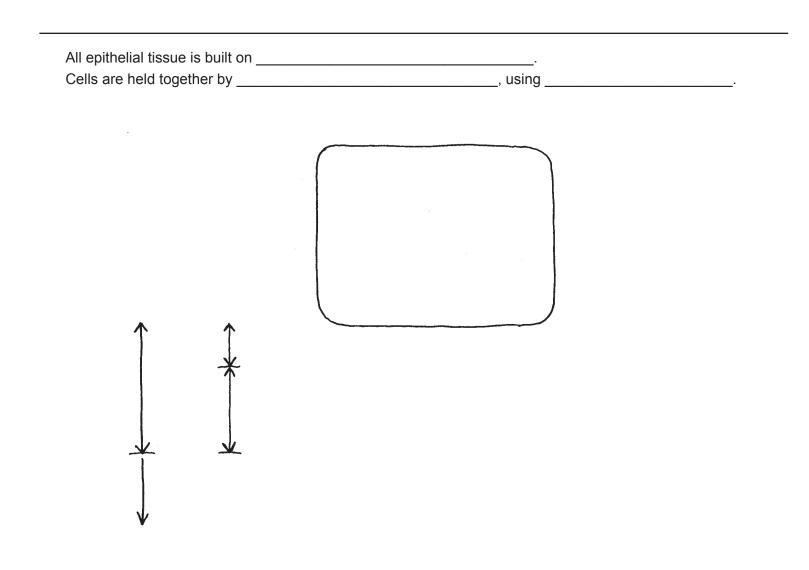
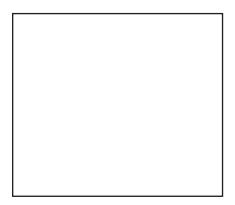
TISSUE TYPES

There are many different types of cells in the body, but all of them can be classified into one of the following categories:

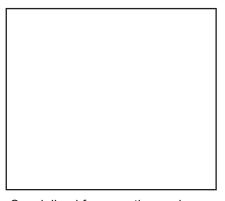
1) _	
2)	
-/-	
-	
3)	
4)	

EPITHELIAL TISSUE (part 1)

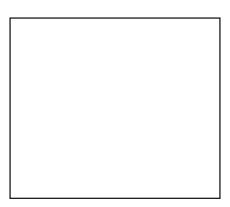




Designed for gas and nutrient exchange because it is very thin. EX: lining of lungs, inside of blood vessels and capillaries

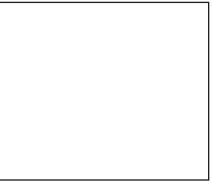


Specialized for secretion and absorption. Some have microvilli. EX: glands such as thyroid, pancreas. Also found in kidney tubules.



Is specialized for secretion and absorption, and also for pushing things along. Can have cila or microvilli. EX: lining of stomach and intestines, Fallopian tubes





Secretes and protects. Not very common EX: eye, throat, uterus, urethra, salivary glands

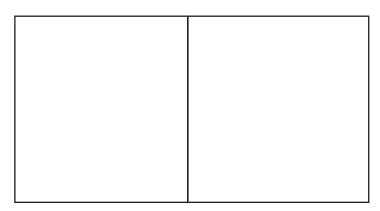
2 Types:

1) KERATINIZED: top layers hard and dead. EX: skin

2) NON-KERATINIZED: top layers soft and alive EX: inside of mouth

Designed for secretion, EX: salivary glands, mammary glands NOTE: usually just 2-3 layers





Nuclei are at different levels. EX: lining of trachea Designed to stretch. EX: Only found in one place: urinary bladder.

CONNECTIVE TISSUE and COLLAGEN

CONNECTIVE tissue is made of 3 thi 1), 2)	•	_ and 3)	
The	and the	_make the	
The protein fibers can be made of 1).	, 2)	or 3)	
There are three types of connective tissues, and several categories under each:			
1)	1)	1)	
2)	2)	2)	
3)	3)	3)	

COLLAGEN is a protein cable made of three separate polypeptide chains (alpha helices). Every third amino acid is glycine, the smallest amino, so that the triple helix can be wound very tightly.

One type of specialized cell is the **FIBROBLAST**, which makes collagen proteins and exports them (using exocytosis) outside the cell, where they then join together and make collagen fibers.

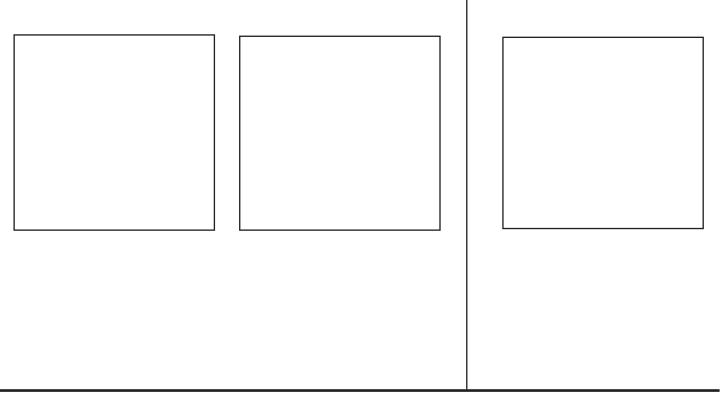
Fibroblasts also made the ground substance which is a mixture of water (90%) and glycoproteins (10%).

Fibroblasts live 2 to 3 months. They multiply rapidly after an injury. Scar tissue is a result of very active fibroblasts.

and
fibers are stretchy.
etwork for capillaries, fat cells and immune cells.
ving
p pathogens are white cells (T and B cells)
cells start the process.
being start the process. to which are attached "bottle brushes" called
and soak up
HOW INFLAMMATION HAPPENS:
1) Mast cells are triggered by or or, which causes them to their
 2) The causes capillaries to and become This causes swelling (). 3) also sends signals to nerve endings, causing and/or 4) The granules also contain which are
chemical messengers that go and recruit more white blood cells to come to this area.

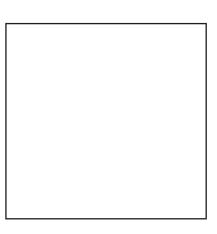
FIBROUS CONNECTIVE TISSUE (part 2: Dense and Adipose)

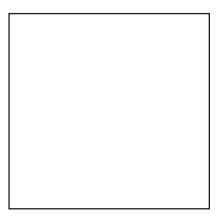
Fibrous connective tissues have specialized cells called ______.



CARTILAGINOUS CONNECTIVE TISSUE

Cartilaginous tissues have specialized cells called _____. Cartilaginous tissues have no ______ and no _____.



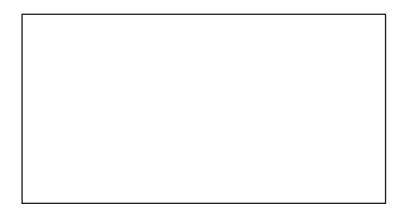


BONE CELLS and the OSTEON				35
Bone is classified as a connective tise 1) Specialized cells (called 2) Protein fibers (called 3) Ground substance, which is a	and)		and	
OSTEOBLASTS secrete collagen, then fill t with minerals. Cells are cuboidal when active		Osteoblasts can become	OSTEOCYTES.	

When osteoblasts are done, they have created an **OSTEON**.

BONES MAKE BLOOD CELLS

Blood cells are made in the ends of the long bones, and also in the red marrow of ribs, vertebrae and pelvic bones.



HEMATOPOIETIC STEM CELLS make all kinds of blood cells. (*He-MAT-o-po-ee-ET-ic*) "Hema" is Greek for "blood," and "poiein" is Greek for "makes."

("HEMATOPOIESIS" is the process of making blood cells.)

BLOOD (as a tissue)

Blood is classified as a connective tissue because it has:

1)	_:	
2)	_:	
3)	_:	

A centrifuge can separate blood into its 3 parts: plasma, "Buffy coat," and red cells.

leaking out!"

PLASMA:	SIDE NOTE: Blood has a pH of 7.4.
1(%)	
、	
2 (%)	
1 Fibrinogen:	
2 Clotting factors:	
3 Albumins:	
4 Globulins:	
(1) α alpha	
(2) β beta	
(3) γ gamma	
3(%)	
FIBRINOGEN the	"fibers" in blood
Fibrinogen is a protein molecule that looks like this:	We can simplify the shape like this:
Clotting factors in the blood can act on fibrinogen to form but only after a special message is sent.	,
Message goes out: "Help! Blood is	

Both float in blood, but don't interact because fibrinogen has a "safety cap" on its active site.

THROMBIN is told to take the safety caps off the central active site of fibrinogen.

The fibrinogens bond with each other to form strings of FIBRIN.

BLOOD: THE CLOTTING (coagulation) CASCADE

The body's way of dealing with damage to blood vessels is called ______

The PRE-STEP is:			
STEP 1:	("primary hemostasis")	INACTIVE PLATELET	
		ACTIVE PLATELET	
1) INJURY: When endothelial cells rip, co		This is the "dendritic" form.	
 ADHESION: Platelets stick to collagen ACTIVATION: Platelets are activated an Changes occur which allow the platelet 	nd release more clotting factors plus calcium.	*Don't forget platelets can also be called "thrombocytes."	
STEP 2:	("secondary hemostasis")		
	Turning fibrinogen into fibrin is a mar ("Cascade" means "waterfall.") The FACTORS and are known by Romar		
		Cascades allow for geometric increase:	
	NOTE: When		
	steps 8, 9 or 11 don't work, we call it Hemophilia A, B and C.		
The fibrin is made of fibrinogens.		Varfarin (rat poison) blocks the action of vitamin K.	
		ed as a medicine, warfarin is called Coumadin.	
What activated fibrinogen? The clotting factor	and P	MBIN also makes ANTI-THROMBIN ROTEIN C, which act to dissolve the clot. in C inhibits VII and V.)	

RED BLOOD CELLS (erythrocytes)

Erythrocytes are produced by the myeloid stem cells in bone marrow.

The **KIDNEYS** control how many are produced. Low oxygen levels in the blood cause the kidneys to make a substance called **<u>erythropoietin</u>** which acts as a signal to the myeloid cells to differentiate into more red cells. This process takes a few days. (This is what happens when you adjust to higher or lower altitudes.)

ERYTHROCYTE	HEMOGLOBI	N I "HEI	ME"		
			CH ₃ CH ₂ Iron (Fe) attracts a molecule of oxygen (O ₂) and holds it loosely. Oxygen can		
Does <u>NOT</u> have:		0 OH	CH ₃ leave heme when pass- ing by cells that need OH oxygen.		
	RECYCLING of hemog	lobin:			
	GLOBIN	HEME			
DOES have hemoglobin molecules.		H ₂ C H ₂ C H ₂ C H ₃ C CH ₂ CH ₃			
Bone marrow can make red cells per!					
The body has red cells at any given time.		Bilirubin OH	Iron (Fe) is taken out		
Red cells live for Old cells are eaten by in the liver and spleen.	GLOBIN is broken down into amino acids.	Heme is broken down in several steps. After the first break, it is called "bilirubin." It is further broken down into yellow and brown molecules that eventually go out in the urine and feces.	of heme and put into <i>transferrin</i> "taxis" to float in the blood and be available to any cells than need iron.		
BLOOD TYPES An erythrocyte has hundreds of proteins on its surface. The most critical ones are, and					

The surface protein called "Rh factor" was named after the _

BASOPHILS (.5% of leukocytes in blood)	1) Normally, they float around in the blood, but they can be recruited into tissues if other cells "call" for them to come.
	2) Are extremely similar to mast cells
	3) Vesicles are filled with histamine (and other chemicals). Histamine dilates blood vessels and makes them leak.(If this happens too fast and too strong, you get a sudden drop in blood pressure and you faint.)
	4) Basophils have many IgE antibodies (from B cells) attached to them. IgEs trigger release of histamine when antigens bind to them.
	5) Basophils also have the ability to "call" other white cells to come and help, including eosinophils, neutrophils and basophils.
MAST CELLS (not in blood)	
	1) Found only in tissues, not in blood. We met these in loose connective tissue, sitting next to capillaries.
	2) Are extremely similar to basophils.
	3) They start the inflammatory process when endothelial cells are damaged.
	 Mast cells are covered with IgE antibodies (from B cells). When allergens bind to the IgEs, histamine is released.
EOSINOPHILS (2% of leukocytes in blood)	
	1) Attack parasitic worms and their eggs. (3 billion people in the world have some kind of worm infection. Some worms are not very harmful and people just live with them.)
	 Vesicles are filled with histamin<u>ase</u>, which neutralizes histamine. (clean up from basophils!)
	3) Other vesicles have chemicals that are helpful for fighting, but can cause damage to body cells, too. For exam- ple, eosinophils have be shown to be very active during asthma attacks.

NEUTROPHILS (60-65% of leukocytes in blood)

These guys are so amazing that they need their own page... (They make several kinds of chemical weapons!)

NEUTROPHILS (60-65% of leukocytes in b	 1) Our body makes about 100 billion per day. 2) We have 5 times as many neutrophils in reserve (in marrow mostly) as we do in circulation. 3) They float in blood until needed in tissues. When they get chemical signals that they are needed, they leave the vessels by squeezing through the cracks between the endothelial cells. 4) Lifespan: a few days 5) "Pus" is mostly dead neutrophils.
HOW THEY GET FROM BLOOD INTO TISSUES:	Neutrophils engulf pathogens by phagocytosis. Then they use chemicals to kill them.
Chemical messages are sent out by cells in distress. The endothelial cells put out "hooks" to slow down and catch the neutrophils that are floating past. The neutrophils then squeeze through the cracks and get into the <u>interstitial</u> space. (the "empty" space between cells) The neutrophils have chemicals that can dissolve the junctions between the endothelial cells, in order to make the crack larger. The endothelial cells then quickly repair the damage. Neutrophils can sense the bacteria, but are also helped out by "yummy" tags placed on the invaders by other parts of the immune system.	 NEUTROPHILS make 3 oxygen-based weapons: 1) "Super-oxide" is an oxygen molecule, O₂, with an extra electron stuck on (by a special enzyme). The electron will go flying off like a bullet, striking the invader. Super-oxide is a very common "free radical" found in your body. It kills pathogens, but it can also damage your cells. 2) Hydrogen peroxide, H₂O₂ (yes, the same stuff that is in your First Aid kit for sterilizing wounds). The "bullet" here is the second O molecule. 3) HOCI, a form of "bleach." (hypochlorous acid) When the neutrophil is making a lot of this, your mucus turns green. (The enzyme that makes it is greenish in color.) Green mucus suggests bacterial infection rather than viral. Other strategies: 4) Digestive enzymes: Lysosomes filled with enzymes can merge (join with the phagosome and dump enzymes all over the pathogen. 5) Iron: Neutrophils can hide (Fe) from bacteria. Bacteria die without iron.

Monocytes in the blood can go into tissues and differentiate into either macrophages or dendritic cells.

MONOCYTES (about 5% of leukocytes in blood)	DENDRITIC CELL : Similar to macro-
50% of them are in spleen	phage except that it stays small, and is
They can do phagocytosis, but are	less involved in secreting cytokines
less efficient than neutrophils.	(messenger molecules).
	Dendritic cells are "professional" <u>A</u> ntigen <u>P</u> resenting <u>C</u> ells (APCs). They eat patho- gens by phagocytosis then put tiny pieces of the antigen on their plasma membranes so they can show them to T cells in the lymph nodes.

Many dendritic cells are found in the skin, the lining of the intestines, and in lymph nodes and spleen

MACROPHAGES

Macrophages are found in all body tissues. In some tissues they go by other names:

- Skin: Langerhans cells
- Liver: Kupffer cells (Macrophages in the liver clear out bacteria and also eat old red blood cells.)
- Lungs: "dust cells"
- Brain: microglia
- Bone: (osteoclasts?) This is being debated...

MACROPHAGES have basically 3 jobs:	(2) Presentation of antigens to T cells (and B cells)
 (1) Phagocytosis of: 1— pathogens 2— old red blood cells (by macrophages called Kupffer cells in liver) 3— dirt, debris, all cellular messes 4— old or sick neutrophils 	(An antigen is anything that is "not self.")
	Pieces of digested pathogen get attached to a "clip" called MHC II, and then moved to the surface of the membrane where they can interact with T and B cells.
The "CD31 handshake" is when a macrophage grabs a neutrophil and won't let it go until it gives a chemical password. Sick or infected neutrophils will not be able do do this. They will get eaten.	MHC = Major Histocompatibility Complex (histo = tissue) but think "My House Cleaning"
	(3) Release of cytokines (messenger molecules), especially the kind called "interleukins" (IL). Interleukins are numbered, such IL1, IL6, IL10. This is how white cells talk to each other and coordinate their actions.

Lymphoid stem cells differentiate into 3 types of cells: B cells, T cells and NK cells.

<u>B CELLS</u>: Stay in the <u>B</u>one marrow until they mature, then they migrate to lymph nodes (also spleen and tonsils). Part of the maturation process is to "learn" to make one particular type of antibody. Antibodies are also called immunoglobulins, or Ig's)

The DNA in the nucleus will direct the production of one kind of antibody. Antibodies are super small, too small to see with a regular microscope. The are the size of enzymes.

Our bodies make10 million different shapes! (most will never be used)

Mature B cells go to lymph nodes to sit and wait until they are needed. These cells are called NAÏVE because they don't know what to do yet.	 Q: What do antibodies do? A: Stick to antigens. Q: What is an antigen? A: Anything "not self"
	Antibodies function as "flags" to alert other cells to the presence of an intruder. They also act like signs that say "Eat me!"

Т

To understand how T cells work, we first need to learn a little more about how body cells work. Cells are like little houses with no windows. How will their neighbors know what is going on inside? What if a thief is inside? (a virus)

The body has a roaming police force that constantly scans for trouble. The police will kill any cell that cannot prove that everything is okay inside. Body cells must "clean house" and cover their outer membranes with samples of the proteins that are floating around inside. If the cellular police detect an intruder or a sickness (virus or cancer) they will kill the cell.

	 WHAT'S GOING ON IN THE PICTURE ABOVE: 1) There are always proteins floating around in the cytosol. 2) A tiny organelle called a proteasome acts like a shredder and chops these proteins up into tiny pieces. The shredded pieces are 5-10 amino acids long. 3) The tiny protein bits go through a portal and into the ER. 4) Meanwhile a ribosome is making a polypeptide, spitting it into the ER. 5) The poly peptide folds up and forms an MHC clip shape. A protein is attracted to the clip part and sticks to it. 6) The ER puts the "loaded" MHC clip into a vesicle. 7) The vesicle goes to the plasma membrane and joins with it (exocytosis). That's how the MHC gets to the surface. 	The little "clips" are called MHC molecules: Major Histocompatibility Complex. (My House Cleaning!) MHC I is found on all body cells MHC II is found only on APCs (antigen-presenting cells)
--	---	---

Now we need to learn about the MHC clip on the APCs (antigen presenting cells such as macrophages).

 A pathogen gets eaten (phagocytosis). The vesicle containing the pathogen is called a phagosome.
 The phagosome merges with a lysosome which contains digestive enzymes.
3) This merger is called a phagolysosome. The lysosome digests the pathogen and dis- solves it into small pieces. The pieces are 15-20 amino acids in length.
4) Meanwhile an MHC II protein is coming out of the ER. (It was made by a ribosome, of course.) Notice the little safety device on the MHC II, making sure the clips stays open until it meets a pathogen protein.
5) The phagolysosome merges with the ves- icle containing the MHC II. The safety device falls off and a piece of pathogen protein sticks to the MHC II.
6) The vesicle merges with the membrane.7) The MHC II is on the outside of the cell.

T CELL RECEPTORS:

T cells have receptors on their membranes that will lock on to either MHC I or MHC II (not both). This means there are two different types of T cells.

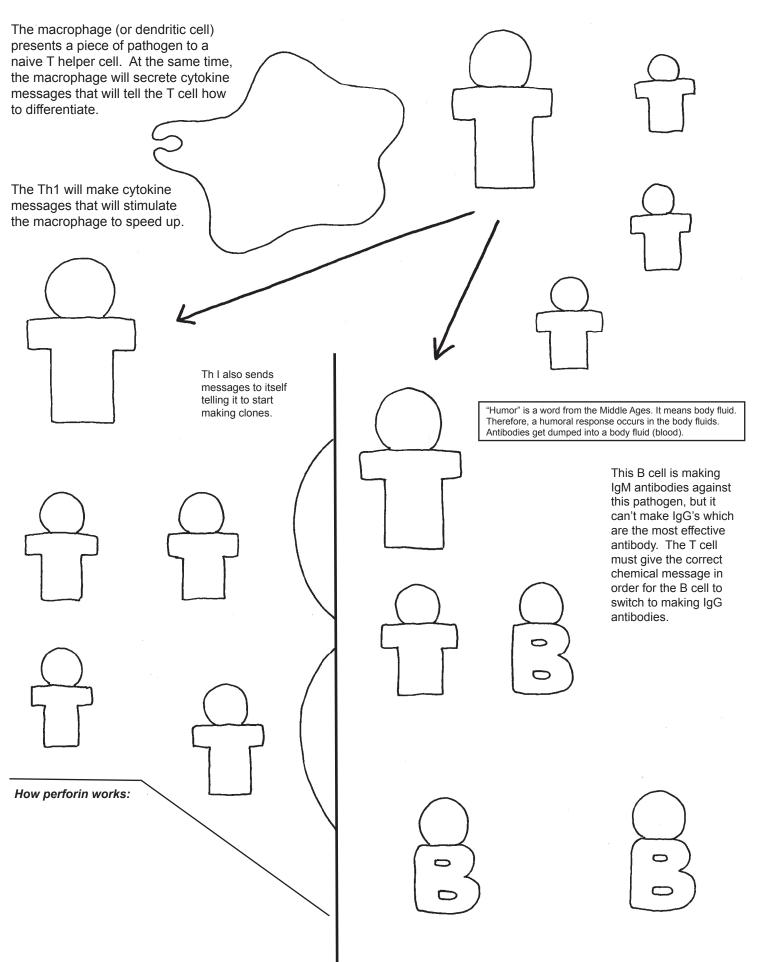
T cells are "born" in the bone marrow, like all leukocytes, then they migrate to the <u>T</u>hymus to mature.
In the thymus the T cells will...
1) differentiate into either CD4 or CD8 cells
2) be tested to see if they will not attack body cells, but will attack pathogens (98% fail and are discarded!)

(T cells don't "know" to go to the thymus. They have special receptors that match those found on the epithelial cells in the thymus. The T cells float in the blood stream until they come into contact with the thymus cells, then they stick there.)

When CD4 and CD8 cells "graduate" from the thymus training school, they go sit in lymph nodes and tonsils until they are needed. (Most will never be needed.)

Since they have no work experience, they are called NAIVE T cells.

Now we must talk about the bad guys: PATHOGENS. They can be viruses, bacteria, protozoans, yeasts, or mul- ticellular animals like worms. Some of these critters stay outside your cells and some like to get inside and hide. Don't forget that cells don't have eyes they can't see the pathogens in or out of cells! Yet they must decide where to look for the pathogens.		
	Examples of pathogens that generally stay outside of cells (extracellular):	Examples of pathogens that like to hide inside of cells (intracelliular):
The decision is made by the macrophages who ate the pathogens. They tell the T helper cells whether to activate the B cells (to fight pathogens hiding outside the cells) or to activate CD8 T cells (for pathogens inside cells).	 anthrax (affects livestock) most E. coli cholera (in intestines) meningococcus clostridium (in intestines) Borrelia (Lyme) some strep (group A) staph (S. aureus) 	 all viruses Listeria (found on food) some strep (group B) candida yeast Yersinia (the plague) Salmonella (food poisoning) mycobacterium (TB) malaria (in erythrocytes)



THE IMMUNE SYSTEM OVERVIEW

The body has several layers of defenses. Scientists have identified three basic layers and given them names. They are: 1) physical barriers, 2) the innate (non-specific) system, and 3) the adaptive (specific) system.

1) **PHYSICAL BARRIERS** that can block pathogens from entering the body.

2) THE INNATE SYSTEM (also known as the NON-SPECIFIC system) ("Nat-" is Latin for "born," so innate means you are born with it.)

	Natural Killer cells are lymphocytes (related to T cells). They mature in bone, thymus, tonsils, spleen and lymph nodes. NK cells have multiple types of receptors and can sense both bad antigens and missing MHC I on body cells.
3) ADAPTIVE SYSTEM (also known as SPECIFIC or ACQUIRED)	

The liver produces tiny proteins called COMPLEMENT (written in the singular, though this sounds strange!). These proteins function as a CASCADE so the response can be fast, hopefully faster than the rate at which the pathogens can multiply! Just like coagulation proteins, the complement proteins float in the blood waiting until they are needed. Once the first protein is activated, then the cascade starts and all the others are activated. Most of the complement proteins are named with the letter C (C1, C2, C3... C9).

 Complement proteins accomplish 4 things:
 C3 is a key protein:

 1) Activates _______
 The "b" part sticks to a membrane and attracts C5, C6, C7, C8 and C9.

 2) __________
 ("eat me" tags)

 3) Acts as ________ (sticks pathogens together into clumps)
 (sticks pathogens together into clumps)

The trigger can be when C1 binds to Ig's that are bound to an antigen

This is a **MOTOR NEURON** (often connected to muscle fibers). Only found in the peripheral nervous system (not in brain or spine).

SENSORY NEURONS connect to our five senses and transmit information to the brain.	

INSIDE AXON

Mitochondria and vesicles are moved along by motor proteins on microtubule "roads" getting them to areas that are experiencing a lot of action potential and therefore need lots of ATPs.

CROSS SECTION of Schwann cell

shows how the cell wraps around the axon many times, forming an insulating sheath that keeps the sodium ions inside. The plasma membrane of a Schwann cell contains a very high proportion of lipids including a lot of cholesterol. These inner layers are called the MYELIN SHEATH. **"Myelin**" is often defined as an "insulating lipid substance" but it is important to remember that it is also the plasma membrane of the Schwann cell.

The axon's terminal knobs connect either to a muscle fiber or to the dendrites of another neuron.

NERVOUS TISSUE in the PNS

Neurons in the PNS (Peripheral Nervous System) are specialized for the jobs they do. The size and length of the axon and the location of the soma can vary.

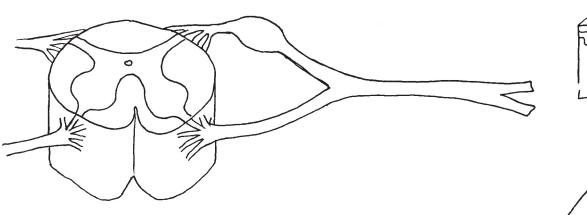
Motor neurons usually run from spinal cord out to a muscle fiber. (The fancy word for this type of neuron is **EFFERENT**.) Motor neurons have many "processes" sticking off the soma, so they are called **MULTIPOLAR**.

Sensory neurons send signals from senses to brain. (The fancy word for this type of neuron is **AFFERENT**.) Sensory neurons can be either **BIPOLAR** (two "processes" sticking off soma) or **UNIPOLAR** (or PSEUDOUNIPOLAR) with one "process" off soma.

A NERVE is a bundle of ______, which is a bundle of _____. A NERVE FIBER is made of an _____ and its ______ and also the _____.

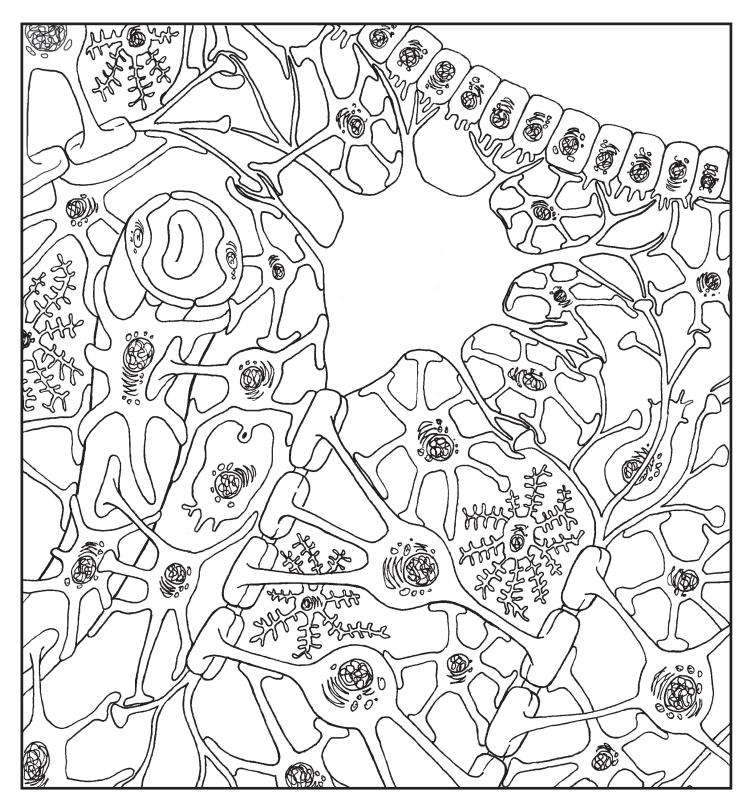
Nerves usually run alongside blood vessels.

Afferent and efferent nerves can be connected by an INTERNEURON, so that they form a REFLEX ARC.





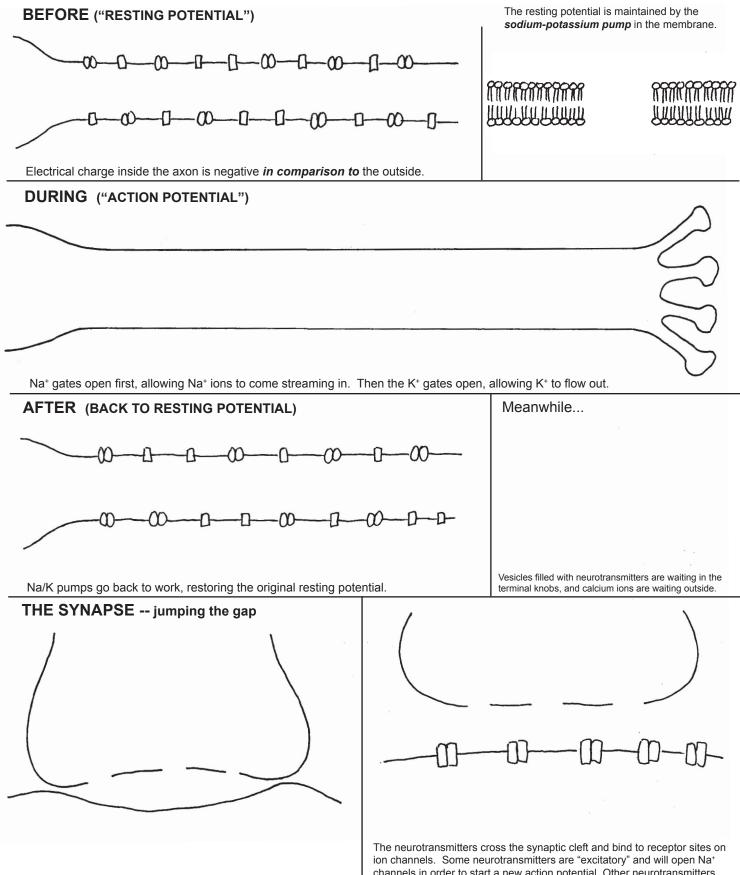
The CNS (Central Nervous System) consists of the brain and the spinal cord. This is a drawing of the cells of the brain. Most of these cells would be in the spine, also, but the arrangement might be different.



Neurons (transmit electrical impulses) Oligodendrocytes (act like Schwann cells) Astrocytes (protect and nourish neurons) Microglia (macrophages of the brain) Ependymal cells (secrete fluid into ventricles) Endothelial cells (form capillary walls) Erythrocyte (carries oxygen) Pericytes (wrap around vessels, regulate blood flow)

THE ACTION POTENTIAL and THE SYNAPSE

Electrical signals start in the hillock, travel down the axon, and end up in the axon terminals.



When the action potential reaches the terminal knob, a sudden influx of Ca^{2+} ions causes the vesicles to do exocytosis.

ion channels. Some neurotransmitters are "excitatory" and will open Na⁺ channels in order to start a new action potential. Other neurotransmitters are "inhibitory" and will open K⁺ channels, preventing a new action potential. Enzymes are present, also, for immediate removal of neurotransmitters.

MUSCLE FIBERS and the NEUROMUSCULAR JUNCTION

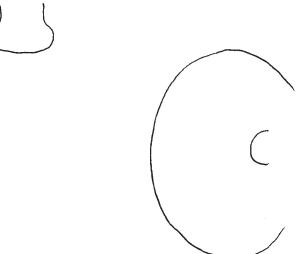
Muscles are bundles of bundles. Nerves run through muscles and attach to muscle fibers.



NOTE: Muscles are covered in connective tissue "bags" called *fascia* that taper off into *tendons*.

MUSCLE CELLS are called MUSCLE FIBERS

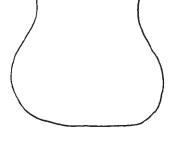
Muscle cells are called *muscle fibers* because lots of cells join together to make one long fiber.

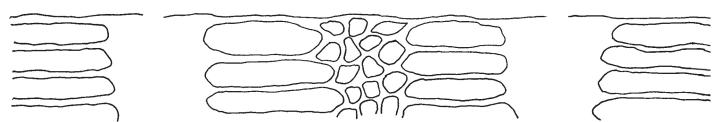


The T tubules carry the action potential down into the fiber so it can reach the myofibrils at the center.

THE NEUROMUSCULAR JUNCTION

This synapse works just like the ones we learned about in the last lesson. A sudden influx of Ca^{2+} ions makes the neurotransmitters flow across the gap and stick to receptors on Na⁺ channels on the other side. The Na⁺ ions begin an action potential.





The smooth ER is called the SARCOPLASMIC RETICULUM. It stores calcium ions that will be needed for contraction.

ACTIN and MYOSIN

Muscle fibers are made of myofibrils. Each myofibril is made of two types of protein filaments: *actin* and *myosin*. Actin and myosin overlap in such a way that the myofibril appears to have stripes. Dark places are where many fibers overlap and light places are where few overlap. The repeating patterns are called *sarcomeres*.

SARCOMERES

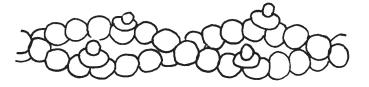
Myofibrils look stripey because of the overlapping actin and myosin filaments.

How Ca²⁺ ions allow myosin to bind to actin:

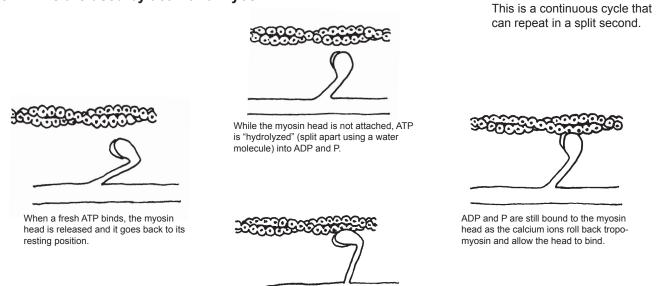
Tropomyosin blocks myosin from binding.



The action potential causes calcium to be released from the SR. Calcium binds to troponin, which causes tropomyosin to move away.



How ATPs are used by actin and myosin:



When the ADP and the P leave, the myosin head moves forward, causing the actin filament to slide the other way.

Where do the ATPs come from?

1) CREATINE is a molecule that holds onto a P. An enzyme can take the P off, and then put it onto an ADP, making ATP. No O_2 needed.

2) The Electron Transport Chain (ETC) This takes place in the mitochondria. Oxygen must be available so that it can receive

the "tired" electrons at the end of the chain.

3) LACTIC ACID FERMENTATION

is a process that enables glycolysis to take place over and over again, generating 2 ATPs each time. No O_2 needed.

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