns the body functions to normal after they have been altered by sympathetic stimulation. In times of danger, the sympathetic system prepares the body for violent activity. The parasympathetic system reverses these changes when the danger is over.


(b)
Ciliary ganglion
Sphenopalatine ganglion
Eye and lacrimal gland
Hypothalamus
III
VII
IX
Blood vessels and glands of the head
Submandibular ganglion
Otic ganglion
C1
Superior cervical ganglion
Sweat glands
Hair follicle
muscle
T1
Respiratory system
X (Vagus nerve)
Heart
Celiac ganglion
Digestive system
Peripheral blood vessels
L1
Kidney
S1
Adrenal medulla
Urinary system
CX
Reproductive system

Central Nervous System

(CNS) is composed of the brain and spinal cord.

The brain is composed of three parts:

1- cerebrum (seat of consciousness),

2- cerebellum,

3-medulla oblongata ("part of the unconscious brain").

The Brain in vertebrate evolutionary trends include:

1-Increase in brain size relative to body size.

2-Subdivision and increasing specialization of the forebrain, midbrain, and hindbrain.

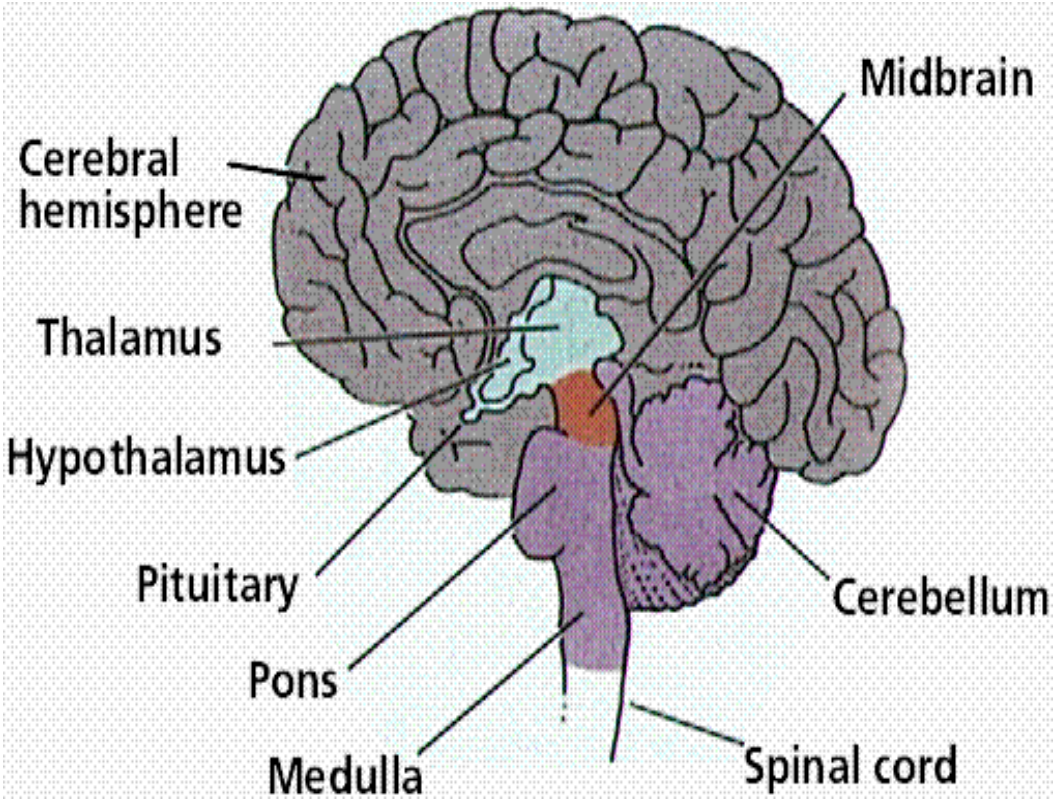
3-Growth in relative size of the forebrain, especially the cerebrum, which is associated with increasingly complex behavior in mammals.

The **medulla oblongata** is closest to the spinal cord, and its function are:

1-is involved with the regulation of heartbeat, 2-breathing, 3-vasoconstriction (blood pressure), 4-and reflex centers for vomiting, coughing, sneezing, swallowing,

The Cerebellum

Functions of the cerebellum include fine motor coordination and body movement, posture, and balance. This region of the brain is enlarged in birds and controls muscle action needed for flight.

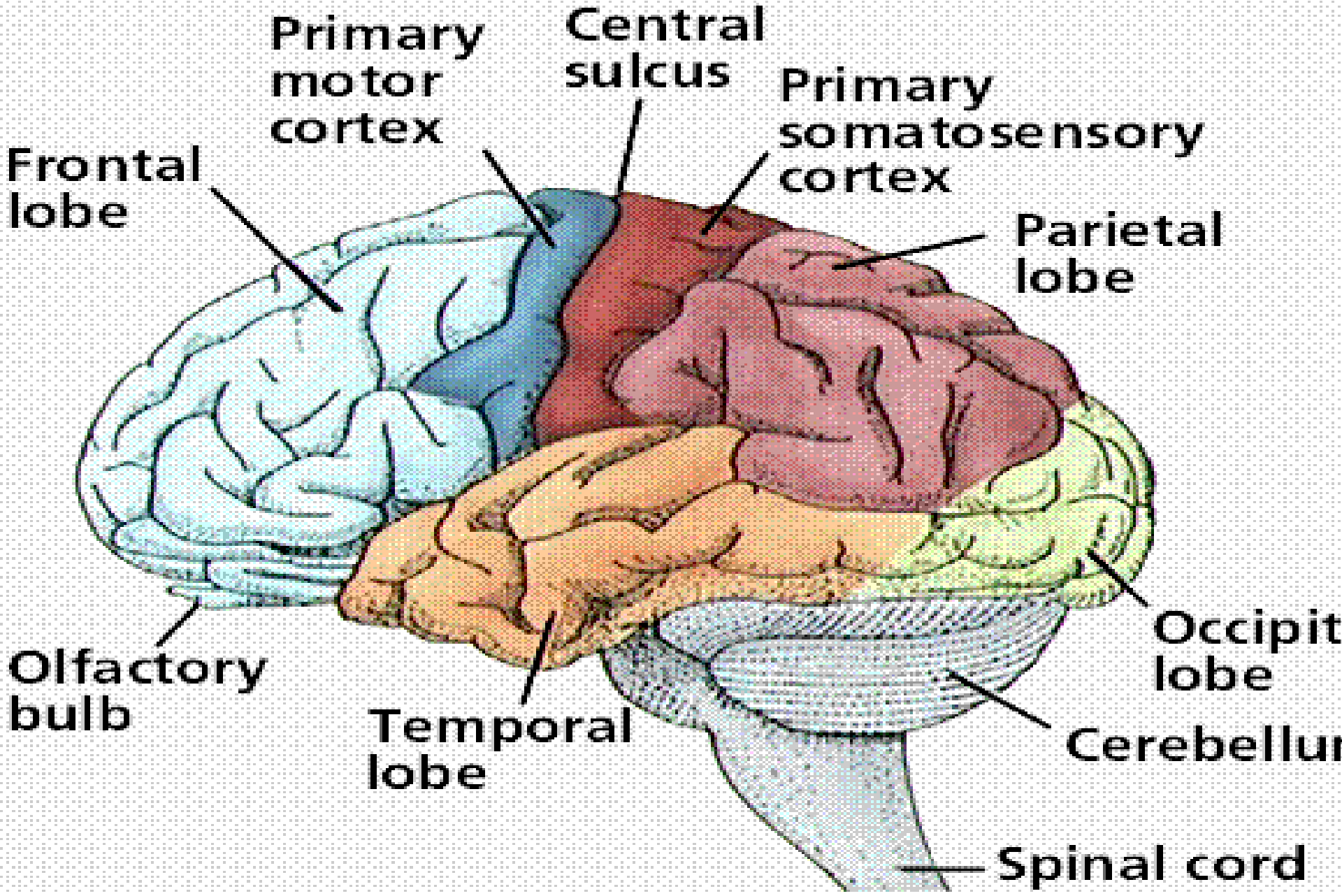

Midbrain
Cerebral hemisphere
Thalamus
Hypothalamus
Pituitary
Cerebellum
Pons
Medulla
Spinal cord

The Forebrain

The forebrain consists of the diencephalon and cerebrum. The thalamus and hypothalamus are the parts of the diencephalon. The thalamus acts as a switching center for nerve messages. The hypothalamus is a major homeostatic center having both nervous and endocrine functions, it regulates homeostasis. It has regulatory areas for thirst, hunger, body temperature.

The cerebrum, the largest part of the human brain, is divided into left and right hemispheres connected to each other by the corpus callosum. The hemispheres are covered by a thin layer of gray matter known as the cerebral cortex, the most recently evolved region of the vertebrate brain. Fish have no cerebral cortex, amphibians and reptiles have only rudiments of this area.

The cortex in each hemisphere of the cerebrum is between 1 and 4 mm thick. Folds divide the cortex into four lobes: occipital, temporal, parietal, and frontal. No region of the brain functions alone, although major functions of various parts of the lobes have been determined.


Primary motor cortex
Central sulcus
Primary somatosensory cortex
Frontal lobe
Parietal lobe
Occipit lobe
Olfactory bulb
Temporal lobe
Cerebellu
Spinal cord

⇨ The occipital lobe (back of the head) receives and processes visual information.

⇨ The temporal lobe receives auditory signals, processing language and the meaning of words.

⇨ The parietal lobe is associated with the sensory cortex and processes information about touch, taste, pressure, pain, and heat and cold.

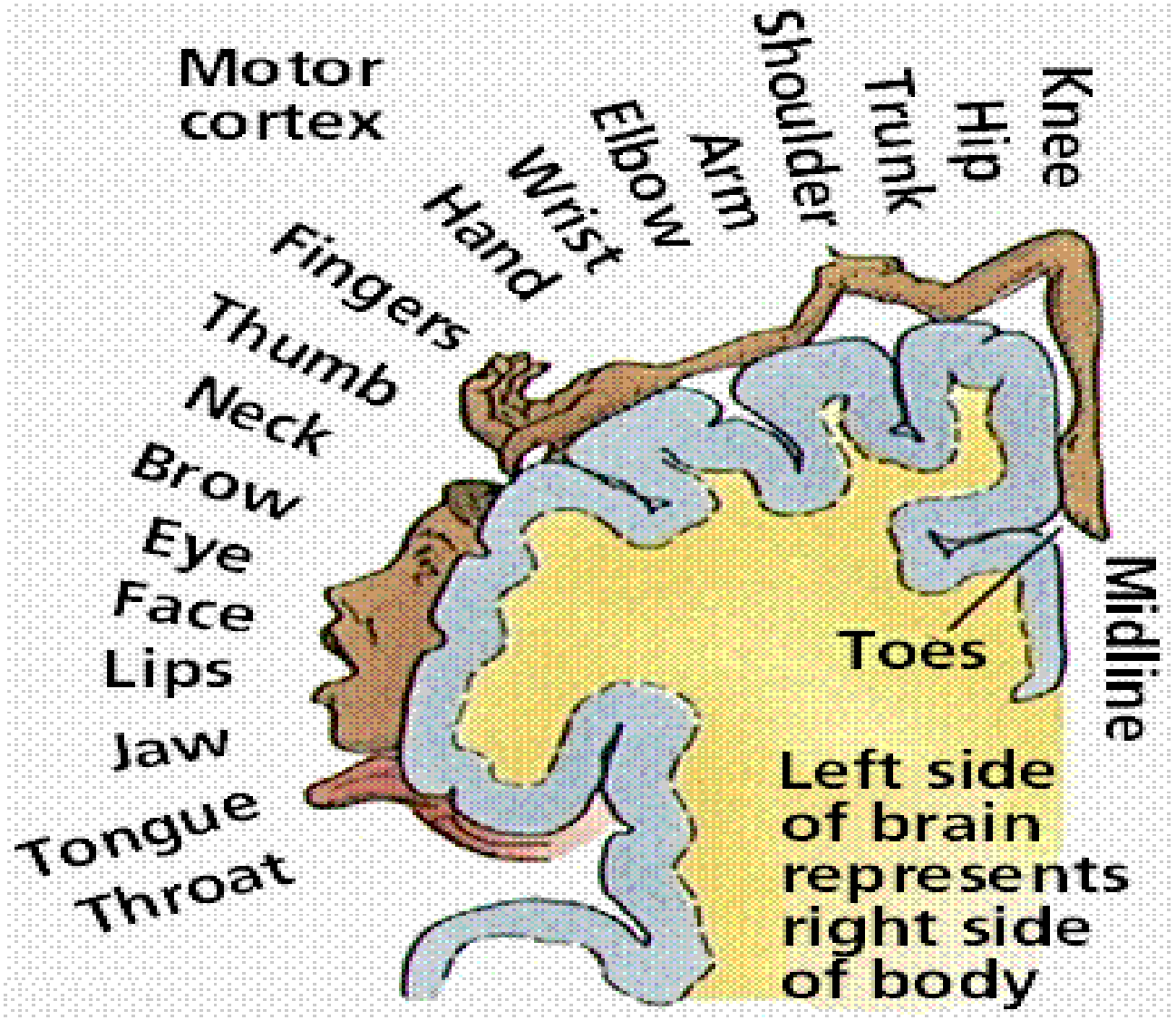
⇨ The frontal lobe conducts three functions:

1-motor activity and integration of muscle activity

2-speech

3-thought processes

- * Not needed
- Functional areas of the brain.
- Most people who have been studied have their language and speech areas on the left hemisphere of their brain.
- Language comprehension is found in Wernicke's area.
- Speaking ability is in Broca's area. Damage to Broca's area causes speech impairment but not impairment of language comprehension.
- Lesions in Wernicke's area impairs ability to comprehend written and spoken words but not speech.
- The remaining parts of the cortex are associated with higher thought processes, planning, memory, personality and other human activities.


Motor cortex
Shoulder
Arm
Elbow
Wrist
Hand
Fingers
Thumb
Neck
Brow
Eye
Face
Lips
Jaw
Tongue
Throat
Trunk
Hip
Knee
Toes
Midline
Left side of brain represents right side of body

- *The Spinal Cord
- 31 pairs of spinal nerves arise along the spinal cord. These are "mixed" nerves because each contain both sensory and motor axons. However, within the spinal column,
- all the sensory axons pass into the dorsal root ganglion where their cell bodies are located and then on into the spinal cord itself.
- all the motor axons pass into the ventral roots before uniting with the sensory axons to form the mixed nerves.
- The spinal cord carries out two main functions:
- It connects a large part of the peripheral nervous system to the brain. Information (nerve impulses) reaching the spinal cord through sensory neurons are transmitted up into the brain. Signals arising in the motor areas of the brain travel back down the cord and leave in the motor neurons.
- The spinal cord also acts as a minor coordinating center responsible for some simple reflexes like the withdrawal reflex.
- The interneurons carrying impulses to and from specific receptors and effectors are grouped together in spinal tracts.

Muscles physiology **Muscular physiology**

Functions of the muscle include:

Types of muscles , skeletal , cardiac, smooth ,

Muscle structure , Anatomy of Skeletal Muscle , **Cellular Organization, Molecular Organization, Sarcomere,**

The Actin Filament, myosin filament,

Mechanism of Muscle Contraction , **Neuromuscular Junction , Neuromuscular Junction , Mechanism of neuromuscular action ,**

Membrane potential , Action membrane potential , Resting potential , Steps of a skeletal muscle contraction & Relaxation, Muscle contraction and Relaxation , Sliding Filament theory , Role of calcium in contraction ,

How does an action potential initiate a muscle contraction? ,

Types of Contractions , Excitation Contraction Coupling ,

Smooth Muscle Contraction , Cardiac muscle contractions ,

Muscles Tetanus and Fatigue , Motor Unit:

- Objective
- To describe muscle’s macro and micro structures
- To explain the sliding-filament action of muscular contraction
- To differentiate among types of muscle fibres
- To describe group action of muscles

Muscular physiology

➡The **muscular system** is the biological system of animals that produces movement.

➡ **Muscle** is contractile tissue and is derived from the mesodermal layer of embryonic germ cells.

Functions of the muscle include:

1-Support of the body

2- Aids in bone movement

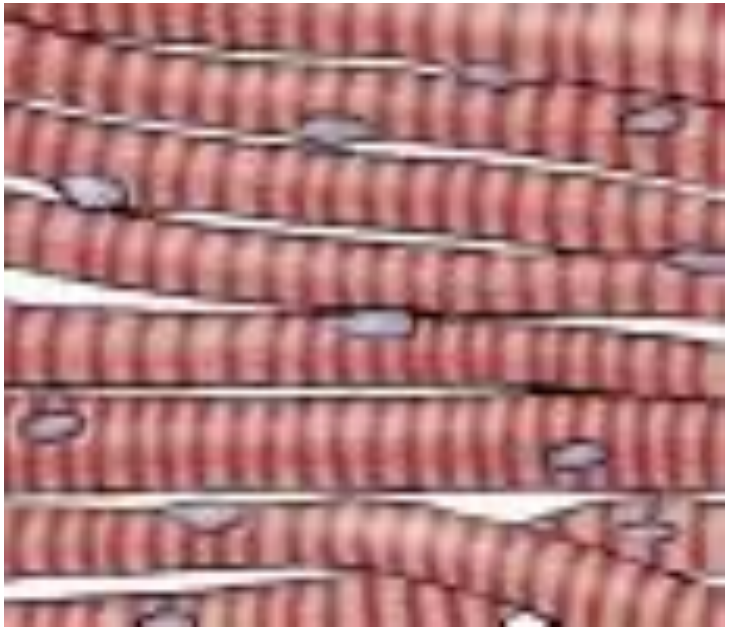
3- Helps maintain a constant temperature throughout the body

4-Assists with the movement of cardiovascular, Gi and lymphatic vessels through contractions

5-Protection of internal organs and contributing to joint stability

6- produce force and cause motion, either locomotion or movement within internal organs.

Types of muscles :



1-Skeletal muscle

- Long cylindrical cells
- Many nuclei per cell
- Striated
- Voluntary
- Rapid contractions

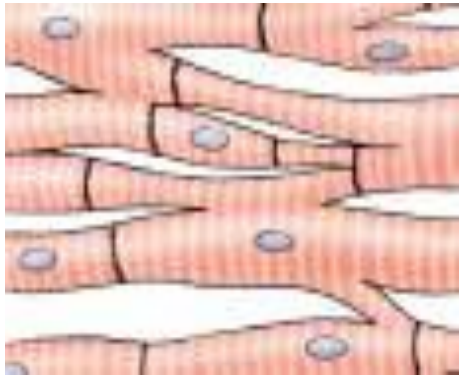
Skeletal muscle is further divided into :

Type I, slow oxidative, *slow twitch*, or "red" muscle is dense with capillaries and is rich in mitochondria and myoglobin, giving the muscle tissue its characteristic red color. It can carry more oxygen and sustain aerobic activity.

Type II, *fast twitch*, "white" muscle that is even less dense in mitochondria and myoglobin. In small animals like rodents or rabbits this is the major fast muscle type, explaining the pale color of their meat.

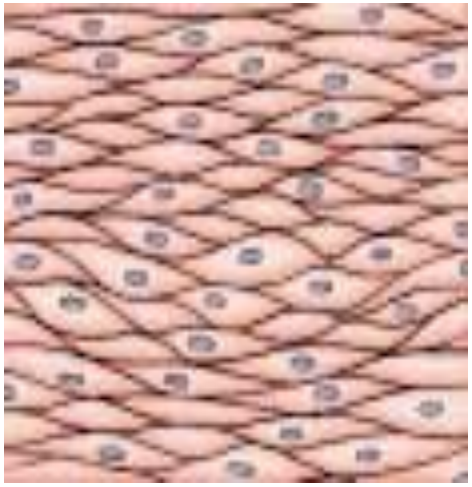
2- **Cardiac muscle**

- Branching cells
- One or two nuclei per cell
- Striated
- Involuntary
- Medium speed contractions



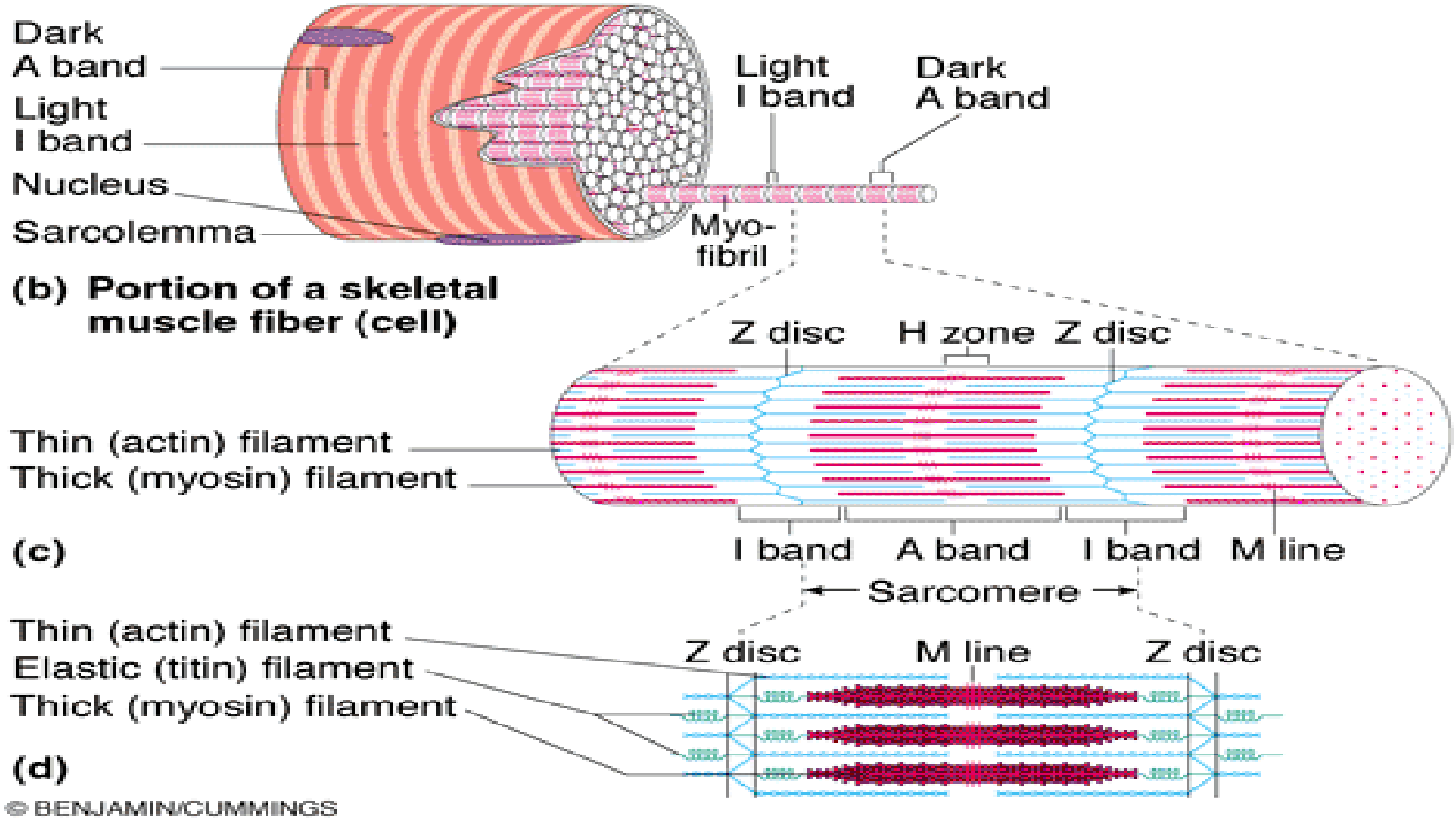
3-Smooth muscles

- Fusiform cells
- One nucleus per cell
- Non striated
- Involuntary
- Slow, wave-like contractions

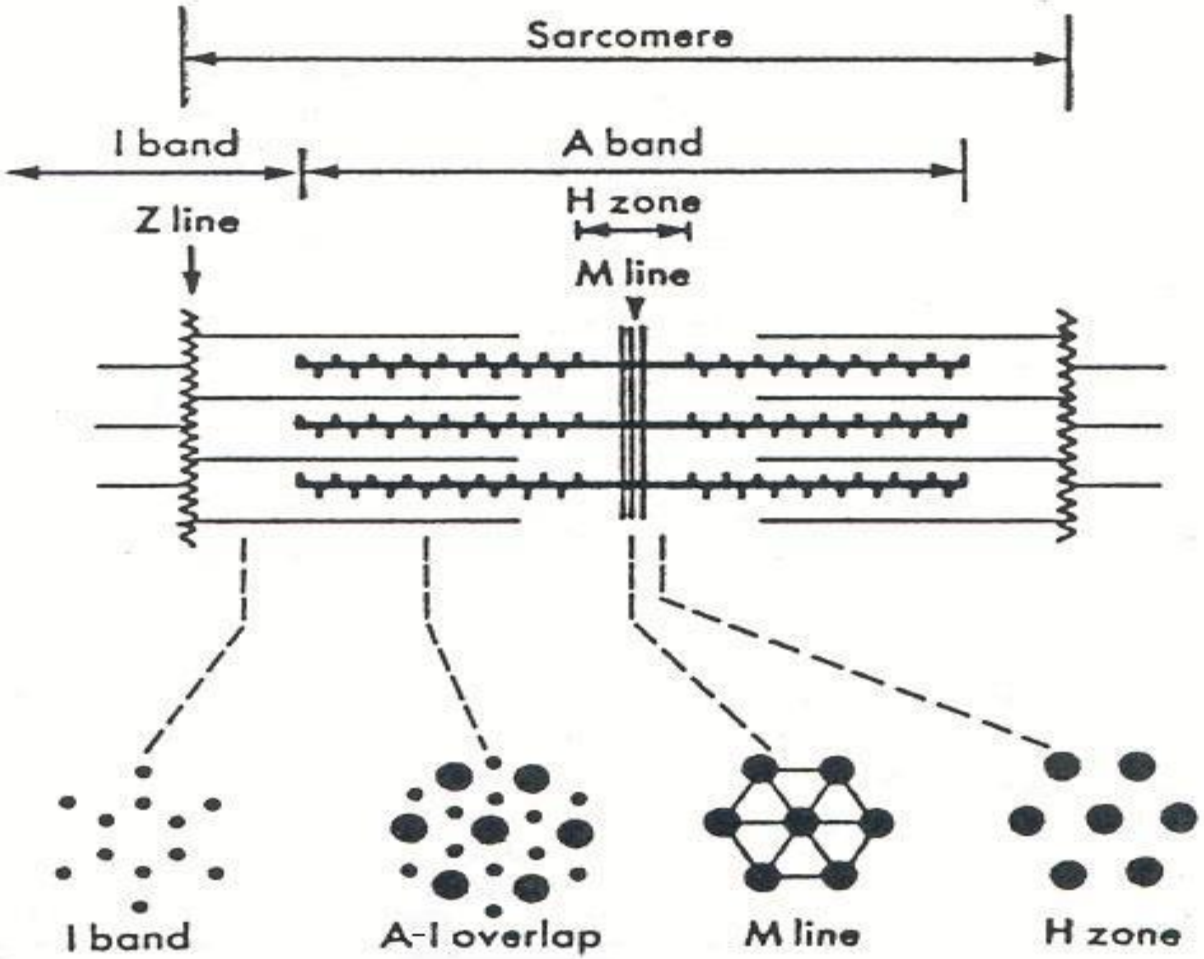


Muscle structure

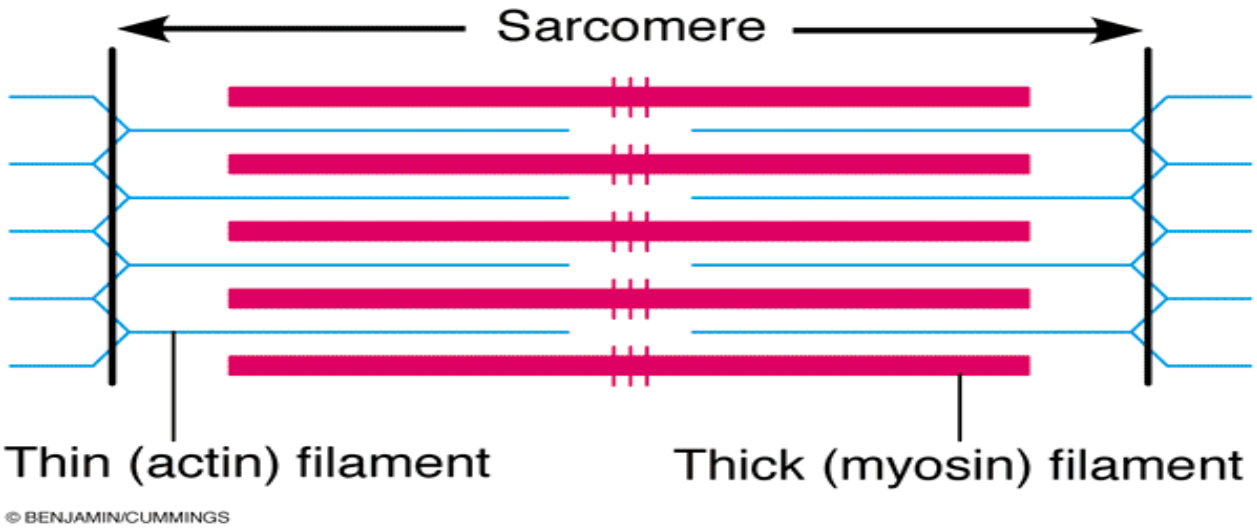
- Skeletal muscle is composed of numerous long, cylindrical cells called muscle fibers, lies in parallel with one another in length and are subdivided into cylindrical subunits called myofibrils.
- Myofibrils are composed of many sub-units in series called sarcomeres, each contains thick filaments of myosin, and thin filaments of actin. *The sarcomere is the functional unit of the muscle during contraction.*
- The striations along filaments are due to light, I band, and dark, A band, alternations. I band separated into 2 part by dark line (Z line), and dark, A band separated into 2 part by light zone (H line)
- A sarcomere is the part of the myofibril between two adjacent Z lines, actin filaments are attached to the Z lines whereas myosin filaments are not, myosin contain globular projections that attach to actin at specific binding sites forming attachments called *cross-bridges*.

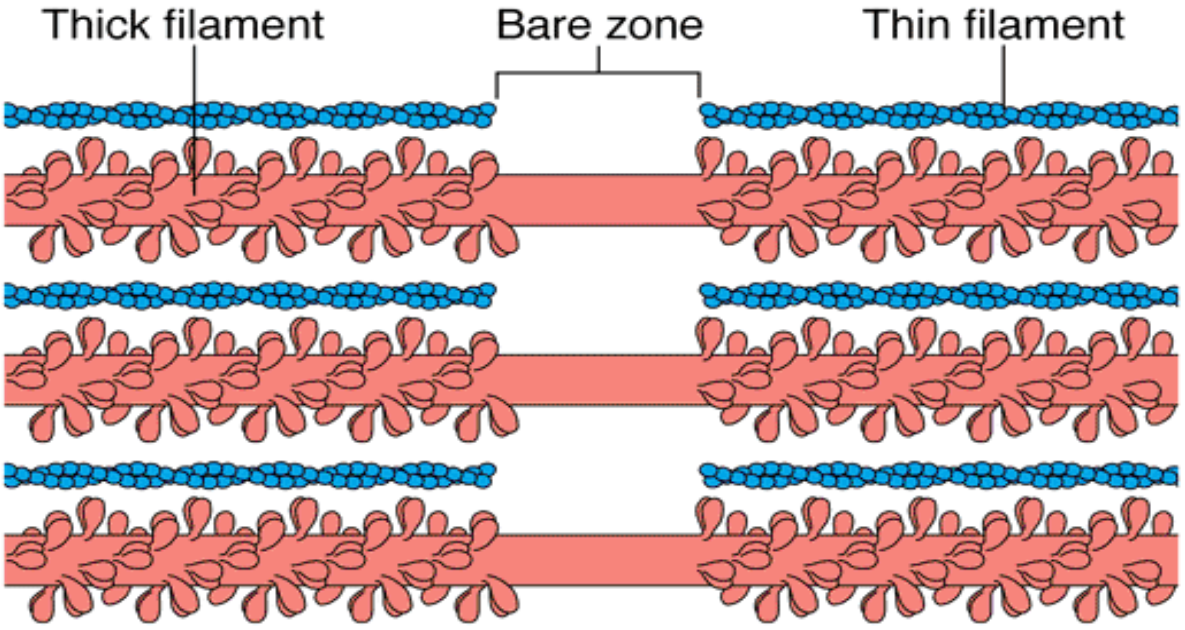


Dark and light bands can be seen in the muscle fiber and also in the smaller myofibrils. An enlargement of the myofibril reveals that they are made of smaller filaments or myofilaments. *There is a thick filament called myosin and *a thin filament called actin.



■ Fig. 22-3. Longitudinal *(top)* and cross-sectional *(bottom)* diagrams showing the relationships between thick *(black)* and thin *(color)* filaments of a sarcomere. (Redrawn from Squire, J.M.: The structural basis of muscular contraction, New York, 1981, Plenum Press.)





(d) Longitudinal section of filaments within one sarcomere of a myofibril

Anatomy of Skeletal Muscle

Gross organization:

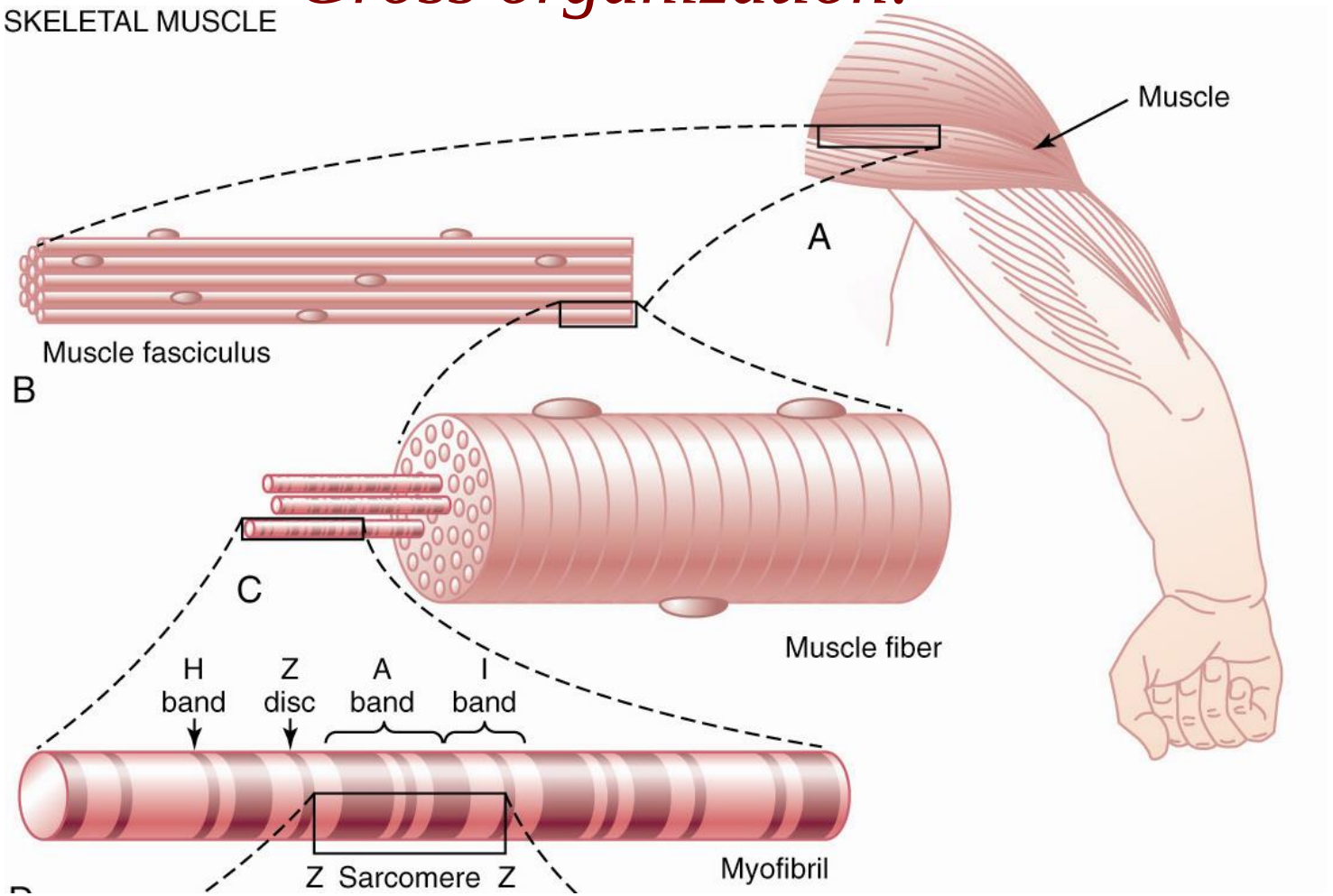


Figure 6-1; Guyton & Hall

Cellular Organization

Muscle fibers

- single cells
- multinucleated
- surrounded by the sarcolemma

Myofibrils

- contractile elements
- surrounded by the sarcoplasm

Cellular organelles - lie between myofibrils (mitochondria, sarcoplasmic reticulum etc.)

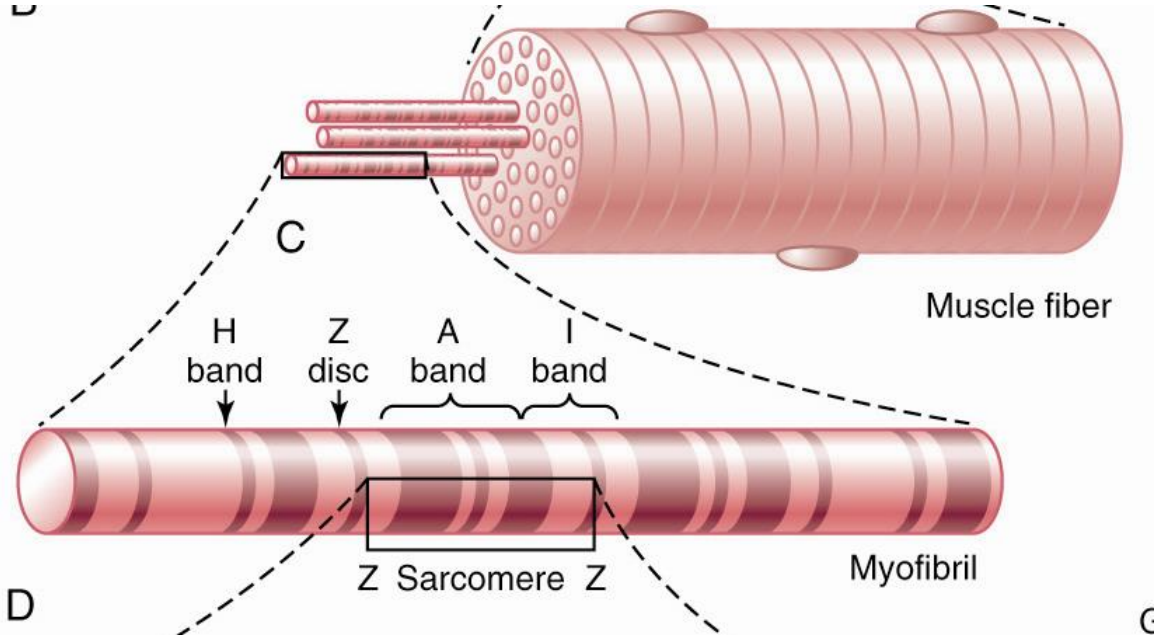


Figure 6-1; Guyton & Hall

Molecular Organization

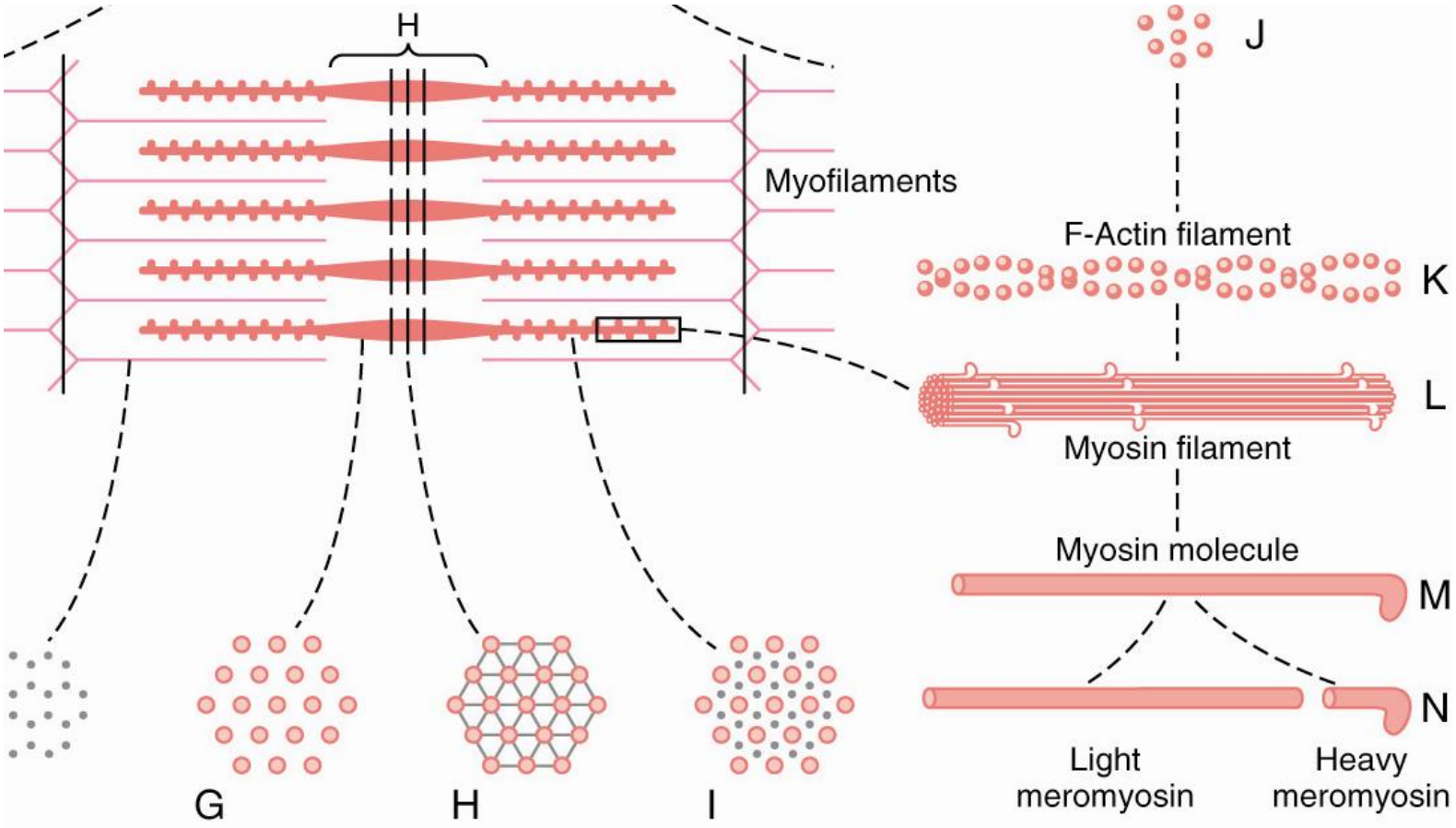
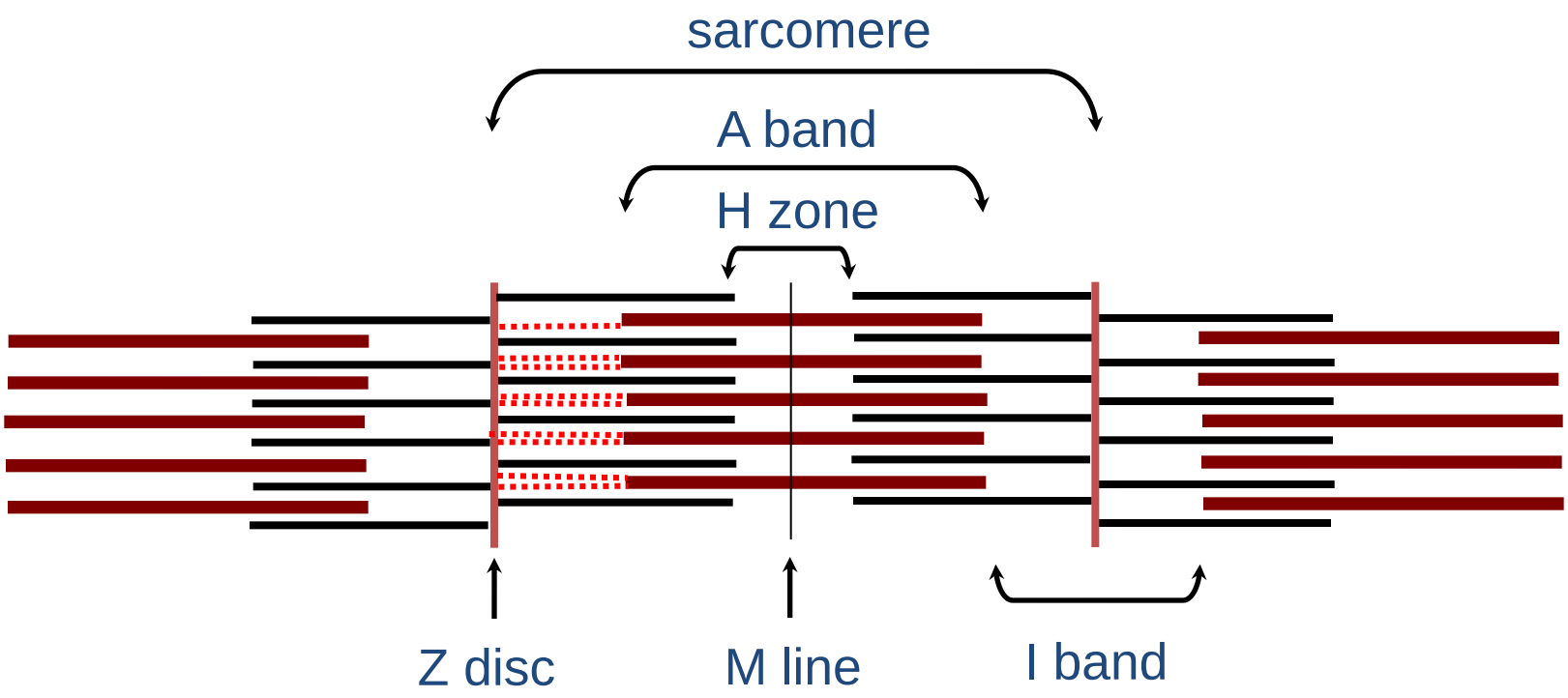


Figure 6-1; Guyton & Hall

The Sarcomere



thick filament (myosin)

thin filament (actin)

titin (filamentous structural protein)

The Actin Filament

- the I band filament
- tethered at one end at the Z disc
- 1 μm long: v. uniform *nebulin* forms guide for synthesis

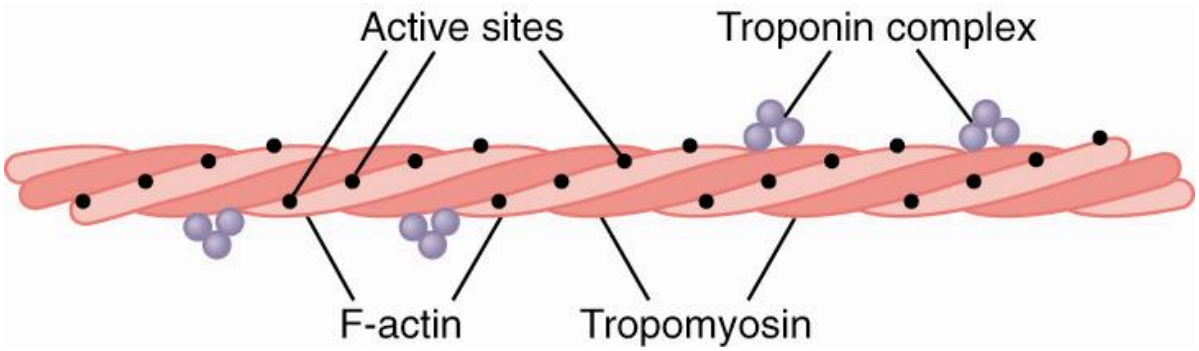


Figure 6-6; Guyton & Hall

F-actin

- double-stranded helix
- composed of polymerized G-actin
- ADP bound to each G-actin (active sites)
- myosin heads bind to active sites

tropomyosin

- covers active sites
- prevents interaction with myosin

troponin

- **I** - binds actin
- **T** - binds tropomyosin
- **C - binds Ca^{2+}**

The Myosin Molecule:

- two **heavy chains** (MW 200,000)
- four **light chains** (MW 20,000)
- "head" region - site of **ATPase** activity

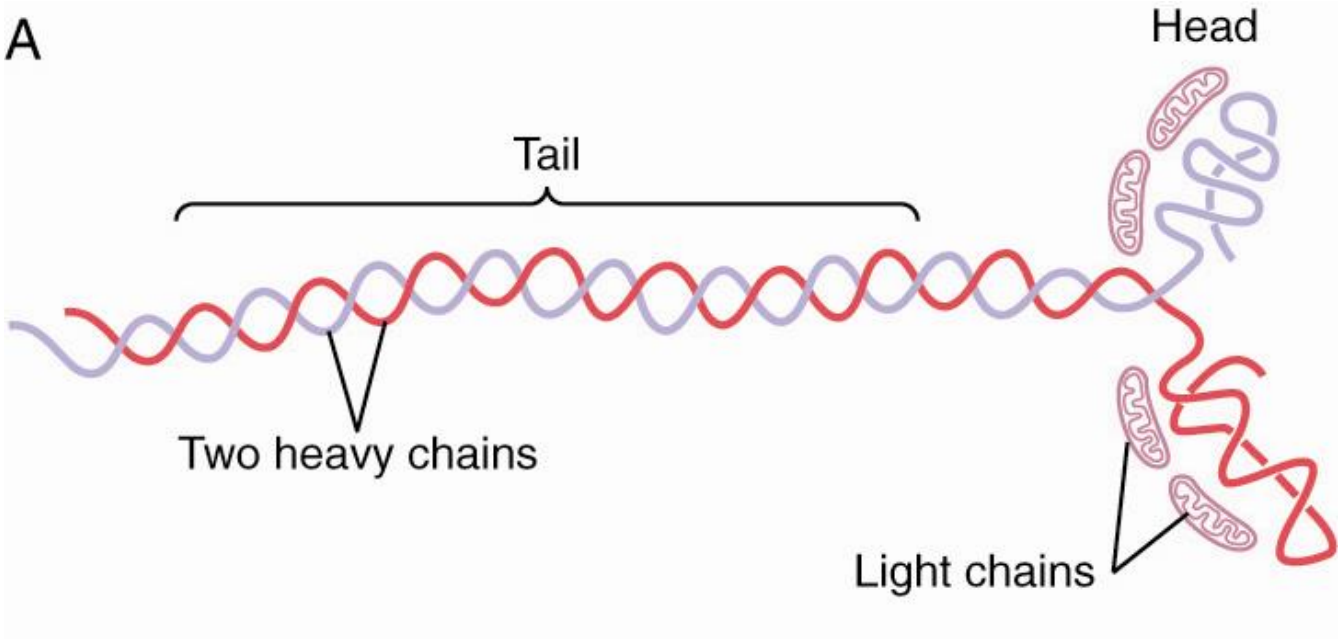


Figure 6-5; Guyton & Hall

Mechanism of Muscle Contraction

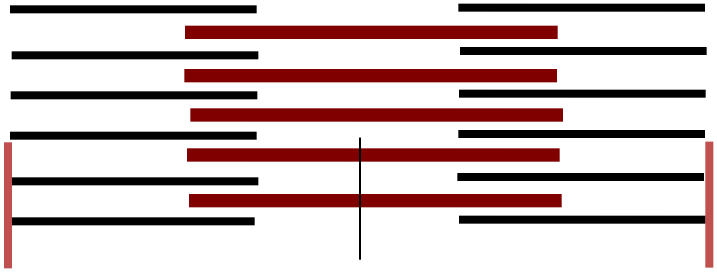
Theory:

Binding of Ca^{2+} to **troponin** results in a conformational change in **tropomyosin** that "uncovers" the active sites on the actin molecule, allowing for myosin to bind.

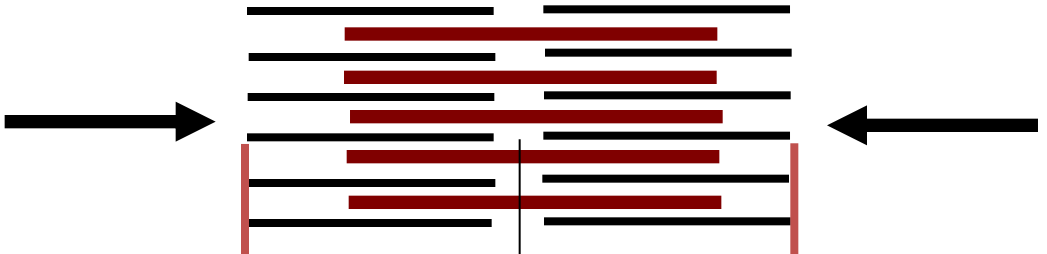
"Sliding Filament" Mechanism

Contraction results from the sliding action of interdigitating actin and myosin filaments

RELAXED:

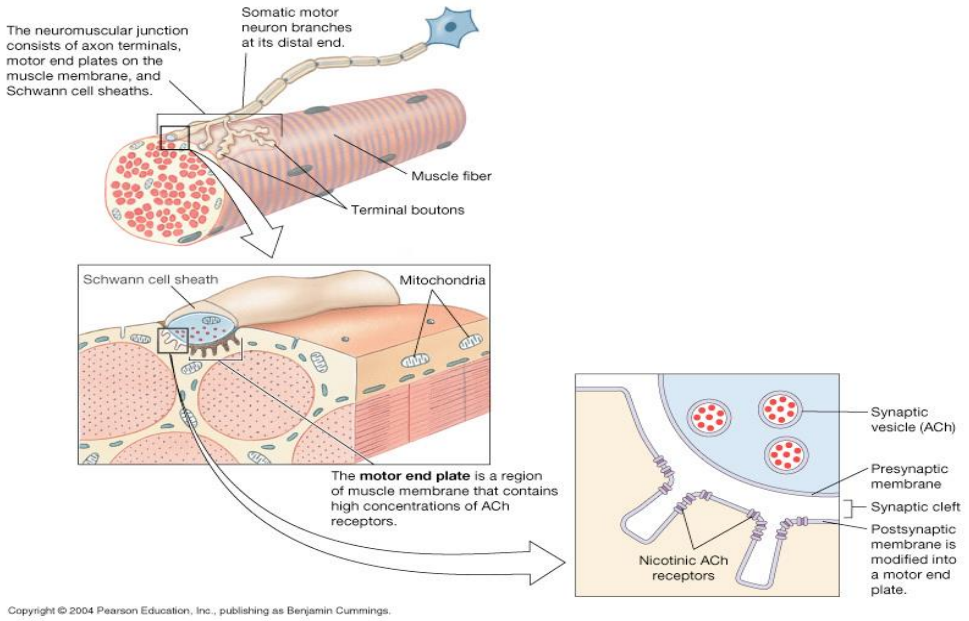


CONTRACTED:



Myoneural junction (Neuromuscular Junction)

There are no structural junction between nerves & muscles which together forms locomotion system, but the junction are functional or physiological. Before motor nerves attach muscles fiber , it branches into many fine fibers, flattened and ended at specialized region on sarcolema called *motor end plate*, each branch innervates one myofibril to form motor unit (which is assume of muscle myofibrils in the unit that attach to one motor nerve fiber by its branches). The region of nerve –muscle communication is called *neuromuscular junction*.



Neuromuscular Transmission

- The Neuromuscular Junction -

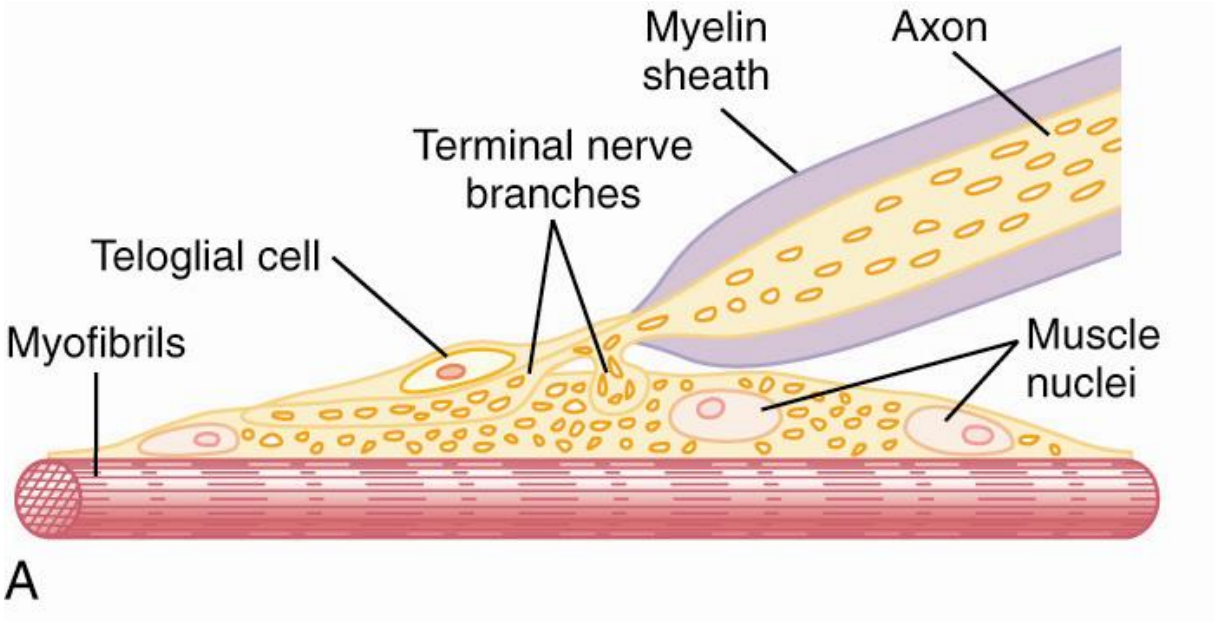


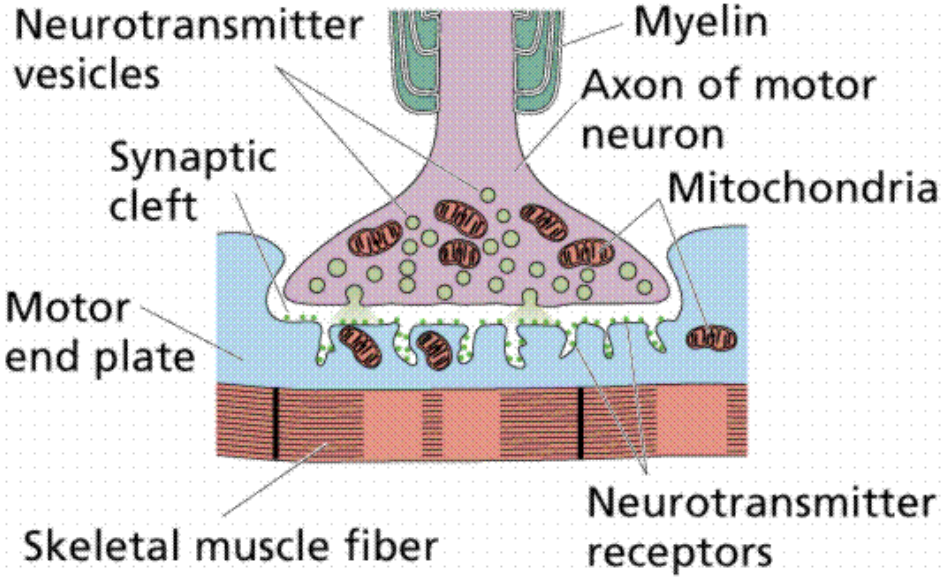
Figure 7-1; Guyton & Hall

- Specialized **synapse** between a **motoneuron** and a muscle fiber
- Occurs at a structure on the muscle fiber called the **motor end plate** *(usually only one per fiber)*

Mechanism of neuromuscular action

When nerve impulse reach the end of the nerve fiber branch, triggers release of Neurotransmitter(ACH) from synaptic vesicles , which diffuses across neuromuscular junction and binds with certain receptors at motor end plate on sarcolema & altered muscle fiber polarity to produce contraction.

Relaxation follows contraction by break down of neurotransmitter with action of acetylcholinestrase and repolarization of muscle fibers.



Membrane potential

muscle & nerve fibers are electrically excitable that mean show voltage changes after stimulation

Electrical potential at resting state called resting membrane potential RMP : is that energy results from a polarized state . RMP is measured in mV , and normally remained by Na-K pump, which removes 3 Na ions from the cell for every 2 K ions it bring in.

and determined by:

1- Diffusion of ions down their concentrations gradients.

2- Selective permeability of plasma membrane.

3-electrostatic attraction.

Action membrane potential

When muscle & nerve cell stimulated Na-K pump (ion gates) open, Na ions rush in and K ions rush out, resulting in changes membrane voltage called action potential .

Resting membrane potential is that energy results from *a polarized state*, where as action potential resulting *in changes membrane voltage* .

*Steps of a skeletal muscle contraction & Relaxation

1- muscle & nerve fibers are electrically excitable (show voltage changes after stimulation)

1-An action potential reaches the axon of the motor neuron, activates voltage gated calcium ion channels on the axon, and calcium rushes in.

2-The calcium causes ACH vesicles in the axon to fuse with the membrane, releasing the ACH into the cleft between the axon and the motor end plate of the muscle fiber.

3-The skeletal muscle fiber is excited by large mylenated nerve fibers which attach to the NM junction. There is one NM junction for each fiber.

4-The ACH diffuses across the cleft and binds to nicotinic receptors on the motor end plate, opening channels in the membrane for sodium and potassium. Sodium rushes in, and potassium rushes out. However, because sodium is more permeable, the muscle fiber membrane becomes more positively charged, triggering an action potential.

5-The action potential on the muscle fiber causes the SR to release calcium ions(Ca++).

6-The calcium binds to the troponin present on the thin filaments of the myofibrils. The troponin then allosterically modulates the tropomyosin. Normally the tropomyosin physically obstructs binding sites for cross-bridge; once calcium binds to the troponin, the troponin forces the tropomyosin to move out of the way, unblocking the binding sites.

7-The cross-bridge binds to the newly uncovered binding sites. It then delivers a power stroke.

8-ATP binds the cross-bridge, forcing it to conform in such a way as to break the actin-myosin bond. Another ATP is split to energize the cross bridge again.

9-Throughout this process, the calcium is actively pumped back into the SR. When no longer present on the thin filament, the tropomyosin changes back to its previous state, so as to block the binding sites again. The cross-bridge then ceases binding to the thin filament, and the contractions cease as well.

Contraction

1-An action potential reaches the axon of the motor neuron, activates voltage gated calcium ion channels on the axon, causes ACH releasing
2- ACH diffuses into the cleft neuromuscular junction.
3-The ACH binds to nicotinic receptors on the motor end plate stimulating sarcolema, opening channels in the membrane for sodium and potassium.
inducing action potential on the muscle fiber surface that travel deep into fibers through T – tubules , reaching the SR.
4- SR release calcium ions(Ca++).
5-The calcium binds to the troponin present on the thin filaments of the myofibrils.
6- troponin-tropomyosin complex moves to shift aside exposing active sites on actin for myosin binding
7-Actin and myosin form linkages.
8- Actin filaments are pulled inward by myosin cross- bridges, leading to shorting muscle fibers as contraction.

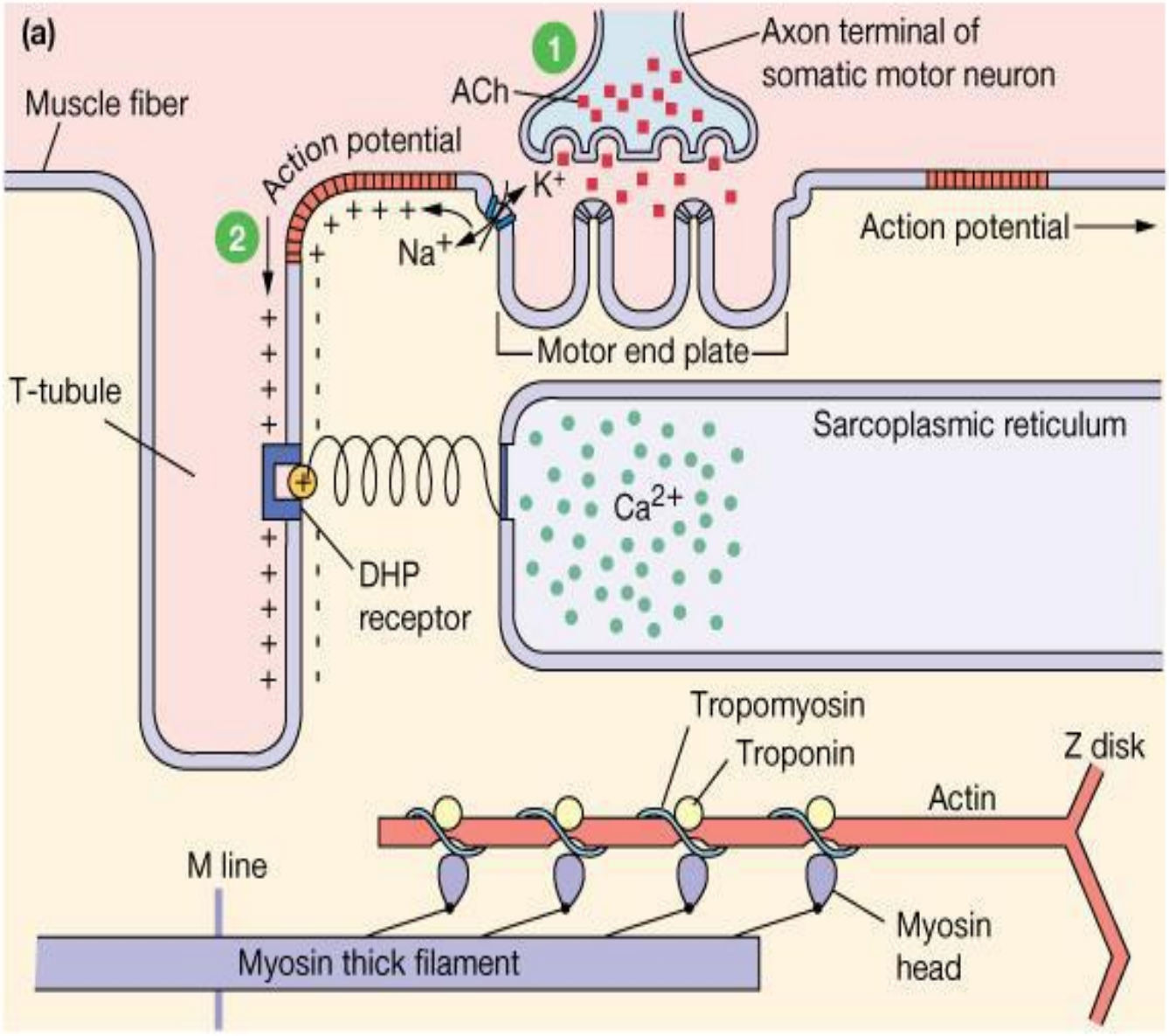
Relaxation

1-Acetylcholineestrase secreted from motor neuron ends, decomposing ACH, and the muscle fibers stimulation stopped.

2- Ca ions actively transported into SR.

3-ATP causes linkages between Actin & Myosin filaments to break.

4-Troponin & tropomyosin molecules inhibit the interaction between actin & myosin, and muscle fiber return to relaxation until stimulated again.



1 Somatic motor neuron releases ACh at neuro-muscular junction.

2 Net entry of Na^+ through ACh receptor-channel initiates a muscle action potential.

Sliding Filament theory

1-During muscle contraction phase , the actin myofilaments is pulled over myosin toward the center of the sarcomere until the actin and myosin filaments are completely overlapped.

2- The head of each myosin molec. Contain myosin ATPase that release energy from ATP, when active sites of actin exposed, myosin heads contacts with it, releasing energy as power stroke for actin sliding over myosin.

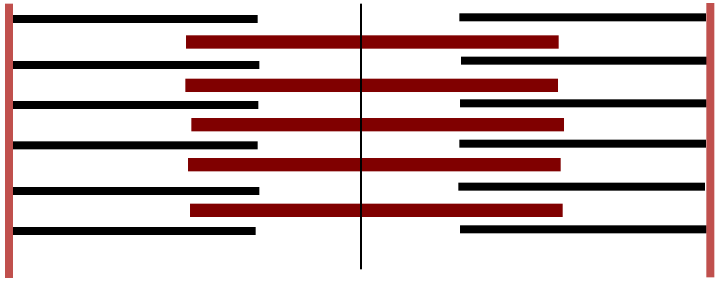
3-The H zone becomes smaller and smaller due to the increasing overlap of actin and myosin filaments, and the muscle shortens. Thus when the muscle is fully contracted, the H zone is no longer visible . Note that the actin and myosin filaments themselves do not change length, but instead slide past each other.

***According to *sliding filament theory*, the Z lines of skeletal muscle fibers move closer together when a muscle contracts because of sliding actin filament over myosin filaments, this process shortens the sarcomere and utilize energy in form of ATP by *ATPase* enzyme which need calcium as cofactor , the combined decrease in length of all myofibrils sarcomeres a count for muscle contraction.**

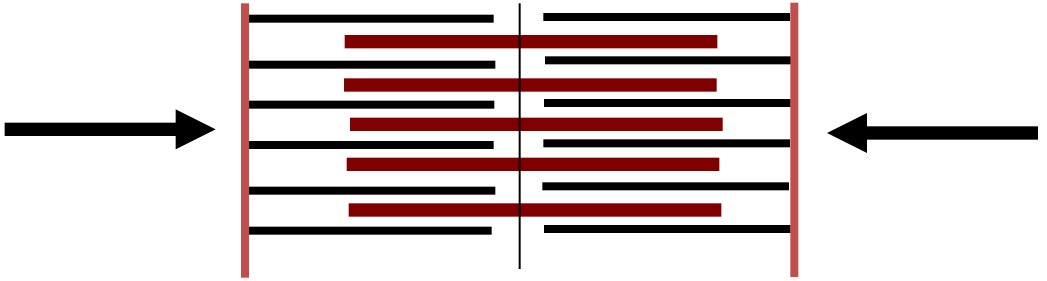
“Sliding Filament” Mechanism

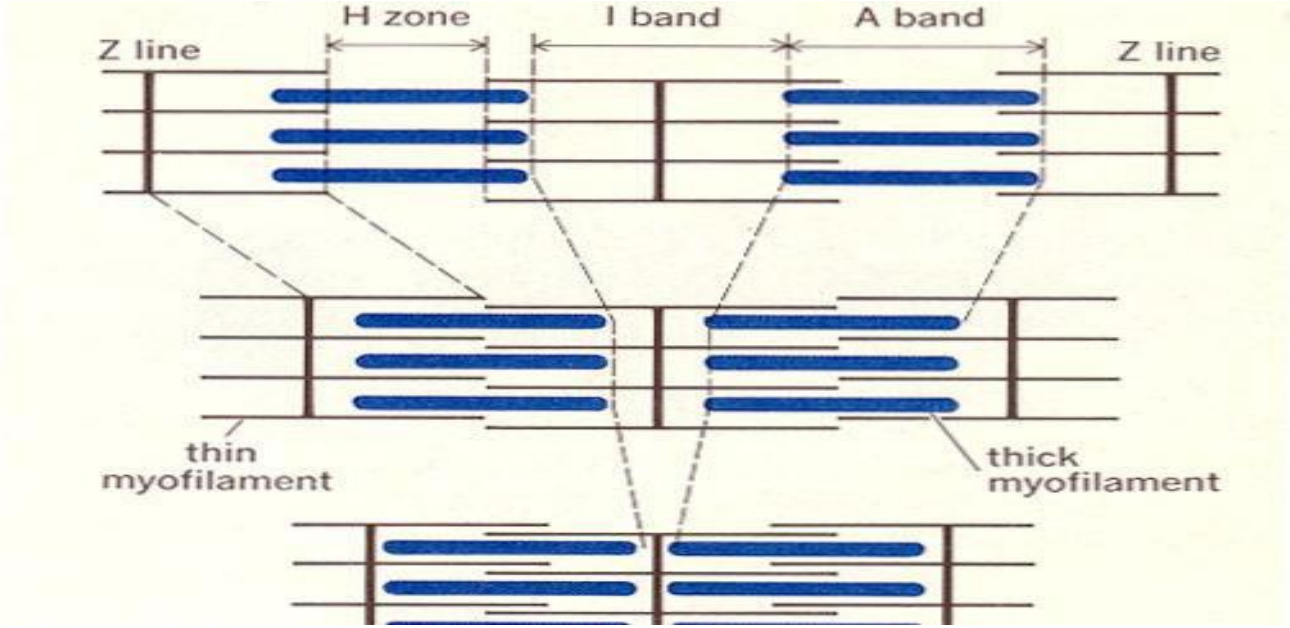
Contraction results from the sliding action of interdigitating actin and myosin filaments

RELAXED:



CONTRACTED:




H zone
I band
A band
Z line
Z line
thin
myofilament
thick
myofilament

Role of calcium in muscle function

1-Calcium is the so called "trigger" for muscle contraction.

2-Calcium aids in the formation of action potential in the motor end plate, and is later released from the terminal cisternae of the sarcoplasmic reticulum into the cytosol of a striated (cardiac and skeletal) muscle cells.

3-Next the calcium ions bind to troponin which causes a change in the conformation of the troponin-tropomyosin complex that exposes the myosin binding sites on the actin filament. The myosin heads then attach to the actin filament and a muscle contraction occurs.

4- In smooth muscle, the influx of calcium leads to depolarization. The calcium binds to calmodulin, causing the calmodulin-caldesmon complex to change its confuguration and pull the caldesmon away from the myosin binding sites on the actin strand. Muscle contraction follows because the myosin heads bind to the actin.

How does an action potential initiate a muscle contraction?

The nerve generates an action potential and it arrives at the axon terminal where it causes a change in the voltage of the axon terminal membrane, thereby causing the calcium channels to open. This allows calcium ions to enter the axon terminal which causes the release of ACh (acetylcholine). As the ACh is released it attaches to the **motor end plate** and the calcium ions are pumped out of the **axon terminal**. Next, the chemically regulated ion channels on the motor end plate open and an influx of sodium ions, and efflux of potassium ions occurs. This causes a depolarization of the motor end plate. The ACh diffuses from the motor end plate and the ion channels close. The depolarization of the motor end plate then moves along the **sarcolemma** and down the**T-tubules**. This depolarization of the T-tubules causes the **terminal cisternae** to release calcium ions into the cytosol of the muscle cell. The calcium binds with troponin and causes the tropomyosin complex to shift, thereby exposing the myosin head binding sites and allowing the myosin heads to attach and perform a "power stroke", or contraction.

Muscle Contraction Summary

- Nerve impulse reaches myoneural junction
- Acetylcholine is released from motor neuron
- Ach binds with receptors in the muscle membrane to allow sodium to enter
- Sodium influx will generate an action potential in the sarcolemma
- Action potential travels down T tubule
- Sarcoplamic reticulum releases calcium
- Calcium binds with troponin to move the troponin, tropomyosin complex
- Binding sites in the actin filament are exposed
- Myosin head attach to binding sites and create a power stroke
- ATP detaches myosin heads and energizes them for another contaction
- When action potentials cease the muscle stop contracting

Types of Contractions:

Isometric contraction--muscle does not shorten during contraction and does not require the sliding of myofibrils but muscles are stiff. Isometric Contraction, Produces no movement, Used in, Standing, Sitting, Posture

Isotonic contraction-- is used to move or work. More energy is used by the muscle and contraction lasts longer than isometric contraction. Produces movement Used in , Walking, Moving any part of the body

Excitation Contraction Coupling

Like most excitable cells, muscle fibers respond to the excitation signal with a rapid depolarization which is coupled with its physiological response:

Resting Potential

If we remember that myofibers are basically water with some dissolved ions separated from the extracellular space, which is also mostly water with some dissolved ions, then the presence of a resting potential may make more sense. In much the same way as a battery creates an electrical potential difference by having different concentrations of ions at its two poles, so does a muscle cell generate a potential difference across its cell membrane. The ATP driven sodium-potassium pump maintains an artificially low concentration of sodium and high concentration of potassium in the intracellular space, which generates a resting potential difference on the order of -75 mV.

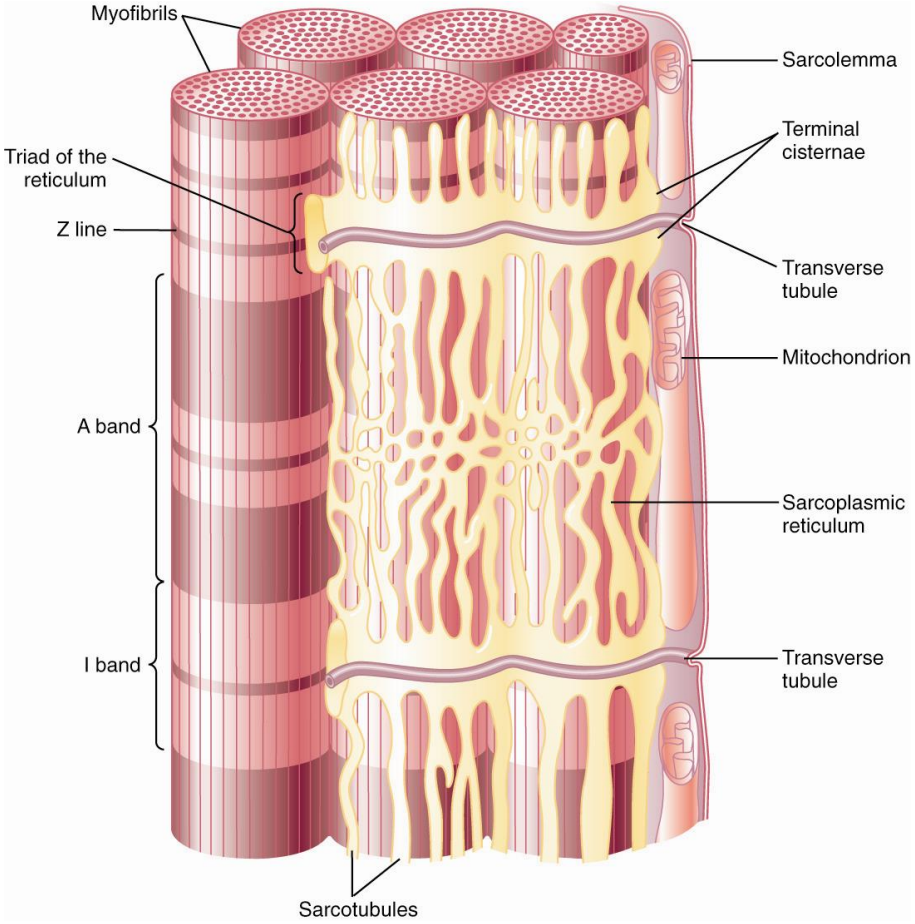
Excitation-Contraction Coupling

T-tubules:

- Invaginations of the **sarcolemma** filled with extracellular fluid
- Penetrate the muscle fiber, branch and form networks
- Transmit AP's deep into the muscle fiber

Sarcoplasmic Reticulum:

- terminal cisternae and longitudinal tubules
- **terminal cisternae** form junctional "feet" adjacent to the T-tubule membrane
- intracellular storage compartment for **Ca^{2+}**



Depolarization

Depolarization is achieved by other transmembrane channel proteins. When the potential difference near these voltage sensitive proteins reaches a threshold level, the protein undergoes a magical conformational change that makes the membrane permeable to sodium. Extracellular sodium immediately rushes in, drawn by both the charge difference and concentration gradient, and locally depolarizes the cell. Almost immediately, potassium also moves along in concentration gradient - out of the cell -- and the membrane potential is restored.

As an interesting side note, this is the mechanism by which potassium chloride is used to induce cardiac arrest: by eliminating the potassium concentration gradient, the depolarized cardiac muscle cells are unable to repolarize for their next beat. Coordination of Depolarization

This depolarization is an extremely localized phenomenon, depending on diffusion over a few milliseconds. Some system is required to carry this signal to the myofibrils deep within the cell body. The sarcolemma, or cell membrane, invaginates to form a network of transverse (or T-) tubules that span the cross section of each fiber, transmitting the depolarization signal uniformly throughout the cell.

From Depolarization to Contraction

Contraction is regulated by calcium ion concentration. In the resting state, a fiber keeps most of its intracellular calcium carefully sequestered in an extensive system of vessicles known as the sarcoplasmic reticuluum. There are at least two receptors in the chain between depolarization and calcium release. Once released, calcium binds to troponin, opening the myosin binding sites on filamentous actin, and force is produced.

- **Smooth Muscle Contraction**
- **Contractions are initiated by an influx of calcium which binds to calmodulin.**
- **The calcium-calmodulin complex binds to and activates myosin light-chain kinase.**
- **Myosin light-chain kinase phosphorylates myosin light-chains using ATP, causing them to interact with actin filaments.**
- **Powerstroke**
- **Calcium is actively pumped out of the cell by receptor regulated channels. A second messanger, IP3, causes the release.**
- **As calcium is removed the calcium-calmodulin complex breaks away from the myosin light-chain kinase, stopping phosphorylation.**
- **Myosin phophatase dephosphorylates the myosin. If the myosin was bound to an actin molecule, the release is slow, this is called a latch state. In this manner, smooth muscle is able to stay contracted for some time without the use of much ATP. If the myosin was not bound to an actin chain it loses its affinity for actin.**
- **It should be noted that ATP is still needed for crossbridge cycling, and that there is no reserve, such as creatine phosphate, available. Most ATP is created from aerobic metabolism, however anaerobic production may take place in times of low oxygen concentrations.**

***Cardiac muscle contractions**

The contraction is due to an increase in the cytoplasmic concentration of Calcium ions.

the release of Ca+ ions from the sarcoplasmic reticulum binds to troponin which allows actin to bind with myosin.

The difference between skeletal muscle and cardiac muscle is that when the action potential opens voltage gated calcium ion channels in the T-tubules. The increase in cytosolic calcium causes calcium ions to bind to receptors on the surface of the sarcoplasmic reticulum. The binding of calcium ions to these receptors causes the opening of more calcium ion channels in the SR membrane. Calcium ions then rush out of the SR and bind to troponin and allow the myosin and actin to bind together which causes contraction. This sequence is called calcium-induced calcium release. Contraction ends when the level of cytosolic calcium returns to normal resting levels.

Tetanus and Fatigue

tetanus

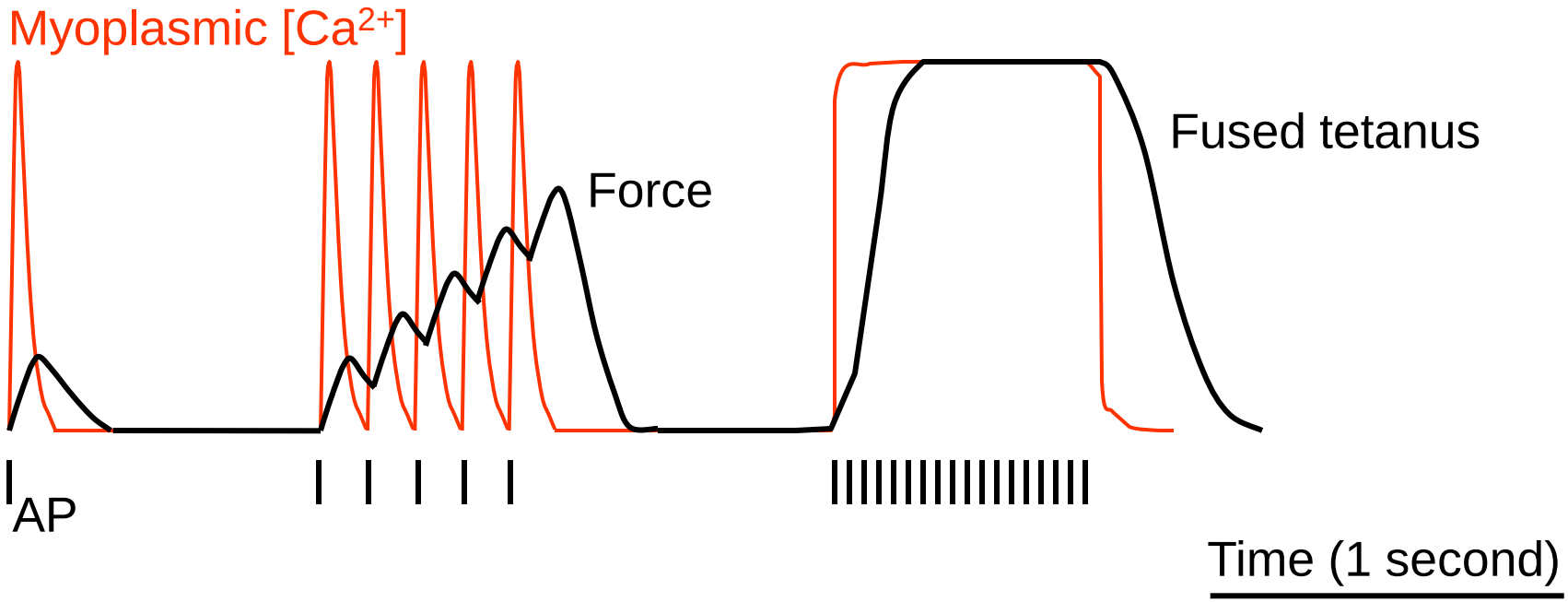
when muscle stimulated continuously with successive stimulus with time period between them not enough for muscle contraction & relaxation,

the affects of the successive stimulus assumes with each other and cause continuous contraction of the muscle, this case of contraction is called *tetanic contraction or tetanus*.

Muscle Fatigue

Long period repeated contraction of skeletal muscle, lead to enter the muscle into a phase that the muscle loss ability for contraction or response to farther stimulation and it gradually returns to its resting length, this phenomenon called *muscle fatigue.*

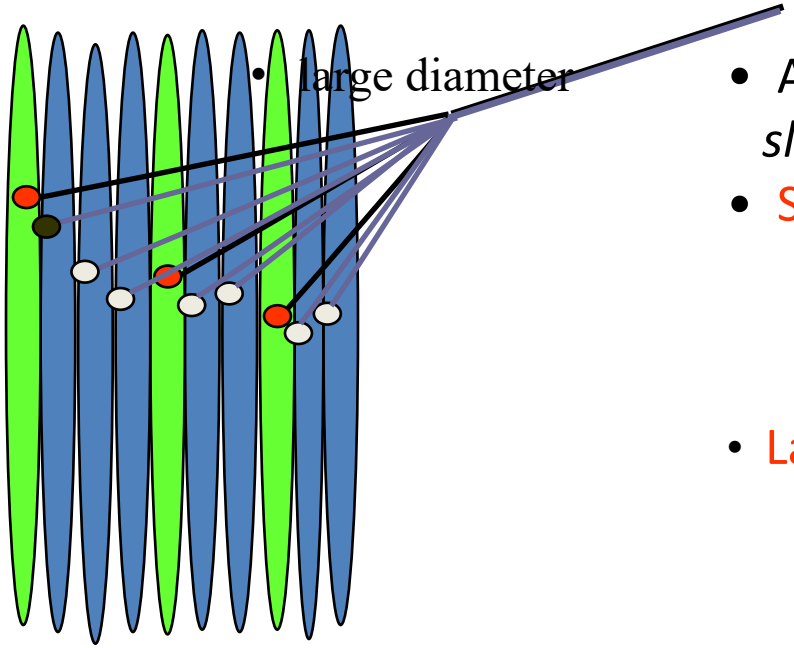
Frequency Summation of Twitches and Tetanus



- Myoplasmic Ca^{2+} falls (initiating relaxation) before development of maximal contractile force
- If the muscle is stimulated before complete relaxation has occurred the new twitch will sum with the previous one etc.
- If action potential frequency is sufficiently high, the individual contractions are not resolved and a ‘fused tetanus’ contraction is recorded.

Motor Unit:

A collection of muscle fibers innervated by a single motor neuron



- All fibers are same type *(fast or slow)* in a given motor unit
- Small motor units *(eg,larnyx, extraocular)*
  - as few as 10 fibers/unit
  - precise control
  - rapid reacting
- Large motor units *(eg, quadriceps muscles)*
  - as many as 1000 fibers/unit
  - coarse control
  - slower reacting
- Motor units overlap, which provides coordination
- Not a good relation between fiber type and size of motor unit

- **Thermal physiology Temperature effects on animals , Animal types according to body temperature**

Thermoregulation , Thermoregulation in birds and mammals , Measurement of body heat production , Types of thermoregulation mechanism, Problems of poikilotherms , Thermoregulation in humans, Sources of body heat production (how heat produced) , Body size and metabolic rates, Thermal tolerance, Lower lethal temperatures , Mechanisms of cold death , Upper lethal temp. , Mechanisms of heat death , Q10 , Mechanisms of regulation of body temperature change, Thermoneutral zone , Hibernation in animals , Role of sweating in thermoregulation , Thermoregulatory center , Adaptation , Acclimatization , Acclimation

Thermal physiology

Effects of temperature on animals *:*

1-Temperature affects the rates of most physical, biochemical, and physiological functions in animals.

2-Play a role in both its distribution and activities of animals ,

there for normal body function related to normal temp. and temp.should be regulated for normal body functions.

3-Most animals must maintain temperature above 0º C and below 45 because proteins tend to denature above 45º C .

4-Temperature conformers operate at the extremes of temperature.

- **Arctic aquatic animals can function with tissue temperatures of -1.9°C.**
- **Insects can endure tissue temperatures of -60° to -70°C**
- **Lizards in the desert can function at tissue temperatures of 45° to 52°C.**

Animal types according to body temperature :

According to ability of animals to regulate their body temp. are of 2 types :

1- Thermoregulaters*:* animals that keeps its core body temperature within certain limits not changed with environmental temp.

2- Thermoconformers : animals changes its body temperature with changes in the outside temperature .

On the basis of the sources of heat that determine the body temperatures animals classifies into :

1-Ectothermic: depend largely on external sources of heat, such as solar radiation, to maintain their body temperature above the environmental temperature. temperature comes mostly from the environment.

2-Endothermic: create most of their heat via metabolic processes. Mammals and birds are endotherms; most other animals behave as ectotherms most of the time.

Also animals can be classified by their response to environmental temperatures into:

1-Homeotherm: Animal that maintains a constant body temperature over a wide range of environmental temperatures

2- Poikilotherm: Animal whose body temperature changes when the temperature of its environment changes

3- Heterotherm: Animal that maintains a constant body temperature some of the time

Thermoregulation

Is the ability of an animal to keep its body temperature within certain boundaries, even when surrounding temperature is very different.

This process is one aspect of homeostasis which is(A dynamic state of stability between an animal's internal environment and its *external* environment).

If the body is unable to maintain a normal temperature and it increases significantly above normal, a condition known as hyperthermia . And when body temperature decreases below normal levels, is known as hypothermia.

Thermoregulation in birds and mammals

In cold environment, birds and mammals employ the following adaptations to minimize heat loss:

1-Using small smooth muscles contractions which are attached to feather or hair shafts leading to thermogenesis by distorts the surface of the skin as the feather/hair shaft is made more erect .

2- Increasing body size to more easily maintain core body temperature (warm-blooded animals in cold climates tend to be larger than similar species in warmer climates).

3-Having the ability to store energy as fat for metabolism.

In warm , birds and mammals employ the following adaptations to maximize heat loss:

1-Behavioural adaptations like living in burrows during the day and being nocturnal.

2-Evaporative cooling by perspiration and panting.

3-Storing fat reserves in one place to avoid its insulating effect.

4-Elongated, often vascularized extremities to conduct body heat to the air

Types of thermoregulation mechanism

There are two types of thermoregulation mechanisms that are used by animals:

1-Physiological or chemical thermoregulation: This is mechanisms of changes body physiology to regulate body temperature either by increasing or decreasing its metabolic reaction. For example, many **Endothermy** tend to sweat in order to lower temperature, muscles may shiver in order to produce heat.

2-Behavioral or physical thermoregulation: This is changes in behavior to change its body temperature. For example, when **Ectothermy** animals warm up in direct sunlight, they may wish to find shade to cool down.

Measurement of body heat production

Direct calorimetry:Mean Direct measuring of kilocalories of heat arise from the body \ time

Indirect calorimetry: Mean measuring of O2 consumed or CO2 produced from the body \ time

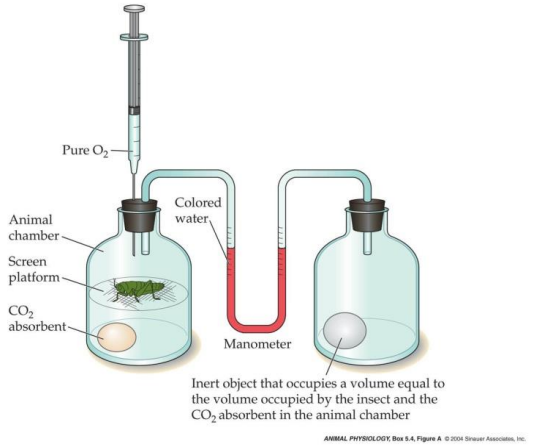


TABLE 6.3 Some factors that affect the metabolic rates of individual animals *(Part 2)*

Factor	Response of metabolic rate	Chapter(s) where discussed in this book
Factors that exert smaller effects		
Ingestion of a meal (particularly protein-rich)	↑ for several hours to many hours following ingestion	6
Body size	Weight-specific rate ↑ as size ↓	6
Age	Variable; in humans, weight-specific rate ↑ to puberty, then ↓	—
Gender	Variable; in humans, ↑ in male	—
Environmental O_2 level	Often ↓ as O_2 ↓ below a threshold, not affected above threshold	7, 22
Hormonal status	Variable; example: ↑ by excessive thyroid secretions in mammals	15
Time of day	Variable; in humans, ↑ in daytime	14
Salinity of water (aquatic animals)	Variable; in osmoregulating marine crabs, ↑ in dilute water	27

Thermal Problems of poikilotherms

Because of changes of body temperature, Therefore Ii poikilotherms

the cold is the main problem of their distribution in various ecosystems especially in cold environments .

For species maintenance and continuity poikilotherms animals exhibit some modes as :

1- producing large number of eggs before their death due to the cold at winter season , the eggs hatch after the cold season .

2-living at deep in aquatic environments to avoid freezing effect of the surface water.

3- some of these animals hibernate during cold seasons.

Thermoregulation in humans

Thermoregulation is an important aspect of human homeostasis.

Most body heat is generated in the deep organs as liver, brain, and heart & skeletal muscles.

For humans adaptation to varying climatic conditions two modes utilized :

1- Physiological mechanisms as a by product of evolution.

2- Conscious development of cultural adaptations.

Heat gain & loss

Four modes of heat loss and gain exhibited : convection, conduction, radiation, and evaporation in order to balance & maintain body temperature.

If skin temperature is greater than that of the surroundings, the body can lose heat by radiation and conduction. But if the temperature of the surroundings is greater than that of the skin, the body actually *gains* heat by radiation and conduction.

Also in hot conditions sweat glands secrete sweat. This causes heat loss via evaporative cooling phenomenon.

There fore the skin assists in homeostasis , it does this by reacting differently to hot and cold conditions, so that the inner body temperature remains more or less constant.

Vasodilation and sweating are the primary modes by which humans attempt to lose excess body heat. Arterioles vasodilation occurs, by relaxation of smooth muscle in arteriole walls allowing increased blood flow through the artery. This redirects blood into the superficial capillaries in the skin increasing heat loss by convection and conduction.

Mechanisms to reduce body heat

1-Cutaneous vasodilatation.

2-Sweating.

3-Hyperventilation due to respiratory centre stimulation.

4-Decreased activity to reduce metabolic heat production.

5-Thermoregulatory mechanism.

Sources of body heat production (how heat produced)

1-**Basic metabolic processes (metabolic heat production).**

2-Metabolically active tissues as liver, kidneys, brain, heart.

3-Food intake by specific dynamic action.

4-Muscular activity.

Metabolic rate depends on:

The metabolic rate is the rate of energy consumption or the rate at which an animal converts chemical energy into heat and external work.

The metabolic rate affected by following factors :

Sex , Age , Muscular activities, Recent food ingestion, environmental temperature , surface area ,Growth , Reproduction state , Lactation, Emotional state , Body temperature , Circulating levels of thyroid hormones, Circulating catecholamine levels.

Body size and metabolic rates

Body size is the most important factor affects metabolism.

Small size animals must respire at higher rates per unit of body mass than larger animals.

Also, there is an inverse relationship between O2 consumption per gram of body mass and the total mass of the animal.

Thermal tolerance

Living cells can function over only a narrow range of temperatures. If cells cool to below 0°C, ice crystals formed damage their structures.

Some animals have adaptations, such as containing antifreeze molecules in their blood, that help them resist freezing; others have adaptations that enable them to survive freezing. Generally, cells must remain above 0°C to stay alive.

The upper temperature limit is less than 45°C for most cells. Some specialized algae can grow in hot springs at 70°C, and some archaea can live at near 100°C, but in general, proteins begin to denature and lose their function as temperatures approach 45°C. Therefore, most cellular functions are limited to the range between 0°C and 45°C, which are considered the upper and lower thermal limits for life.

Thermal death

If an organism cannot regulate its body temperature , then it phace two problems:

1. **Lethal temperature effect .**
2. **Disturbance of body activities .**

Lethal temperature (LT 50) is defined as(that temperature at which 50% of organisms exposed to it die.

LT50, depends on exposure time, some organisms may be killed by a long exposure to a temperature that they would survive for a short period.

Prolonged exposure to less extreme temperatures usually increases thermal tolerance, as a result of organisms adjust to the new temperature.

Lower lethal temperatures

Many ectoderms adapted to survive & even function normally at low temperature . Some tropical species are less tolerant of low temp. , especially aquatic species , they died due to exposed to cold as a result of freezing, but some ectoderms accumulate high concentrations of specific solutes in their fluides to lower their freezing point , theses solutes typically:

1. Sugars – glucose, fructose, trehalose
2. Sugar alcohols – glycerol, sorbitol.

Mechanisms of cold death

The death of the animals resulted by exposure to colds called cold death , these case resulted by these mechanisms:

1- Freezing formig ice crystals leading to the mechanical injiury of the cell structure .

2- Lowring of Hb and O2 combination affenity.

3- Disregulation of the body fluids ionic and osmotic balance.

Upper lethal temp.

Many ectotherms adapted to survive & even function normally at high temp. , but most of them tolerance of high temperautre are limited , even died due to hot as a result of hot.

Mechanisms of heat death

The death of the animals resulted by exposure to heat called heat death , these case resulted by these mechanisms:

1-Protein denaturation – permanent loss of function of enzymes.

2. Thermal inactivation – reversible loss of enzyme activity faster than synthesis.

3. Failure of oxygen supply. Can be disproved by increasing the partial pressure of oxygen.

4. Failure of metabolic regulation.

5. Loss of membrane function. Cell membranes are lipid bilayer with attached proteins, held together by weak interactions of several types.

6- Dehydration in terrestrial animals.

*Q*10 :

Is a measure of temperature sensitivity of animals body biochemical reactions or process to the surrounding temperature. It mean changes in body temperature in response to changes in environmental temperature by 10 degree.

Terms of *Q*10, calculated by dividing the rate of a reaction at a certain temperature, by the rate of that reaction at a temperature 10°C lower,

***Q*10 can be measured for a simple enzymatic reaction or for a complex physiological process, such as rate of oxygen consumption.**

Most biological *Q*10 values are between 2 and 3.

A *Q*10 of 2 means that the reaction rate doubles as temperature increases by 10°C, and a *Q*10 of 3 indicates a tripling of the rate by 10°C increasing in temperature .

If a reaction or process is not temperature sensitive, it has a *Q*10 of 1.

- $Q_{10} = {}^{R}T / {}^{R}T\text{-}10$
  - **rate of a reaction at temperature R_T divided by the rate of the same reaction 10º C lower**

Mechanisms of regulation of body temperature change

There are several ways that an animal can absorb or lose heat from or to the environment: conduction, convection, radiation, and evaporation.

1-Conduction :Is the transfer of heat between objects and substances that are in contact with each other. The transfer of heat from the skin surface to molecules of gas in the air is an example of conduction.

2- Convection :Is the transfer of heat contained in a mass of a gas or liquid, by the movement of that mass. A simple example of this is when you sit in front of a fan on a hot day and the movement of air takes the heat away.

3-Radiation : Is the transfer of heat through electromagnetic radiation without objects coming into contact. An example of radiation is the warming that can occur to animals in sunlight.

4-Evaporation: Is a change in state from liquid to gas, which requires energy. Heat is dissipated from the body during evaporation because large water molecules with high energy content accumulate at the skin surface and enter the gaseous phase. When the larger molecules vaporize, they take thermal energy with them and any water left behind becomes cooler.

The amount of heat that will transfer into or out of an animal depends on :

- **Surface area**
- **Temperature difference,**
- **Specific heat conductance of an animals body surface.**

Thermoneutral zone

Is a range of environmental temperature at which the animal not loss or gain any heat or it mean ,range of temperatures that are optimal for physiological processes.

At TZ metabolic rate is minimal and at this range the endothermic animals not gain or loss temp.

The metabolic rate of a resting animal at a temperature within the thermoneutral zone is called the basal metabolic rate BMR.

Hibernation in animals

Hibernation mean a reduction in body activities or metabolic rate to offers an energetic advantage during these states.

During hibernation, thermoregulatory control continues with a lowered set point and reduced sensitivity. With the lowered body temperature characteristic of hibernation, body functions are greatly slowed. All true hibernators are mid-sized mammals weighing at least several hundred grams and large enough to store sufficient reserves for extended hibernation.

Role of sweating in thermoregulation

Evaporative heat loss through sweating is a very efficient modes for balancing metabolic heat production and heat absorbed from surroundings by radiation and convection.

Secretion of sweat occurs in human when the ambient temperature rises above 30-31°c, and/or when internal body temperature rises above 37°C .

Humans and some primates, and a few other species sweat. Cats and dogs not sweat but pant to cool by evaporation of water .

Thermoregulatory center

Regulation of body temperature is established at temperature-sensitive neurons and nerve endings in the brain in the brain is located in the hypothalamus called Thermoregulatory center. This center act as thermostatic centers.

This center contain heat and cold sensitive specialized receptor cells. This physiological system for thermoregulation operates like an automatic control system that responds to negative feedback.

This system act when the hypothalamus detects temperature change , and it release hormones that essentially carry information to other parts of the body to change their metabolic activities according to body demands for temperature.

Cooling the hypothalamus produced an increase in metabolic rate. Warming the hypothalamus resulted in a decrease in metabolic rate and an increase in heat dissipating mechanisms.

Adaptation , Acclimatization , Acclimation

Adaptation : Physiological, biochemical, or anatomical modifications occurring within a species over several generations that facilitate an enhanced ability to survive and reproduce in a particular environment.

Acclimatization: Physiological, biochemical, or anatomical modifications occurring within the lifetime of an individual organism that result from chronic exposure to a naturally occurring environmental challenge , mean physiological change in response to seasonal climate changes accomplished through metabolic compensation.

Acclimation : Physiological, biochemical, or anatomical modifications within an individual organism that result from exposure to a single environmental factor in a laboratory or field setting ac change in temperature .

Physiology of Reproduction

Male reproductive system , Testes structure , Functions of sertoli cells
Functions of Leydig cells , Epididymis , Ductus Deferens ,
Accessory sex organs:Seminal Vesicles, Ejaculatory Ducts, Prostate Gland, Bulbourethral Glands.
Male Hormone Regulation , Luteinizing Hormone (LH), Follicle-Stimulating Hormone (FSH):
Process of sperm production : Spermatocytogenesis , Spermatidogenesis
Spermiogenesis , Spermiation
Spermatogenesis Hormonal Control Flow Chart , Puberty.

Female Reproductive System

Functions

Hormones of Ovary : Progestin , Estrogens
Mammary glands , The development of mammary glands
The Female Reproductive Cycle , Oogenesis , Infertility ,
Factors of Infertility ,
The Menstrual Cycle
Changes occur to allow parturition

Physiology of Reproduction

Reproduction: Is the process by which organisms create descendants and their species .

Male reproductive system

Male reproductive organs include: (Primary sex organs **&** Accessory sex organs).

Primary sex organs (gonads, Testes)

Testis has two functions:

1- production of sperm, by Spermatogenesis occurs within *Seminiferous tubules*.

2- secretion of androgens by *Leydig cells*, which are found in interstitial spaces between seminiferous tubules . It play a role in:

A-developing secondary sexual characteristics.

B-Involved in feedback mechanisms relating to spermatogenesis.

Testes structure

Each testis contains over 100 yards of tightly packed seminiferous tubules. The seminiferous tubules are the functional units of the testis, where spermatogenisis takes place.

- **Interstitial Cells (Cells of Leydig)**
  In between the seminiferous tubules within the testes, They are responsible for secreting the male sex hormones (i.e., testosterone).
- **Sertoli Cells**
  A Sertoli cell (a kind of sustentacular cell) is a 'nurse' cell of the testes which is part of a seminiferous tubule.
  It is activated by follicle-stimulating hormone, and has FSH-receptor on its membranes.
  Its main function is to nurture the developing sperm cells through the stages of spermatogenesis.

Functions of sertoli cells:

1- Convert androgens into estrogens via the enzyme **aromatase** present in sertoli cells.

2- Secrete androgen binding protein (ABP) & EstrogenBP (EBP).

3-Secrete **inhibin & activin**– which inhibit & stimulate the release of FSH from ant. Pituitary respectively.

4- Secrete **Mullerian regression factor (MRF)** or Mullerian inhibiting substance (MIS) in fetal testes. MRF is responsible for regression of Mullerian duct during sex differentiation in fetus.

Functions of Leydig cells

1-Produce androgens : testosterone, androstenedione and dehydroepiandrosterone (DHEA.

2- Increase spermatogenesis.

3-Influence secondary sexual characteristics.

4-Stimulated to produce androgens by luteinizing hormone (LH)

5-FSH increases the response to LH by Leydig cells

Epididymis

The seminiferous tubules join together to become the epididymis, is coiled. Within the epididymis the sperm complete their maturation and their flagella become functional. This is also a site to store sperm until the next ejaculation.

Ductus Deferens

The ductus (vas) deferens, also called sperm duct, or, spermatic deferens, extends from the epididymis. The smooth muscle layer of the ductus deferens contracts in waves of peristalsis during ejaculation.

Accessory glands functions :

is to secrete seminal fluid (99% of semen volume)

- Components of seminal fluid
  - Mucus
  - Water
  - Nutrients
  - Buffers
  - Enzymes
  - Prostaglandins
  - Zinc

Accessory sex organs:

Seminal Vesicles

The pair of seminal vesicles are posterior to the urinary bladder. They secrete fructose to provide an energy source for sperm and alkalinity to enhance sperm mobility.

Ejaculatory Ducts

There are two ejaculatory ducts. Each receives sperm from the ductus deferens and the secretions of the seminal vesicle on its own side. Both ejaculatory ducts empty into the single urethra.

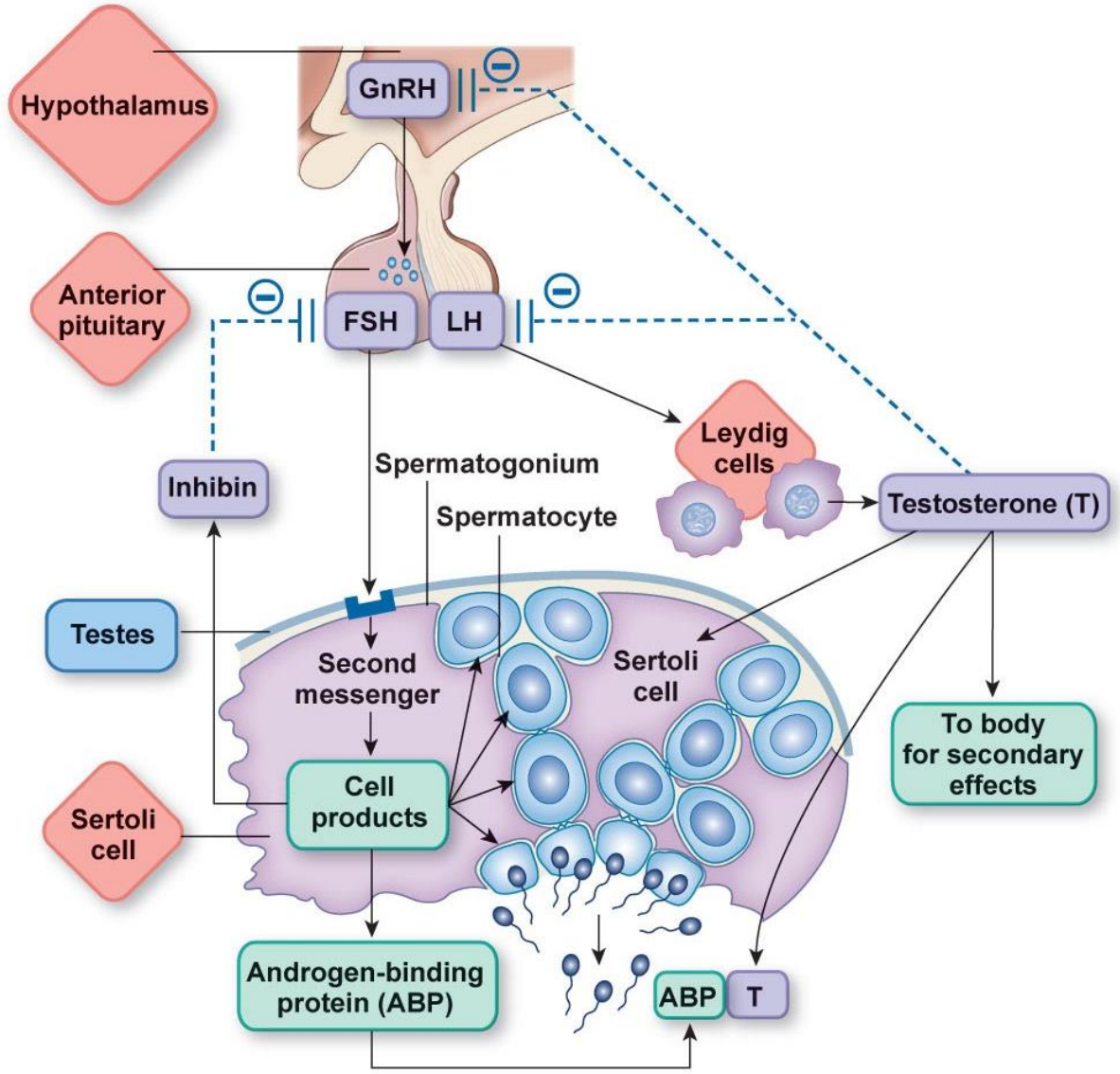
Prostate Gland

The prostate gland is a muscular gland that surrounds the first inch of the urethra as it emerges from the bladder. The smooth muscle of the prostate gland contracts during ejaculation to contribute to the expulsion of semen from the urethra.

Bulbourethral Glands

The bulbourethral glands also called Cowper's glands are located below the prostate gland

Spermatogenesis Hormonal Control Flow Chart



Male Hormone Regulation

Hormones which control reproduction in males are:

Gonadotropin-Releasing Hormone (GnRH), secreted by hypothalamus into the pituitary gland.

There are two gonadotropic hormones, FSH and LH.

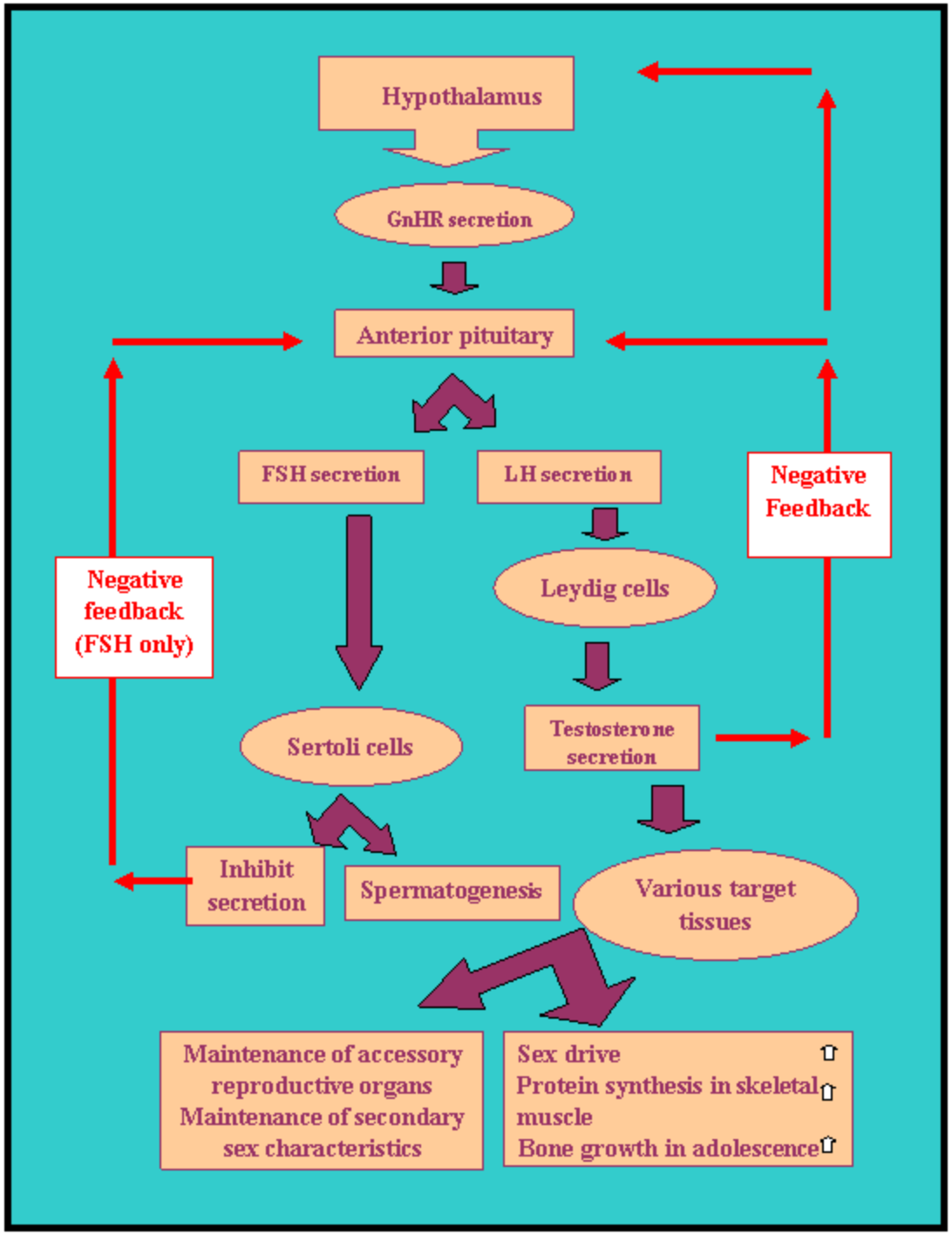
Luteinizing Hormone (LH):

The pituitary gland secretes this hormone after receiving a GnRH signal from the hypothalamus. LH stimulates Leydig cells, in the testes to produce testosterone.

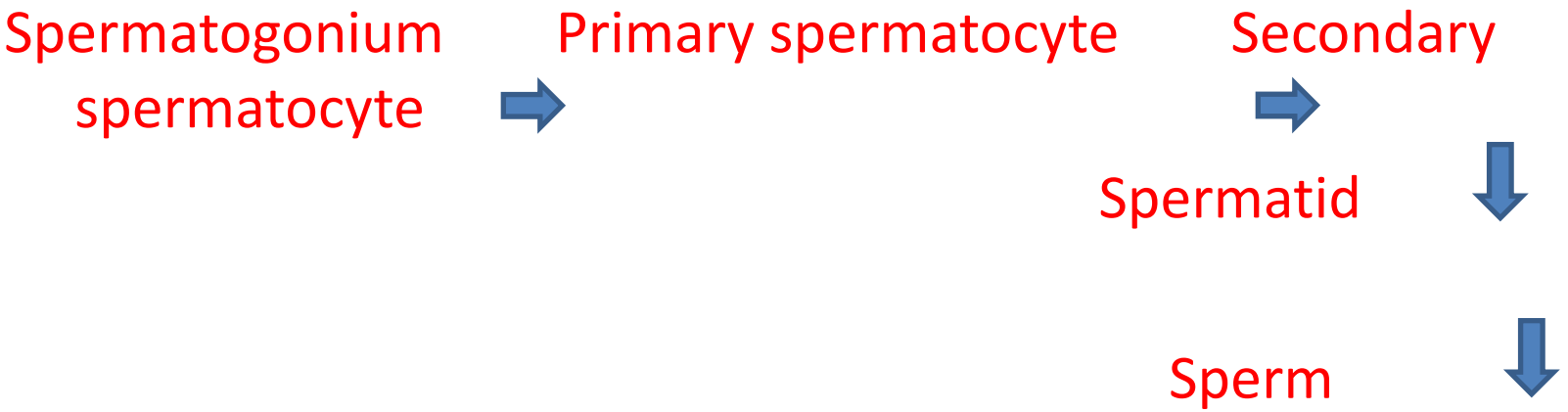
Follicle-Stimulating Hormone (FSH):

The pituitary gland secretes this hormone.

FSH help in maturation of sperm.


Hypothalamus
GnHR secretion
Anterior pituitary
FSH secretion
LH secretion
Negative Feedback
Negative feedback (FSH only)
Leydig cells
Sertoli cells
Testosterone secretion
Inhibit secretion
Spermatogenesis
Various target tissues
Maintenance of accessory reproductive organs
Maintenance of secondary sex characteristics
Sex drive
Protein synthesis in skeletal muscle
Bone growth in adolescence

Spermatogenesis is the process of forming sperm cells by meiosis (in animals, by mitosis in plants) in specialized organs known as gonads (in males these are termed testes). After division the cells undergo differentiation to become sperm cells. Sperm production begins at puberty at continues throughout life, with several hundred million sperm being produced each day. Once sperm form they move into the epididymis, where they mature and are stored.



Process of sperm production: involves three stages

1-Spermatocytogenesis

produces secondary spermatocytes from spermatogoium

2-Spermatidogenesis

stage where meiosis I & II occur

results in spermatid formation

3-Spermiogenesis

final stage of sperm development

spermatid becomes a motile spermatozoa during spermiation

4-Spermiation

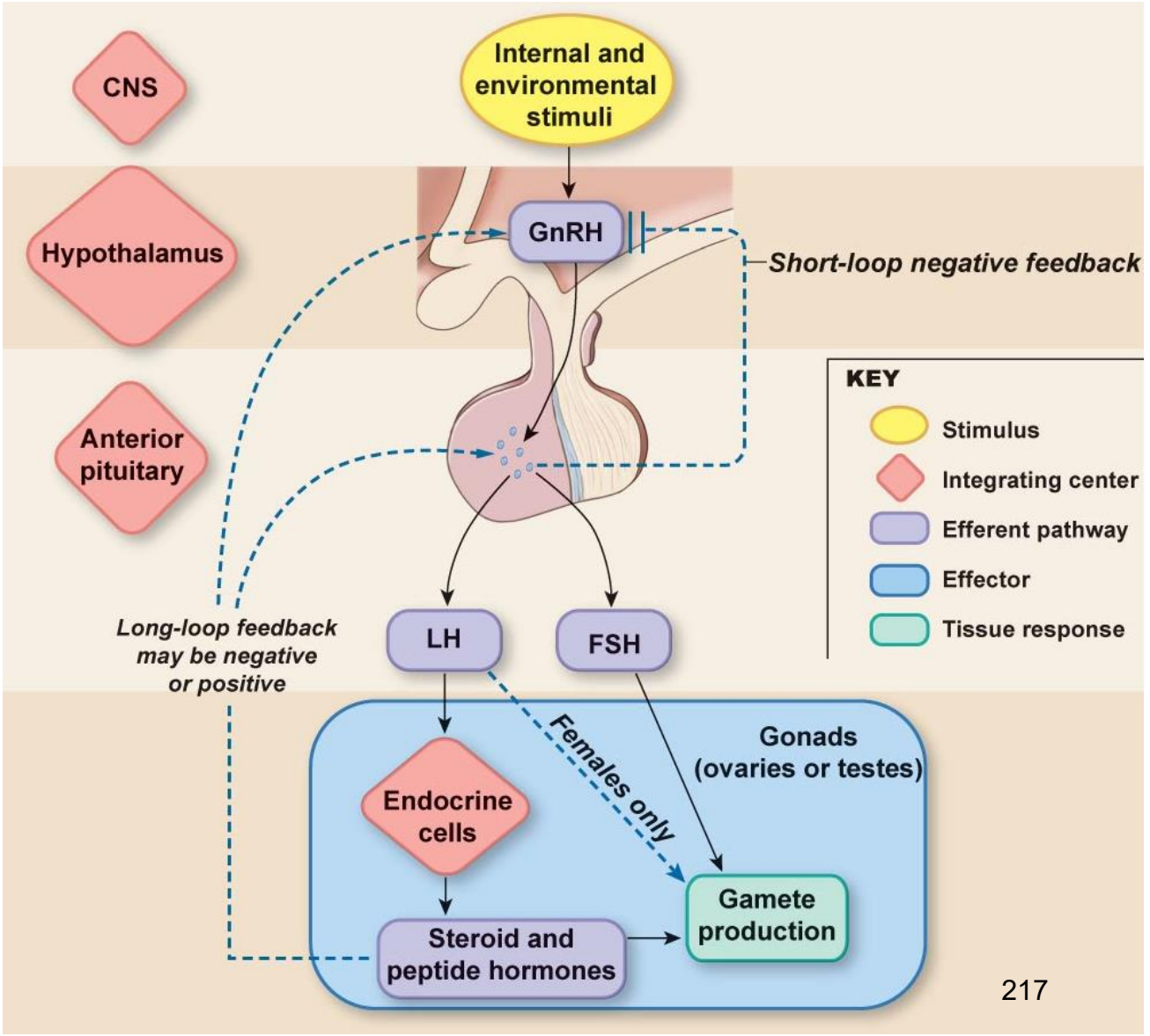
The spermatozoa that are formed are initially unable to move.

The flagella must become motile

Not used however until ejaculated

Prior movement through the male reproductive tract is via peristalsis

The Pituitary-Gonad Axis



Puberty

In addition to producing sperm, the male reproductive system also produces sex hormones, which help a boy develop into a sexually mature man during puberty. the stages of puberty generally follow a set sequence.

First stage: the scrotum and testes grow larger, the *apocrine glands* develop.

Second stage: the external sex organ and the seminal vesicles and prostate gland grow. Hair begins to grow . Reproductive capacity has usually developed by this stage.

Third stage: hair begins to appear on the face and underarms. During this time, a male's voice also deepens. Fertility continues to increase.

Female Reproductive System

Functions

- Produces eggs (ova)
- Secretes sex hormones
- Receives the male spermatazoa during
- Protects and nourishes the fertilized egg until it is fully developed
- Delivers fetus through birth canal
- Provides nourishment to the baby through milk secreted by mammary glands in the breast

Hormones of Ovary

Two of hormones secreted by ovary:

Progestin (progesterone)

Which play a role in following :

1-Act on reproductive tract.

2-Prepare uterus for fetus growth.

3-Keep pregnancy to continue.

4-It act as thermogenic factor during pregnancy.

5-Play a role in plantation of fertilized egg in uterus.

Estrogens

play a role in:

1-Increase growth of mammary ducts.

2-Increase general protein anabolism.

3-Increase growth of ovarian follicles.

4-Affect on secondary sexual feature.

- **Mammary glands**

  These exocrine glands are enlarged and modified sweat glands.

  Structure

  The basic components of the mammary gland are the alveoli (hollow cavities of a few millimetres large) lined with milk-secreting epithelial cells and surrounded by myoepithelial cells. These alveoli join up to form groups known as lobules, and each lobule has a lactiferous duct that drains into openings in the nipple. The myoepithelial cells can contract, similar to muscle cells, and thereby push the milk from the alveoli through the lactiferous ducts towards the nipple,

- **The development of mammary glands**

is controlled by hormones. The mammary glands exist in both sexes, but they are rudimentary until puberty when - in response to ovarian hormones - they begin to develop in the female. Estrogen promotes formation, while testosterone inhibits it.

True secretory alveoli only develop in pregnancy, where rising levels of estrogen and progesterone cause further branching and differentiation of the duct cells, together with an increase in adipose tissue and a richer blood flow.

The suckling of the baby causes the release of the hormone oxytocin which stimulates contraction of the myoepithelial cells.

The cells of mammary glands can easily be induced to grow and multiply by hormones. If this growth runs out of control, cancer results.

The Female Reproductive Cycle

Towards the end of puberty, girls begin to release eggs as part of a monthly period called the female reproductive cycle, or menstrual cycle.

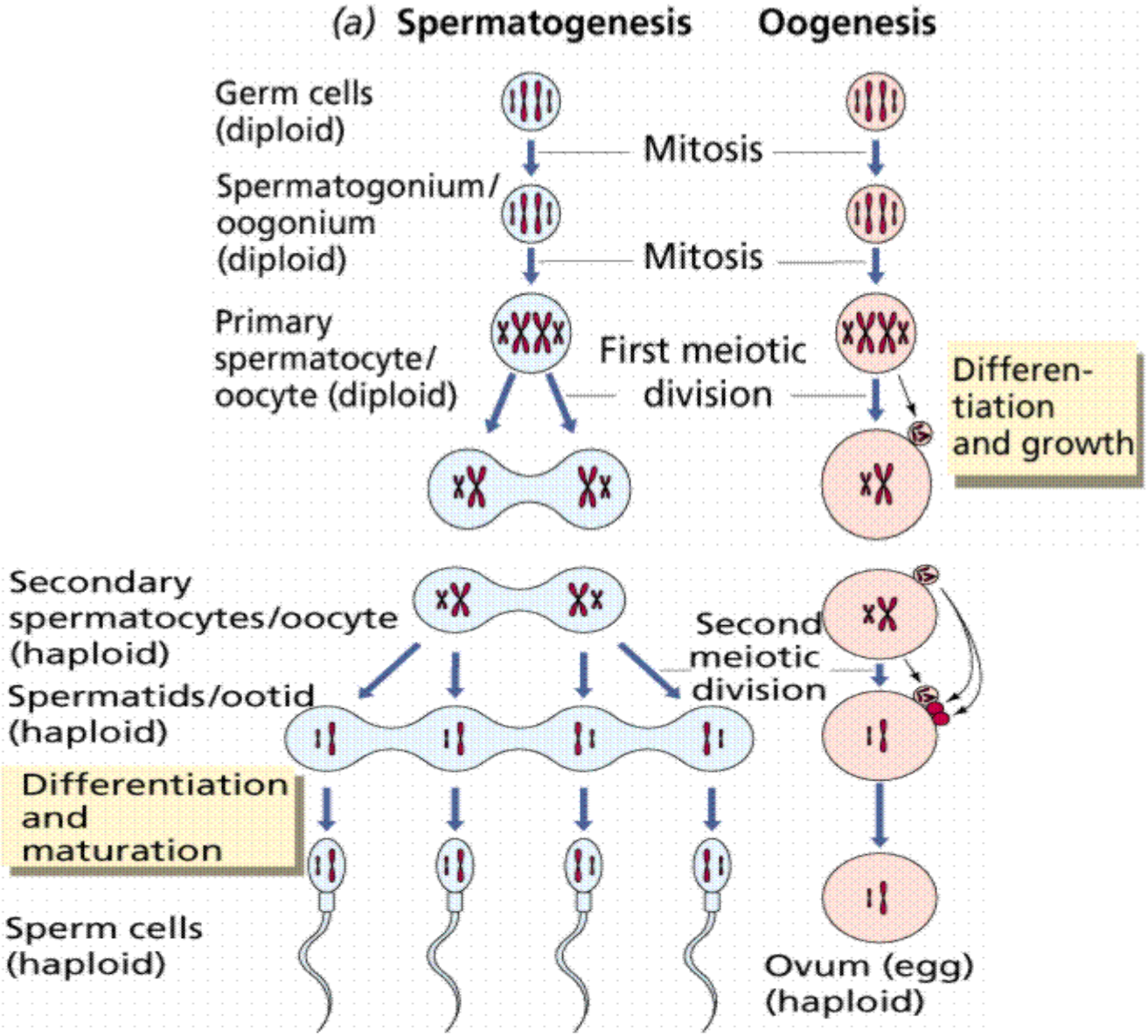
Approximately every 28 days, during ovulation, an ovary sends egg into one of the fallopian tubes. Unless the egg is fertilized by a sperm while in the fallopian in the two to three days following ovulation, the egg dries up and leaves the body about two weeks later . This process is called menstruation.

Menstruation forms a normal part of a natural cyclic process occurring in healthy women between puberty and the end of the reproductive years.

Oogenesis is the process of forming an ovum (egg) by meiosis in animals.

*Whereas in spermatogenesis all 4 meiotic products develop into gametes, oogenesis places most of the cytoplasm into the large egg. The other cells, the polar bodies, do not develop.

This all the cytoplasm and organelles go into the egg. Human males produce 200,000,000 sperm per day, while the female produces one egg (usually) each menstrual cycle.


(a) Spermatogenesis
Oogenesis
Germ cells (diploid)
Mitosis
Spermatogonium/ oogonium (diploid)
Mitosis
Primary spermatocyte/ oocyte (diploid)
First meiotic division
Differen- tiation and growth
Secondary spermatocytes/oocyte (haploid)
Second meiotic division
Spermatids/ootid (haploid)
Differentiation and maturation
Sperm cells (haploid)
Ovum (egg) (haploid)

Infertility

is the inability to naturally conceive a child or the inability to carry a pregnancy . There are many reasons why a couple may not be able to conceive without medical assistance. Healthy couples in their mid-20s having regular sex have a one-in-four chance of getting pregnant in any given month. This is called "Fecundity".

Primary vs. secondary

"Secondary infertility“Secondary infertility" is difficulty conceiving after already having conceived and carried a normal pregnancy. Apart from various medical conditions (e.g. hormonal), this may come as a result of age and stress felt to provide a sibling for their first child. Technically, secondary infertility is not present if there has been a change of partners.

Factors of Infertility

Factors relating to female infertility are:

1-General factors

Diabetes mellitus,thyroid disorders,adrenal disease

Significant liver, kidney disease , Psychological factors

2-Hypothalamic-pituitary factors:

Kallmann syndrome , Hypothalamic dysfunction , Hyperprolactinemia

Hypopituitarism

3-Ovarian factors

Polycystic ovary syndrome , Anovulation , Diminished ovarian reserve

Luteal dysfunction , Premature menopause , Gonadal dysgenesis (Turner syndrome) , Ovarian neoplasm

4-Tubal/peritoneal factors

Endometriosis , Pelvic adhesions , Pelvic inflammatory disease, Tubal occlusion

5- Uterine factors

Uterine malformations , Uterine fibroids (leiomyoma) , Asherman's Syndrome

6- Cervical factors

Cervical stenosis , Antisperm antibodies

Insufficient cervical mucus (for the travel and survival of sperm)

7- Vaginal factors

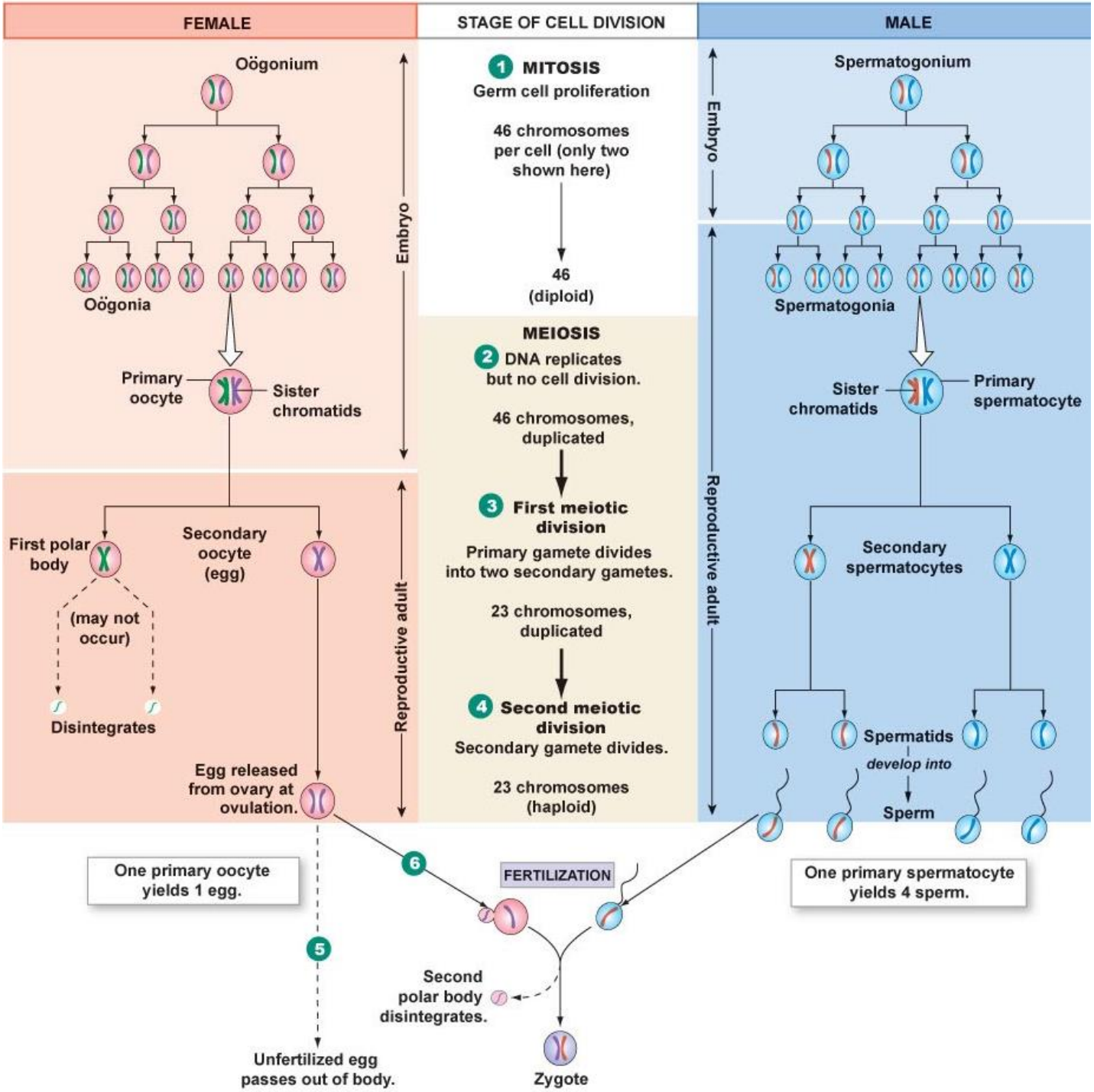
Vaginismus , Vaginal obstruction

8- Genetic factors

Various intersexuality|intersexed conditions, such as androgen insensitivity syndrome

- The Menstrual Cycle
  - Duration
    - Approximately 28 days (ranges 24 – 35 days)
    - Starts with the removal of the endometrium & release of FSH by the anterior pituitary
  - The ovarian cycle
    - Development of ovarian follicle
    - Production of hormones
    - Release of ovum during ovulation
  - The uterine cycle
    - Removal of endometrium from prior uterine cycle
    - Preparation for implantation of embryo under the influence of ovarian hormones

- Changes occur to allow parturition
  - Increasing levels of corticotropin-releasing hormone (CRH) from the placenta a few weeks prior to delivery
    - Early deliveries have been linked to early elevated levels of CRH
    - During delivery
      - progesterone levels drop off
      - Oxytocin levels rise
        - » Oxytocin receptors on the uterus are upregulated during gestation
      - Inhibin levels increase
        - » Relax the cervix and ligaments of the pelvis
        - » Allows for increased stretch of the cervix which triggers additional oxytocin which triggers stronger uterine contractions which increase stretch of the cervix which triggers oxytocin which triggers stronger uterine contractions which increases stretch of the cervix which increases oxytocin release which increases uterine contractions which increases stretch on cervix which….


FEMALE
STAGE OF CELL DIVISION
MALE
Oögonium
Oögonia
Primary oocyte
Sister chromatids
Embryo
1 MITOSIS
Germ cell proliferation
46 chromosomes per cell (only two shown here)
46 (diploid)
MEIOSIS
2 DNA replicates but no cell division.
46 chromosomes, duplicated
3 First meiotic division
Primary gamete divides into two secondary gametes.
23 chromosomes, duplicated
4 Second meiotic division
Secondary gamete divides.
23 chromosomes (haploid)
Spermatogonium
Spermatogonia
Embryo
Sister chromatids
Primary spermatocyte
Secondary spermatocytes
Reproductive adult
First polar body
Secondary oocyte (egg)
(may not occur)
Disintegrates
Reproductive adult
Egg released from ovary at ovulation.
Spermatids
develop into
Sperm
One primary oocyte yields 1 egg.
6
FERTILIZATION
One primary spermatocyte yields 4 sperm.
5
Second polar body disintegrates.
Unfertilized egg passes out of body.
Zygote

Physiology of body homeostasis

Homeostasis , Basic Cell Functions , Balancing the Internal and External Environment , Homeostasis mechanism , Control of Homeostasis , External stimuli , Internal stimuli , Components of an control system , Control path way of Homeostasis , Homeostatic Control Systems,

Feed for ward Term , Feedback Term , Negative feedback loop , Positive feedback loop ,

Homeostatic Regulation of Blood Sugar through Negative Feedback ,

Homeostatic Regulation of Body Temperature through Negative Feedback ,

Homeostasis of Blood Pressure , Positive Feedback during Childbirth ,

Pathways That Alter Homeostasis , Variables that need to be maintained by Homeostasis,

Homeostasis Throughout the Body , Role of Body Systems in Homeostasis , Nervous System , Endocrine System , Integumentary System , Digestive System , Skeletal System , Muscular System , Cardiovascular System , Respiratory System , Lymphatic System , Urinary System , Reproductive System.

Homeostasis

Homeostasis It is the body's attempt to maintain a constant internal environment balance or equilibrium. Homeostasis requires constant monitoring and adjustments of physiological systems within the body is called *homeostatic regulation*.

Homeostasis is essential for survival and function of all cells.
Each cell contributes to maintenance of a relatively stable internal environment

Basic Cell Functions

1- Sensing and responding to changes in surrounding environment.

2- Control exchange of materials between cell and its surrounding environment :

- **Obtain nutrients and oxygen from surrounding environment.**
- **Eliminate Co2 and other wastes to surrounding environment.**

3-Perform chemical reactions that provide energy for the cell.

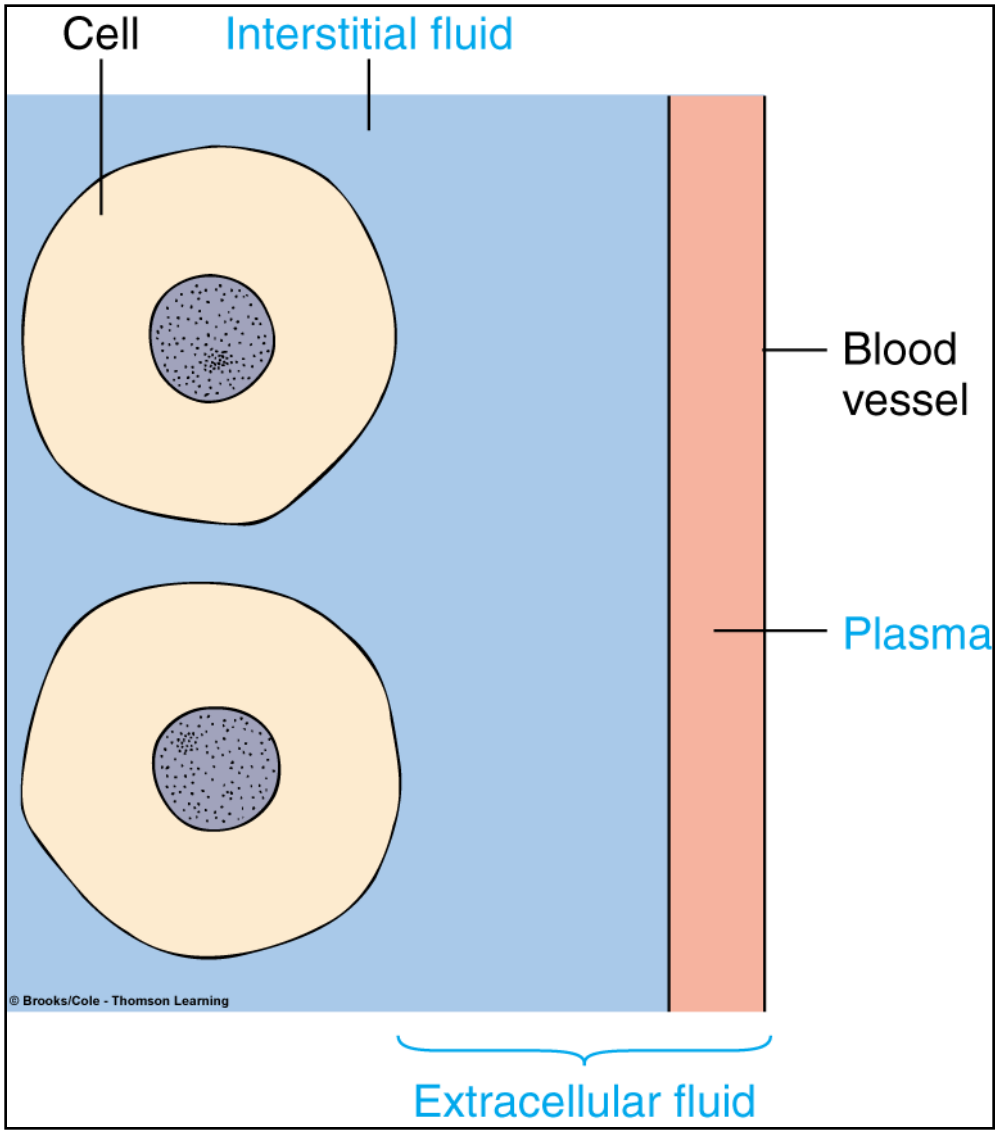
4-Synthesize needed cellular components.

Intracellular fluid (ICF) - Fluid contained within all body cells

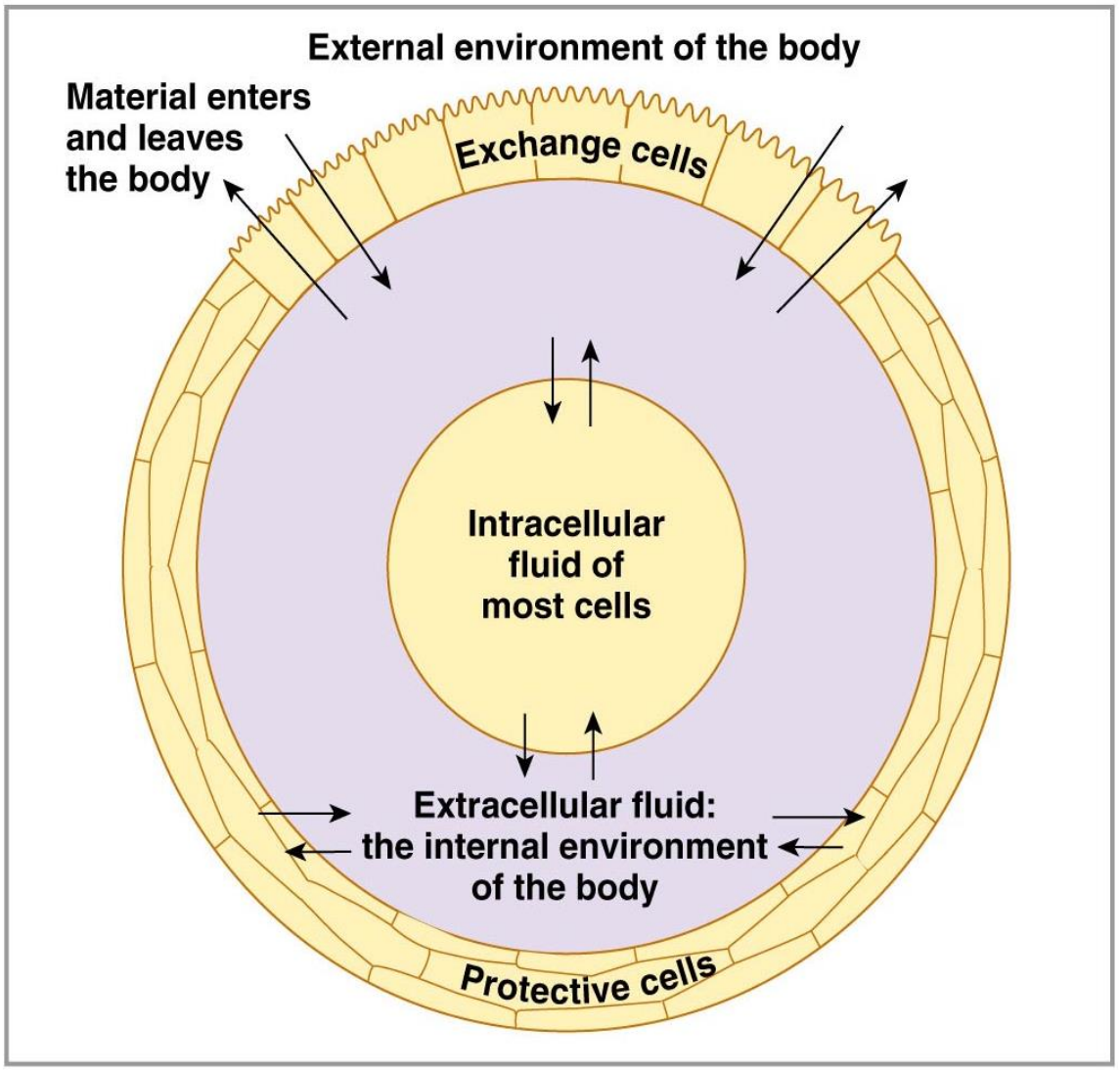
Extracellular fluid (ECF) - Fluid environment in which the cells live (fluid outside the cells)

Include two components:

- **Plasma**
- **Interstitial fluid**



Homeostasis



Balancing the Internal and External Environment

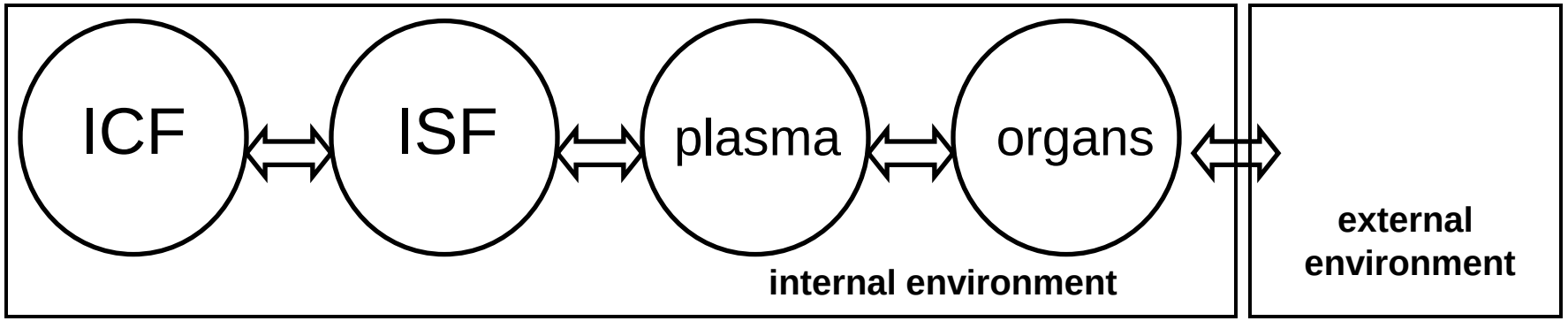
Cells, the fundamental units of life, exchange nutrients and wastes with their surroundings:

The intracellular fluid is "conditioned by"…

the interstitial fluid, which is "conditioned by" …

the plasma, which is "conditioned by" …

the organ systems it passes through.



Homeostasis mechanism

- **Homeostasis involves dynamic mechanisms that detect and respond to deviations in physiological variables from their "set point" values by initiating effector responses that restore the variables to the optimal physiological range.**
- **Two systems that maintain homeostasis are: Nervous system & Endocrine system .**

- **Homeostatic regulation involves three parts or mechanisms:**
  1) the *receptor*
  2) the *control center*
  3) the *effector*

The *receptor* receives information that something in the environment is changing. The *control center* or *integration center* receives and processes information from the *receptor*. And lastly, the *effector* responds to the commands of the *control center* by either opposing or enhancing the stimulus.

Control of Homeostasis

- Homeostasis is continually being disrupted by :

  1- External stimuli

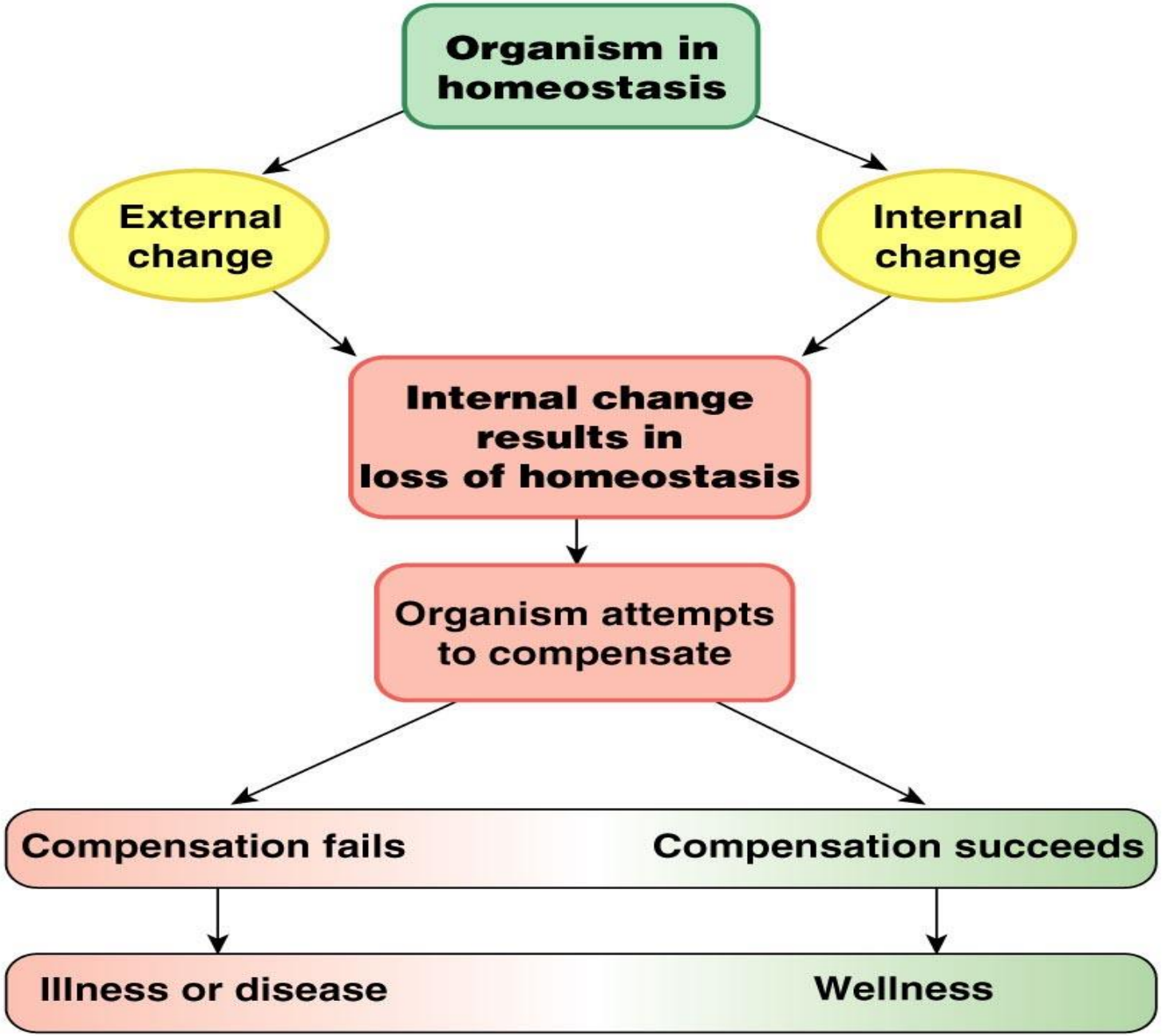
  As : heat, cold, lack of oxygen, pathogens, toxins.

  2-Internal stimuli

  - As :
  - Body temperature
  - Blood pressure
  - Concentration of water, glucose, salts, oxygen, etc.
  - Physical and psychological distresses
- Disruptions can be mild to severe
- If homeostasis is not maintained, death may result

Components of an control system

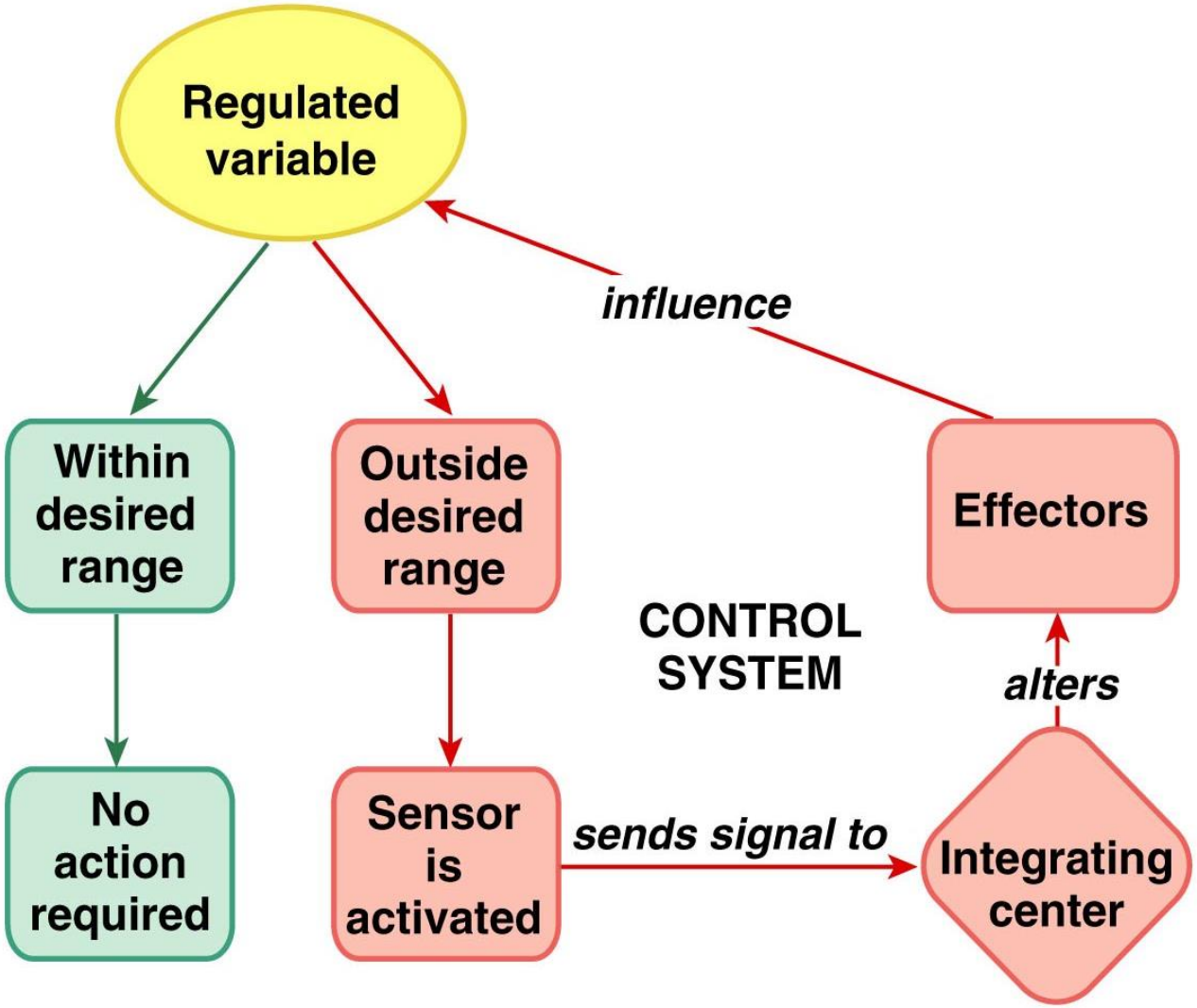
Variable	is the characteristic of the internal environment that is controlled
Sensor	(receptor) detects changes in variable and feeds that information back to the integrator (control center)
Integrator	(control center) integrates data from sensor and stored "setpoint" data
Set Point	is the "ideal" or "normal" value of the variable that is previously "set" or "stored" in memory.
Effector	is the mechanism that has an "effect" on the variable



Control path way of Homeostasis

Control Pathways

Physiological control systems keep regulated variables within a desired range during homeostasis



Homeostatic Control Systems

In order to maintain homeostasis, control system must be able to :

1-Detect deviations from normal in the internal environment that need to be held within narrow limits

2-Integrate this information with other relevant information

3-Make appropriate adjustments in order to restore factor to its desired value.

Control systems are grouped into two classes :

1-Intrinsic controls : Local controls that are inherent in an organ

2-Extrinsic controls : Regulatory mechanisms initiated outside an organ , Accomplished by nervous and endocrine systems

Feed for ward Term :

term used for responses made in anticipation of a change.

Feedback Term

refers to responses made after change has been detected.

- **Types of feedback systems :**

1-Negative feedback loop

– original stimulus reversed

– most feedback systems in the body are negative

– used for conditions that need frequent adjustment

2-Positive feedback loop

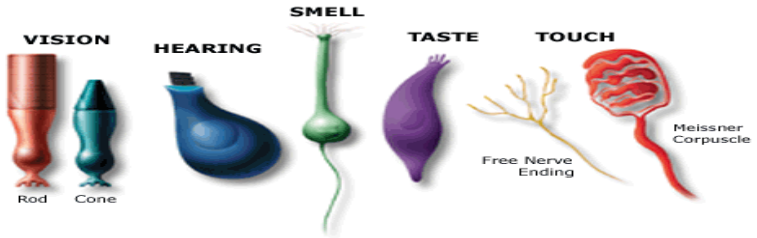
– original stimulus intensified

– seen during normal childbirth

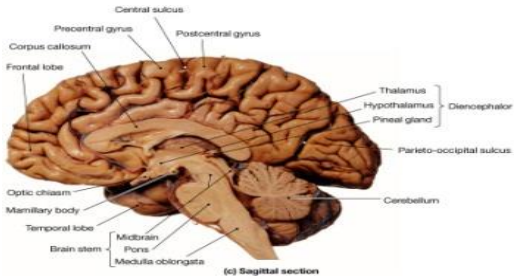
Negative Feedback Loop

Negative feed back loop consists of:

1-Receptor - structures that monitor a controlled condition and detect changes

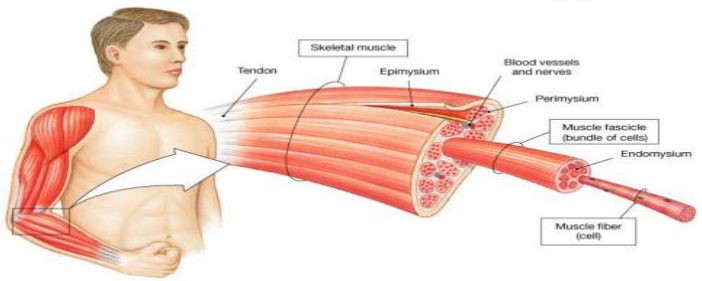


2-Control center - determines next action

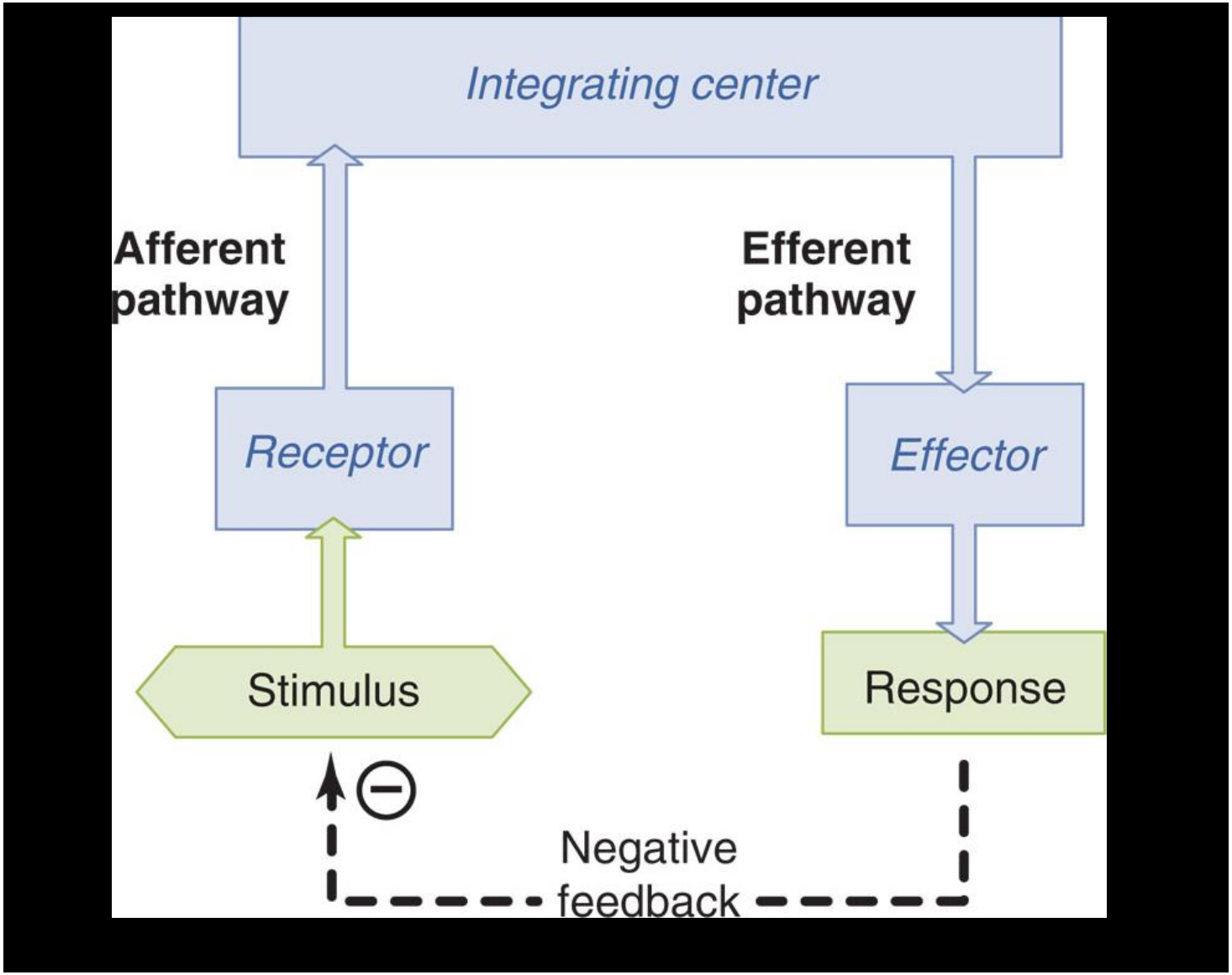


3-Effector

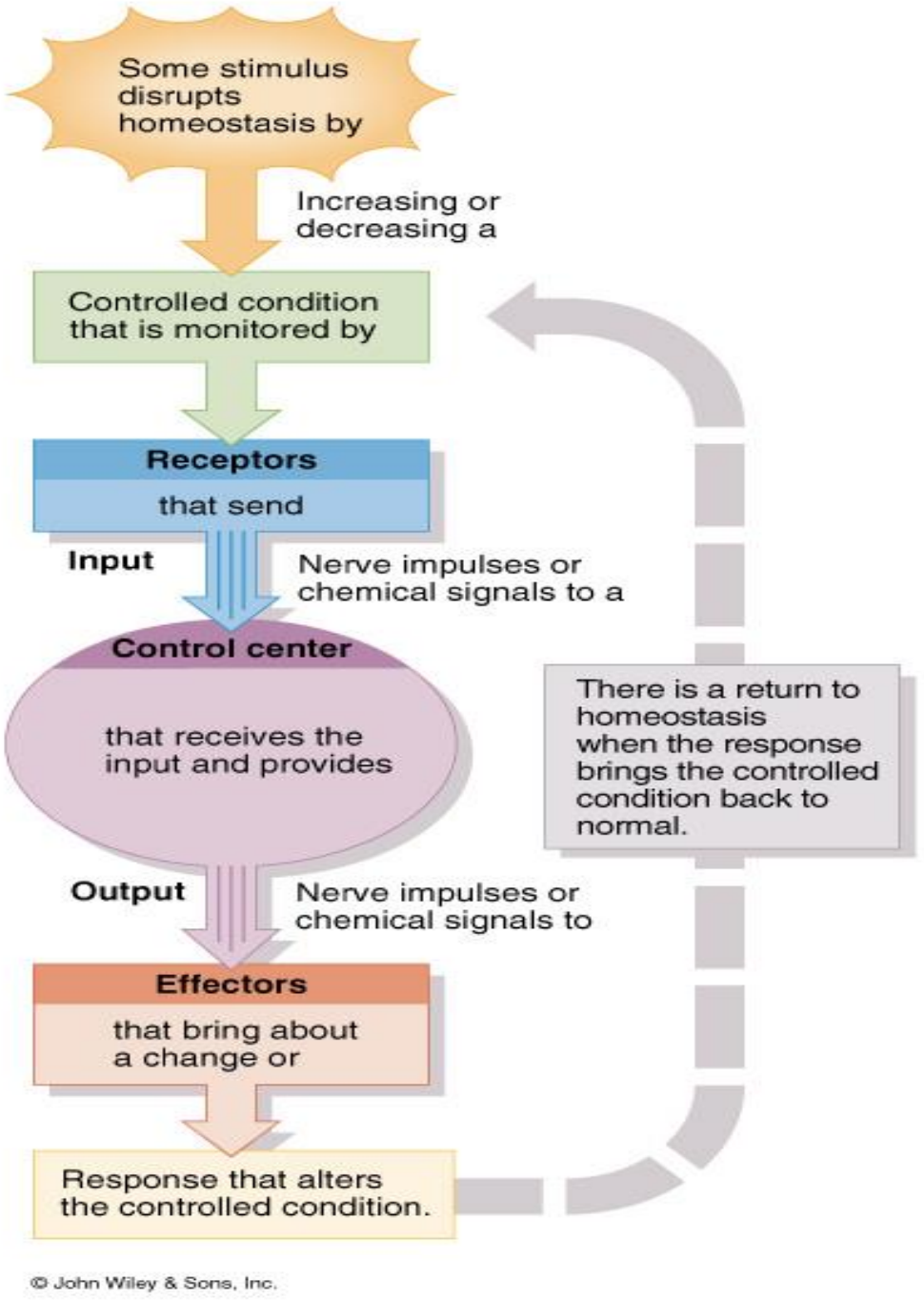
- receives directions from the control center
- produces a response that restores the controlled condition



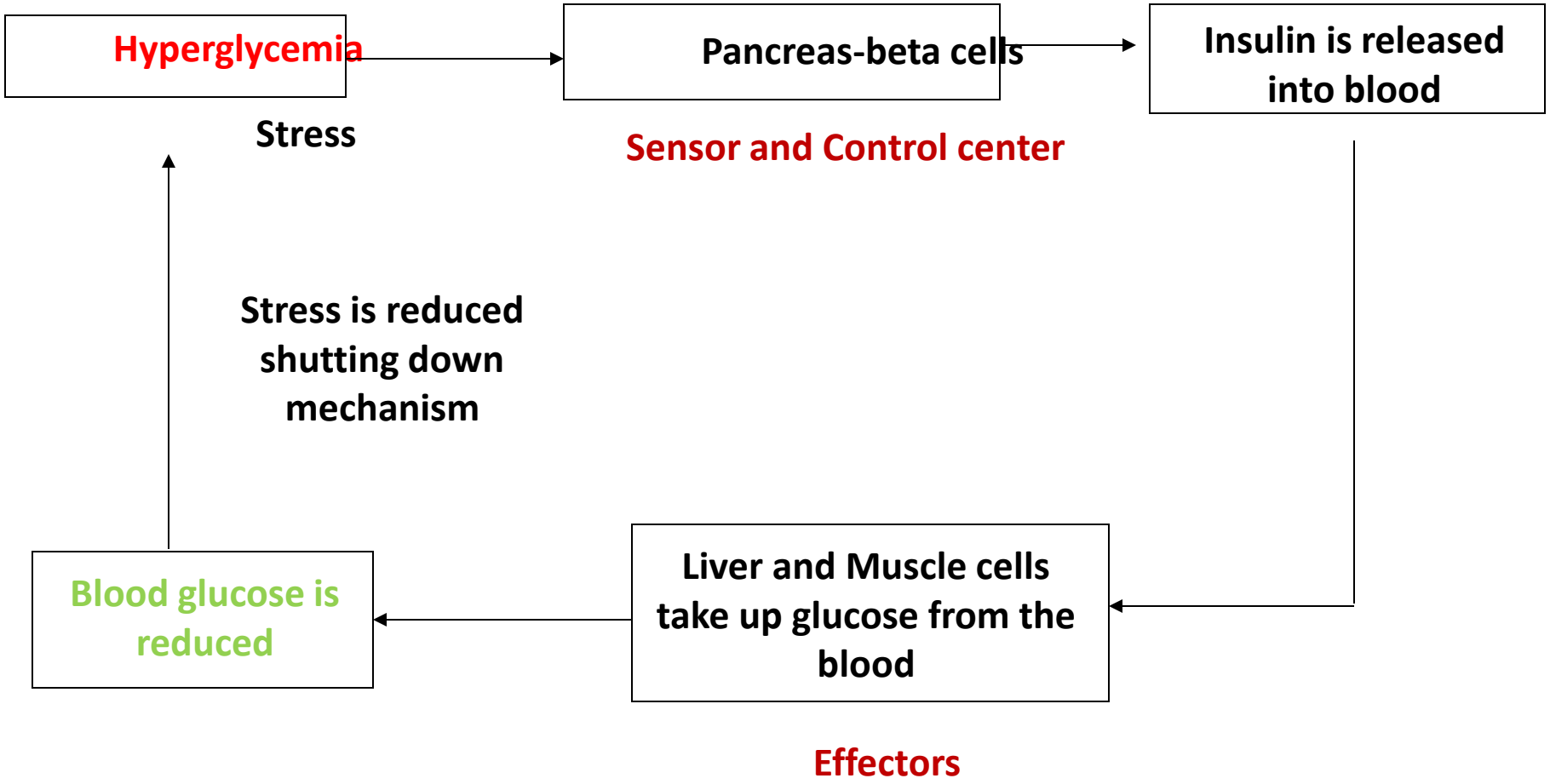
Negative Feedback Loop



Negative Feed

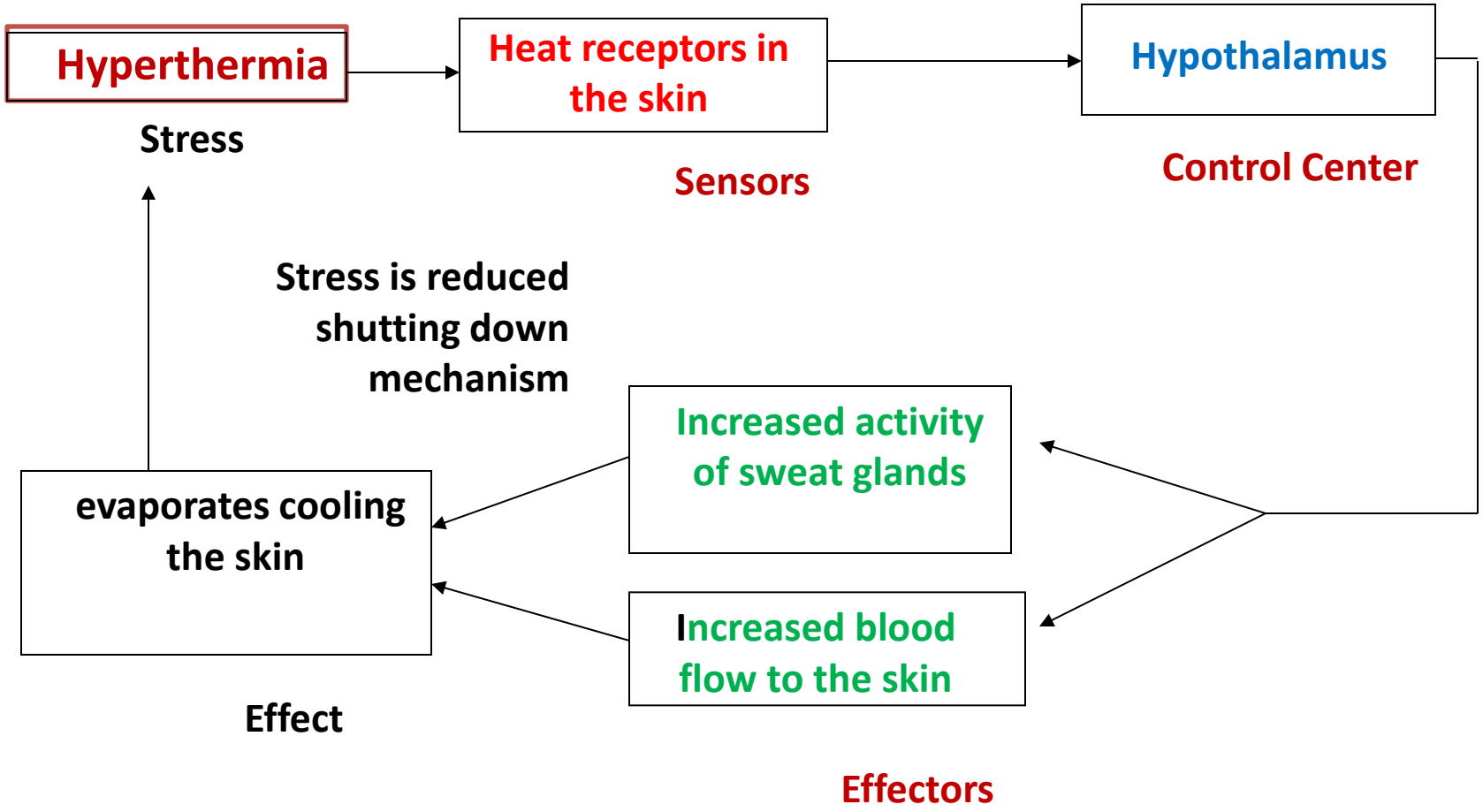


Homeostatic Regulation of Blood Sugar through Negative Feedback



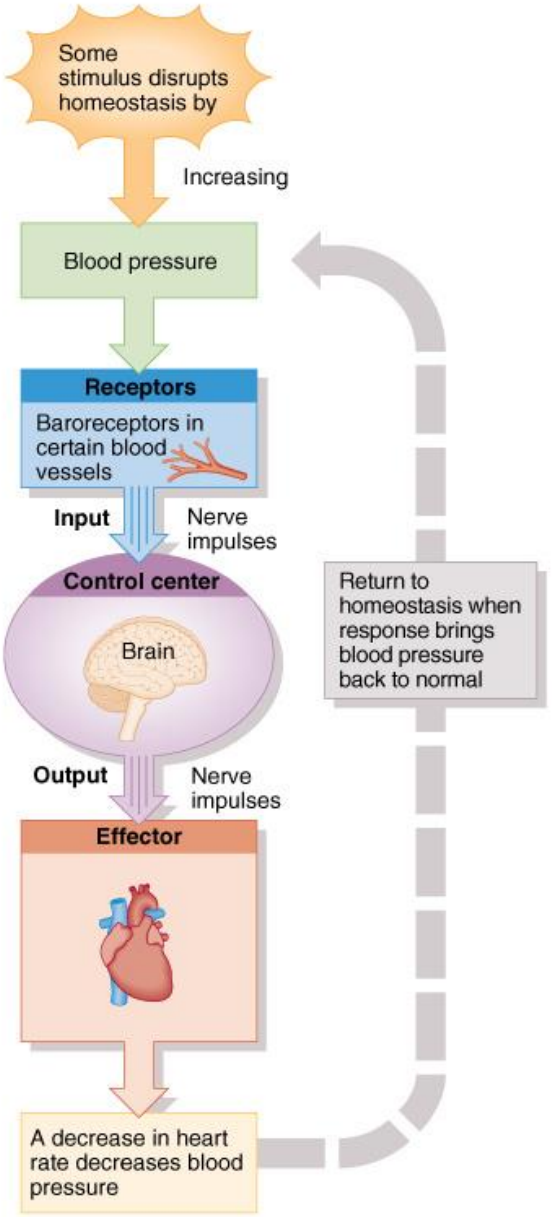
- Blood glucose concentrations rise after a sugary meal (the stimulus), the hormone insulin is released and it speeds up the transport of glucose out of the blood and into selected tissues (the response), so blood glucose concentrations decrease (thus decreasing the original stimulus).

Homeostatic Regulation of Body Temperature through Negative Feedback



Homeostasis of Blood Pressure

- Baroreceptors in walls of blood vessels detect an increase in BP
- Brain receives input and signals blood vessels and heart
- Blood vessels dilate, HR decreases
- BP decreases



Positive Feedback during Childbirth

- Stretch receptors in walls of uterus send signals to the brain
- Brain induces release of hormone (oxytocin) into bloodstream
- Uterine smooth muscle contracts more forcefully
- More stretch, more hormone, more contraction etc.
- Cycle ends with birth of the baby & decrease in stretch

- **Pathways That Alter Homeostasis**

- **When the cells in the body begin to malfunction, the homeostatic balance becomes disrupted, this leads to disease or cell malfunction that caused in two basic ways:**

1- either, *deficiency* (cells not getting all they need) or

2- *toxicity* (cells being poisoned by things they do not need).

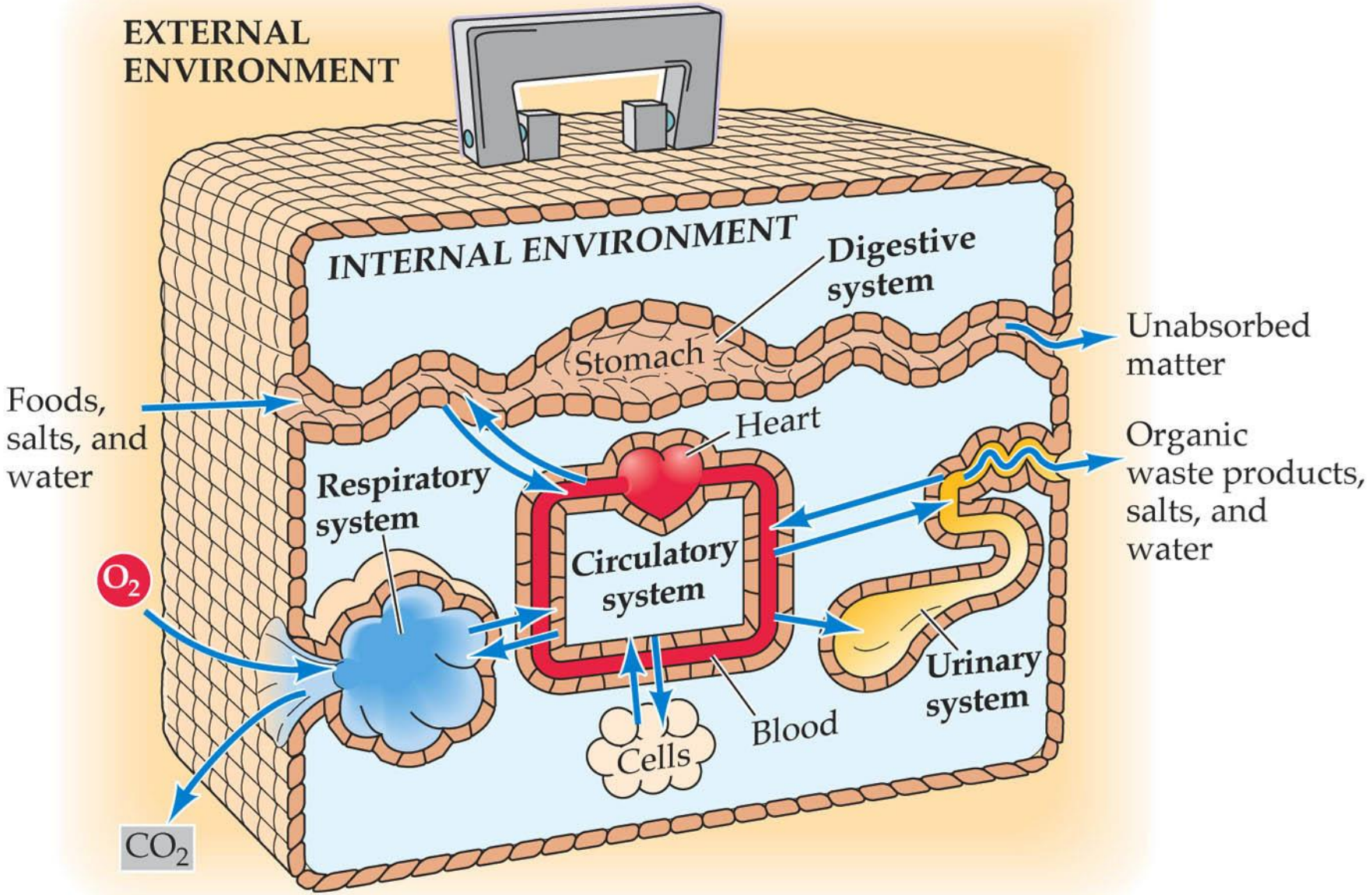
When homeostasis is interrupted in the cells, there are *pathways* to correct the problem.

The factors have their effects at the cellular level, whether harmful or beneficial are (Nutrition, Toxins, Psychological, Physical, Genetic/Reproductive, Medical).

By removing negative health influences, and providing adequate positive health influences, the body is better able to self-regulate and self-repair, thus maintaining homeostasis.

Variables that need to be maintained by Homeostasis:

- ion concentrations (e.g. sodium and potassium)
- water volume
- blood pressure
- nutrient concentrations (e.g. glucose)
- wastes
- Oxygen
- Concentration of water, salt, and other electrolytes
- Concentration of O_2 = 100mmHg and CO_2 = 40 mmHg
- pH = 7.35
- Blood volume 4-6 L and pressure 120/80
- Temperature = 37^o C

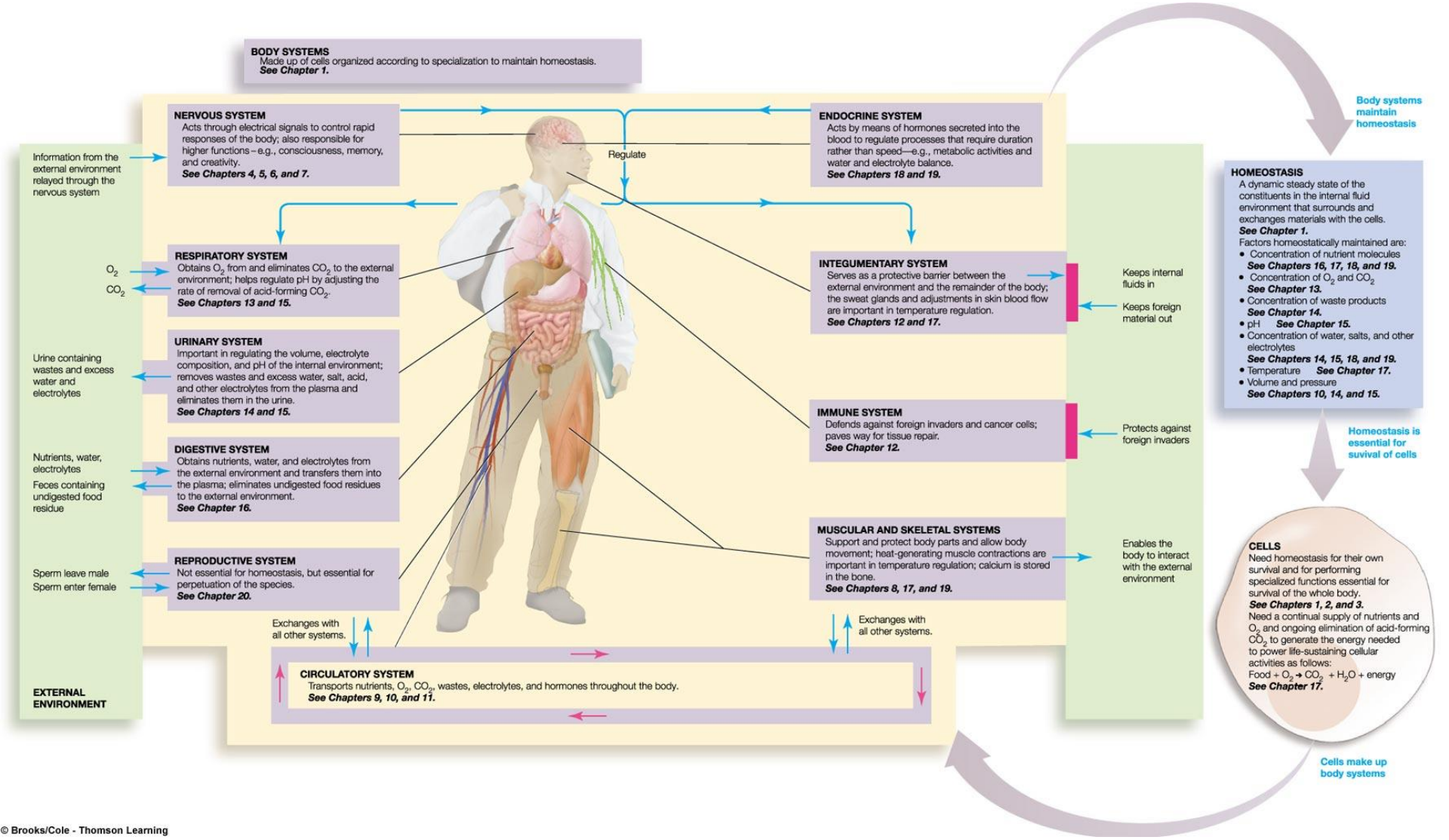


LIFE: THE SCIENCE OF BIOLOGY, Seventh Edition, **Figure 41.1 Maintaining Internal Stability while on the Go**

Homeostasis Throughout the Body

Each body system contributes to the homeostasis of other systems and of the entire organism. No system of the body works in isolation, A disruption within one system generally has consequences for several additional body systems.

Role of Body Systems in Homeostasis



Nervous System

- **The nervous system, along with the endocrine system, serves as the primary control center of the body .** Nervous system

  1-Controls and coordinates bodily activities that require rapid responses

  2-Detects and initiates reactions to changes in external environment

For example,

1-Hypothalamus is the body's "thermostat“ & also stimulates the pituitary gland to release various hormones that control metabolism and development of the body.

2-sympathetic and parasympathetic nervous system alternatively stimulate or inhibit various bodily responses (such as heart rate, breathing rate, etc) to help maintain proper levels.

3-The nervous system also regulates various systems such as respiratory , cardiovascular system, endocrine organs, the digestive system, and the urinary system.

4-The nervous system is also involved in our sexual behaviors and functions.

Endocrine System

1-Secreting glands of endocrine regulate activities that require duration rather than speed

2-Controls concentration of nutrients and, by adjusting kidney function, controls internal environment's volume and electrolyte composition

3-Each hormone has an effect on one or more target tissues, regulates the metabolism and development of most body cells.

4-Endocrine system has sex hormones that activate sebaceous & mammary glands development .

5-bone growth is regulated by several hormones, and the endocrine system helps with the mobilization of calcitonin and calcium.

6-In the muscular system, hormones adjust muscle metabolism, energy production, and growth.

7-In the nervous system, hormones affect neural metabolism, regulate fluid/electrolyte balance and help with reproductive hormones influence CNS development and behaviors.

8-In the Cardiovascular system, hormones regulate the production of RBC's, which elevate and lower blood pressure.

9-Hormones also have anti-inflammatory effects and stimulate the lymphatic system.

Systems for regulation

Endocrine System	Nervous System
Chemical massage	Electrical massage
Generalized action throughout body	Local action
Secretes Hormones	Secretes Neurotransmitters
Target Cells	Neurons
Controls Every Cell	Controls only muscles and glands
Long Lived	Short Lived

Integumentary System

1-The integumentary system is involved in protecting the body from invading microbes,

2-regulating body temperature through sweating and vasodilation, or shivering

3-regulating ion balances in the blood.

4-helps synthesize vitamin D which interacts with calcium and phosphorus absorption needed for bone growth, maintenance, and repair.

5-Hair on the skin guards entrance into the nasal cavity

6- helps maintain balance by excretion of water and other solutes

7-It also provides mechanical protection against environmental hazards.

- **Digestive System**

1- regular supply of energy and nutrients .

2-The digestive system absorbs organic substances, vitamins, ions, and water.

3-In the skin, the digestive tract provides lipids for storage in the subcutaneous layer.

- **Skeletal System**

1-skeletal system consists mainly of the 206 or so bones of the skeletal system but also includes cartilages, ligaments, and other connective tissues that stabilize and interconnect them.

2-Bones work in conjunction with the muscular system to aid in posture and locomotion.

3-Protection of organs are encased within the skeletal cavities (cranial, and spinal "or dorsal").

4-The skeletal system also serves as an important mineral reserve.

5-Also, the skeletal system provides calcium needed for all muscular contraction.

6-Finally, red blood cells, lymphocytes and other cells relating to the immune response are produced and stored in the bone marrow.

Muscular System

1-The muscular system contains the heart, which constantly pumps blood through the body.

2-The muscular system is also responsible for involuntary actions.

3- Muscles also help protect organs in the body's cavities.

Cardiovascular System

1- plays a role in maintenance of other body systems by transporting hormones and nutrients , taking away waste products, and providing all living body cells with a fresh supply of oxygen and removing carbon dioxide.

2-Homeostasis is disturbed if the cardiovascular or lymphatic systems are not functioning correctly.

- **Respiratory System**

1-provide oxygen to cells for cellular metabolism.

2-removes carbon dioxide.

3-helps maintain proper blood pH levels,

4-The respiratory system also helps the lymphatic system by trapping pathogens and protecting deeper tissues within.

- **Lymphatic System :has three principal roles**

1-in the maintenance of blood and tissue volume. Excess fluid that leaves the capillaries when under pressure would build up and cause edema.

2-Secondly, the lymphatic system absorbs fatty acids and triglycerides from fat digestion

3-Third,is involved in defending the body against invading microbes, and the immune response.

- **Urinary System**

1-Removal of toxic nitrogenous wastes.

2-involved in maintaining proper blood volume, blood pressure and ion concentration within the blood.

3-One other contribution is that the kidneys produce a hormone (erythropoietin) that stimulates red blood cell production.

4-The kidneys also play an important role in maintaining the correct water content of the body and the correct salt composition of extracellular fluid.

- **Reproductive System**

1- the reproductive system relates to the maintenance of the species.

2- the sex hormones do have an effect on other body systems, and an imbalance can lead to various disorders (e.g. a woman whose ovaries are removed early in life is at much higher risk of osteoporosis).