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BLOOD AND LYMPHATIC CAPILLARIES

Blood and Lymphatics

The blood and lymphatic system are tied in close together with the same cells in both. The beginning of blood cells takes place in the bone marrow once adulthood is reached. Prior to this, the cells can be made in blood islands around the head during embryology. Blood can whole blood can be spun down and separated into three parts based on this centrifugation.

The top layer of blood is composed of the non-cellular matrix and makes up about 55% of whole blood. It can be divided into the clotting proteins Fibrinogen) and the serum which is the fluid and most proteins. Most of the proteins found in blood come from the Liver. In fact 55% of all blood proteins are Albumin. 35% are other globulins such as immunoglobulins. There is then a roughly 7% of the proteins which are fibrinogens which are from the liver and used for clotting. There is a group of regulatory proteins in the blood which make up <1% of all proteins. Besides the proteins, serum is the liquid found in the blood with electrolytes, and sugars.

Under the Plasma we find a cloudy white layer which makes up about 1% of the whole blood called the buffy layer. This is where the white blood cells are contained. These cells include granulocytes, lymphocytes, monocytes and platelets. As mentioned, these cells begin life in the bone marrow.

The last division of blood makes up 45% of all blood by volume. This is the erythrocytes or red blood cells layer. In the past, this layer was used to determine the hematocrit which was considered an indirect way to check for anemia. In a normal individual the range for hematocrit should be 45-52% of the whole blood volume.

When looking at the blood, most will divide the contents into two parts. The matrix or non-cellular is the plasma while the cellular aspect of it would be the formed elements. As stated, the formed elements included both the buffy coat and erythrocytes.

When new cells need to be made, the circulatory cells start in the bone marrow with Pleuripotent hematopoetic Stem cells. These cells will divided forming a replacement and either a Myeloid stem Cell or a lymophoid stem cell. If we start with the Lymphoid stem cells, the lymphoid stem cell can develop into a lymphoblast (Blast means maker) which will become a prolymphocyte until it becomes either a B or T lymphocyte.

The fate of myeloid stem cells can vary a bit more. The Myeloid stem cells can sometimes develop into a Proerythrocyte, which can become an erythroblast. When maturing the erythroblast will destroy its nucleus while a reticulocyte until it finally becomes a mature erythrocyte. The fact that erythrocytes destroyed the nucleus before it is mature leads the a major difference in the appearance of the bone marrow and a blood smear. This also leads to the red blood cell to have a maximum life of 120 days as it is not able to repair itself. When part of its cytoskeleton begins to show, it is eaten by phagocytic cells which break its cytoskeleton forming unconjugated bilirubin.

Another possible fate for myeloid stem cells is that they can develop into myeloblast which can become one of three types of granule containing cells known collectively as granulocytes. These three cells contain a variation of granules in vacuole form. There is one cell where most granules stain with a basic blue colored dye which are the basophils, another which will stain with an acidic red/orange dye called eosinophils, and one cell that has both types of granule called a neutrophil.

Still a third type of variety of the cells that the myeloid stem cells can develop start by becoming a monoblast. These monoblast will mature to become a promonocyte. The mature version of this cell which you will find in the blood is called a monocyte. The last possible fate of the Myeloid stem cell is that it can develop into a megakaryocyte which will fragment to form platelets. These cell fragments are vital for blood clotting.

The last fate of the myeloid stem cell is that it can become a megakaryocyte which break apart to form platelets (thormbocytes) which are needed for clotting. Platelets tend to react to the basement membrane of the endothelial lining which is a sign of a cut vessel. This is the reason why smoking is a big problem as it can lead to endothelial

damage.

There is a condition when, usually due to some sort of trauma to the veins, the platelets will begin the clotting cascade in the deep veins of the legs. This is called a deep vein thrombosis. The problem with this is that the clot can be thrown and go to the heart. Eventually the clot can get stuck in the bifurcation of the pulmonary truck which is called a Pulmonary embolism. While this allows ventilation of the lungs, there is a lack of perfusion which can lead to a rapid death. The conditions that can lead to Deep vein thrombosis are referred to Virchow's triad. The triad is made up of Endothelial damage, venous stasis, and a hyper-coagulable state.

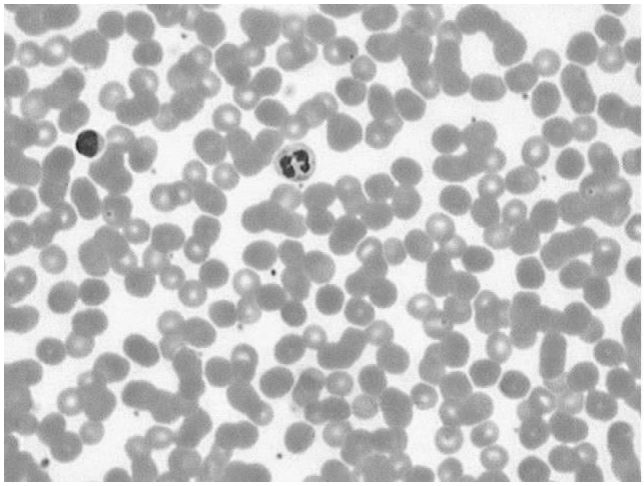
Once all the cells are formed they can be classified by how they act in the blood. The Erythrocytes will be the red blood cells which are mostly concerned with transport of Oxygen. The other full cell are the white blood cells. These are your granulocytes which have been described earlier and your Agranulocytes which are the lymphocytes and monocytes.

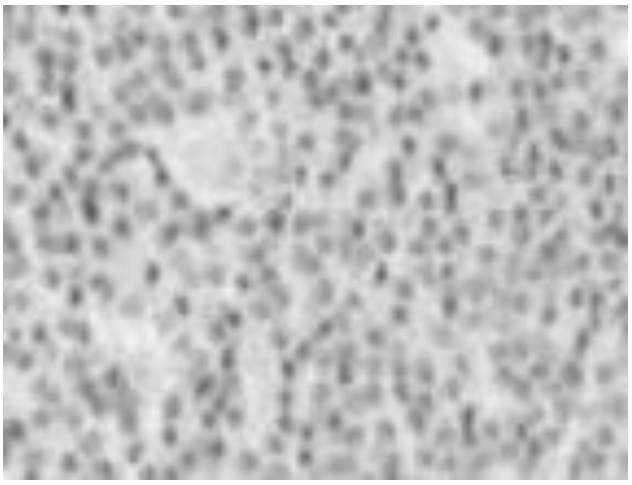
1. What are the two divisions of whole blood?

2. What does each division of blood contain?

3. Draw a schematic of the development of all blood cells from the Pleuripotent Hematopoetic stem cell to all the derivatives.

4. Compare a slide of a blood smear to that of bone marrow. Label the erythrocyte and determine the difference?





5. In the picture above explain why the dark dots on the right are missing in most cells on the left picture.

As blood travels through the vessels, it is under pressures of various types even as it flows through smaller and smaller vessels until it reaches the capillary bed. There only one normal shaped erythrocyte can pass at a time. This is why genetic conditions such as Sickle Cell Anemia can be so dangerous. In Sickle Cell anemia, there is a change in one amino acid which causes the cytoskeleton of the erythrocyte to change shape when under hypoxic condition. This can cause the red blood cell to become trapped in capillaries leading to severe pain and can even lead to death.

There is a hydrostatic pressure which is produced by the heart and gravity and a pressure from the proteins within the blood. The proteins and other large molecules in the blood also cause a pressure which attempts to pull back the fluid lost to the tissues due to the hydrostatic pressure. This pressure is called Oncotic pressure. In the surrounding tissues you will also have hydrostatic pressure and oncotic pressures. When these the pressures of both sides are equal, then there is no net flow of fluid.

Sometimes the pressures of the blood vessels and the tissue around them, interstitial space is not even. If the hydrostatic pressure on the blood vessel increases or the oncotic pressure of the blood vessel decreases (by lack of proteins) then fluid will move into the interstitial space to cause edema. To compensate, the body has a group of capillaries which take the extra interstitial fluid and return it to the vascular system. The capillaries which return the excess fluid back are called your lymphatic capillaries and the fluid inside the lymphatic capillaries is called lymphatic fluid.

6. The need for lymphatic stems from the fact that fluids leak out of capillaries due to pressure within the vessels. This is counteracted in part by the pressure caused by large proteins, what is this pressure called? Where are most of these proteins made?

7. The fluid in tissue from above is taken up by capillaries that take this fluid back to the heart, what is the name of this fluid, what is the name of these capillaries.

Prior to returning the lymphatic fluid directly to the heart, the lymphatic capillaries send the fluid collected to collections of lymphocytes within the lymph nodes. These lymph nodes are located everywhere and are named after the area they are located. For instance the lymph nodes around the neck are called the cervical lymph nodes, the ones in the axilla are the axillary lymph nodes, the ones near the femoral triangle are called the inguinal lymph nodes and so on.

To understand how this system works better we need to look at the cells involved in the immune response. Starting with the non-specific immune system we have barriers such as the keratinized stratified squamous epithelium of the skin, the Stratified squamous epithelium of the mouth, to name a few. These barriers keep things outside of the body. If something were to get past the barrier, the body reacts by sending messages via cytokines. We experience this as pain and they are signals to the white blood cells that there is something wrong in an area.

The cytokines call Basophils, which have a two lobed nucleus, and Mast Cells to the area for the beginning of an immune response. These cells contain granules with histamine, and heparin which will cause the capillaries in the area to become leaky and allow other cells, such as neutrophils, to enter.

Basophils, neutrophils, eosinophils, and monocyte enter the site of tissue damage and attempt to eat or destroy any infectious agents. Along the way, a series of proteins come together which is called the complement cascade As leaking does occur, the excess fluid and immune cells are picked up by the lymphatic capillaries and taken to the lymph nodes. This is how the non-specific immune system works.

These reactions lead to the cardinal signs of inflammation. The first is dolor which is caused by the damage and cytokines. Calor is the heat which is due to increase blood flow the area and the chemical reactions. Tumor is the swelling caused by increased blood supply and leaking of fluid from the capillaries. Rubor is the redness caused by increased blood flow to the area. The last state is Functio laesa which is loss of function which occurs if inflammation continues.

8. Explain how barriers are used by the body as first lines of defense against invasions?

9. What cells are involved in non-specific immune reaction?

10. What is the complement?

11. What are the cardinal signs of inflammation?

Besides the innate or non-specific immune system, the human body also has a specific immune system. This is made up of many cells which need to be "educated" in order to function. The B and T cells are said to have memory which means that they remember what they have seen previously. They are both born in the bone marrow but the T-cells are moved to the thymus for education while the B-cells remain in the bone marrow for their education.

To truly understand the specific immune system, there are a few words that must be defined. The first is an antigen. If we break apart the word we can see that it is composed of the roots Anti which means against and Gen which is beginning of. In short an antigen is anything that causes an immune response.

Once B-cells are born they begin to make antibodies in the form of immunoglobulins. These immunoglobulins have an area which is made randomly. Once a B-cell can make a particular immunoglobulin, it can only make an immunoglobulin that can attack that specific antigen. As the immunoglobulin is made at random, it must be checked to make sure that the cell cannot attack anything that is self.

Education begins when the B-cells are introduced to a chaperone cells which present the normally present antigens of that human body. If the B-cell can make an immunoglobulin that can attack the body, it is triggers Apotosis, cell death. If it does not, it is rescued. Once the B-cell is educated, it travels to the blood to secondary lymphoid tissues such as lymph nodes, spleen, tonsils and associated lymphnoid tissues. The B-cells remain there until they are activated by an Antigen presenting cell.

The T cell moved to the thymus to be educated. There, they go through the same process as the B-cell in that if they recognize self-antigens, they go through apoptosis. In this way, the body ensured the maximum number of immunoglobulins and yet decreases the chance of the body attacking itself. Once educated, T-cells are sent though the blood to protect the body. These T-cells can be specialized into T-helper cells, or T-killer cells. The only way to differentiate these two cells is by an cell surface protein called Cluster Differentiation (CD) factors. CD 4 cells are T-helper while CD 8 are the T-killer cells.

When working in concert, the nonspecific immune system attacks things that cause damage to the body. Those cells that can eat other cells, then are transported into the lymphatic capillaries where they are sent to the lymph nodes to trigger B-cells. Once B-cells are activated, they begin to produce antibodies for the antigen that activated them. This

antibody will be sent to the heart with the lymph fluid and will circulate looking for more of that antigen.

The phagocytic cells can also remain in the blood and trigger T-cells. If the phagocytic cells is an antigen presenting cell (APC) it can activate T-helper cells to better react to antigens as well as get the T-killers to recognize and attack the antigen which activated them. Together, as the B-cells and T-cells have memory, they can attack the antigen better next time it is found in the body.

Most people are unaware but the first use of vaccines was in 1796 when Edward Jenner MD, discovered that milkmaids who had been infected by cow-pox were resistant to small pox. After various experiments, he published his finding in 1798. At the time it was not entirely known but the antigens found in cowpox were similar enough to small pox to cause a memory of the disease. As the illness originally came from cows we name vaccines after them. Vaca meaning cow in Latin.

By the 1800's cowpox vaccination programs were being practiced throughout Europe and the US. While today some suggest that these vaccination programs lead to conditions such as autism, we must understand that Psychology, the science that deals specifically with autism, did not have a diagnosis of Autism in their DSM until 1980. The word Autism was in fact first used describe schizophrenic patients in 1908, more than 100 years after the first vaccine programs.

12. What is the name of a Macrophage when in the blood rather than another tissue?

13. What are the cells that stain with basic dye?

14. What are the cells that stain with acidic Eosinophil?

15. What Cells are permanent residence in the Lymph nodes?

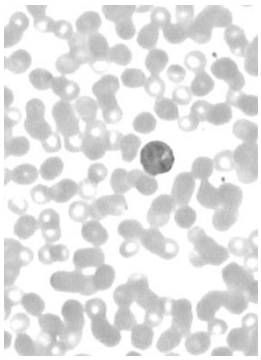
16. What is an antigen?

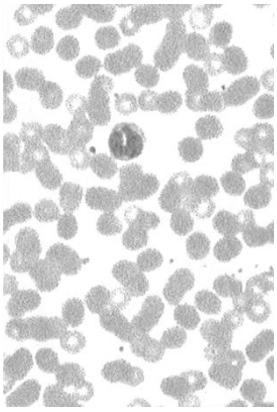
17. What is an immunoglobulin?

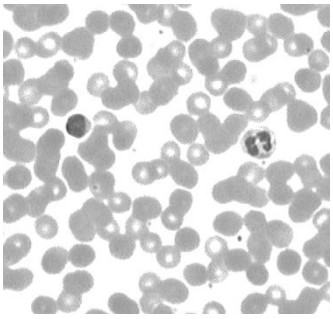
Lymphocytes in blood:

Name	Granules	Shape of nucleus	Specific or nonspecific	Normal WBC percent
Eosinophil	Basic granules	Bilobed	Non-specific	1-5%
Basophil	Acidic granules	Bilobed	Non-specific	0.5-1%
Neutrophil	Acidic and basic	Multilobed	Non-specific	40-75%
Monocyte	None	Unilobar	Non-specific	2-10%
Lymphocyte	None	Unilobar	specific	20-40%

18. Based on the table above, label the cell type based on the nucleus:







It is now known that B-cells can form immunoglobulins which are the proteins that can attack other molecules and they live in lymph nodes or any secondary lymphoid tissue. These tissues are specialized connective tissues called reticular tissues.

Immunoglobulin (Ig)	**Structure**	**Function**
IgA (immunoglobin A)	Dimerized	Excreted and secreted
IgD (immunoglobin D)	Monomer	unknown
IgE (immunoglobin E)	Monomer	Attacks parasites
IgG (immunoglobin G)	Monomer	Second Ig, can cross the placenta most common Ig
IgM (immunoglobin M)	Pentamer	First If does not cross placenta

Immunology is vital for understanding blood-typing and other organ donations and rejections. First remember that the body can make immunoglobulins to any antigen not found in self. That would include foreign proteins found on other bodies. As we can separate the immunoglobulins out we can take a sample of blood and place it in a visible container. Then we can add the immunoglobulins to particular types of blood.

As in 1900 Landsteiner wrote down the two proteins found in blood as A, B, and O if neither antigen was present we can use immunoglobulin Anti A and Anti B to test. If a sample of blood is introduced to Anti A antibody and it causes the blood to develop grains it means that anti A found the antigen A on the sample of blood. If the same is done with Anti B and it develops grains the blood sample is contains antigen B. The grains that appear are due to a process called agglutination which is when red blood cells are bound together and fall out of the liquid blood.

Later on, the rh factor was discovered which is another antigen found on some blood. Unlike the A and B where someone could have one, both, or none, the rh factor is a have or not. The rh factor is checked with an Anti rh immunoglobulin as well.

19. Fill out the table for how blood types react:

Blood type	Reaction with Anti A	Reaction with Anti B	Reaction with rh
A+			
B+			
AB+			
O+			
O-			
AB-			
A-			
B-			

When looking at a slide of a Lymph node, one can see that it is covered by capsule. This capsule is attached to the lymphatic vessels which are brining lymph to the lymph nodes. The vessels are called the Afferent lymphatic vessels. Inside the capsule we find the outer layer called a cortex and within the cortex there are some round follicles and within those follicles we fine the germinal center. The germinal center are the B-cells or the activated B-cells called plasma cells. The activated B-cells will be secreting one of the many types of Immunoglobulins.

Deep to the follicles are the paracortex and Medulla. The paracortex usually holds T-cells while the Medullary cords hold plasma cells and might be an area of highest Ig production. This is followed by the medullary sinus which is attached to the Efferent lymphatic capillary which takes fluid from the lymph node to the heart.

20. Draw and label a slide of a lymph node include all parts described above:

21. What cells are in the germinal center?

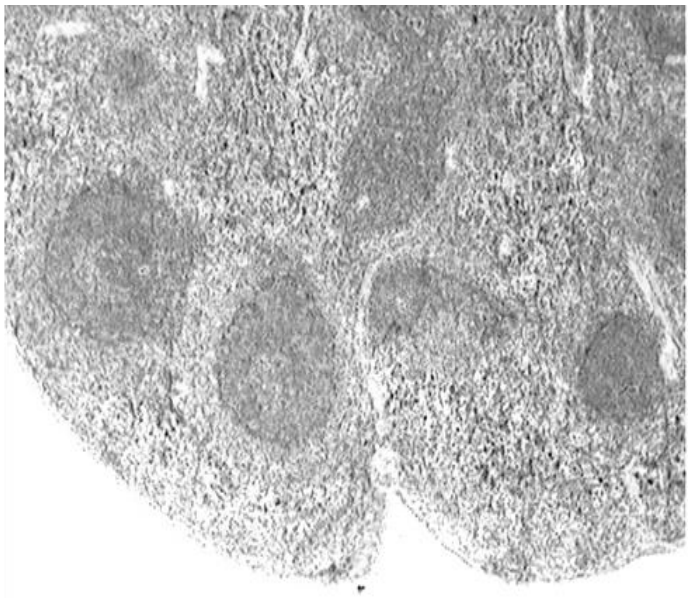
22. What cells are in the Paracortex?

From the lymph nodes the lymphatic fluid drains into a collection of capillaries leading to one of five major trunks. These are the subclavian trunks, the bronchomediastinal trunks, intestinal trunks, and lumbar trunks, all but the intestinal trunks are paired. Then, the lower part of the body converge into the lymphatic vessels which become the Cisterna Chyli which rest at around L2. Then the Cisterna Chyli comes together with the lymphatic drainage of the left are and side of the face to form the thoracic duct. This will drain into the left subclavian vein.

Unlike 75% of the bodies lymphatic drainage described above, the right side is a bit different. The Right arm, chest, and side of the head will drain into the right lymphatic duct prior to draining into the right lymphatic duct. This then drains into the Right subclavian vein and together both vessels come together to drain into the Superior Vena Cava.

The lymphatic and circulatory system in general is also composed of many accessory organs located throughout the body. Some of these are tonsils which are located within the mouth. These are the adenoid tonsils, tubal tonsils, palatine tonsils and lingual tonsils. When one looks at a slide of tonsils, they find that the structures are similar to the lymph node in fact both have follicles made up of B-cells.

23. Look at a tonsil slide and compare it to the lymph node, what similarities do you find?

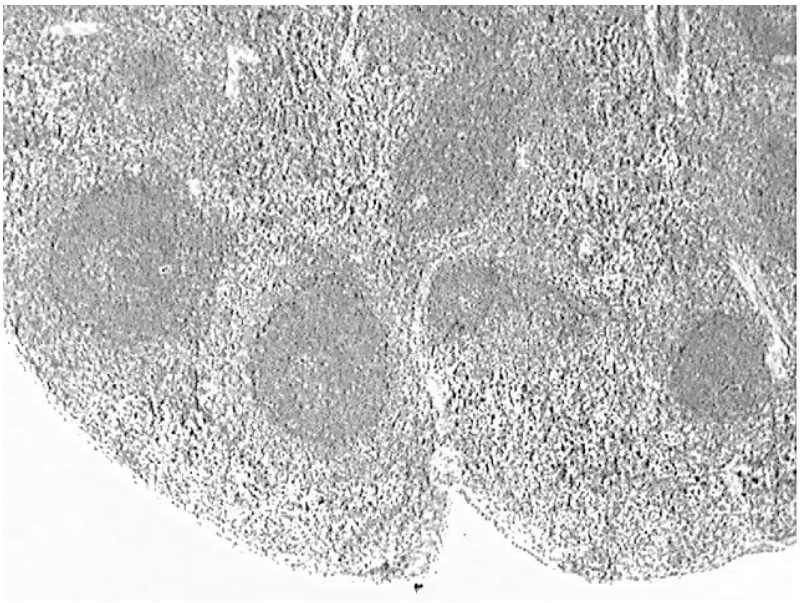


Another accessory lymphoid tissue is the Thymus which is a place T-cells mature. While in utero and even when a human is an early neonate, it produces thymosin, a hormone used in T-cell maturation. As a human grows, the thymus is becoming a fat pad over the heart.

24. What cells develop in the Thymus?

The spleen is an important accessory lymph organ that is located on the left lateral posterior and superior aspect of you abdominal cavity. That is the reason which, if the spleen is punctured and cannot be repaired the splenic artery and vein are tied off and the organ is removed. It has been found that the spleen has many important roles in immunology and hematology such as storage of both read and white blood cells. Its histology shows follicle like areas called white pulp which is surrounded by red pulp. Within the white pulp we can see the central artery which is surrounded by the periarterial lymphatic sheath. Within the red pulp we have red blood cells and macrophages.

25. Looking at a slide of the spleen, label the white pulp, red pulp, central artery, and the periarterial lymphatic sheath.



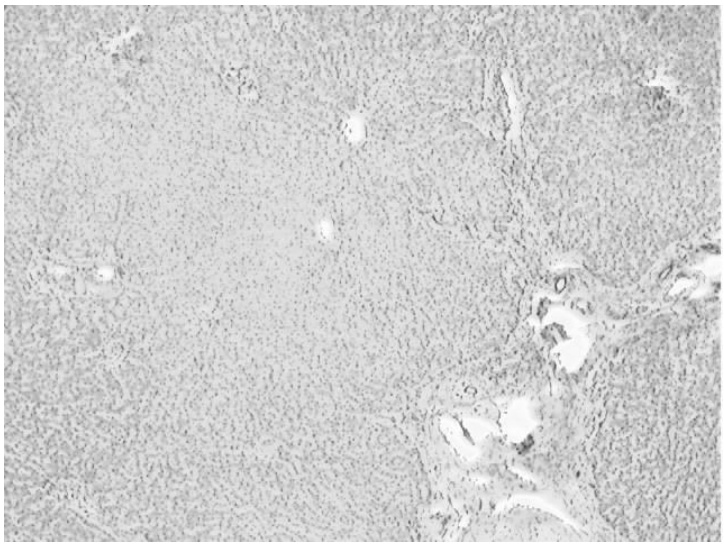
26. What cells are found in the white pulp?

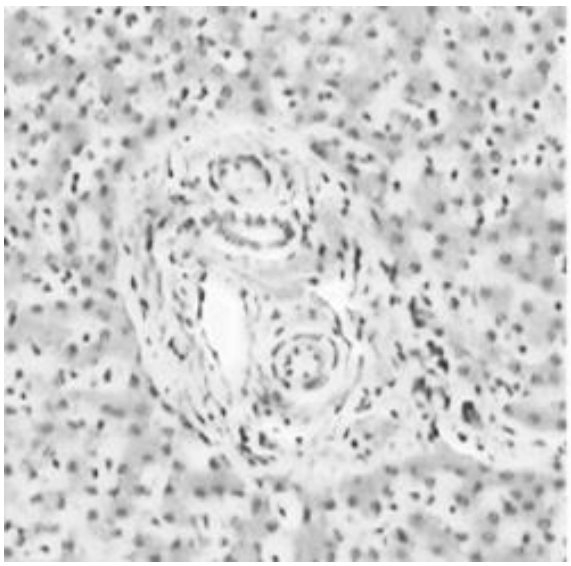
27. What cells are found in the red pulp?

One of the most important accessory organs of the circulatory and lymphatic systems is the liver. Like most soft organs, the liver is made of reticular tissue which is set up in lobules with a hexagon arrangement. These lobules contain a variety of structures such as the central vein, which connects to the hepatic vein and is located in the middle of the lobule. The portal triad made up of the portal venule, which branches from the hepatic portal vein, the hepatic arteriole, and the bile duct which transport bile to the intestines are all located on the corners outside the lobule.

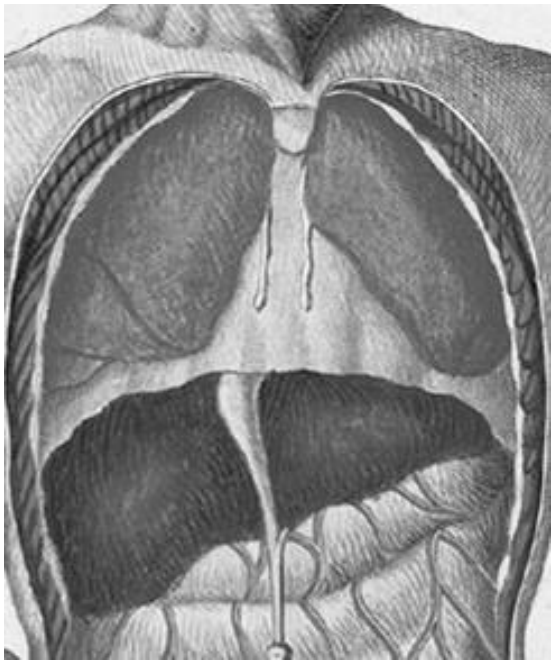
Connecting the portal venule to the central vein are a series of sinusoids which are lined by Kupffer cells, a satellite macrophage which are surrounded by the liver cells called Hepatocytes. The hepatocyte is the cell which conjugates bilirubin to make it water soluble and takes cholesterol to make bile salts which are needed for digestion.

28. On the picture below label the parts of the liver lobule





The liver is a blood-filled organ located in the upper right quadrant of the abdominal cavity. Grossly, we find that it has many different lobes which are divided by ligaments. Starting with the anterior view, we can see that it has a diaphragmatic surface where it attaches to the diaphragm via the coronary ligament. It is divided into right and left by the falciform ligament and attached to the umbilicus by the round (teres) ligament.



29. Label the following on the picture provided:
    a. right and left lobes
    b. falciform ligament
    c. ligamentum teres.

If one were to turn the liver around, one could see that the caudate lobe, meaning the tale lobe, is separated from the right lobe by the Inferior Vena Cava. The left side of the caudate lobe is separated from the left lobe by the ligamentum venosum which runs from the to the left hepatic vein.

The inferior border of the caudate lobe is the location where the Hepatic Portal Vein, the hepatic artery, and the common hepatic duct connect to the liver. This three-vessel structure is called the Porta Hepatis. Inferior to the Porta Hepatis is the quadrate lobe.

30. On the image provided, label the following structures.
    a. ligamentum venosum
    b. Inferior vena cava
    c. Hepatic veins
    d. Right lobe
    e. Left lobe
    f. Quadrate lobe
    g. Caudate lobe
    h. Gall bladder
    i. Porta hepatis
    j. hepatic artery
    k. hepatic vein
    l. common bile duct
    m. cystic duct