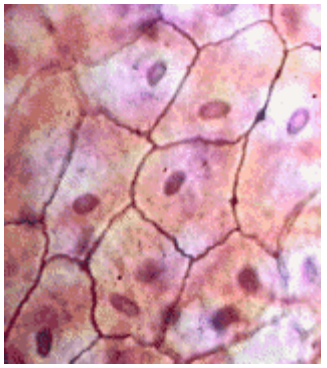
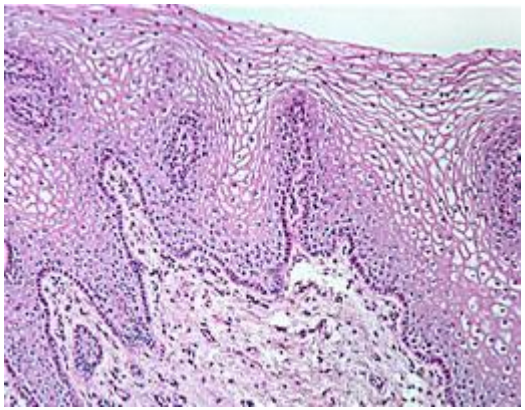
Tissues

Simple Squamous Epithelium



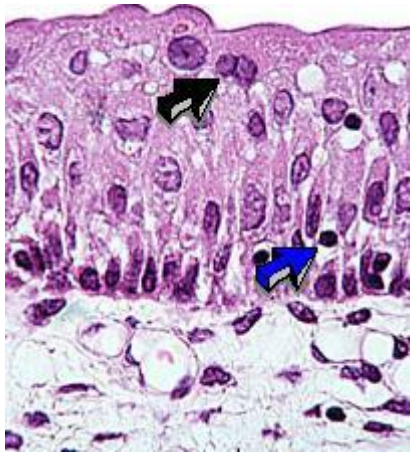
- In Bowman's capsule in the kidney, in the alveoli in the lungs, and serous membranes.
- Oblong, polyhedral-shaped cells with a prominent nucleus.

Stratified Squamous Epithelium



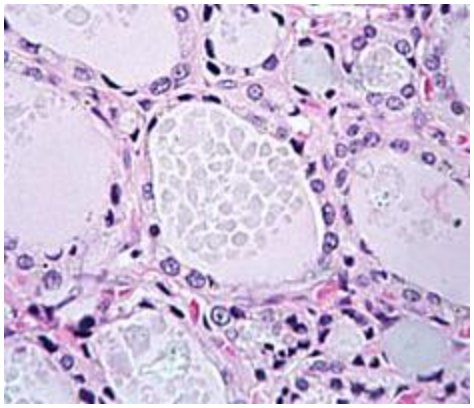
- Epidermis of the skin (keratinized),
- in mucous membranes (NON-keratinized),
- linings of vagina and esophagus.
- Stacked in symmetrical layers.

Transitional Epithelium



- In bladder, ureters;
- you may have noticed that sometimes when a smoker quits smoking at a late age that they seem to develop lung cancer -- this is due to the smoking-differentiated tissue getting stuck in a transitional phase instead of re-differentiating into "normal tissue"; the transitional tissue grows out of control (cancer).

Simple Cuboidal Epithelium

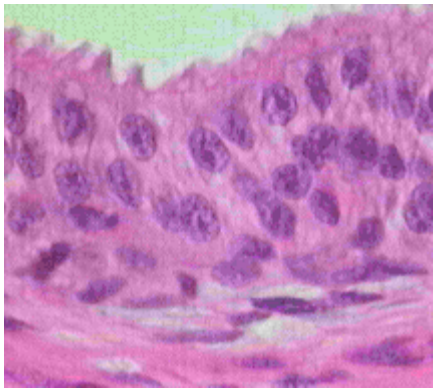


- Found in the collecting tubules in the kidney and in the ovary.
- Shaped like a cube.

Simple Columnar Epithelium

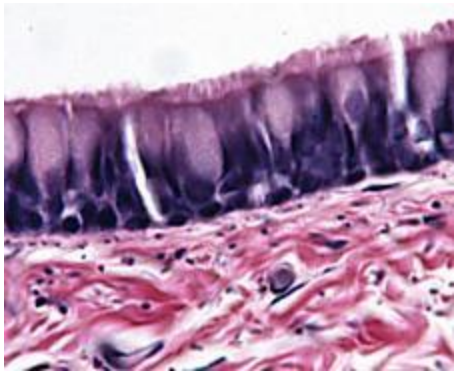
- In mucous membrane of the stomach and large and small bowel.
- Shaped like a column (think of the porch columns you remember from "Gone With The Wind").

Stratified Columnar Epithelium



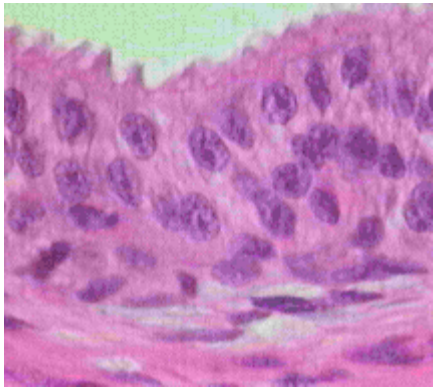
- Seems to be found only in the male urethra.
- Shaped in columns and stacked on each other in symmetrical layers.

Pseudostratified Ciliated Columnar Epithelium



- In tracheal mucosa of airways.
- Has cilia (little fingers) on its surface, stacked in a sort of hodge-podge of layers of columns.

Stratified Cuboidal Epithelium

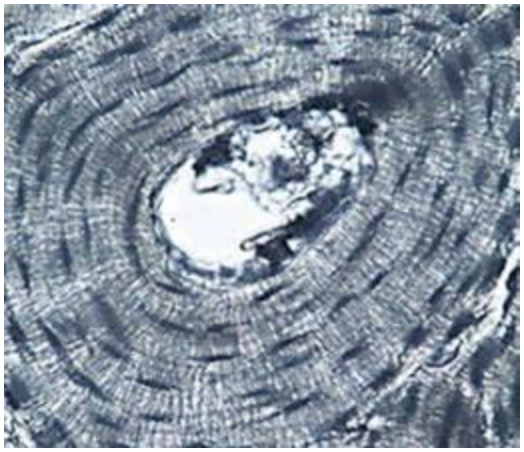


- In sweat glands.
- Cubic shaped in layers.

Osseous Tissue – Bone

The skeletal system is the framework of bones and cartilage that protects our organs and allows us to move.

Bone Tissue



- In bones.
- We'll talk more about this in the skeletal section.

Function of the Skeletal System

- The framework supports soft tissue and muscle attachment.
- The skeletal system protects our brains by the cranial bones, the spinal cord by the vertebra, the heart and lungs by the ribs and the internal reproductive organs by the pelvis.
- The skeletal system facilitates movements as bones are levers to which muscles are attached.
- The combination of levers (bones), joints and muscles provide movement when directed to do so by the nervous system.

Function of the Skeletal System

- The skeletal system provides for some mineral storage, e.g., Ca and P when we need it.
- The skeletal system provides for an energy store.
- Inside long bones is a cavity which stores yellow marrow – this is fat that can be used for energy.

Function of the Skeletal System

- The skeletal system stores blood-cell producing cells.
- This is done in the red marrow which is in the adult proximal epiphyses of the humerus and femur, in the flat bones of the cranium, sternum, ribs, vertebra and pelvis.
- The production of any blood cell is called either hemopoiesis or hematopoiesis
  - if it is red blood cells (RBC) that are being produced, it is called erythropoiesis;
  - WBC production is called leucopoiesis.
- Red bone marrow contains blood cells in immature stages, fat cells and macrophages.
- Red bone marrow produces RBC and WBC, as well as platelets.

Histology

- There are at least three types of connective tissue that are involved in the skeletal system:
  - Cartilage,
  - Dense connective tissue and
  - Bone – where our attention will focus.
- There are 4 types of bone cells that require our attention:
  - Osteoprogenitor cells,
  - Osteoblasts,
  - Osteocytes and
  - Osteoclasts.

Osteoprogenitor cells (osteogenic cells)	Osteoblasts ("blast" = germ, bud)	Osteocytes (mature bone cells)	Osteoclasts ("clast" = to break)
Found in the inner portion of the membrane that surrounds the bone (periosteum). Found in the membrane that lines the medullary cavity (endosteum). Found in both Haversian and Volkmann's canals which contain blood vessels. Differentiate into osteoblasts.	Associated with bone formation. Secrete some organic compounds and mineral salts involved in bone formation. Found on surface of bone.	Are the primary cell of bone tissue. Are actually osteoblasts which are isolated within bony intercellular substance deposited around themselves and whose structure changes.	Develop from circulating monocytes (WBC-type). On the surface of the bone. Function in bone resorption (degradation).

To help you remember these cells' functions, try this: 'blasts build bone, 'cytes maintain daily cellular activities of bone tissue, 'clasts are important in development, growth, maintenance and repair of bone.

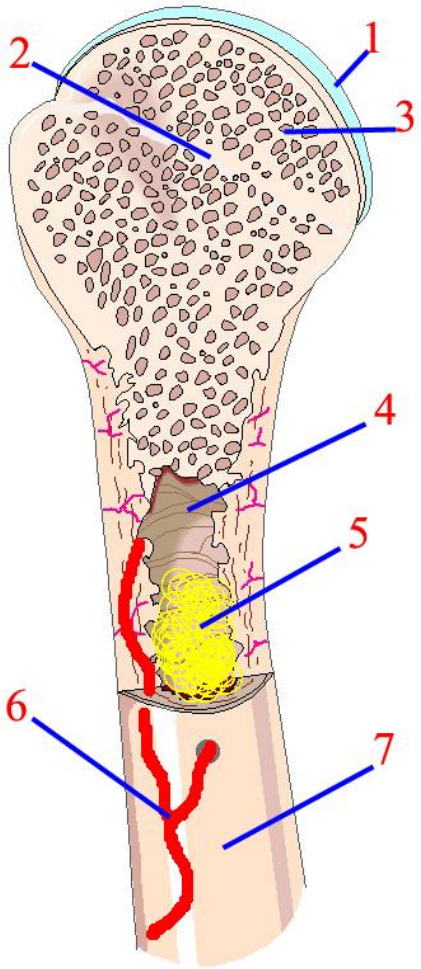
Intercellular Substances

- Mineral salts make up about 67% of the weight of a bone.
- These salts consist primarily of a calcium phosphate-type of salt called hydroxyapatite.
- The best chemical formula to date for hydroxyapatite is $Ca_3(PO_4)_2 \cdot (OH)_2$.
- Secondarily, calcium carbonate is found in bones, as well as small amounts of magnesium hydroxide, magnesium fluoride, magnesium sulfate.
- As all salts deposit in the protein framework (collagenous fibers), tissue hardens and is called calcification or ossification.
- The remaining 33% of bone is made up of these collagenous fibers.

Macroscopic Structure of Bone

- There are two kinds of bone that we're interested in:
  - compact and
  - spongy (cancellous) tissue.

Macroscopic Structure of Bone

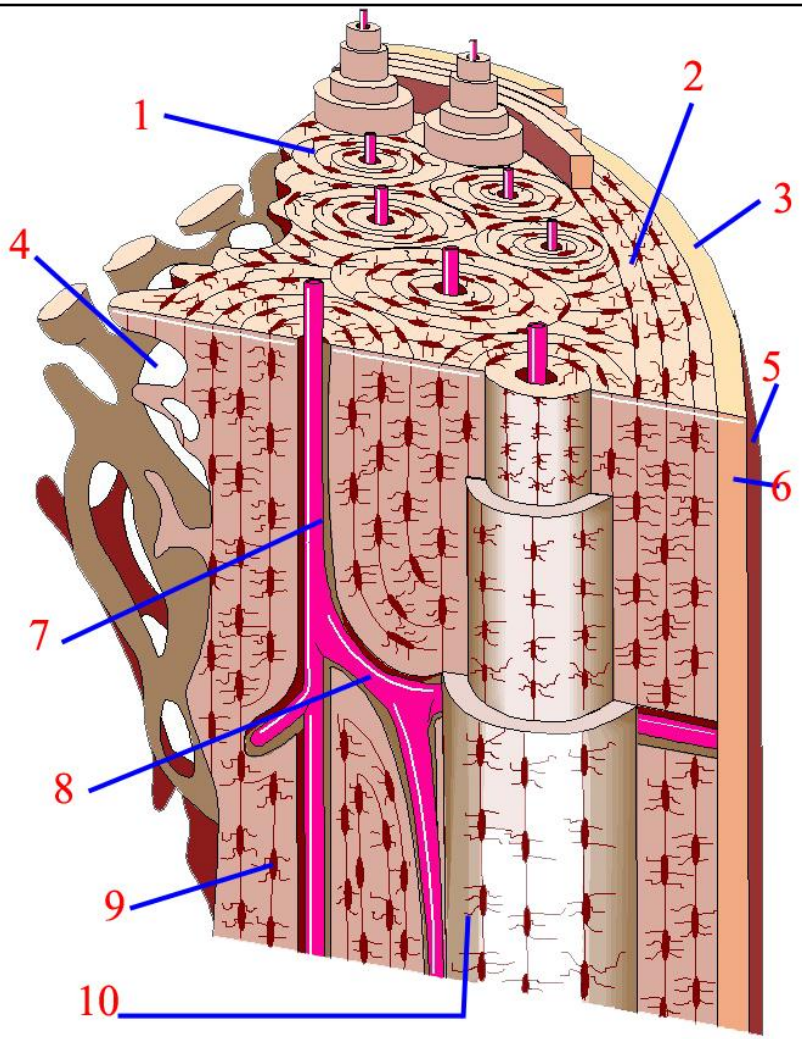
Compact bone		Spongy bone
Has few spaces. Is found over spongy bone. Is thicker in the diaphysis than on the epiphysis. Provides protection and support and helps long bones resist the stress of weight placed on them.		Contains many large spaces filled with red marrow. Makes up most of the bone tissue of short, flat and irregularly shaped bones and most of the epiphyses of the long bones.
1 – Articular cartilage 2 – Metaphysis 3 – Spongy bone 4 – Medullary cavity – lined by endosteum		5 – Yellow Marrow 6 – Nutrient blood vessel 7 – Diaphysis (shaft)

- Note when you pull away the periosteum, you'll note there are fibers anchoring it to the bone – these are Sharpey's fibers.
- Also note that the spongy bone in the epiphysis is covered by compact bone.
- The articular cartilage at the ends of bones is used to reduce friction and absorb shock during movement.
- The endosteum contains osteoprogenitor cells, and osteoblasts with scattered osteoclasts.
- The periosteum is essential for bone growth, repair and nutrition – it is also the point of attachment for ligaments and tendons.

There are two layers to the periosteum. These layers are summarized, below:

Periosteum	
Outer Fibrous Layer	Inner Osteogenic Layer
This layer has blood vessels, lymph vessels and nerves traversing it.	This layer consists of elastic fibers, blood vessels, osteoprogenitor cells, osteoblasts and osteoclasts.

Microscopic Structure of Bone



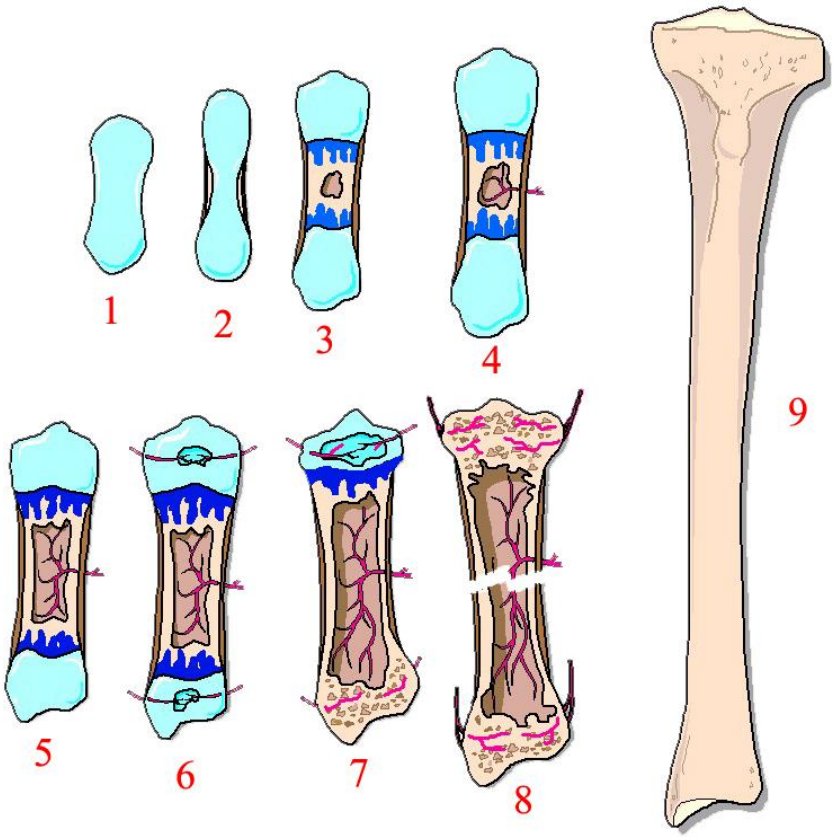
1 – Concentric Lamella
2 – Interstitial Lamella
3 – Periosteum
4 – Spongy Bone
5 – Fibrous Layer of Periosteum
6 – Osteogenic Layer of Periosteum
7 – Haversian Canal with blood vessel
8 – Volkmann's canal with blood vessel
9 – Lacunae with Osteocyte
10 -- Canaliculus

Physiology of Ossification

- Most bones are formed by endochondral ossification, aka, intracartilaginous ossification.
- In this process, cartilage is replaced by bone.

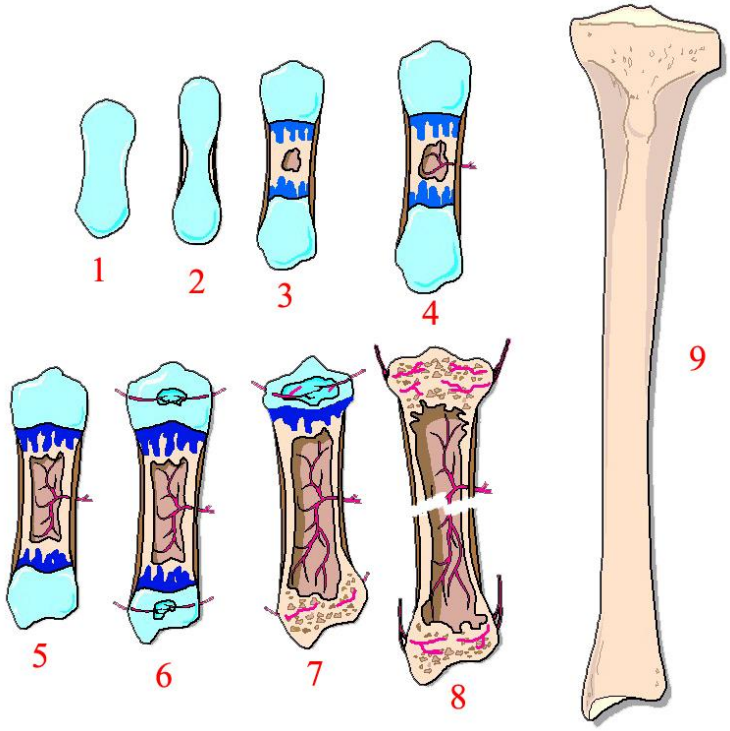
Physiology of Ossification

- Stage 1 is the embryonic "cast" of the developing bone.
- As it differentiates and matures, Stages 2 and 3, the cartilage differentiates into a bony collar and "grows" periosteum over it.



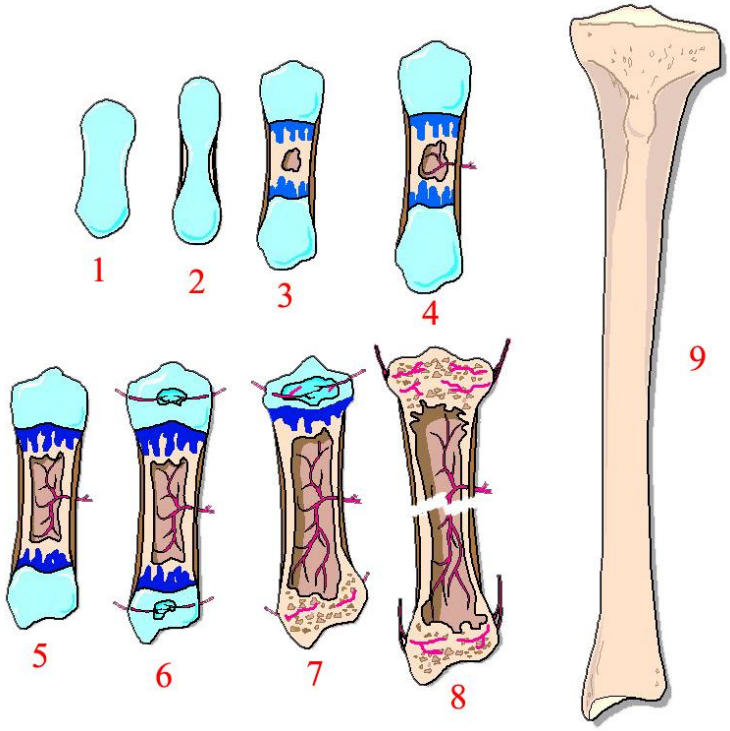
Physiology of Ossification

- The bone collar and cavity (primary ossification center) continues to grow and blood vessels penetrate into/through the developing bone into the “medullary cavity”, Stages 4 and 5.



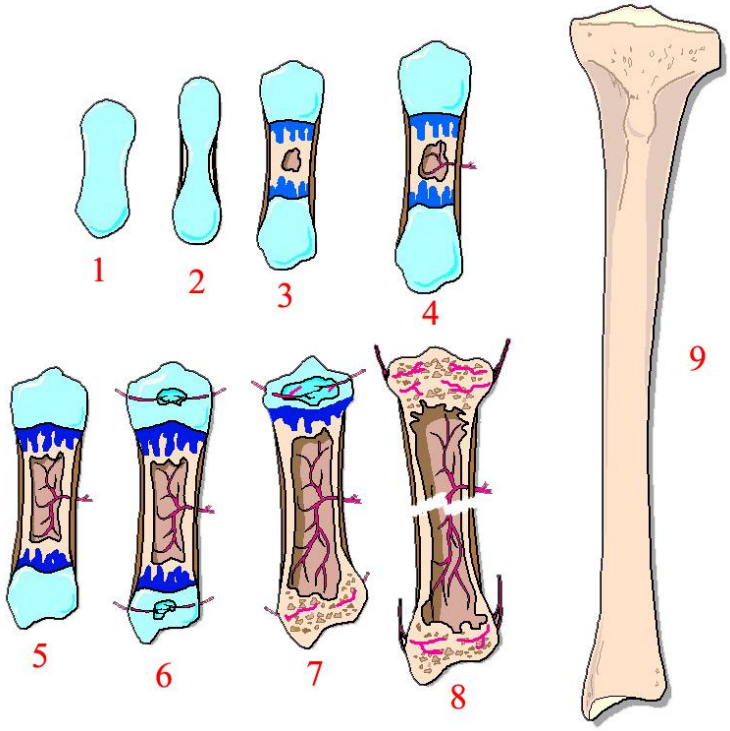
Physiology of Ossification

- These blood vessels stimulate osteoprogenitor cells to differentiate into osteoblasts to form spongy bone which will eventually transistion to compact bone, Stages 6 and 7.



Physiology of Ossification

- In Stage 8, you can see the ossification of the bone.
- Between Stages 8 and 9 the epiphyseal plate (metaphysis) ossifies to form the epiphyseal line.
  - At this point, there is no more longitudinal growth of the bone.
- Stage 9 illustrates an adult tibia.



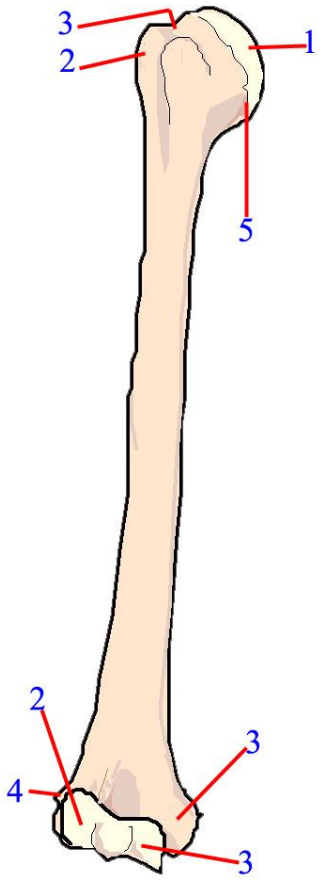
Physiology of Ossification

- The formation of the epiphyseal line occurs because the cartilage cells stop growing due to the effects of growth hormone and testosterone (or estrogens) and become bone.
- The clavicle is usually the last bone to stop growing in humans around the age of 25, more or less.
- This is also the usual (average) age at which ossification in most bones is complete.
- As a general rule (and most of us remember this from our own puberty), females stop growing first and males second – this is due to the effects of estrogens, ad nauseum.

Secondary Ossification Centers

- Typically, proximal secondary centers of ossification occur roughly at birth and the distal secondary ossification centers present at various ages.

Secondary Ossification Centers

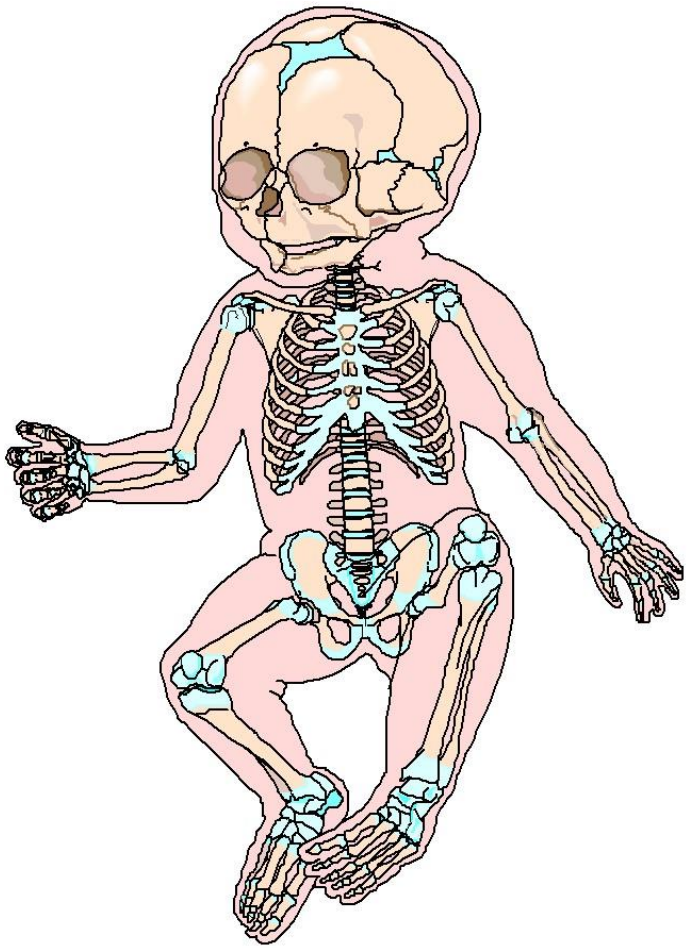
Humerus Illustration	Time (approximate) of Appearance of Secondary Ossification Centers in the Humerus
	1 – Head of Humerus appears at 3 months of age 2 – Greater Tubercle appears at about 2 years of age; Capitulum appears about 2 years of age 3 – Head and Greater Tubercle unite at about 6 years of age; Trochlea appears at about 9 years of age; Medial Epicondyle at about 6 years of age 4 – Lateral Epicondyle appears at about 11 years of age 5 – Epiphyseal Line – appears with cessation of longitudinal bone growth

Other representative secondary sites of ossification

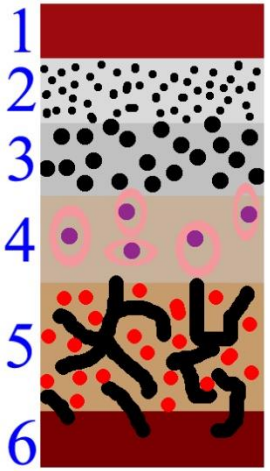
Age of Appearance	Site of Appearance	Age of Appearance	Site of Appearance
Birth	Distal epiphysis of femus; proximal epiphysis of tibia; cuboidal	6 years of age	Trapezoid; ulnar styloid
Birth to 1 year of age	Hamate (4 months); capitate (6 months); radial styloid, femoral head (9 months); 3d cuneiform; distal tibial epiphysis	7 years of age	Ischium and pubis fuse
2 years of age	Lateral malleolus	8 years of age	Epiphysis of os calcis (calcaneus)
3 years of age	Triangular; epiphyses of metacarpals and phalanges; 1st cuneiform; epiphyses of metatarsals	9 years of age	Olecranon process
4 years of age	Lunate; greater trochanter; fibular head; 2d cuneiform; navicular	10 years of age	Pisiform, epiphysis of Lesser Trochanter
5 years of age	Radial head; trapezium; scaphoid, patella	11 years of age	Tibial tuberosity

Infant's Cartilage Sites

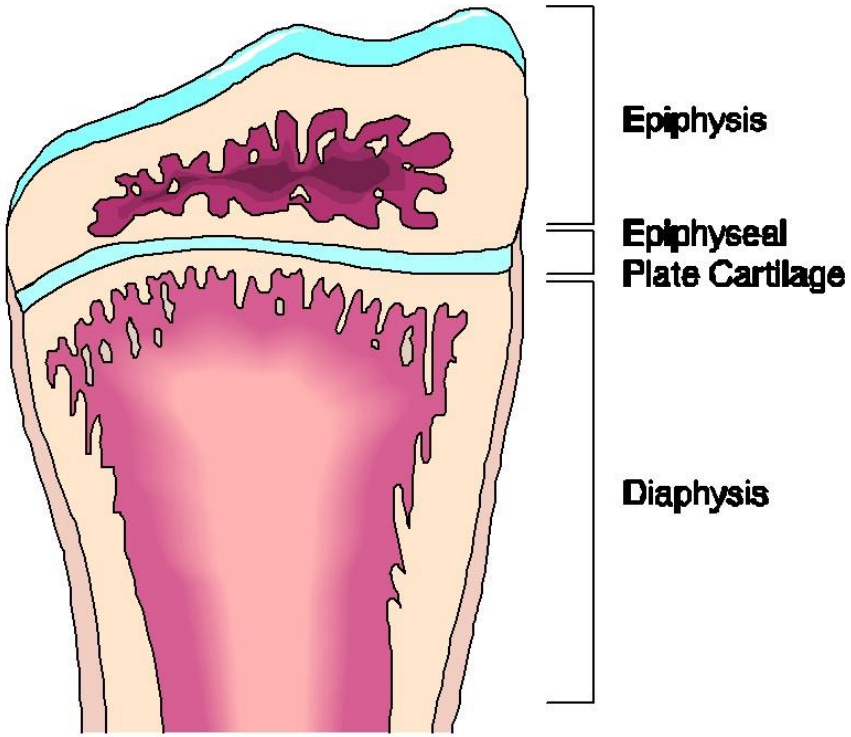
- For reference, refer to the following (not quite complete, although ok for us) illustration of a newborn infant's skeleton – all in blue is cartilage, BTW:



These secondary sites of ossification are the metaphyses (growth plates; epiphyseal plates).

Growth Zones	Artist's Rendition of Metaphysis (Epiphyseal Plate)	Comments
1 -- Epiphysis 2 – Zone of Reserve Cartilage 3 -- Zone of Proliferating Cartilage 4 – Zone of Hypertrophic Cartilage 5 – Zone of Calcified Matrix 6 -- Diaphysis		#2 anchors the epiphysis to the metaphysis and contains small chondrocytes #'s 3 and 4 have increasingly larger chondrocytes going towards the diaphysis #5 cements the diaphysis to the metaphysis; the red dots represent marrow space

Epi-, Dia- and Metaphyseal Relation



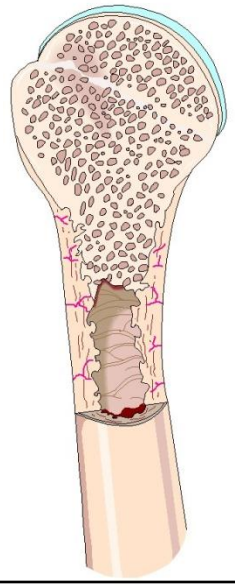
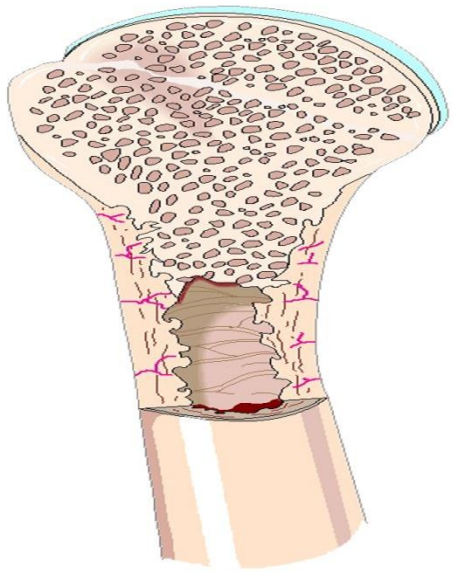
Bone Remodeling – Homeostasis and Fracture Repair

- Bone is never metabolically at rest – it constantly remodels itself and reappropriates matrix and minerals along lines of mechanical stress.
- It is due to this mechanical stress that the long bones are, more often than not, curved.
- The curvatures are “built in” through our genes so as to evenly distribute the stress due to our weight making our bones stronger – were these bones straight, there would be uneven distribution of stress which would lead to fractures.

Bone Remodeling – Homeostasis and Fracture Repair

- When bone remodels, it occurs by replacing old bone tissue with new bone tissue.
- New compact bone is formed by the transformation of cancellous bone.
- This is well demonstrated by examining the increase in diameter of a long bone.
- This increase occurs due to destruction of the bone closest to the medullary cavity and the construction of new bone around the outside of the diaphysis.

Bone Remodeling – Homeostasis and Fracture Repair

Starting "point"	Final remodel
	

Note the enlarged medullary cavity as well as the thickened diaphysis in the right illustration, above.

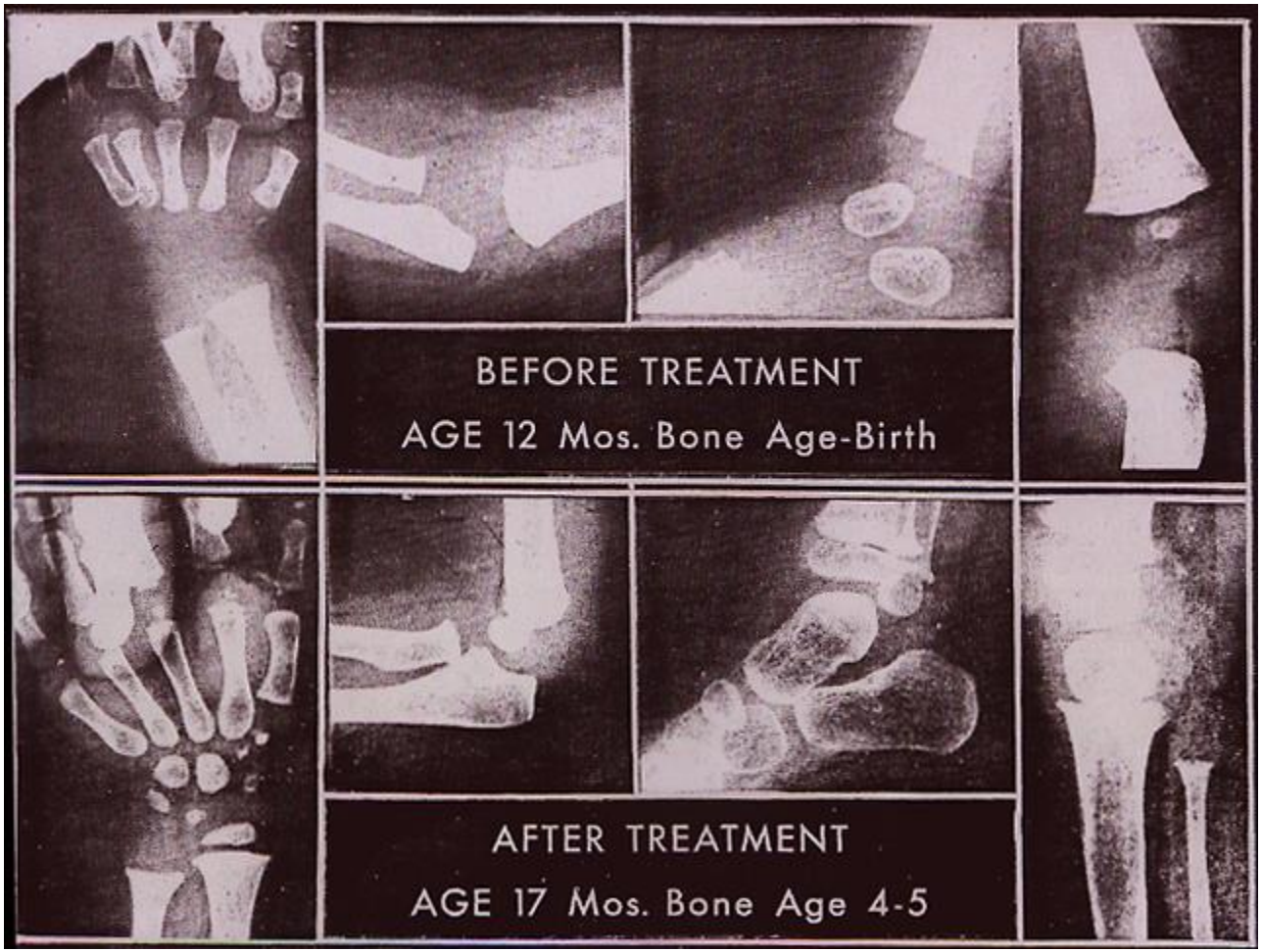
Normal Bone Growth

- Normal bone growth requires calcium, phosphate, boron, estrogens (for women), testosterone (for men), manganese (via parathyroid hormone), vitamins A, C and D.
- Vitamin D is required for calcium absorption across the gut, for bone calcium resorption and for renal calcium reabsorption.
- Vitamin C maintains connective tissue growth by aiding collagen synthesis from lysine.
- Reduced vitamin C levels leads to reduced collagen production which leads to retarded bone growth and delayed healing of fractures.
- Vitamin A controls the activity, distribution and coordination of osteoblasts and osteoclasts during development.
- Reduced vitamin A levels leads to reduced growth rates of bone.

Hormones Required for Normal Bone Growth

Growth hormone	Parathyroid hormone	Calcitonin	Estrogens	Testosterone
Responsible for bone growth (giant vs dwarf)	Increases activity and numbers of osteoclasts; increases calcium and phosphate release from the bone to the blood; increases renal calcium reabsorption; increases phosphate excretion	Decreases osteoclastic activity; increases calcium absorption BY bone	Increases osteoblast activity; increases bone growth; decreases chondrocytes; stops bone growth	Increases osteoblast activity; increases bone growth; decreases chondrocytes; stops bone growth
During adolescence, there is a surge in hormone release. This surge drives the growth spurt. As the bone grows, it "outgrows" the metaphysis, sealing the epiphyseal plates to form the epiphyseal lines. At this point we are at our adult height. These hormones (estrogens and testosterone) are a double edged sword: they stimulate and stop bone growth.				

Effects of Thyroid Hormone on Bone Development



Health Applications

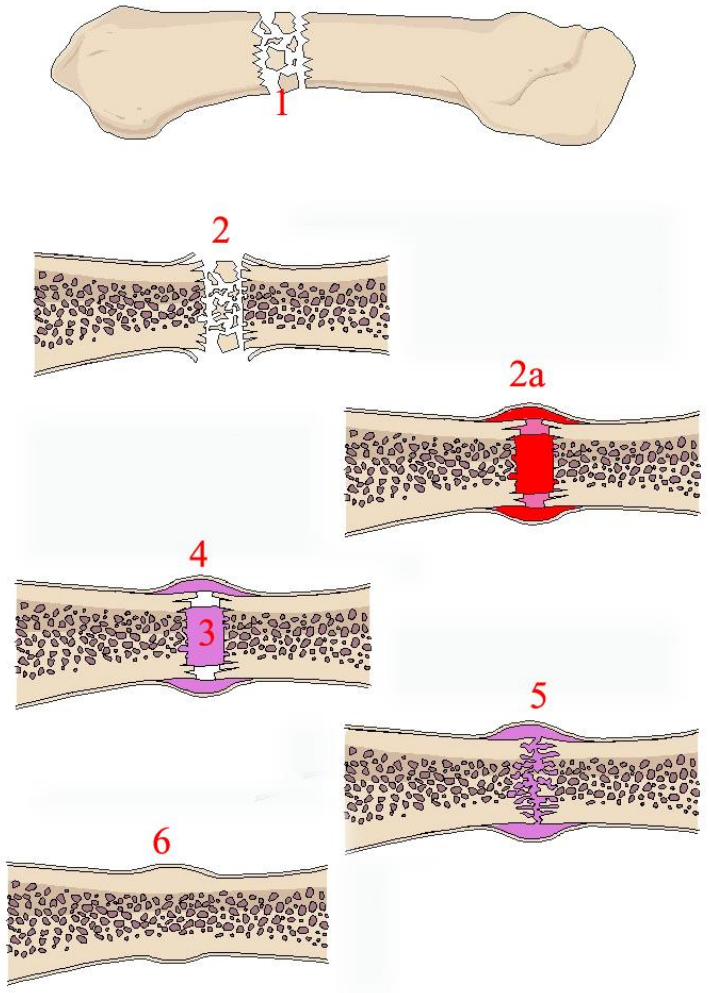
- Body build – short females are at greater risk since they have less total bone mass
- Weight – thin females are at greater risk since adipose tissue is a great source of estrone, an estrogen that retards bone loss
- Smoking – smoking decreases blood estrogen levels
- Calcium deficiency and malabsorption

Health Applications

- Vitamin D deficiency – can lead to rickets in the young or osteomalacia in adults – in either case, this leads to “soft bones”; rickets is characterized by bowed arms and legs (due to the weight of the body on these extremities) and chest deformities;
- Osteomalacia is characterized more by bowed legs, shortening of the back bone and flattening of the pelvic bones (it mainly effects women who live on poor cereal diets devoid of milk, are seldom exposed to the sun and who have repeated pregnancies close together that deplete their body of calcium).
- Exercise – sedentary people are more likely to develop bone loss
- Certain drugs – alcohol, some diuretics, caffeine, cortisone and tetracycline promote bone loss or block calcium uptake across the gut

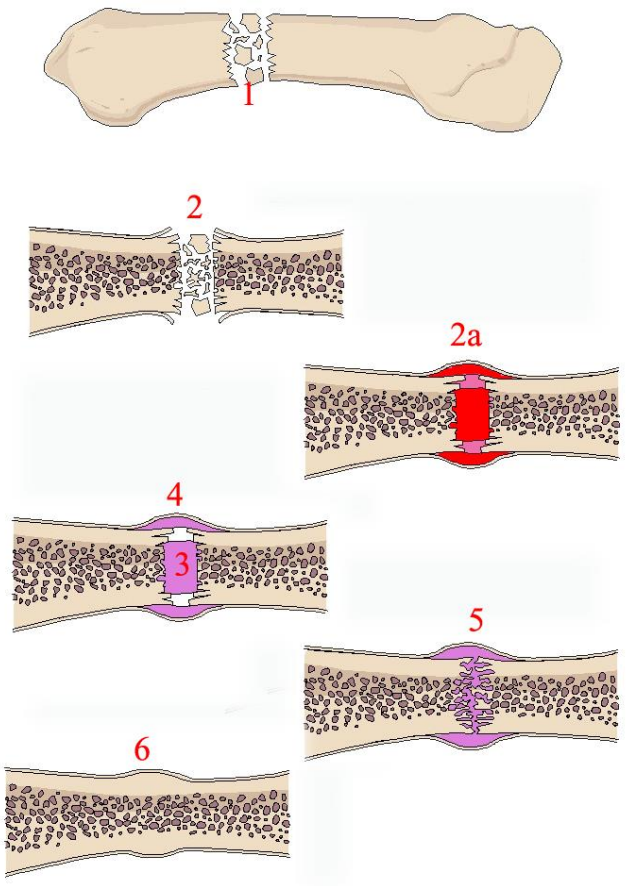
Fractures

- Stages 1 and 2 illustrate the appearance of a comminuted fracture.
- Stage 2a illustrates the formation of the fracture hematoma.
- This generally is present within 6-8 hours of the trauma.
- Stage 3 – callus formation – begins within 48 hours of the fracture and is driven by endosteal osteoblasts that are activated within the first week of the trauma.



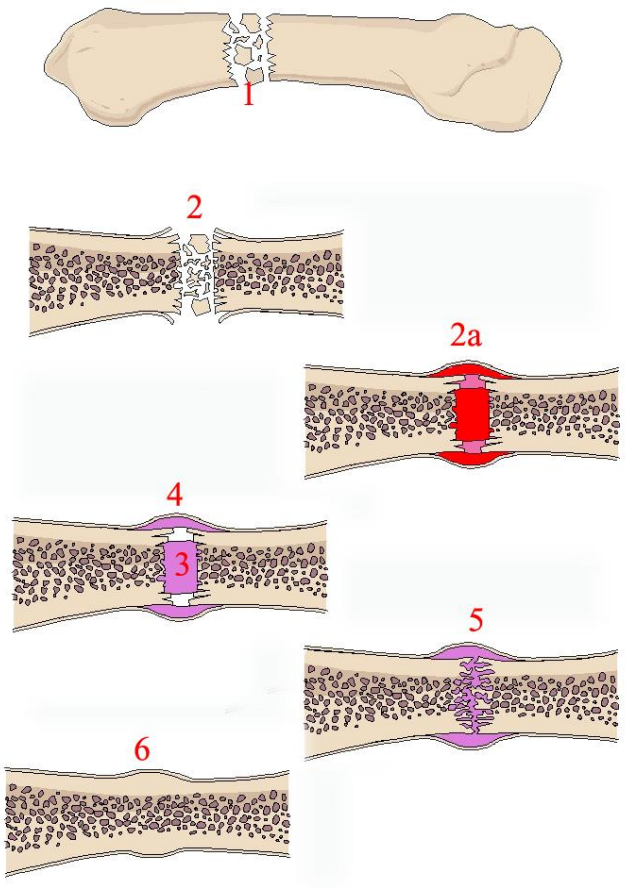
Fractures

- Stage 4 – callus formation – again, begins within 48 hours of the trauma and is driven by periosteal osteoblasts that are at full activation by day 10-14.
- Note that the inside of the bone is the first portion set up for repair.
- Also note that the early callus consists of cancellous bone laying down the trabecullar network.



Fractures

- Stage 5 and 6 illustrate the final stage of repair.
- Note that the younger one is when they have a fracture that the less permanent callus formation will remain – the opposite is equally as true.

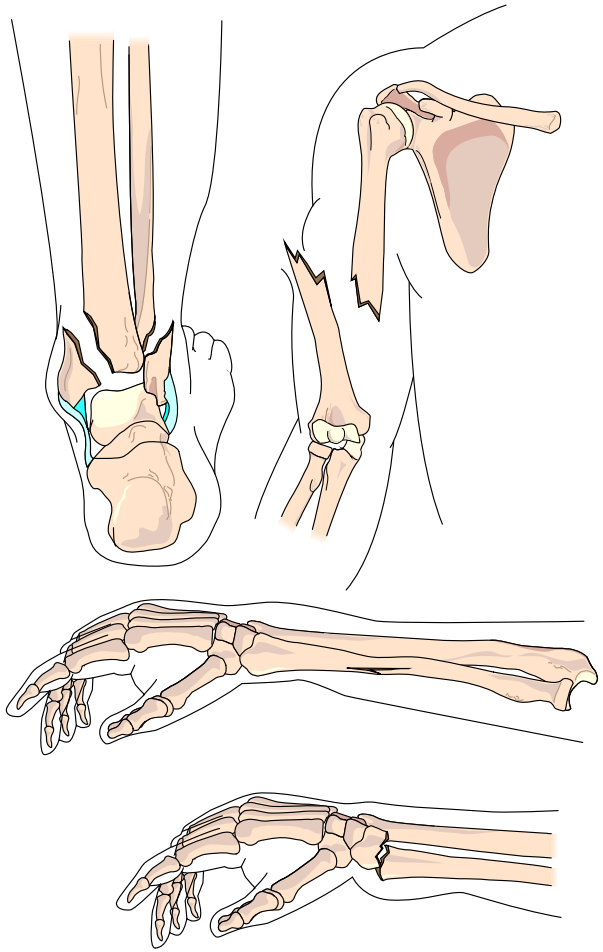


Fractures

- It is also of interest that bone development is actively driven by weight bearing activities.
- It seems that when a person put weight on his/her bones that it causes a “spark” to emit between osteoblasts/cytes via the Piezo electric effect that causes mineralization of the protein matrix – probably explains why (besides reducing the incidence of pneumonia) patients who have undergone hip repair surgery are up and about as soon as possible.

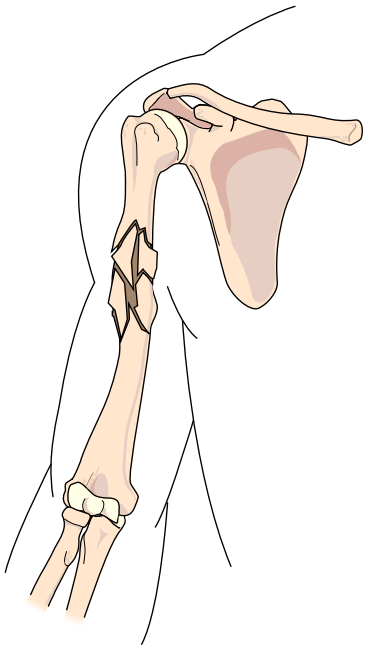
Fracture Types

Fracture Type	Comment
Colles' (BOTTOM)	From falling down; posterior dislocation of the radial head.
Pott's (TOP LEFT)	Fracture through the distal fibula, above the lateral malleolus.
Greenstick (MIDDLE BOTTOM)	Like the name implies, a partial fracture; usually in kids, one side "breaks" and the other doesn't – just like a green stick when you try to snap it.
Simple (NOT SHOWN)	Bone is fractured, not displaced.
Compound (TOP RIGHT)	Bone is sticking through the skin.



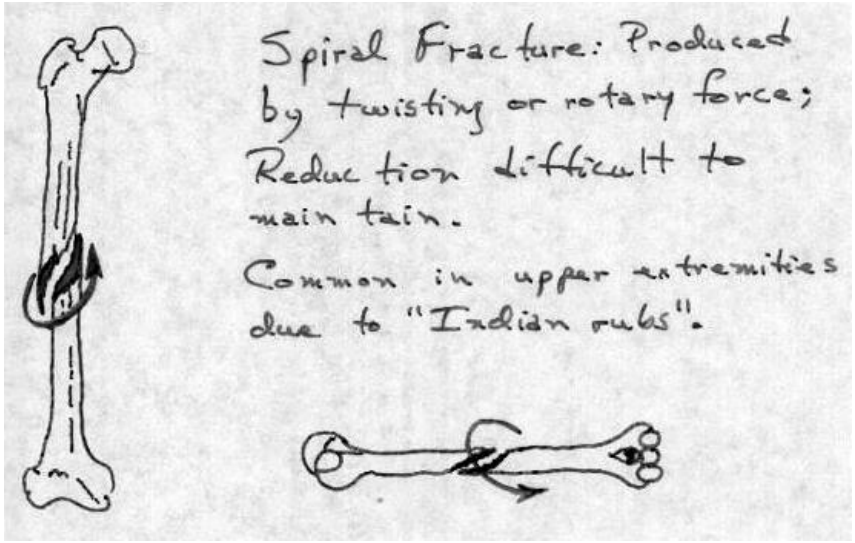
Fracture Types

Fracture Type	Comment
Impacted	Another sort of falling type of fracture; when the humeral diaphysis impacts into the humeral head.
Transverse	Fracture goes perpendicular to the diaphysis.
Oblique	Fracture goes at an angle to the bone – not at 90° (then it's transverse)
Comminuted (at RIGHT)	Essentially, "shattered" into tiny pieces; the diagram, above, of fracture repair is a comminuted fracture.
Pathological	Due to excessive sedentariness, glucocortocoid use, osteogenic sarcoma – bone gets "soft" and breaks.



Fracture Types

Spiral	Fracture runs spirally down the bone – just like a spiral-cut ham.



Piezo Electric Effect

- Piezoelectricity = pressure electricity.

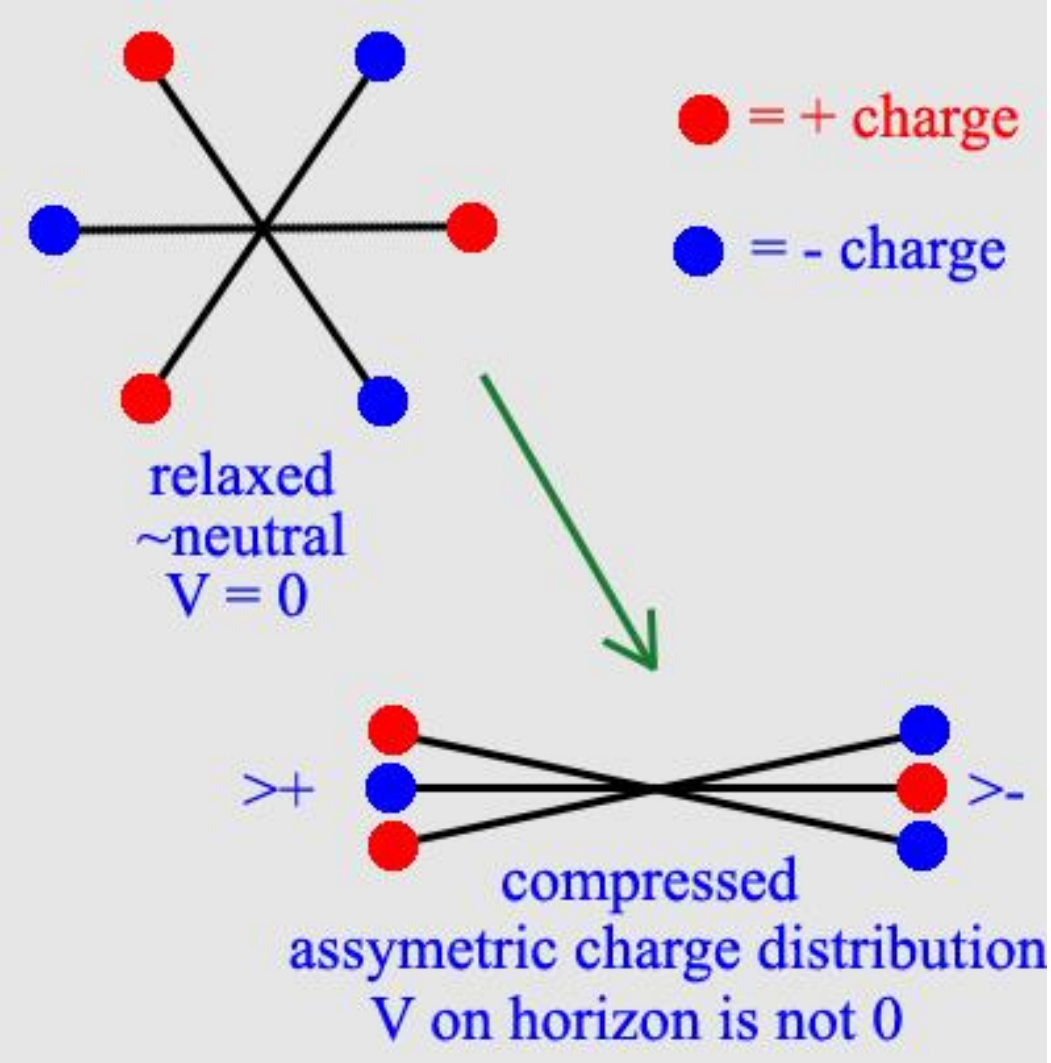
- We know it from BBQ grills with the propane "starter".

- 1st discovered in quartz and tourmaline
- Found in tendon, dentin, aorta, trachea, elastin and BONE!

Piezo Electric Effect

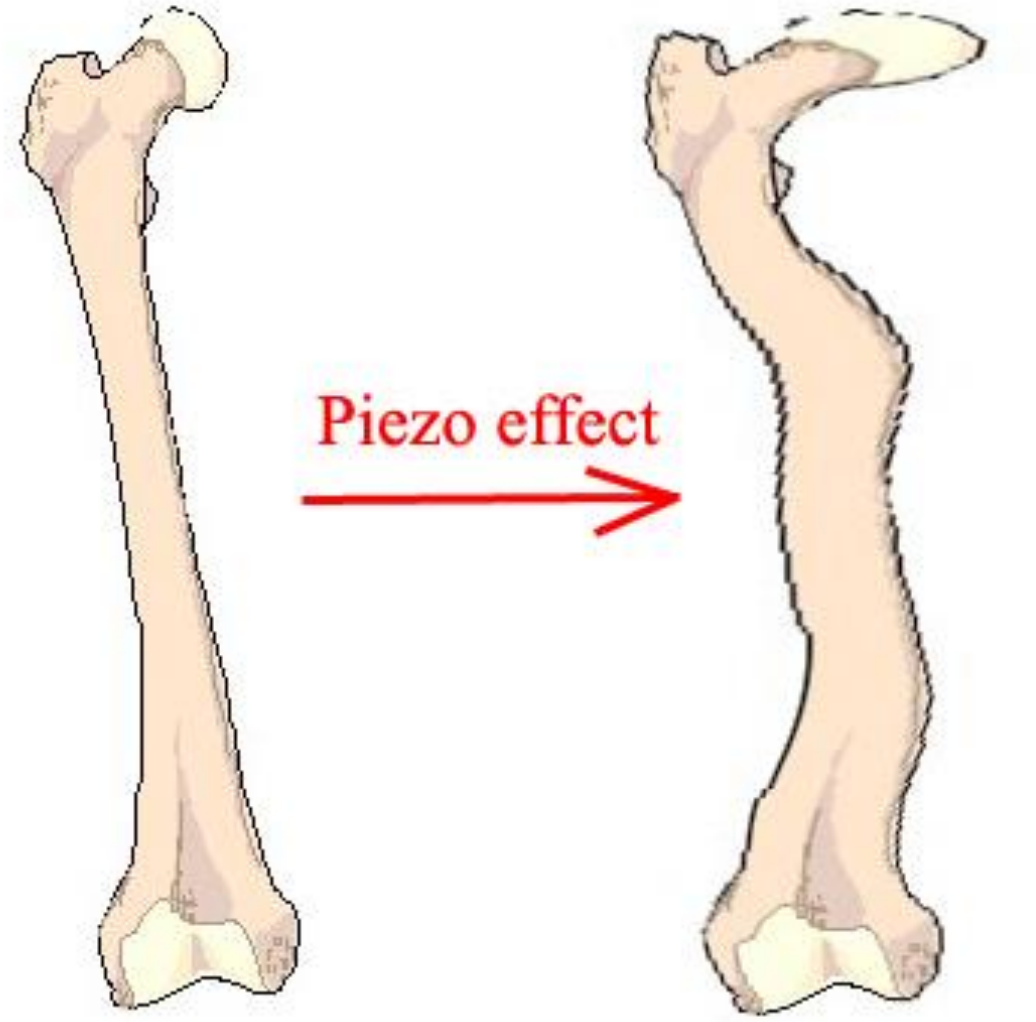
- The effect is the ability of a mineral or crystal to acquire opposing electrical charges on opposing surfaces when bending, stretching or compression is applied to the crystal.
- Is caused by displacing ionic charges within a crystal structure – the magnitude of the charge is usually proportional to the amount of stress applied.

Piezo – How It Works

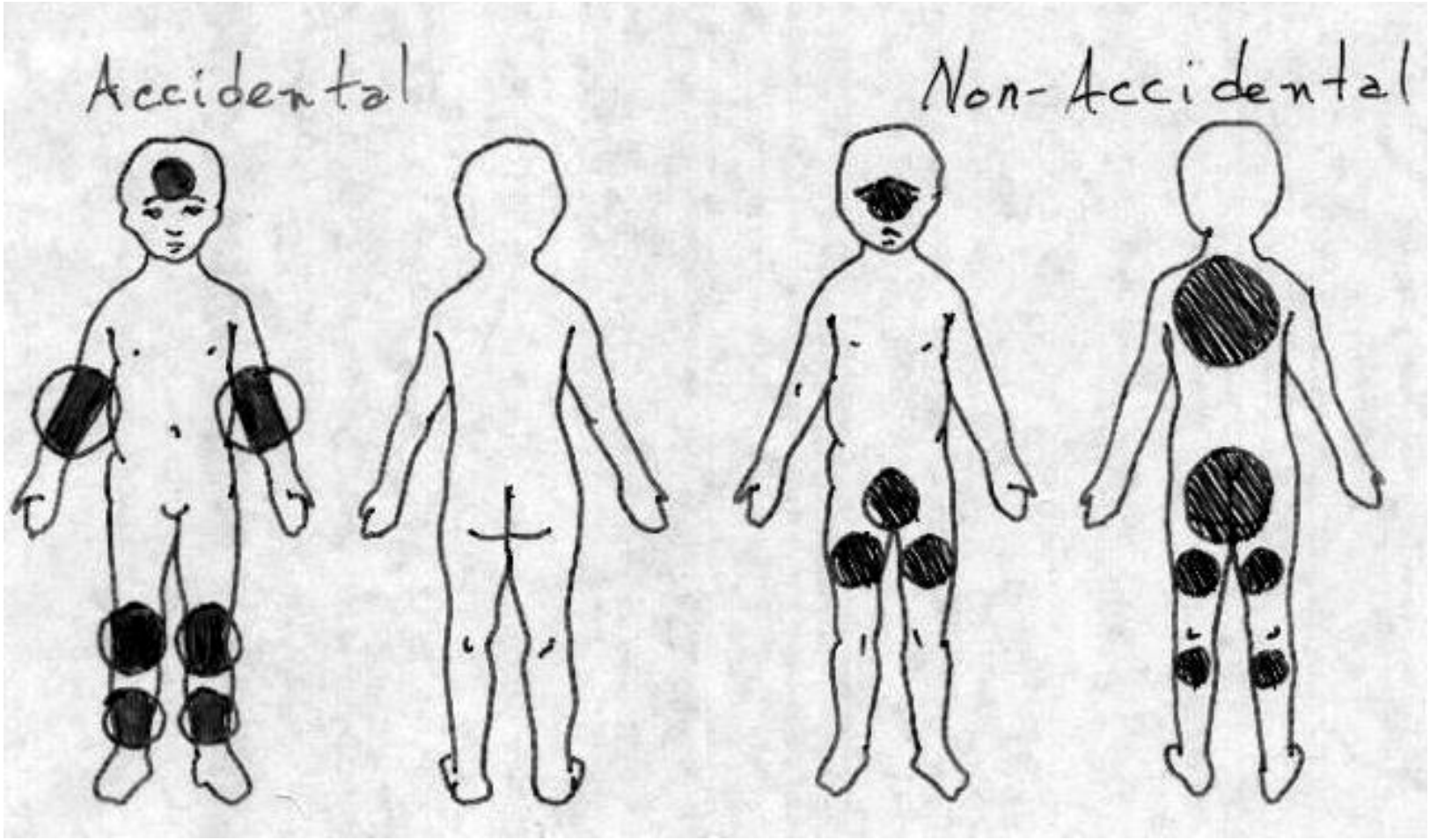


Piezo -- Bone

- This stress effect causes osteoblasts to secrete osteoid (CHON that permits Ca salt ppt'ation on/in it) to make/remodel new bone.



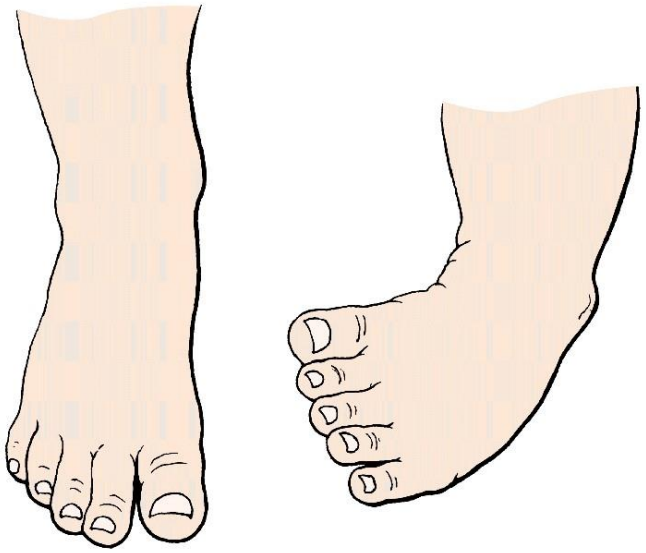
Accidental vs Non-Accidental Injury Sites



4 Prominent Types of Clubfoot

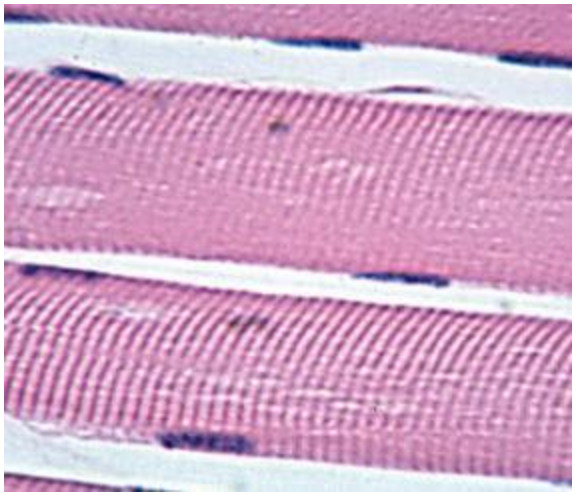
Clubfoot occurs in about 1 in 700 to 1 in 1000 live births. The cause is unknown.			
Talipes varus	Talipes valgus	Talipes equinus	Talipes calcaneus
The foot is inverted (shoe salespersons call this supination).	The foot is everted (shoe salespersons call this pronation).	The foot is plantarflexed.	The foot is dorsiflexed.

Talipes equinovarus is the most common form of clubfoot and is, more or less, illustrated, below:



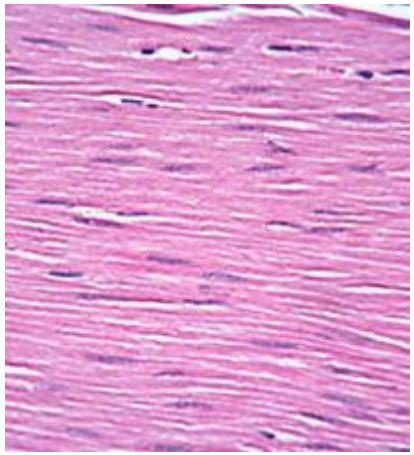
An Overview of Muscle Tissue

Striated Muscle



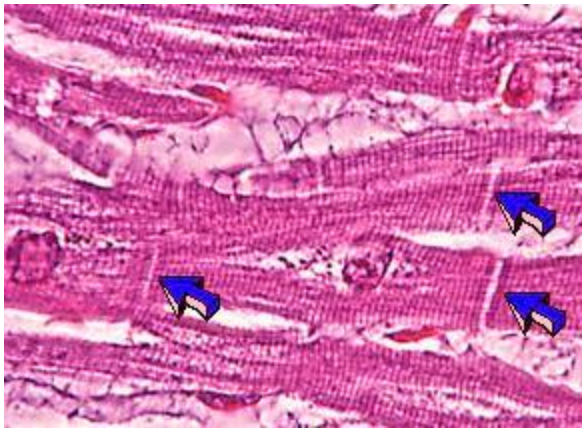
- In skeletal muscle.
- Has lines in the tissue.

Smooth Muscle



- Around hollow organs like arteries, the small bowel, esophagus.
- Has NO lines in the tissue.

Cardiac Muscle



- In the heart.
- Looks like striated with one BIG exception: the thicker lines are called intercalated disks -- these help to accelerate impulses between cells to get the heart muscle cells to contract, more or less, simultaneously.

Muscle tissue makes up 40-50% of the total body weight of an individual. There are 4 characteristics that are found in muscle:

Characteristic	Description
Irritability	The ability of muscle tissue to receive and respond to stimuli.
Contractility	The ability of muscle tissue to shorten and thicken after sufficient stimulus.
Extensibility	The ability of muscle tissue to be stretched.
Elasticity	The ability of muscle tissue to return to its original shape after contraction or extension.

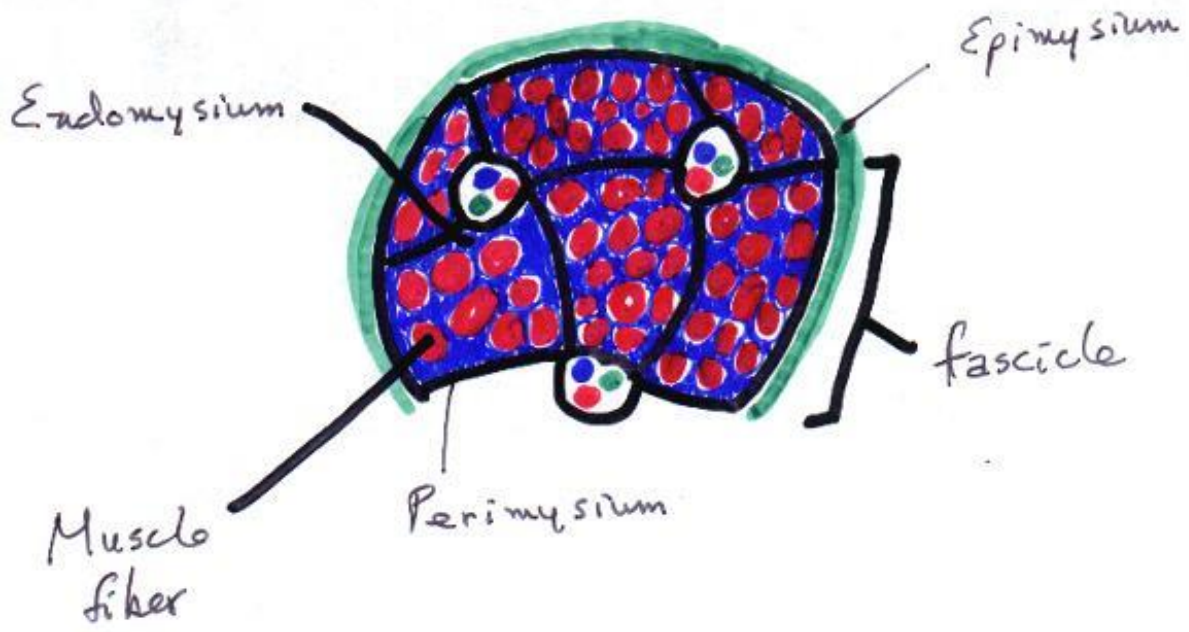
- The functions of muscle are as follow: Motion, Maintenance of Posture and Thermogenesis. Some motion is obvious: walking, running -- any form of locomotion. These motions rely on integrated functioning of bones, joints and muscles attached to bones. The less obvious motions include the motion of the myocardium, the peristalsis of the GI tract, contraction of the gall bladder and contraction of the urinary bladder.
- Muscles are necessary to maintain our posture. The contraction of the muscles holds the body in stationary positions such as sitting or standing.
- Muscles are necessary for heat production (thermogenesis). Skeletal muscle contractions produce heat and are important in maintaining normal body temperature during shivering or exercising.

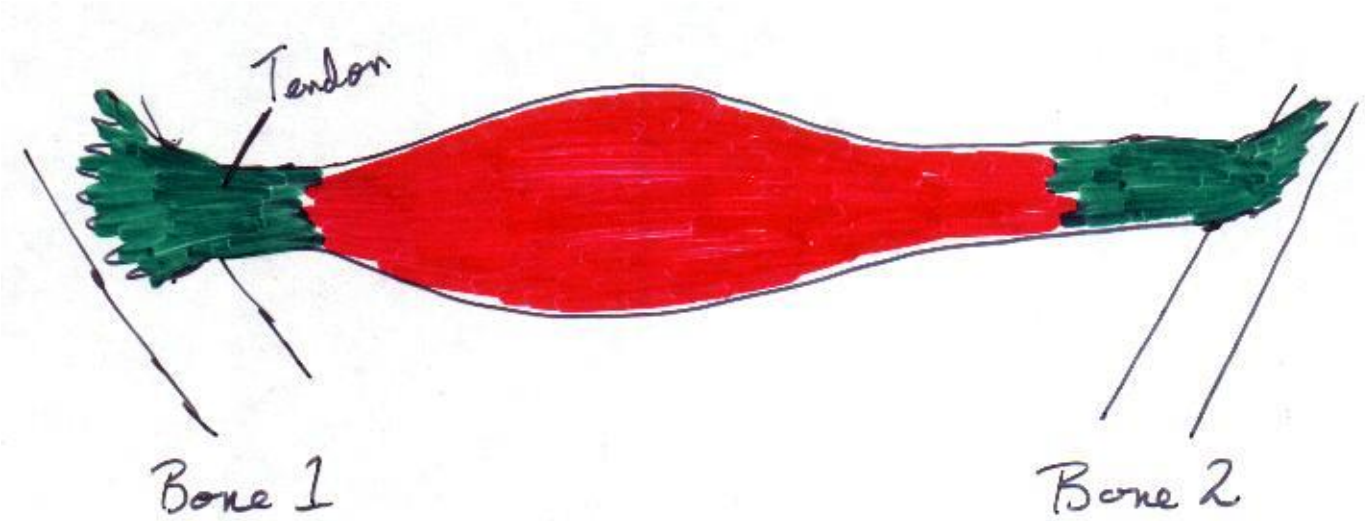
There are three kinds of muscle tissue as we discussed earlier in the course: skeletal, smooth and cardiac:

Skeletal	Smooth	Cardiac
This muscle is attached to bones.	This muscle is also known as visceral muscle.	This muscle is found in the walls of the heart.
This muscle is striated due to bands in it.	This muscle lines the walls of hollow internal structures, e.g., blood vessels, stomach, bowel.	This muscle is striated and contains intercalated disks to speed up fiber contraction.
This muscle is voluntary (under conscious control).	This muscle is involuntary, i.e., it is NOT under conscious control.	It is involuntary.
	This muscle is called smooth muscle because it is NON-striated.	

- When describing tissues around and in muscle, they are described by "fascia". Fascia is a sheet or broad band of fibrous connective tissue beneath the skin or around muscles and other organs of the body. There are three types of fascia: superficial, deep and subserous.
- Superficial fascia is also known as (aka) subcutaneous (SQ; SC) fascia. It is immediately deep to the skin. It is thin over the back of the hand and thick over the inferior abdominal wall. The outer layer consists of adipose tissue and the inner layer consists of reticular tissue. Between the inner and outer layers lie arteries, veins, nerves, mammary glands and the facial muscles.
- Deep fascia is the most extensive of the three types. It consists of dense connective tissue and has NO fat associated with it. It lines the body wall and extremities and holds the muscles together to form functioning groups and to form protective compartments.
- The subserous fascia is between the internal layer of the deep fascia and a serous membrane. It covers the external surfaces of the viscera in the thoracic and abdominal cavitites.

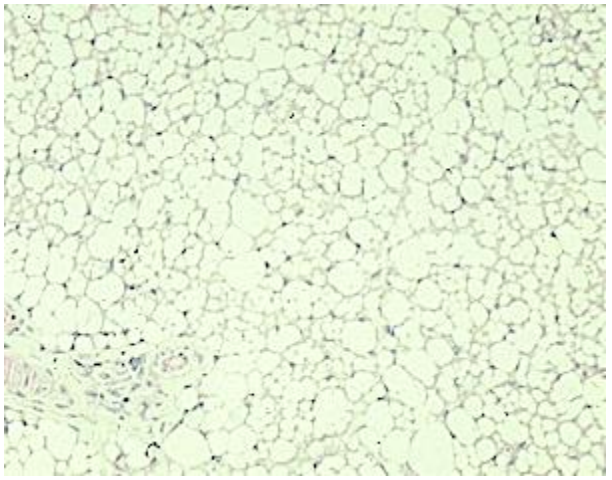
- Muscles attach to the periosteum of bone via tendons. Tendons are extensions of the epimysium, perimysium and endomysium. If you were to slice across a muscle, you would notice its similarity to steak. You would also notice three sorts of skeletal muscle fascia: endomysium, perimysium and epimysium. The epimysium is wrapped around the entire muscle. It is an extension of the deep fascia.
- The perimysium is invaginations of epimysium which divide muscle tissue into fasciculi.
- The endomysium is invaginations of the perimysium which separate each individual fiber.





- In addition to these three sorts of deeper fascia, there are three more terms one needs to become familiar with: tendon, aponeurosis and tendon sheath. As we said, before, a tendon is extensions of the epimysium, perimysium and endomysium beyond the end of the muscle. It is a cord of connective tissue that attaches muscle to periosteum.
- An aponeurosis is a broad flat band of tendons which also attaches to coverings of a bone or another muscle.
- A tendon sheath is a fibrous connective tissue (fct) tube, which encloses a certain tendon, e.g., what you would find in the wrist and ankle. It is lined by a synovial membrane that permits the tendon to slide easily within the sheath. It also prevents the tendon from slipping out of place.

Adipose Tissue

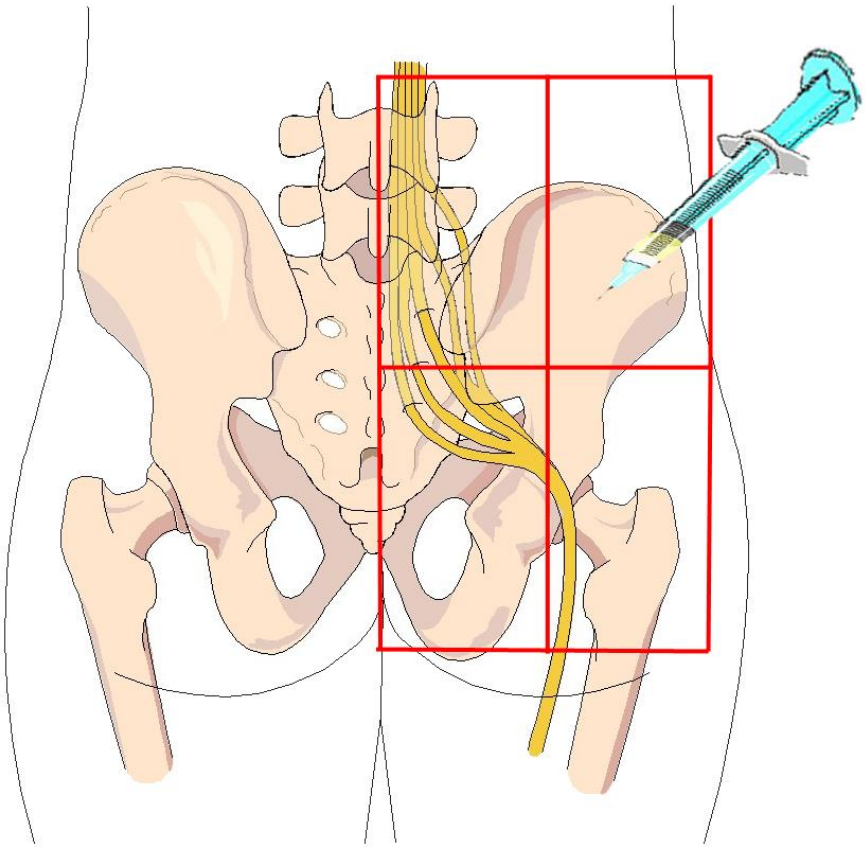


- Fat tissue -- pick a spot.
- Looks like chicken wire with the nucleus pushed to the side.

Neuroglia – Nervous Cells and Tissue

Neuroglia – The Brief Version

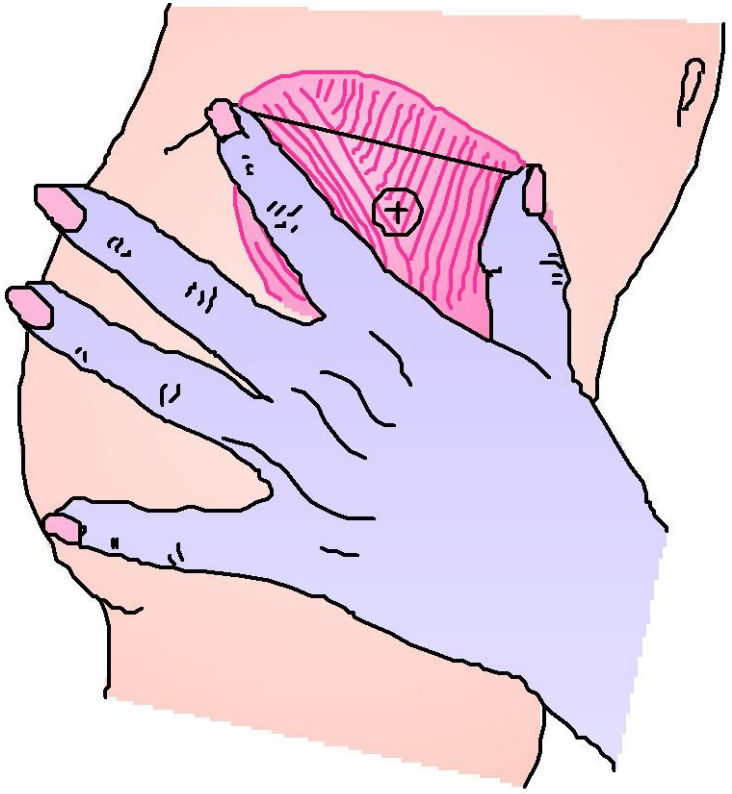
Why would anyone going in to health care at any level need to know anything about the nervous system? The graphic, right, illustrates why having a working knowledge of this system is so important:



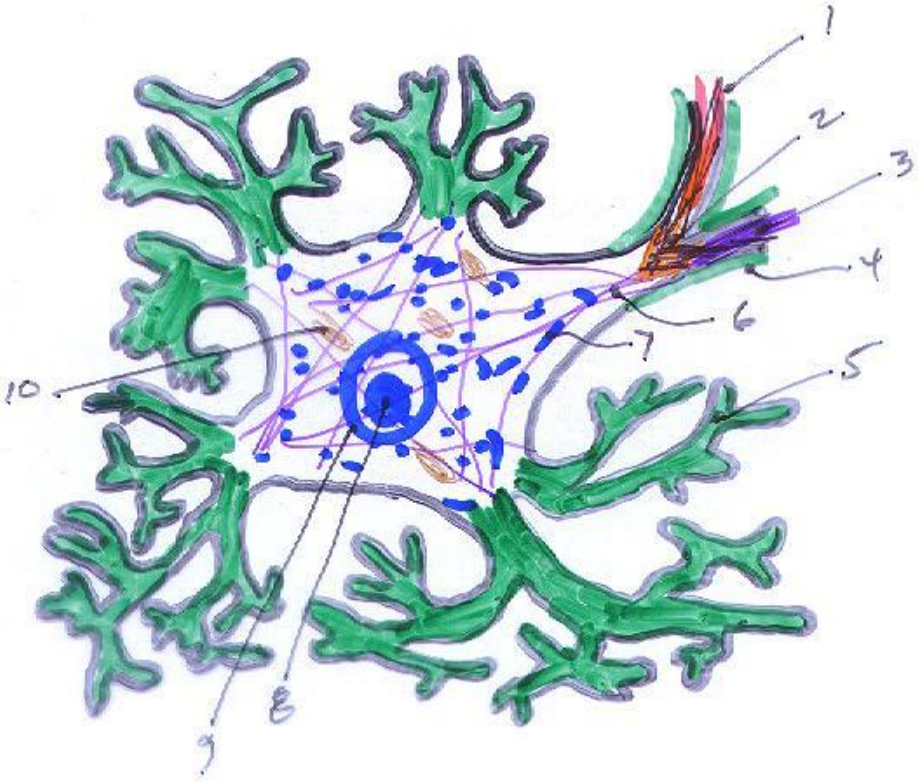
A working knowledge of the nervous system will prevent injuries to your patients. Remember that the first maxim of health care is “Do No Harm”.

On the surface, so to speak, the graphic, below, illustrates one technique for determining proper injection location to miss the sciatic nerve (which was illustrated, above – the needle goes in the upper outer quadrant (above) or in the triangle bounded by your thumb, forefinger and an imaginary line between the two digits at about the “+” mark):

There are other sites, e.g., deltoideus and vastus lateralis, for which that knowledge is important, as well.



- For all intents and purposes, the general term neuroglia covers all nervous tissue. Before we get into the different kinds of cells in nervous tissue, we first need to get a grasp on a single neuron or nerve cell.



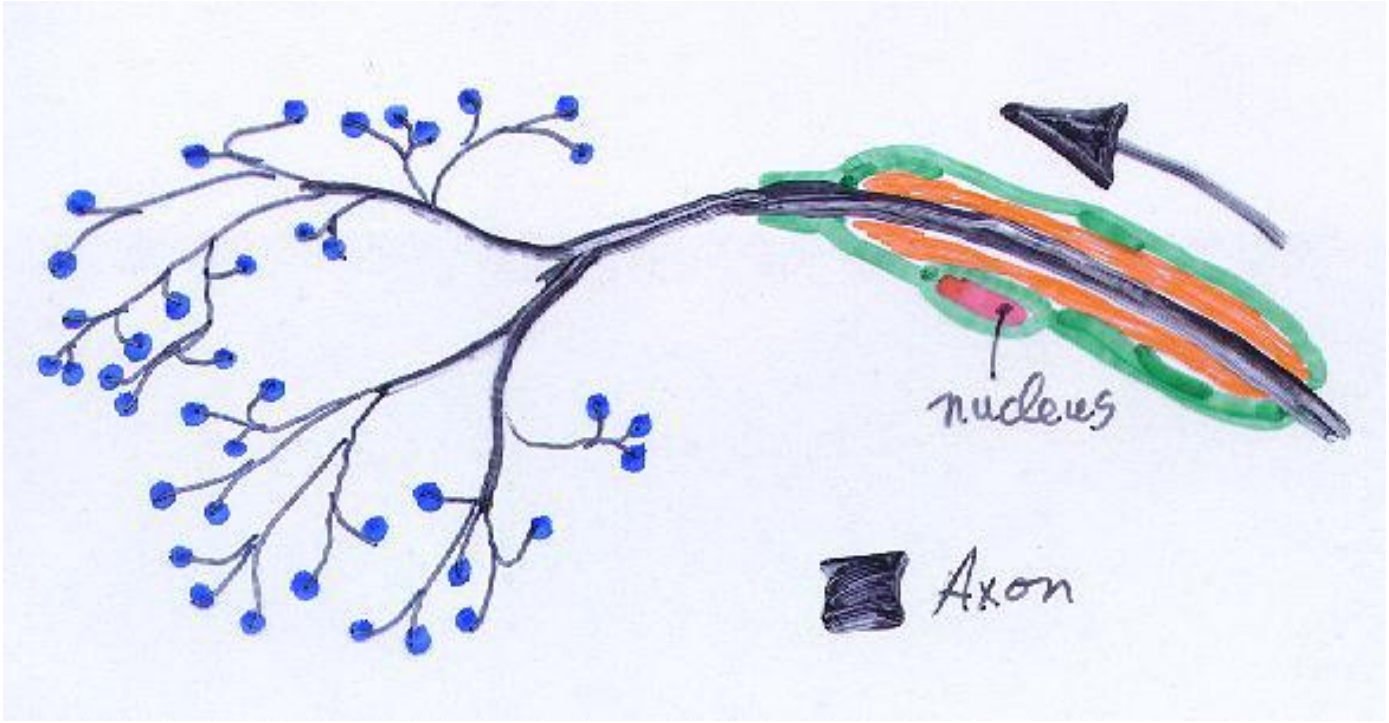
Number	Region	Number	Region
1	Axon collateral	6	Nissl bodies
2	Axon hillock	7	Neurofibrils
3	Axon	8	Nucleolus
4	Axolemma	9	Nucleus
5	Dendrites	10	Lipofuscin

- The cell body is also known as the soma or perikaryon. It has a well defined nucleus and nucleolus which is surrounded by a granular cytoplasm. The cytoplasm contains typical sub-cellular organelles.

- Dendrites are highly branched thick extensions of the cytoplasm of the cell body. Their function is to conduct nerve impulses TOWARDS the cell body. It is because of dendrites that some people have to have their lower central incisors anesthetized individually when the trigeminal nerve block doesn't catch them as well.

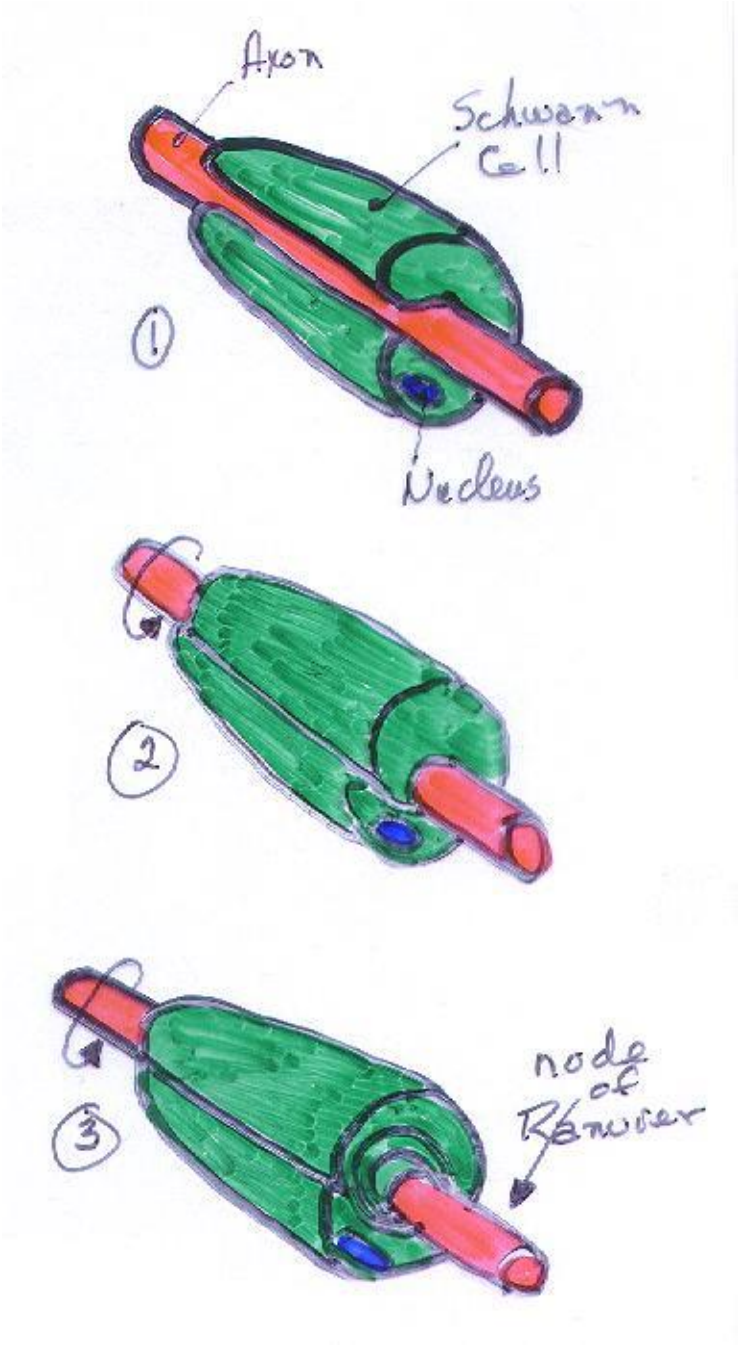
- An axon is a single highly specialized, usually long process that conducts impulses AWAY from the cell body to another neuron or tissue.

- The axon hillock is the point of origin of the axon from the cell body. An axon collateral is a side branch (or are side branches) along the length of the axon.
- The axolemma is the plasma membrane which surrounds the axoplasm (the cytoplasm in the axon).
- Lipofuscin is clumps of yellowish-brown granules. This substance is related to aging, i.e., the amount increases with increasing age.
- Nissl bodies are also known as chromatophilic substance. This is an orderly arrangement of rough endoplasmic reticulum. Its function is protein synthesis.
- Neurofibrils are long thin fibrils of microtubules. Their function is to provide support (intracellular skeleton) and “irrigation” (nutrient transport).

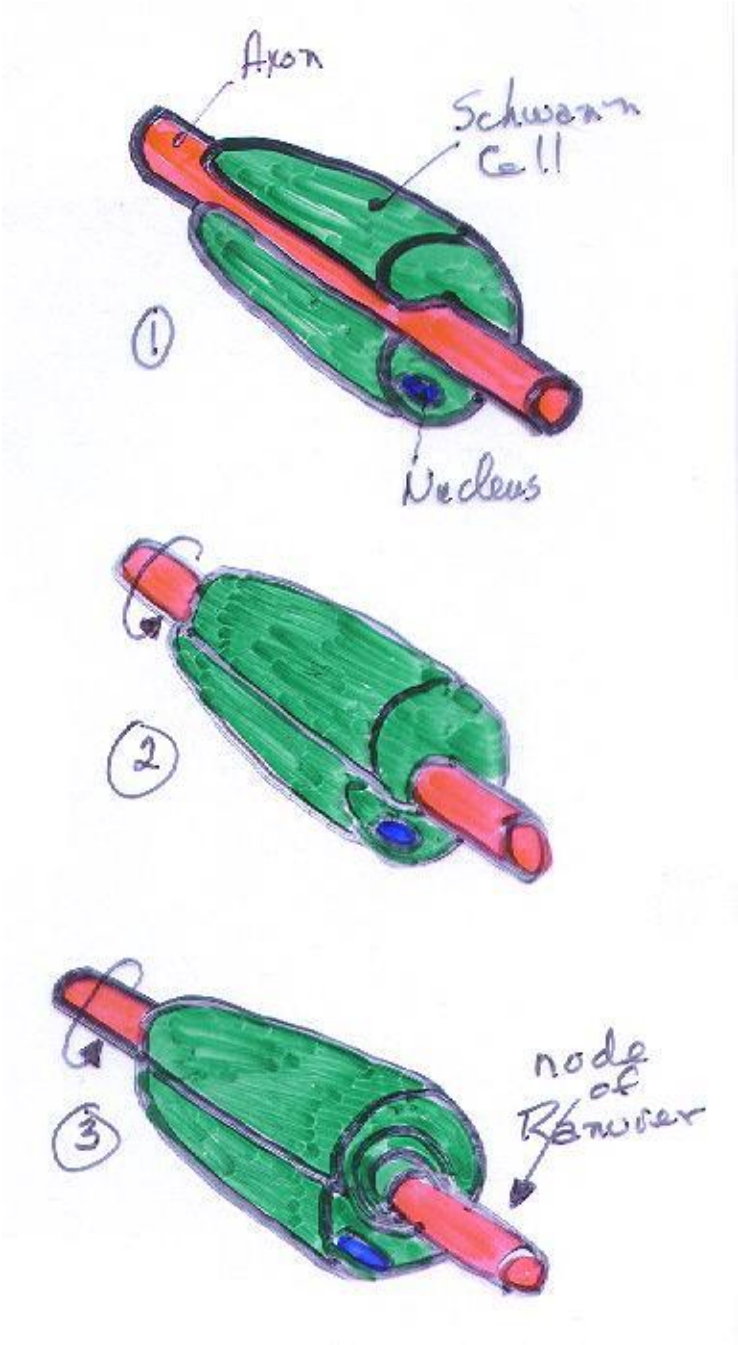


- The <u>neurolemma</u> is best illustrated in the graphic
- The neurolemma is in **green**. It is also known as the Sheath of Schwann. Note the peripherally located nucleus is in the sheath. The neurolemma is found ONLY around fibers in the peripheral nervous system (everything in the nervous system except the brain and spinal cord). The function of the neurolemma is to provide a "tube" for axonal regeneration following nerve section. Schwann cells are flattened cells which produce the myelin sheath.

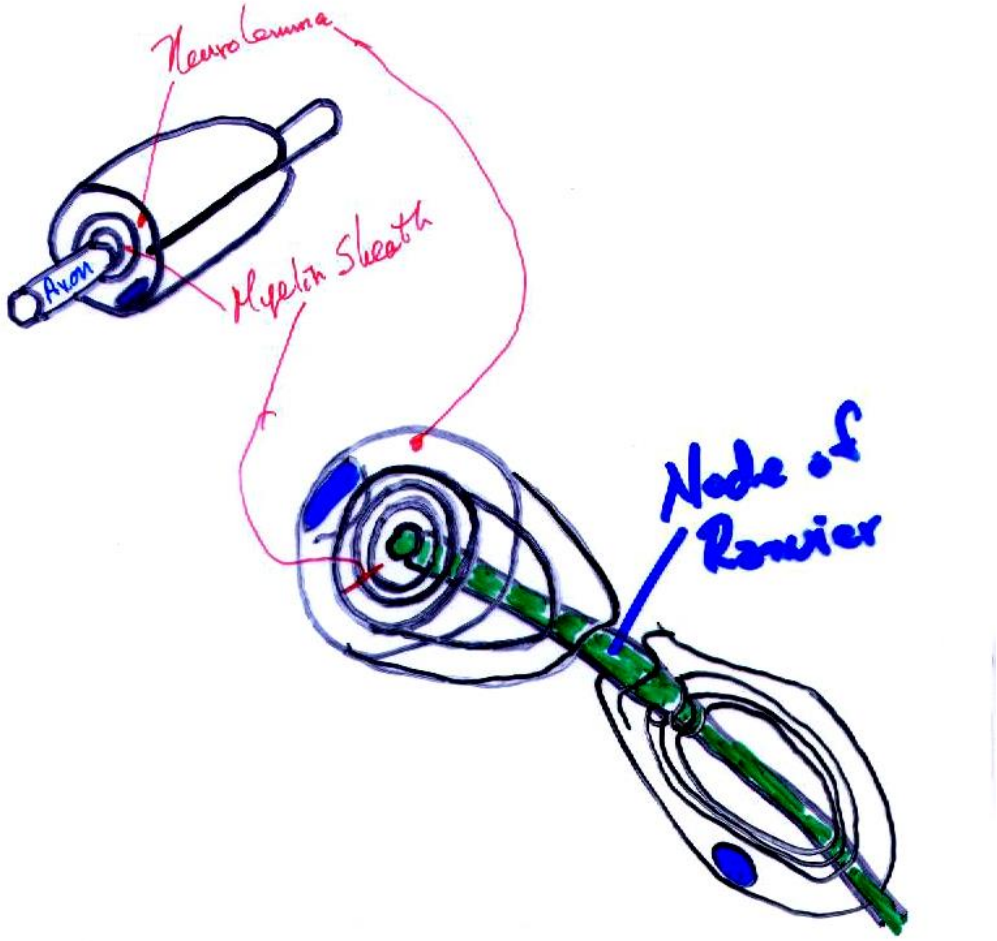
- The illustration shows how the myelin sheath wraps around the nerve fiber:
- Note that Schwann cells surround the large axons outside the central nervous system (CNS). The myelin sheath is a multi-layered, white segmented covering containing phospholipids. Its function is to increase the speed of nerve impulse conduction and to insulate and maintain the axon. Myelin gives the color to white matter in nerves, the brain and the spinal cord. Note also that the Schwann cell wraps beneath itself as it winds around the nerve tissue.



- The myelin sheath protects and insulates nerve fibers from each other – note, too, that one Schwann cell is wrapped around one segment of one nerve fiber. The space between the Schwann cell and the axon is on the order of 10-20 nm – this is called the peri-axonal space.



- Myelin is first laid down during the later part of fetal development and during the first year of life. The amount of myelin increases from birth to maturity and its presence greatly increases the rate of nerve impulse conduction. Due to lower levels of myelination in infancy, an infant's responses to stimuli are not as rapid OR as coordinated as those of an older child or an adult. Myelination is generally "complete" by 5-7 years of age. It is because of this that a diagnosis of ADD or ADHD is not best determined until after the age of 7 – and this is a minimum, given the immaturity of boy childrens' nervous systems. This creates problems when their elementary school teachers don't have the energy or the self-discipline necessary to keep up with them and seek medication for the children to make the adults' lives easier.



In between each Schwann cell is a gap that exposes the nerve segment. This gap is called the Node of Ranvier. The gap acts as a sort of "spark plug" to speed up nerve impulses even more. The internodal segments (Nodes of Ranvier) range in distance from 200-300 nm up to 2000 μm.

In general, small fibers have short internodes (gaps) and large fibers have long internodes. The table, below, summarizes the rate of impulse difference between myelinated and un-myelinated fibers:

Myelinated fibers	vs	**UN-myelinated fibers**
150 m/sec		**1 m/sec**
Primarily peripheral		**Primarily CNS**

Large diameter fibers with long internodes and thick myelin sheaths conduct impulses up to 50 times faster than small myelinated fibers.

The Nodes of Ranvier also seem to have the following three additional functions:

- ion-exchange buffer – the gaps have a capacity to concentrate and maintain a high, but osmotically **IN**active, reservoir of sodium ions (Na^+) close to the nodal axolemma.

- The "paranodal apparatus" (ends of the Schwann cells and node) may provide a source of energy rich compounds for the nodal axolemma OR play a role in controlling the ionic milieu in the node gap.

- It is possible that the paranodal apparatus is concerned with the active concentration of sodium ions in the nodal gap (the space between the axon and the neurolemma in the node) by using Schwann cell mitochondria to provide energy necessary to pump sodium ions outside the sheath into the microvillous surface at the node.

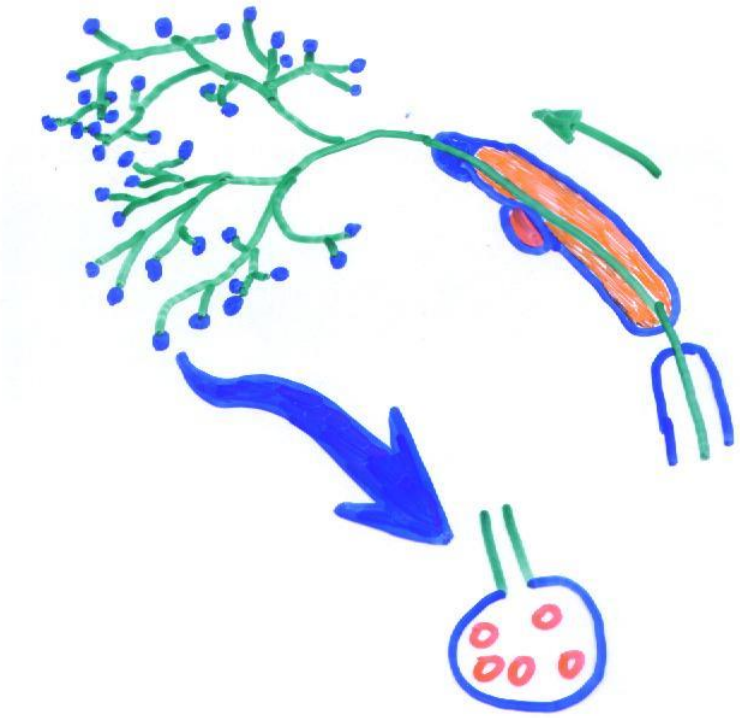
Schwann cells appear to also serve as a source of general metabolic support for peripheral axons with two transport systems, each having a different rate:

- 1-3 mm/day – this system is distally directed and the rate of transport is about the same as the rate of regrowth of severed axons.

- 400 mm/day – this is the fast transport system. It is energy dependent and appears to be largely concerned with particulate constituents of the axoplasm and materials such as enzymes, glycoproteins and membrane components.

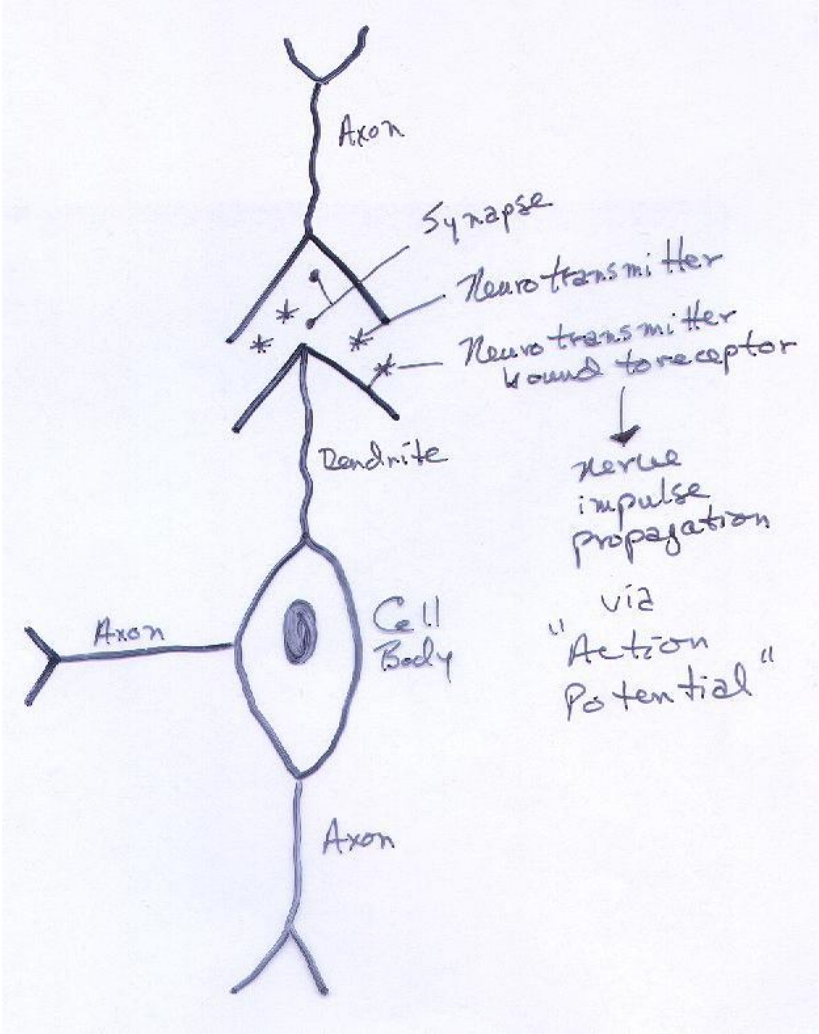
- In the CNS, oligodendrocytes form the myelin sheath.
- Each oligodendrocyte can coil around as many as 60 different axons at once vs the Schwann cell's coiling around one axon.
- Oligodendrocytes also lack the neurolemma which does not permit nerve re-generation if the nerve is damaged.
  - White matter in the CNS is primarily fiber tracts wrapped in myelin.
  - Gray matter in the CNS contains mostly nerve cell bodies and UN-myelinated fibers.
- The term "nerve fiber" may be applied to any process projecting from the neuron and primarily refers to the axon and sheath.

The last neuronal bit of anatomy is illustrated, below:

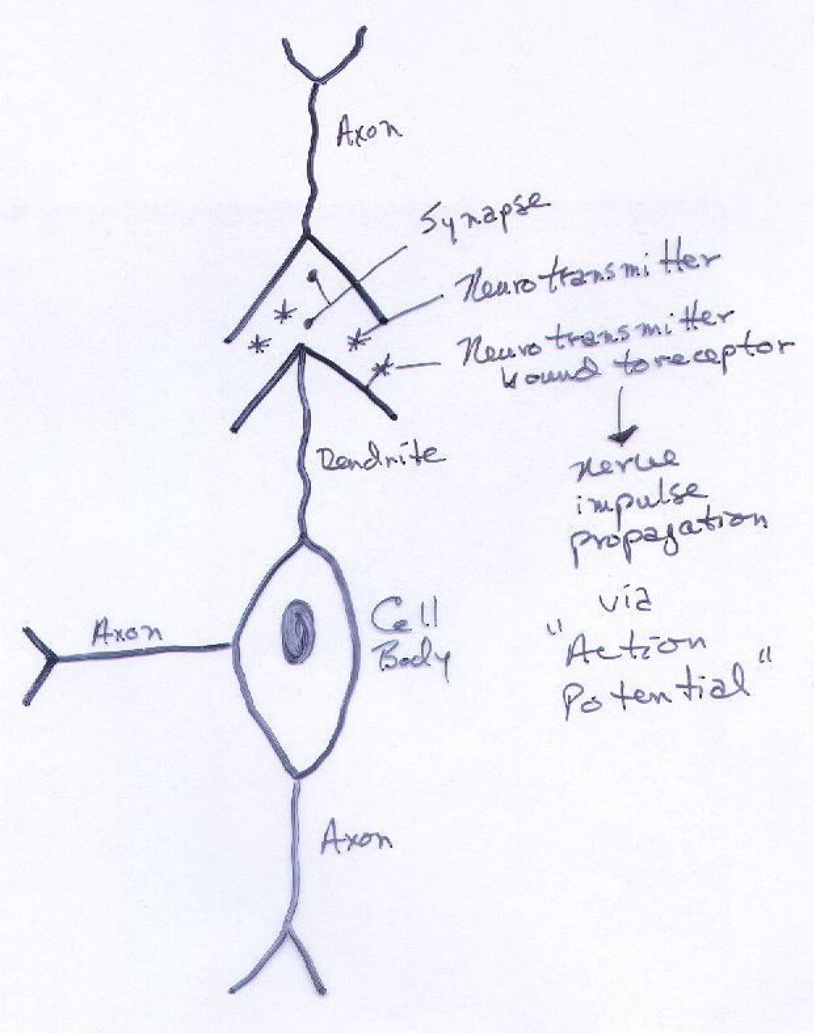


The small blue dots represent the distal ends of the axon terminals. They are bulb-like and are necessary for nerve impulse conduction between neurons or between a neuron and muscle or gland. In the exploded view (green stalk with blue sac containing red circles, above) are the synaptic vesicles. These are membrane-enclosed sacs in the ends of the bulbs. They store neurotransmitters that determine where a signal is sent.

The gap between an axon and another cell's dendrite[s] is called the synapse. This is crudely illustrated, below, for you:

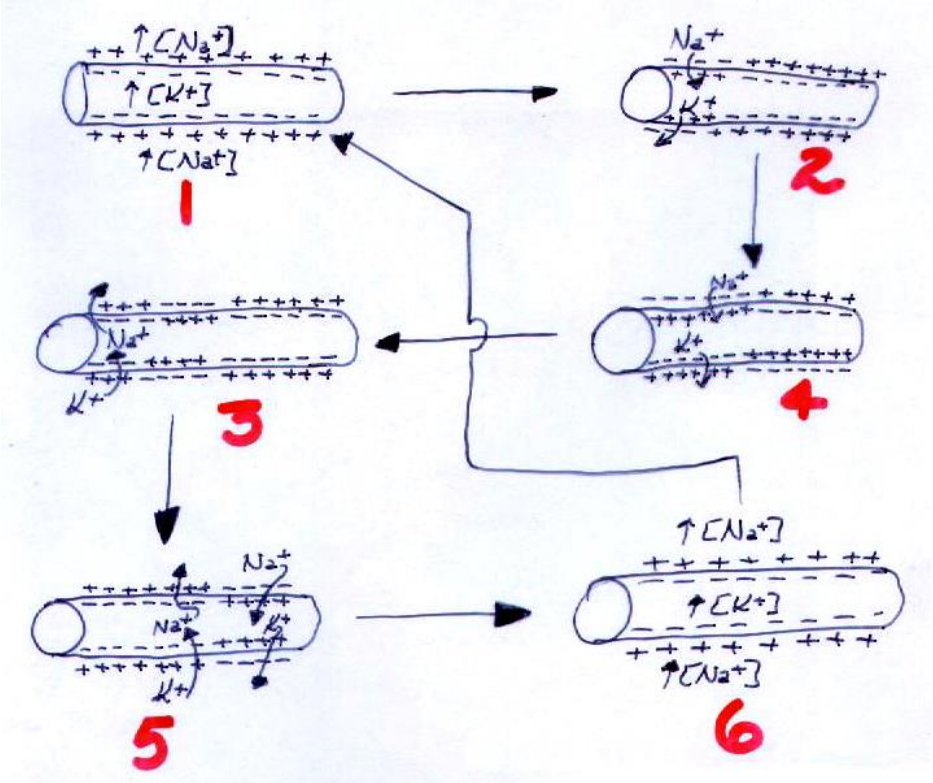


- Each portion is labeled. In order to get neurons to communicate from axon to dendrite[s], they must be “hit with” a small electrical current – a way to think about this is to take a 9V battery and touch the terminals to your tongue. This current is called an “action potential”. The action potential – as long as you don’t get carried away with its intricacies – is pretty basic. It simply reflects the movement of sodium ions, potassium ions and the hydrolysis of ATP to form ADP and P_i.



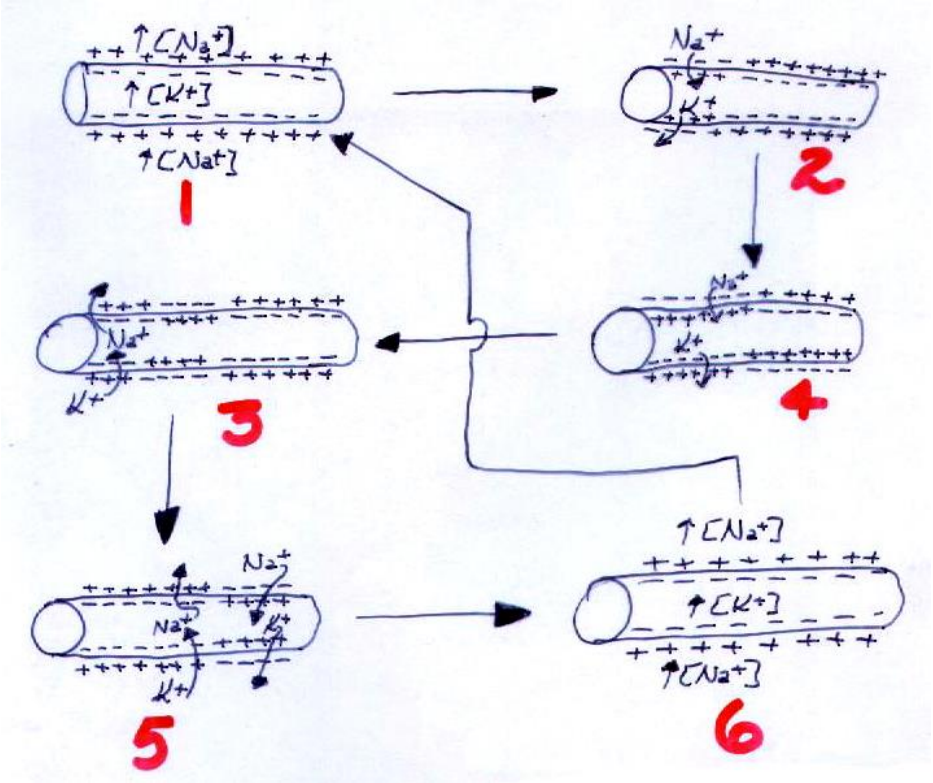
- In general, for every 3 sodium ions that move across the membrane and for every 2 potassium ions that move across the membrane concurrently (more on this in the Heart and EKG lectures in BIOL 224), 1 ATP molecule is hydrolyzed so that there is enough energy to drive the potential along the membrane.

The action potential is roughly illustrated below:



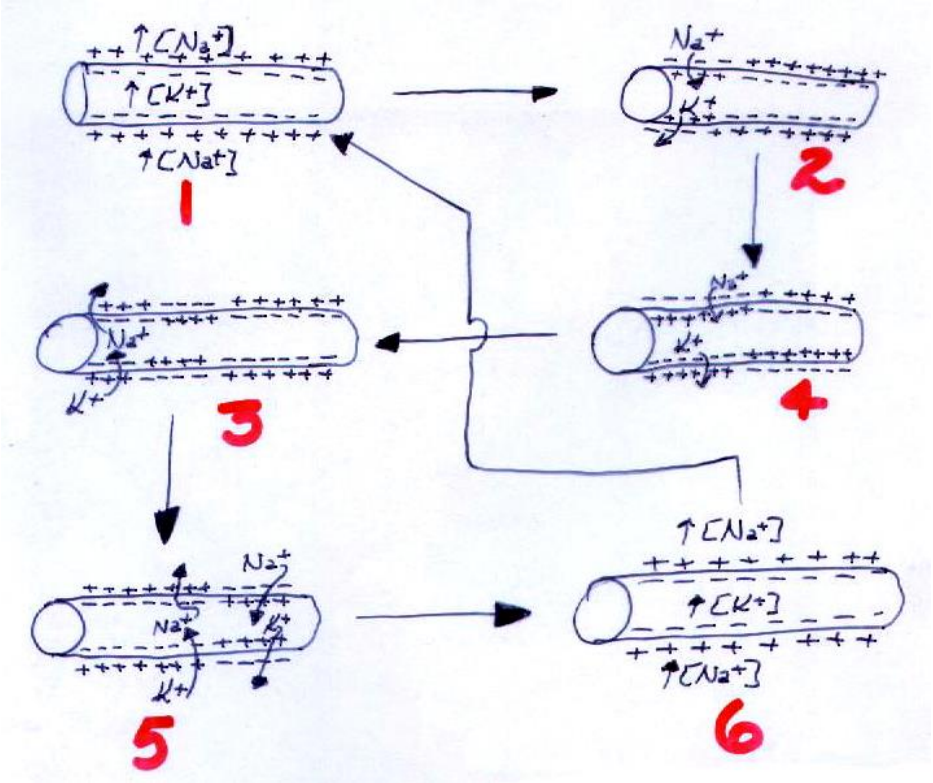
- Briefly, the action potential is sort of like the “wave” people do at sporting events – it just uses ions in this case.
- In cartoon #1, the membrane is resting – potassium ion concentrations are high inside the fiber and sodium ion concentrations are high outside the fiber.
- Once the fiber depolarizes (cartoon #2, above; this is equivalent to a muscle contracting), the sodium and potassium ions exchange places moving across the membrane.

The action potential is roughly illustrated below:



- This movement causes part of the outside of the membrane to become negatively charged and the inside to become positively charged.
- The ion exchange (via the Na-K pump or Na-K ATP'ase) continues down the membrane (cartoon #4).
- Once depolarization has progressed far enough down the membrane, the ions are returned to their original spaces, i.e., Na^+ to the outside and K^+ to the inside of the membrane (cartoon #3).

The action potential is roughly illustrated below:



- This is called repolarization (this is equivalent to a muscle relaxing).
- The movement of ions continues along the membrane depolarizing and repolarizing the membrane (cartoons #5 and #6) until the full sequence has caused a neurotransmitter to be released and can rest (cartoon #1) until the next time it's needed to elicit a response.

- Since we're discussing nervous tissue, it seems appropriate to discuss the regeneration of nervous tissue. Neuronal death or atrophy may result as a consequence of trauma, circulatory insufficiency, tumors, infections, metabolic insufficiencies, developmental/degenerative defects and heredo-degenerative diseases.
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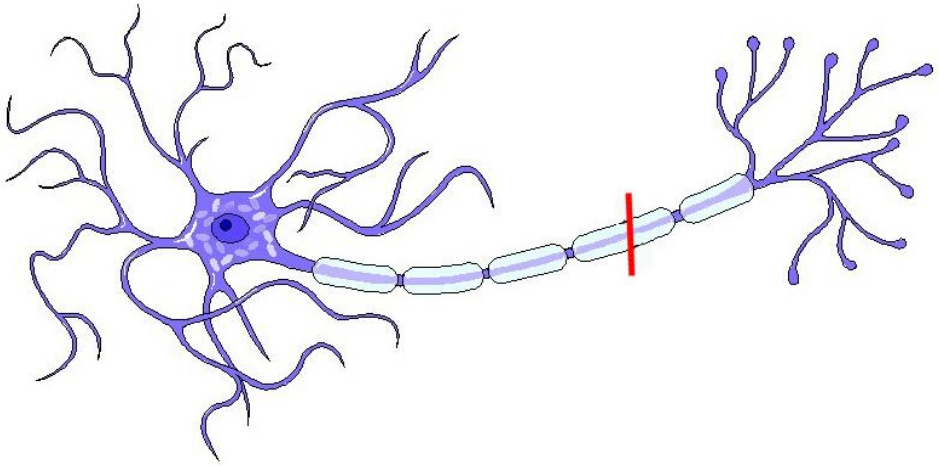
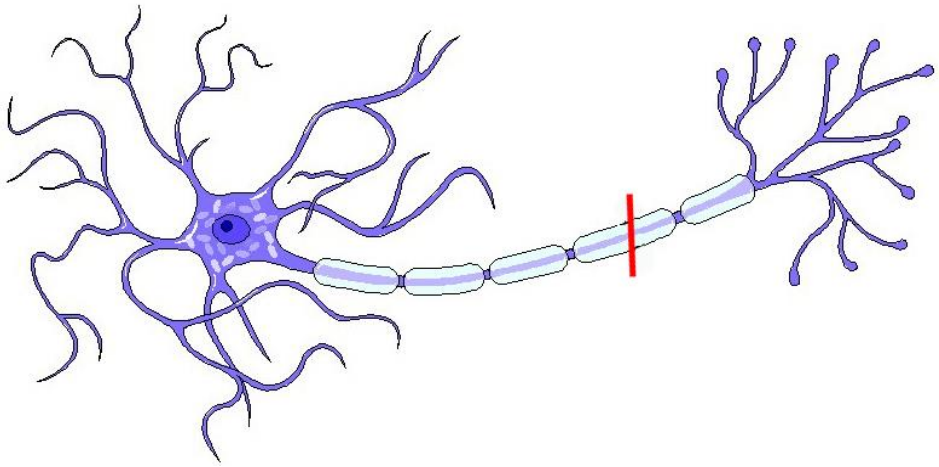
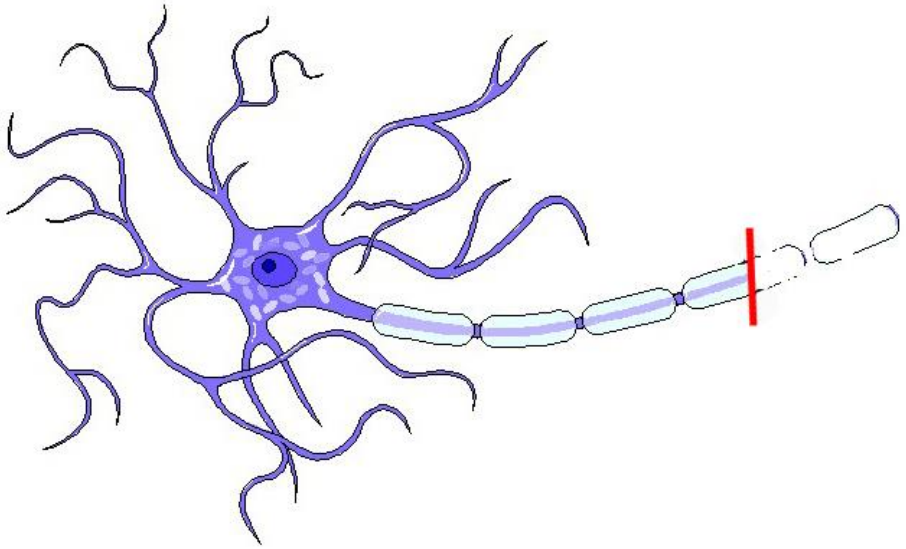


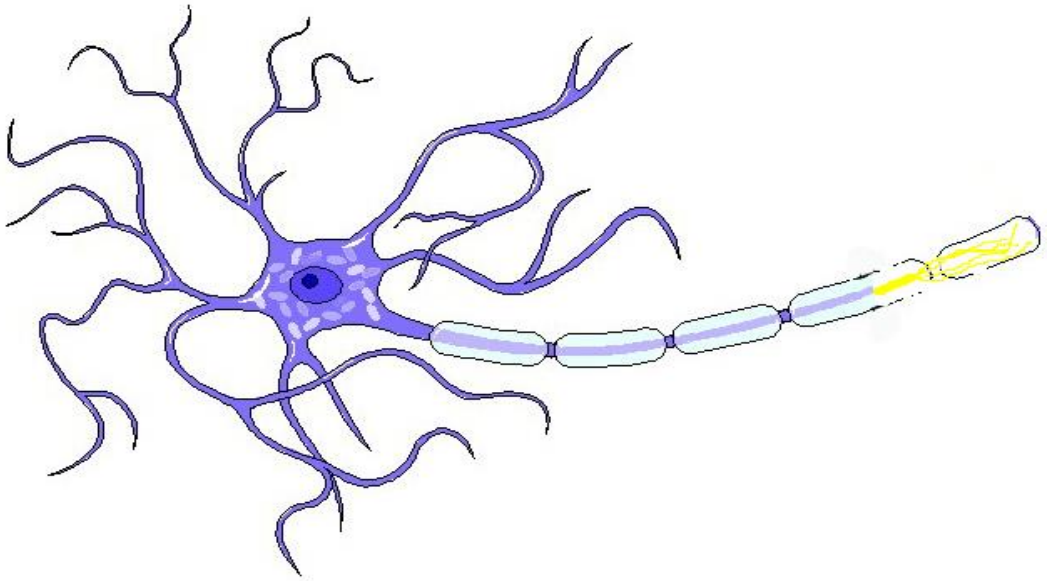
- The neuronal response to injury occurs following section of the axon or direct injury to the cell body and leads to the following sequences/series of responses:

- Response 1: axonal section (red line).
- The nucleus (assuming cell body involvement), cell body and nucleolus all swell.

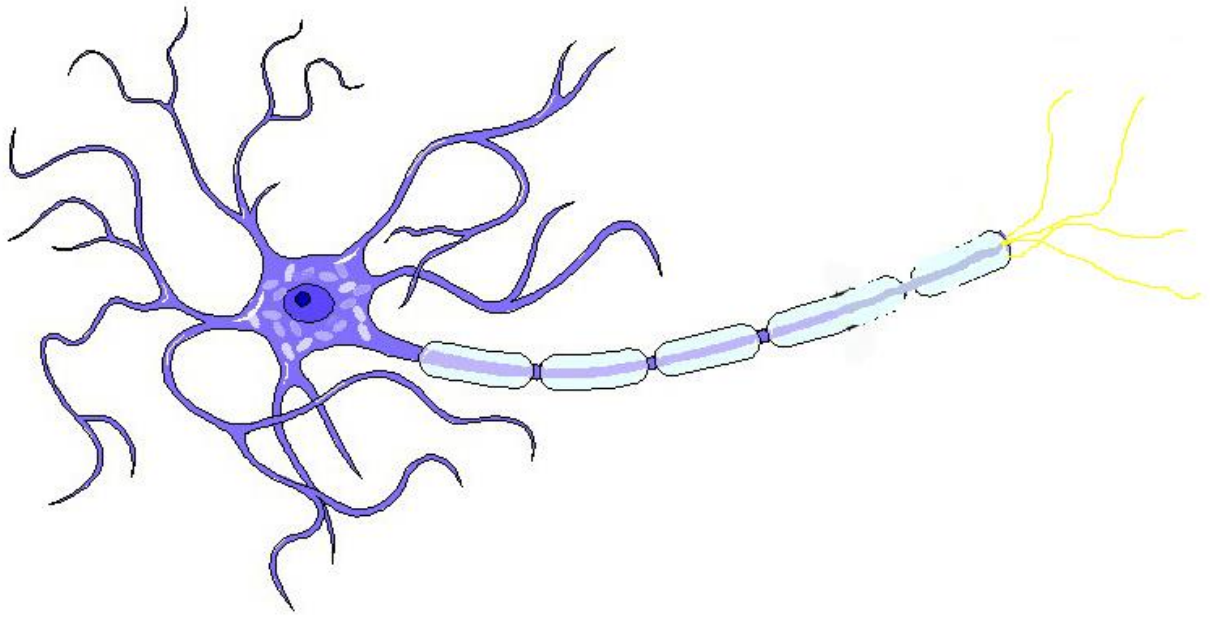




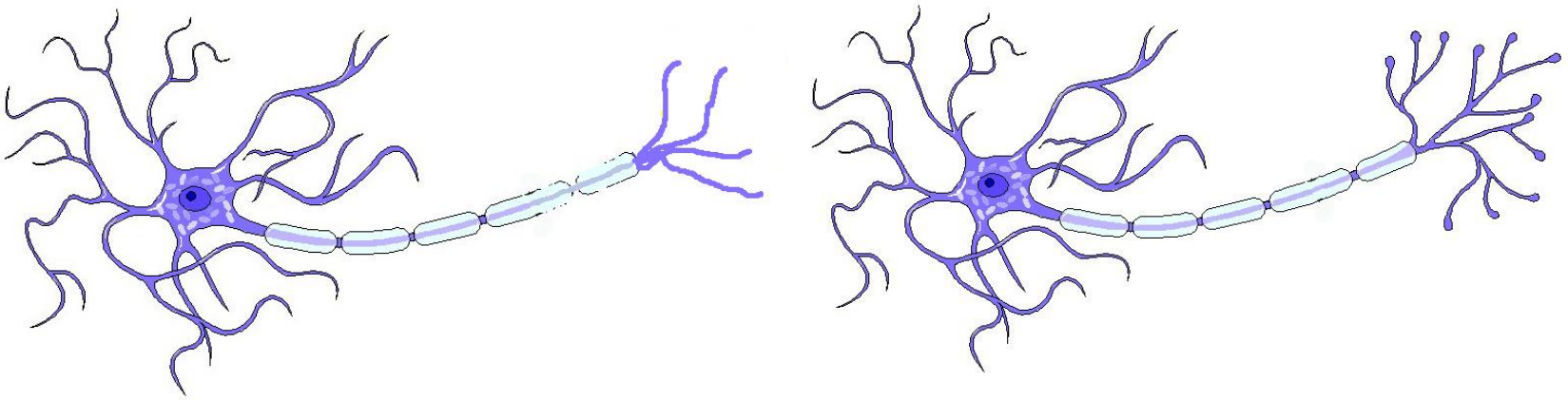
- Atrophic changes occur if the neuron is too damaged to repair itself. Everything shrinks down and by 7-10 days post injury, the nerve cell is phagocytized – if it is not this drastic, only the portion of the axon distal to the section is phagocytized, above.
- Degeneration has already begun within 12 hours. By 4-7 days the axon is being phagocytized by macrophages of circulatory origin.



- Typically, a peripheral nerve will regenerate a new tube in the remaining myelin sheath (specifically the neurolemma that gets “left behind”) within a week for new nerve growth, above.
- The central stump of the axon sends out sprouts (see above in yellow) from the proximal root through the new myelin tunnel.



- Regeneration occurs at a rate of 1-5 mm/day (sources conflict, here), with sprouts crossing the lesion (section) region after about 2-3 weeks.



- The amount of time between nerve re-growth and the beginning of function return may be estimated on the basis of a rate of regeneration of 1.5 mm/day. The rate of regeneration is also dependent on where and how wide the lesion is.

- The greater the distance across the lesion site, the less the chance of recovery due to adjacent tissues blocking re-growth by “plugging” the larger gaps.
- The axonal sprouts escape into the surrounding tissues and form a tissue mass called a neuroma.
- Neuroscar tissue biochemistry is not well known – it does, however, block regeneration.
- Teflon, believe it or not, has had limited success as a “myelin” tube to guide new axonal re-growth.

- A new myelin sheath is deposited around the new axon over time along with healing. Note that post-trauma growth is never exactly the same as what existed before the injury. In contrast to the peripheral nervous system (PNS) fibers, those within the CNS never re-generate under normal circumstances.
- Recent research may be close to challenging this

- The previous discussion on nerve re-generation was dealing with the PNS.
- This next brief section deals with the CNS. In the case of damaged nerve tracts in the CNS, the oligodendrocytes that are surrounding the injured tracts die which causes demyelination of the tracts.
- NO guiding tunnels are formed as the oligodendrocytes lack the neurolemma.
- Glial scar replaces the oligodendrocytes and blocks regeneration of sprouting axons.
- Wouldn't it be interesting to see if anyone has isolated the gene or genes necessary for neurolemma growth in Schwann cells and if they have attempted to insert these genes into the genome of oligodendrocytes?
- THAT would be a break-through were it successful! Of interest, too, is that CNS axons WILL grow through segments of cut peripheral nerves containing Schwann cells and they WILL establish functional connections.

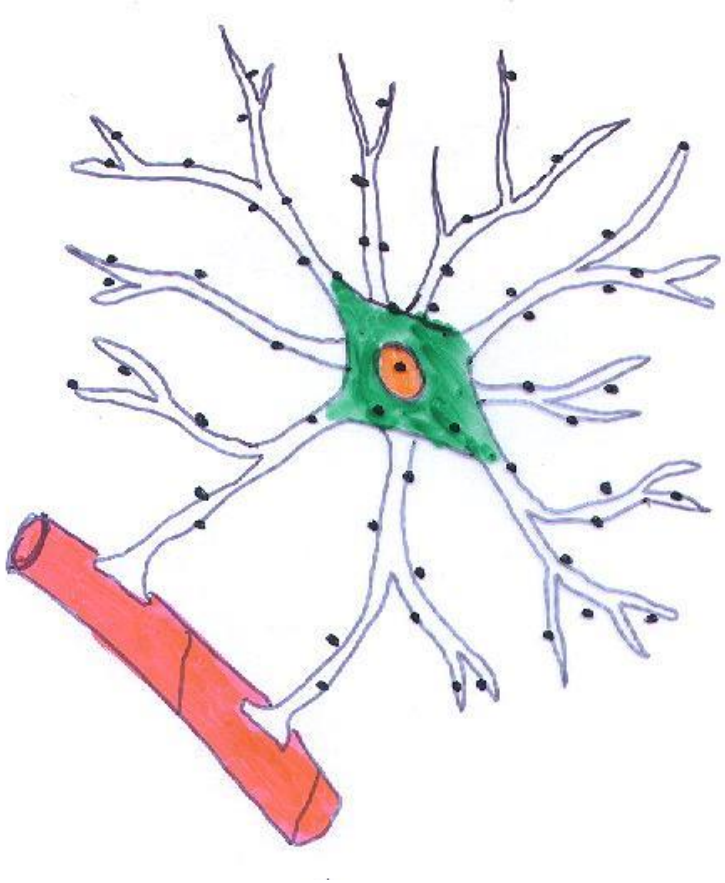
The following is a very succinct and graphic tabular rendition of the various neuroglia that you need to know cold.

Fibrous Astrocyte

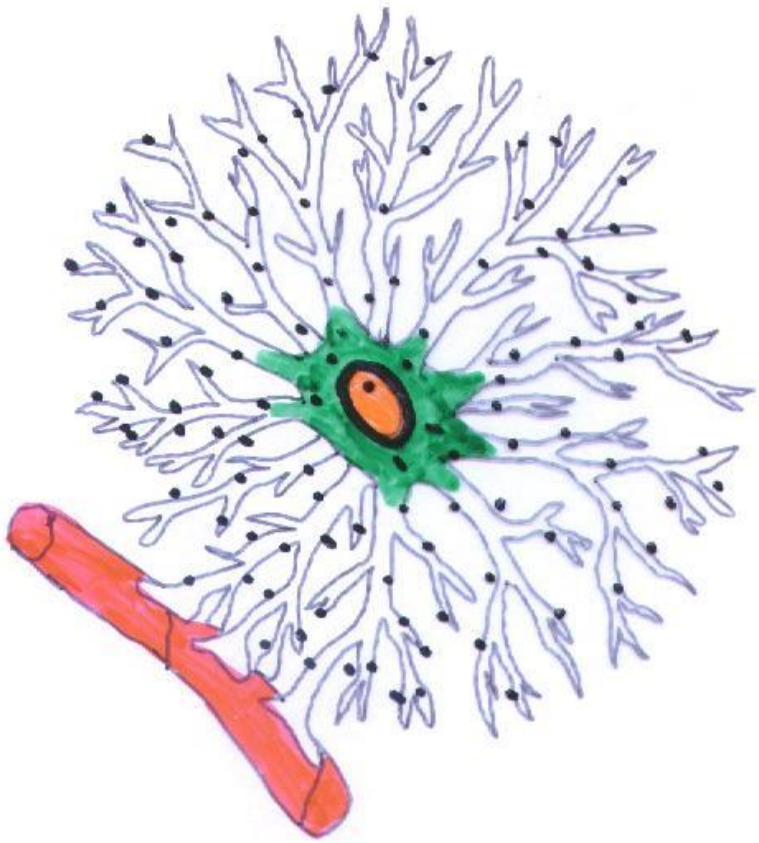
found in white matter;
tends to be “star-shaped” with numerous processes.

They help form the blood-brain barrier by “twining” about the neurons and blood vessels (makes it very difficult to get many drugs into the CNS when needed).

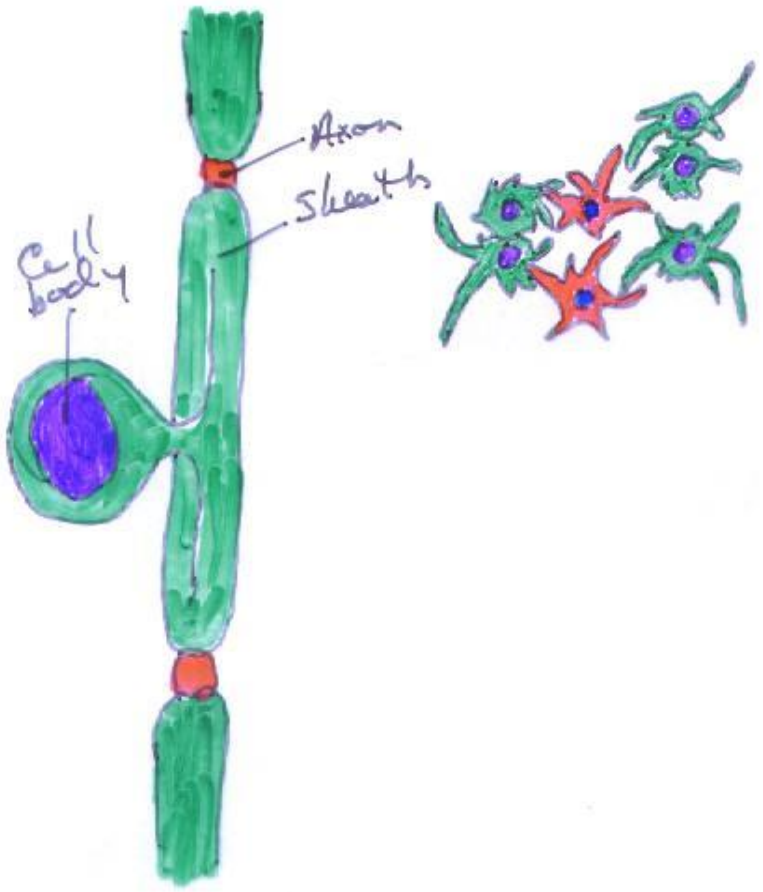
They also provide a support network in the CNS and attach neurons to local blood vessels.



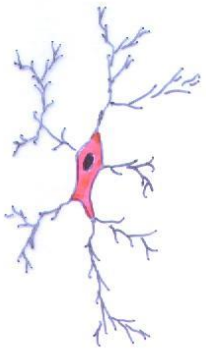
- Protoplasmic Astrocyte –
- differs in numbers of processes – performs same function as above.
- Both populations of astrocytes maintain the blood/brain barrier, give the framework (shape) for the CNS, repair damaged neuroglia, guide neuron development, regulate electrolytes and gases in the CNS, regulate capillary flow in nervous tissue and are involved in neurotransmitter recycling/catabolism.



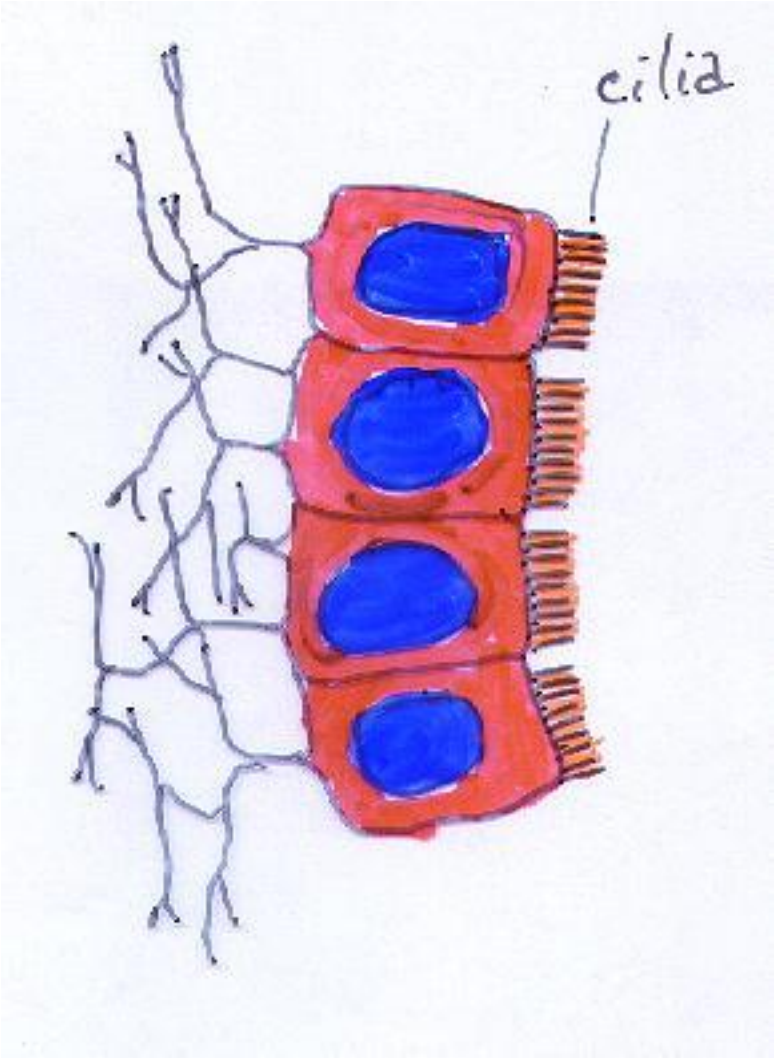
- Oligodendrocytes –
- their processes are shorter and fewer than in astrocytes.
- They produce the phospholipid (thick, fatty) myelin sheath around axons IN THE CNS.



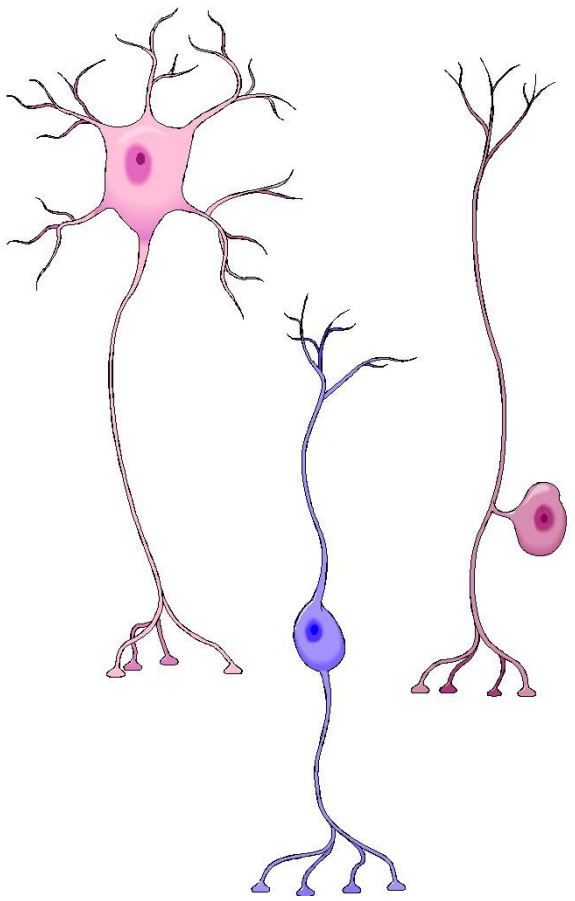
- Microglia – these are small cells with few processes.
- They are monocyte derived (as are osteoclasts) and function as the brain macrophages.
- They engulf and destroy microbes and cellular debris with their phagocytic activity.



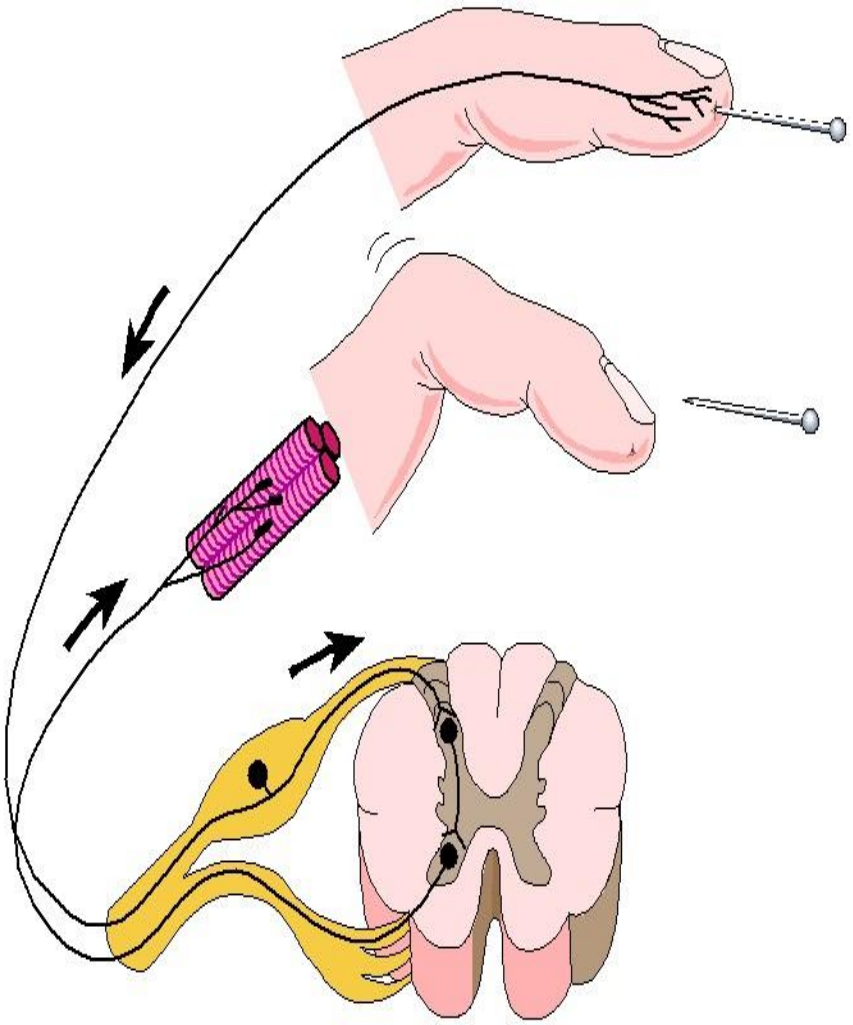
- Ependyma (or ependymal cells) –
- these are epithelial cells arranged in a single layer, ranging in shape from squamous to columnar.
- Many are ciliated to assist with the production, circulation and monitoring of cerebral spinal fluid (CSF).
- They are located in the linings of the brain and in the ventricles, as well.



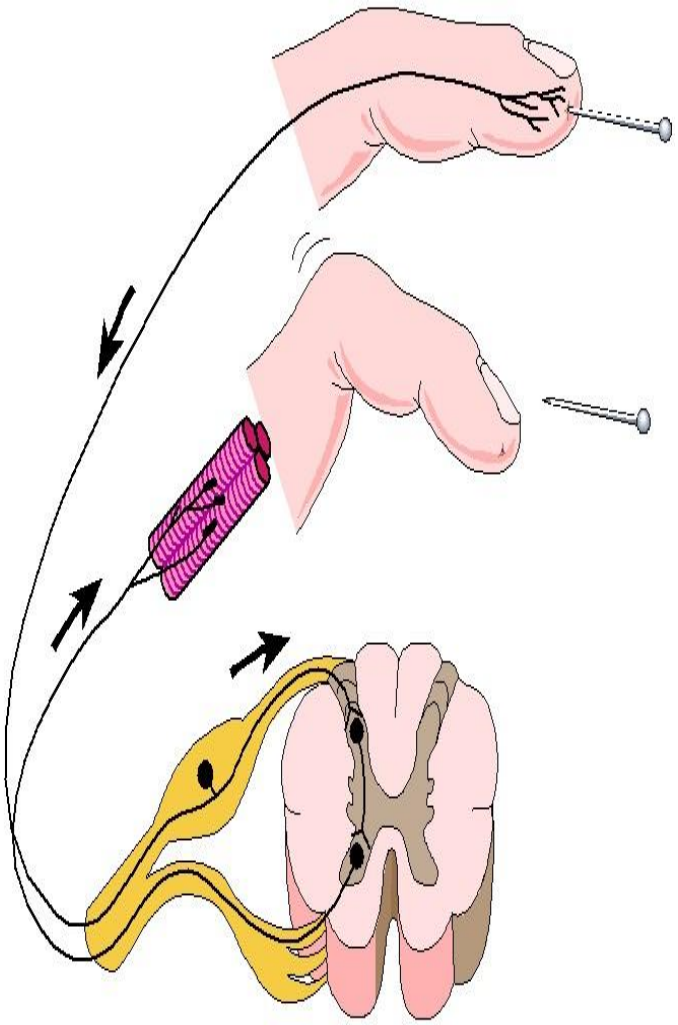
Neurons can also be classified, below, based upon their structural appearance.

Neuron – Structural Classification Graphic	Individual Comment/Description
	***Far left***: Multipolar Neuron – has several dendrites (short off the cell body) and one axon; most neurons in the CNS are of this type.
	Middle: Bipolar Neuron – has one dendrite with processes and one axon with processes; found commonly in the retina, inner ear and olfactory areas.
	Close Right: Unipolar Neuron – has one process that exits the body. This process splits into an axon and a dendrite. These are found in the posterior root ganglia (sensory) of the spinal nerves and cranial nerve ganglia that carry general somatic sensations.

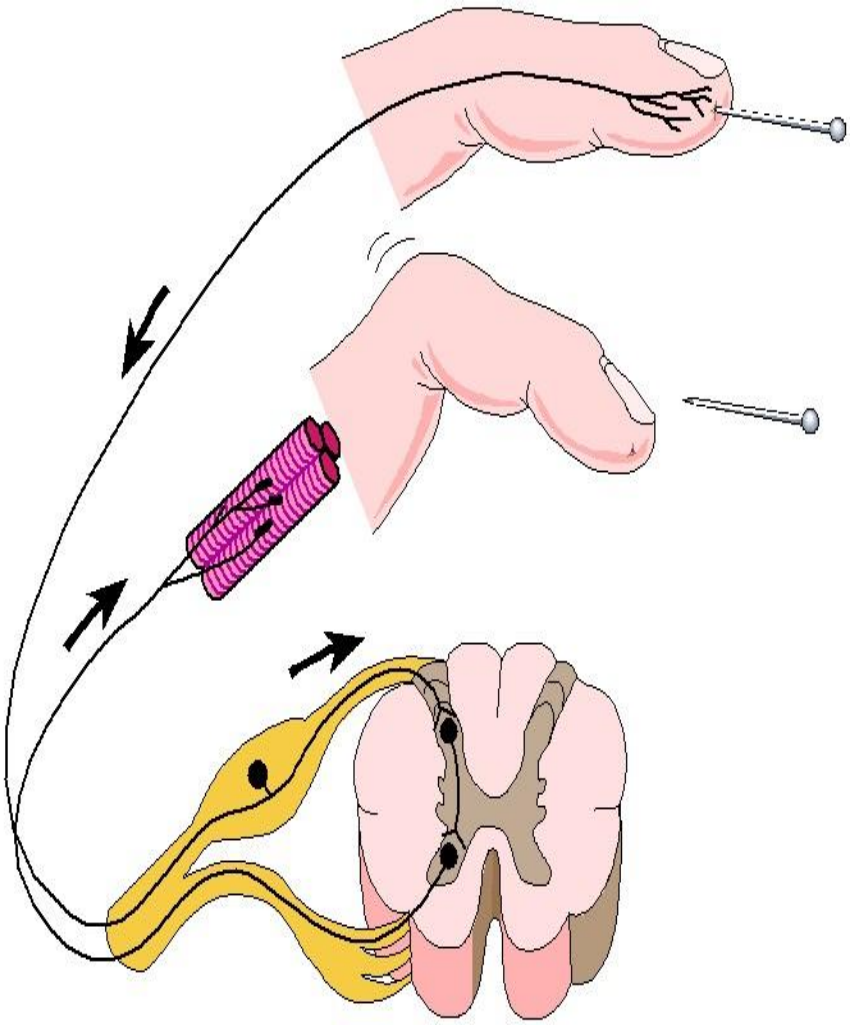
If one can classify neurons based on structure, then it follows that neurons can be classified by function:



In this graphic, the finger that is pricked by the pin contains receptors that transmit that sensation to the spinal cord through the "bump" along the back of the cord around through the cord and back to the finger so's that the fella'd say, "Gee I wish I hadn't done that!" and pulls his finger (or her) away from the pin.



- The former is a sensory neuron which transmits sensations/impulses from receptors TO the CNS, as well as from lower CNS centers to higher CNS centers.
  - ➢ These cells are usually unipolar – the “bump”, BTW, is called a ganglion.
- The latter are motor neurons.
- These cells carry impulses AWAY from the CNS to effectors like muscles or glands, as well as from higher CNS centers to lower CNS centers.
  - ➢ These neurons are usually multipolar.



- Note, too, that there is another neuron between the two in the brown/gray region of the graphic, above.
- This is an association neuron and we'll discuss it shortly.

- Another name for **S**ensory fibers is **A**fferent fibers.
- Large myelinated afferent fibers propagate impulses at a speed of 75-100 m/sec – this is 1082-1443 mph. The finest UN-myelinated fibers run at 0.3-1.5 m/sec – this is 4.3-21.6 mph.
- For a little more perspective, per square centimeter ($[cm^2]^{-1}$), there are about 200 pain points (afferent nerve endings) in the tip of the nose, the sole of the foot and the palm of the hand; there are about 55, more or less, in less sensitive regions of the body.
- Another name for **M**otor fibers is **E**fferent fibers.
- The mnemonic to remember these two sets of terms is **SA**-**ME**.

- In general, the processes of afferent and efferent neurons are arranged into bundles called **nerves if they are outside the CNS** or **tracts if they are inside the CNS**.

- Nerves belong to the peripheral nervous system.

Functional components of nerves are the nerve fibers, which may be grouped (for now) according to the following scheme:

General Somatic Afferent Fibers	General Somatic Efferent Fibers	General Visceral Afferent Fibers	General Visceral Efferent Fibers
Conduct nerve impulses from the skin, skeletal muscles and joints to the CNS.	Conduct nerve impulses from the CNS to the skeletal muscles. Impulses over these fibers cause the contraction of skeletal muscles.	Convey nerve impulses from the viscera and blood vessels to the CNS.	Belong to the autonomic nervous system (aka autonomic fibers). They convey nerve impulses from the CNS to cause contractions of smooth and cardiac muscle and secretion by glands.

- The remainder of this monograph is about **association neurons**.
- They are also known as **connecting neurons or interneurons**.
- They carry impulses from sensory neurons to motor neurons and are located in the brain and spinal cord.
- Association neurons are responsible for the distribution of sensory information and coordination of motor activity.
- The more complex the response to a given stimulus, the more interneurons involved.
- ***More than 99% of the neurons in the body are association neurons.***