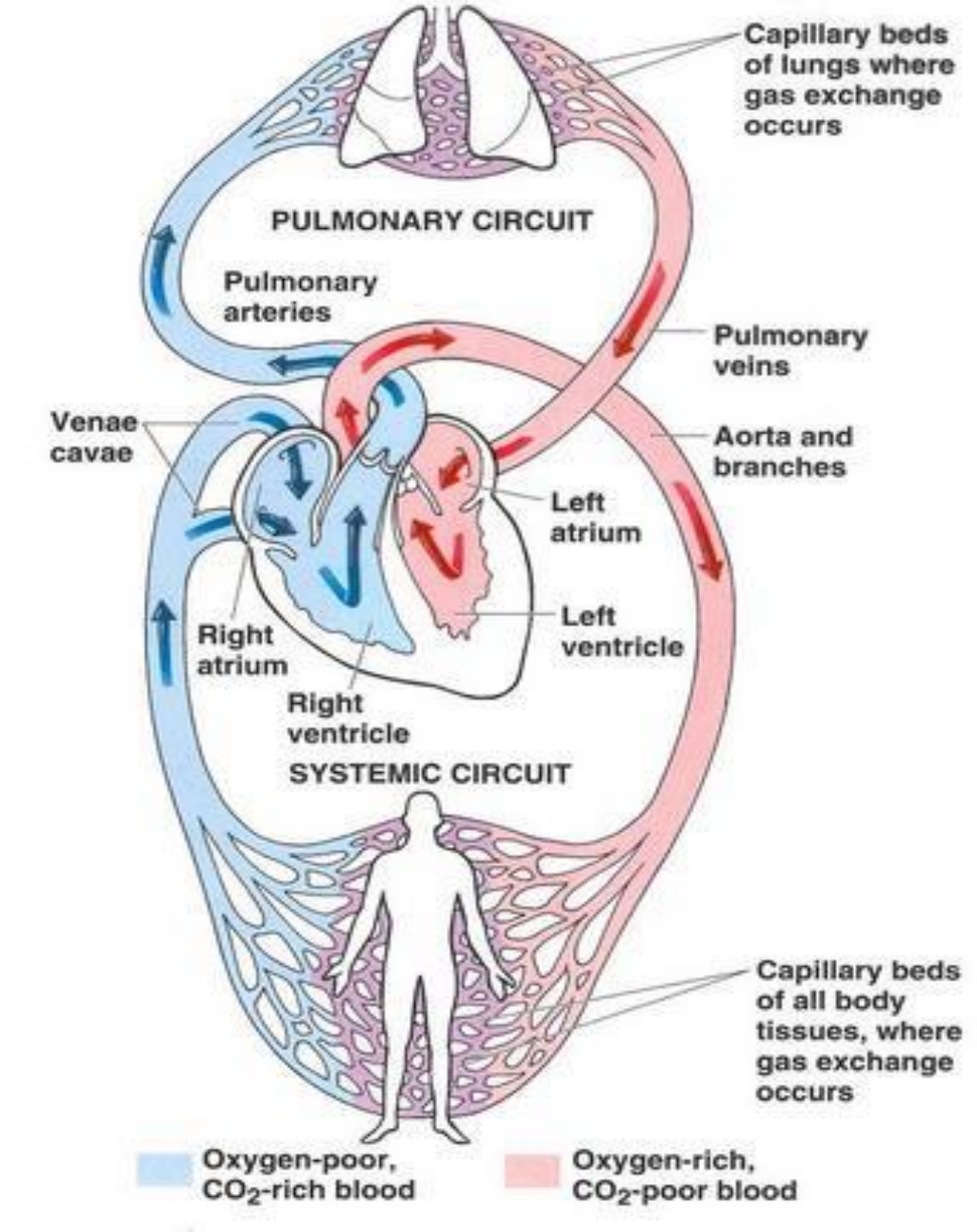
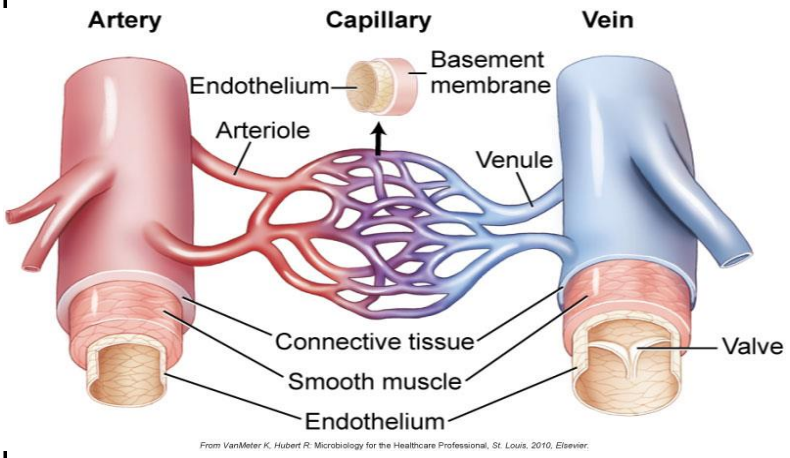
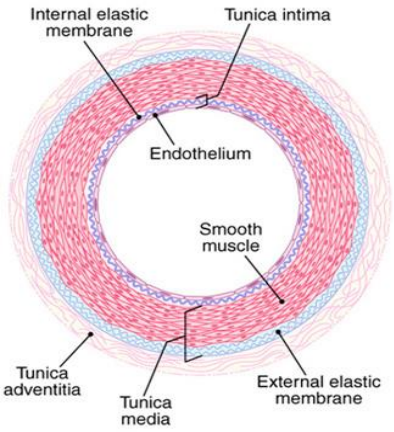
	BIOS 2015 … CHAPTER 10- Blood and the Circulatory System
Page	**Note**

	"Circulatory System" - refers to blood vessels.
	"Cardiovascular System" - refers to the heart and blood vessels.
	"Hematopoietic System" - refers to the bone marrow and blood.
	Circulation:
	From the heart > arteries > arterioles > capillaries > venules > veins > to the heart.
	Systemic Circulation: Exits left heart, returns to right heart.
	Pulmonary Circulation: Exits right heart, returns to left heart.



BLOOD VESSEL ANATOMY





CAPILLARIES: The lumina of all blood vessels are lined by a single layer of thin flat squamous cells known as endothelium. Capillaries are the smallest blood vessels (**the lumen is the diameter of a single red blood cell**). They consist of nothing more than a tube of endothelial cells surrounded by interstitium (connective tissue). This makes sense because gases (oxygen and carbon dioxie) and nutrients and waste have to pass from red blood cells across the endothelium and into the interstitium.

ARTERIES, ATERIOLES, VENULES AND VEINS

These differ from capillaries by having coats of smooth muscle.

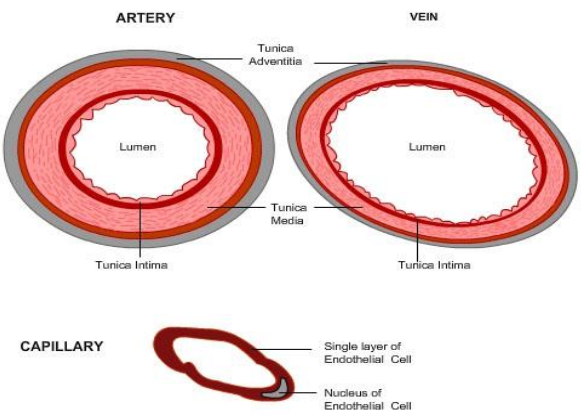
These vessels have layers:

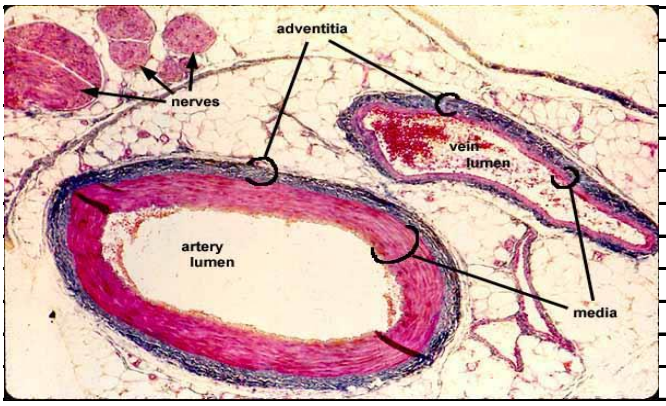
Intima: this is the inner layer and consists of the endothelium and the small amount of connecive tissue beneath the endothelium.

Media: this is the middle layer and consists of smooth muscle.

Adventitia: this is the outer layer and consists of the connective tissue external to the muscle layer.

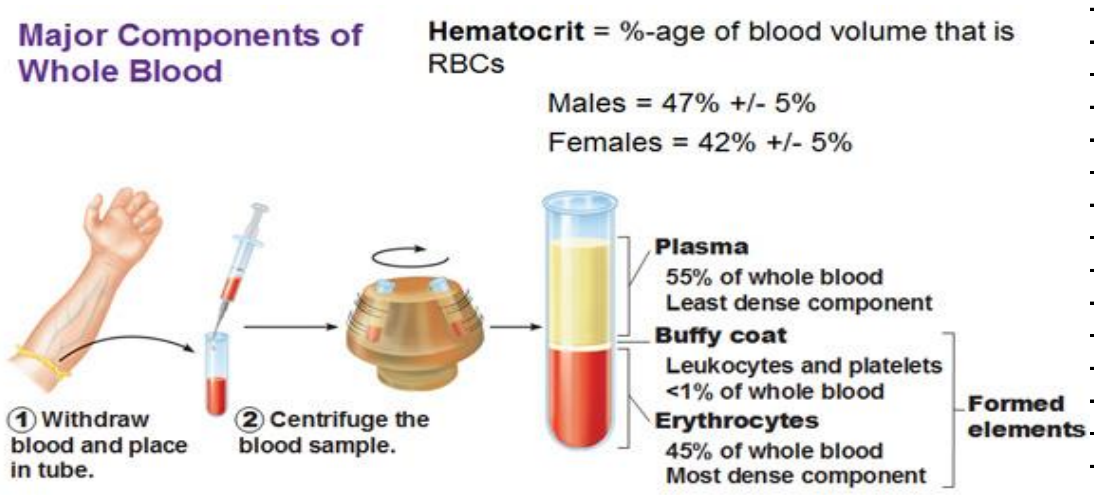
Difference in veins and arteries: see below diagrams : the arteries have a thicker layer of smooth muscle and also have elastic membranes that add recoil to balance the pressure wave from when the heart contracts.

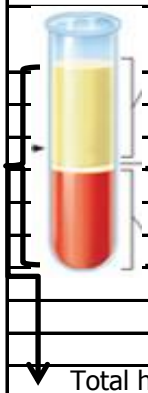




BLOOD

Blood is composed of a protein rich fluid called "plasma" in which there are red blood cells (also called erythrocytes and red corpuscles), white blood cells (also called leukocytes) , and platelets (also called thrombocytes).





If the blood is centrifuged, the red cells go to the bottom and the plasma is on top

Height of red cells

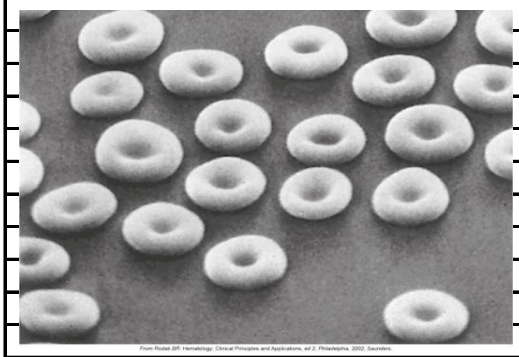
Total height of red cells and plasma

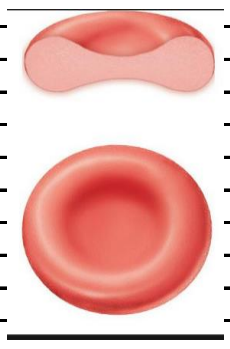
HEMATOCRIT
- Measured as percent
- Calculated by dividing the height of the red cells by the total height of the red cells and plasma.

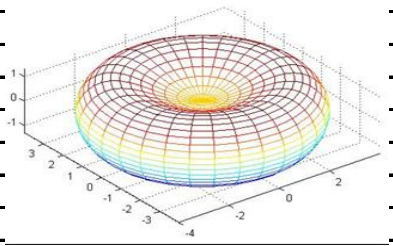
Cellular components
- Erythrocytes
- Leukocytes
- Thrombocytes (platelets)

Plasma components
- Albumin (oncotic / osmotic pressure)
- Globulins (immunoglobulins)
- Fibrinogen (clotting)
- Biomolecules, nutrients, electrolytes.

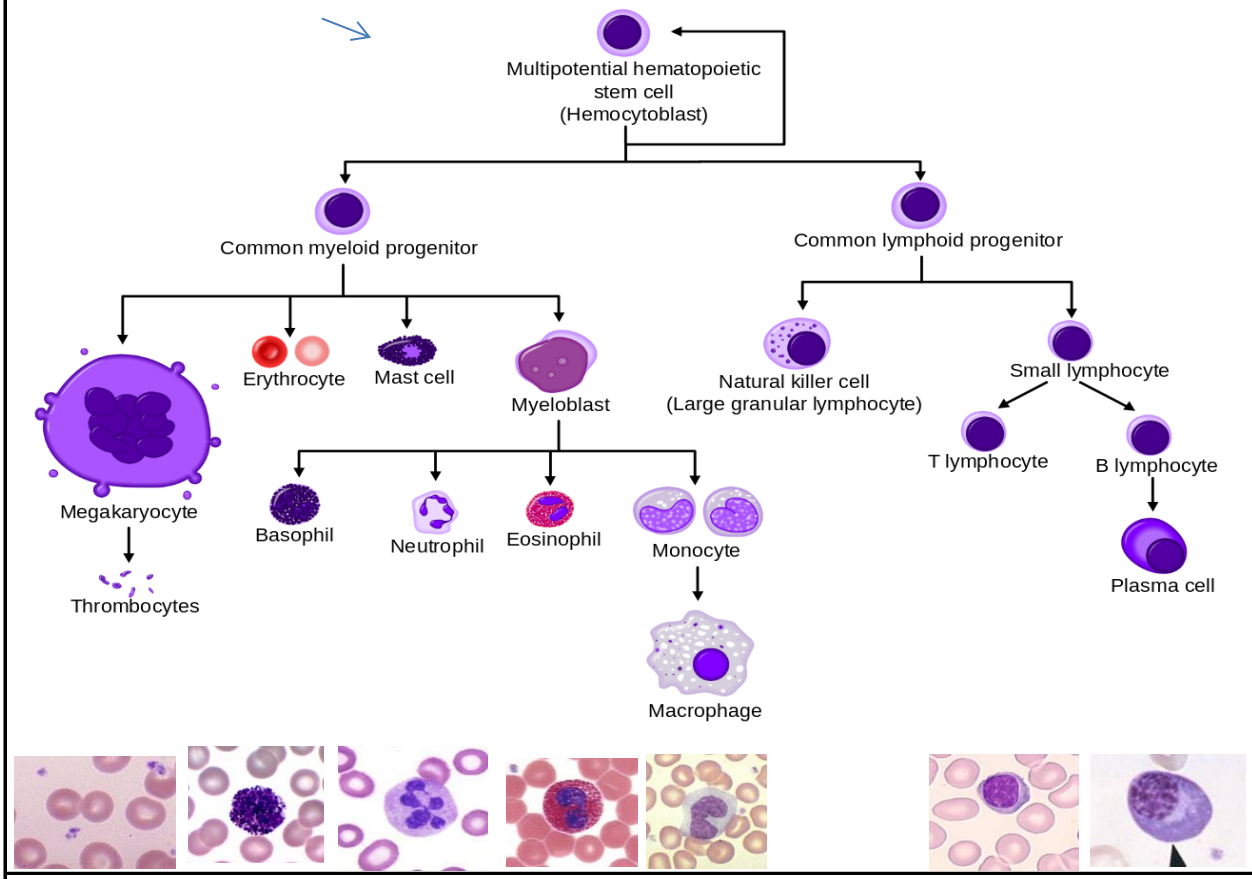
Red Cells: have a shape known as a biconcave disc - look like donuts, but there is no hole.







LEUKOCYTES- The below diagram shows how stem cells give rise to all the different white blood cells. Do not memorize chart but **do know what the different cells do.**



Thrombocytes (platelets) - get sticky when activated, form clumps, stop bleeding by plugging hole in blood vessels.

Basophil - less than 1 percent of circulating cells, granules have heparin and histamine, sometimes seen in allergic reactions and certain parasitic infections.

Neutrophil - most common cell in the circulation, nonspecific phagocytosis, kills bacteria. In CBC differential count, **think bacterial infection when the percentage of neutrophils are elevated**.

Eosinophil - elevated in allergic reactions and parasitic infections. **Think of allergic condition and parasite when the CBC differential count shows a high percent of eosinophils.**

Monocyte - these cells give rise to macrophages when they leave the blood stream and go into the tissues. **Nonspecific function:** phagocytosis, clear debris. **Specific function:** antigen presentation to Cytotoxic T cells and B cells by presenting a fragment of the original molecule, tacking it onto an MHC molecule and showing it to the T and B cells. T helpper cells help both B cells and cytotoxix T cells.

Lymphocytes - Think of **viral infection when the CBC differential count shows a high percent of lymphocytes.**

T Cells - Lymphocytes that participate in "cell mediated immunity" **(a "specific immunity" because the T cells are activated by specific antigens presented by macrophages).**

B Cells - Lymphocytes that participate in "humoral immunity" **(a "specific immunity" because the B cells are activated by specific antigens presented by macrophages).**

memory trick > **B**e Humorous *(reminder that B Cells are the "humoral" immune system)*

ERYTHROCYTES, aka RED BLOOD CELLS, RBC, CORPUSCLES

- big bags of hemoglobin.

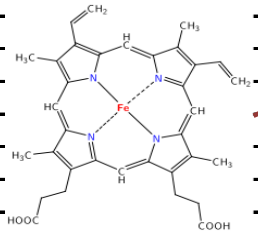
- no nucleus (it is lost in maturation in the bone marrow and circulating RBCs have no nucleus)

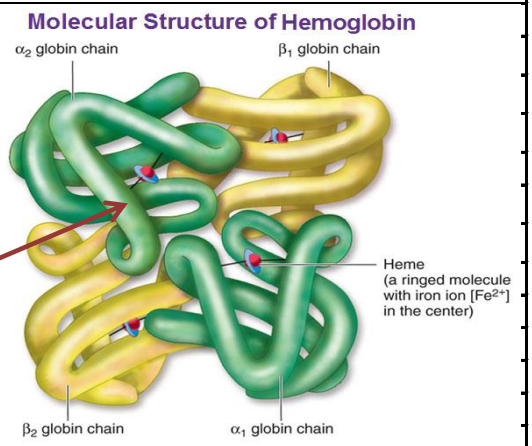
- have surface membrane antigens (A antigen, B antigen, Rh antigen) that allow them to be typed
- live 120 days in the circulation.

Hemoglobin:

-Composed of 4 proteins (alpha 1 globin chain, alpha 2 globin chain, beta 1 globin chain, and beta 2 globin chain) each of which has a heme ring.

Heme Ring: is a porphorin class molecule that has a ring shape and hold an Iron molecule in the center.





Oxygen gas in the form of O_2 (O=O) binds to the Iron for delivery from the lungs to the tissues.

T+ :C≡O: Carbon monoxide can also bind to the iron. It does not detach as easily as oxygen; so it blocks oxygen binding - a very toxic situation.

Most of the RBC is hemoglobin, so after the RBC does its 120 day tour, it is removed by the spleen and degraded. Three parts are dealt with globin chains, heme ring, and iron.

1. Globin chains are degraded by spleen into amino acids that can be recycled to build new proteins.
2. Ion is recycled and can be used in new erthrocytes.
3. The heme ring is broken and the linear molecule bilirubin is formed and sent to the liver where it is excreted in the bile. **NOTE: bilirubin is yellow, so if the liver is sick and can not get rid of the bilirubin, one turns yellow - known as jaundice.** This can also happen when a non-sick liver is overwhelmed with more bilirubin than it can handle. Example - someone has a hemolytic disease that lyses or pops red cells in the circulation. Large amounts of bilirubin form in the circulation and turn them yellow.

Yellow Bruise:
Heme is converted to biliverdin (green) and then into bilirubin (yellow) . So, the reason a bruise changes color is because the blood in the bruis e is being degraded locally and bilirubin is produced.

BLOOD TYPING - learn the chart below you will be tested on what blood types and plasma types are compatible. Just remember that the plasma will have antibodies of opposite blood type.

TABLE 10-1 ABO Blood Groups and Transfusion Compatibilities

Blood Group	RBC Antigens	Antibodies in Plasma	For Transfusion, Can Receive Donor Blood Group
O	None	Anti-A and anti-B	O
A	A	Anti-B	O or A
B	B	Anti-A	O or B
AB	A and B	None	O, A, B, or AB

NOTE: When you give type O blood to someone who is type A or B, the plasma must be removed and only the erythrocytes are given. This is because the O blood plasma has anti A and anti B antibodies that would attack the recipient's cells. The plasma is removed by centrifugation and the erythrocyte product (minus the plasma) is called "packed red cells".

Blood Clotting—Hemostasis

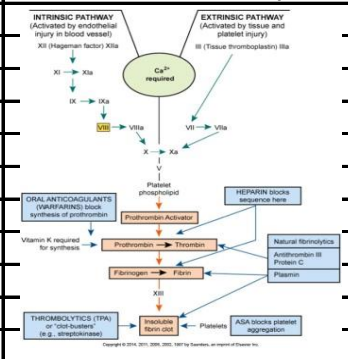
Three Steps:

1. Vasoconstriction (smooth muscle in arterioles contracts and narrows the arteriolar lumen cutting blood flow to the bleeding area).

2. Platelets are activated, stick to tissue, and stick to each other forming aggregates to plug up the hole.

3. Coagulation Mechanism - the clotting cascade results in proteins forming masses with erythrocytes. These erythrocyte - protein clumps are known as blood clots.

After the damaged blood vessels that lead to the bleeding are repaired, the blood clot has to be broken down. **"Plasmin"** is a protein that assists in this process.



The picture of the clotting cascade is to remind you that clotting is a cascade with many steps. Interuptng any step may shut down clotting and make one prone to bleeding.
Thus:
1. For patients that may clot too easily leading to emboli and strokes - "anticoagulant medicine " is given to inhibit clotting on purpose.
2. diseases that inactivate a clotting factor may lead to a bleeding disease like hemophilia.

Anticoagulants:

1. Medicines like heparin **that affect clotting factors.**

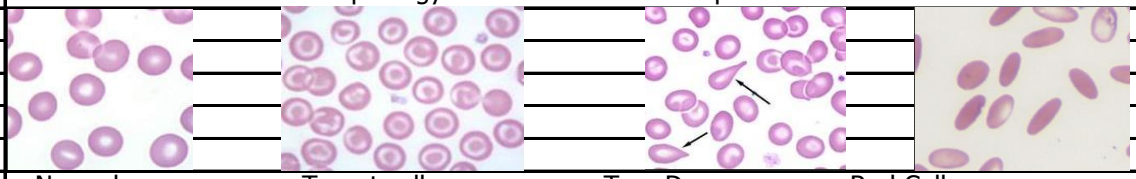
2. Molecules like EDTA and citrate, known as chealators, **bind up all the available calcium** and the clotting cascade (that requires calcium to work) is shut dowm.

3. Medicines like aspirin (chemical name aceto-salicylic acid, o ASA) will **inhibit platelet aggregaation.**

CBC - Complete Blood Count

The CBC is a comprehensive report on the blood and its components. Listed are:

1. The concnetration of red blood cells (RBC).
2. The concentration of white blood cells (WBC).
3. The concentraion of platelets (Plt).
4. The concentraion of hemoglobin (Hb).
5. The hematocrit (Hct).
6. The mean volume of the red cells or mean corpuscular volume (MCV).
7. The size distribution of the red cells - RDW
8. The mean volume of the platelets or mean platelet volume (MPV).
9. Comments on red cell morphology to discuss unusual shapes:



Normal Target cells Tear Drops Rod Cells

Abnormal Results:

RBC - too few = anemia, too many = polycytemia

WBC- too few = leukopenia, too many = leukocytosis

Platelets - too few = thrombocytopenia, too many = thrombocytosis

MCV - small size RBC = microcyte, normal size RBC = normocyte, large size RBC = macrocyte

thus in anemia there are **microcytic, normocytic, and macrocytic anemias.**

Differential count of WBC - abnormalities discussed above in discussion of leukocytes.

Recap elevations and associations - **know the following three:**

Elevated neutrophils in bacterial infections.

Elevated lymphocytes in viral infections.

Elevated eosinophils in allergic reactions.

ANEMIA:

- too little red cell mass from too few RBCs or adequate number but the RBCs are small.
- many types of anemia, we will focus on three:

- patient is pale, fatigued, may have dyspnea (difficult breathing) and tachycardia (fast heart beat).

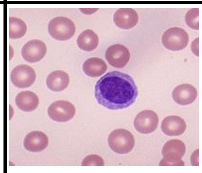
1. Iron deficiency anemia - from too little iron in diet or from inadequate replacement of iron loss. Mainly lost by bleeding (menstrual losses or by abnormal bleeding like gastrointesinal bleeding).

2. Pernicious Anemia - from vitamin B12 deficiency. Not usually from diet. Usually because the stomach is affected by an inflammatory disease ("gastritis") that affects the acid producing cells that also make "intrinsic factor" that is needed to absorb dietary vitamin B12. Affects nerves, there may be pins and needles tingling in limbs. Tongue may be enlarged, red, sore.

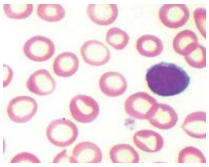
3. Sickle Cell Anemia - from a mutation in the globin beta chain that results in deformed cells that plug up capillaries and are prone to hemolysis. Recessive inheritence means one bad gene is a "sickle cell carrier" and two bad genes is "sickle cell disease".

Diagnosis of Anemia

1. Iron deficiency anemia -



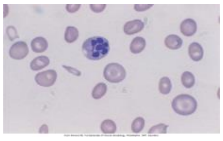
Nomal



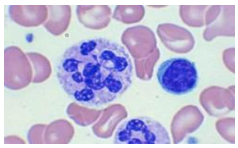
Microcytic Hypochromic

1. Pale, fatigue, lethargy, tachycardia.
2. CBC: MCV is low
3. Serum iron level is low

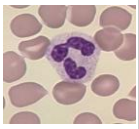
2. Pernicious Anemia -



Macrocytic



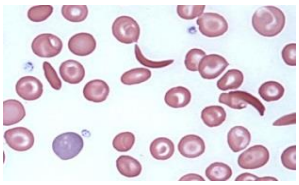
Hyperlobated Neutrophils vs



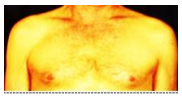
Normal

1. Red Tongue, Tingling extremities
2. CBC: MCV is high
3. Serum Vitamin B12 level is low.
4. Reduced or no acid in stomach.

3. Sickle Cell Anemia -



1. Usual signs of anemia plus **pain from ischemia.**
2. CBC: shows abnormal sickle forms.
3. Hemoglobin Elecroporesis shows Hemoglobin S.
4. Bilirubin in blood is elevated from hemolysis.
   May cause jaundice (yellow skin).



Brief Mention:

Aplastic anemia:

- Bone marrow depressed by radiation, chemicals, drugs, virus, or genetic disorder
- **CBC shows pancytopenia** (decrease in RBC, WBC, platelets)

Hemolytic Anemia:

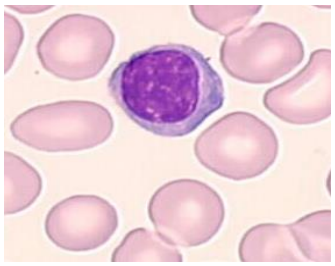
- **conditions that lyse (pop) red blood cells**. **Bilirubin is elevated** in the circulation.
- causes are many, **Incompatible Blood Transfusion** is an important one to remember.
- immune reactions may produce antibodies in the circulation that lyse the RBCs.
- other causes include genetic disease, malaria, toxins, and abnormal bood chemistry.

Clotting Disorders:

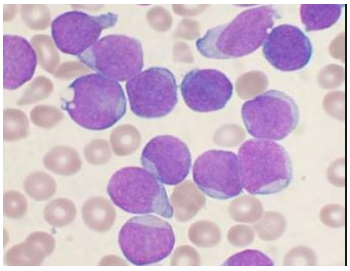
Present with abnormal bleesing:

- Bleeding from gums.
- Epistaxis (nose bleed).
- Petechiae (pinpoint hemorrhages).
- Purpura (sheet like skin hemorrhages).
- Ecchymoses (bruises).
- Hemarthrosis (blood in joint space).
- Hemoptysis (coughing up blood).

	- Hematemesis (vomiting blood).
	- Melena (tary stool from digested blood).
	- Hematuria (blood in urine)
	Blood loss may result in anemia, low blood pressure, and rapid pulse.
	on these terms but will expect you to know that clotting disorders produce abnormal bleeding in a variety
	Clotting Disorders:
	Hemophilia A - caused by a genetic abnormality involving a member of the clotting cascade (Factor VIII).
	Batteries of blood tests are run to diagnose clotting disorders.
	Some, like PT, PTT, and bleeding time are entry level tests.
	Final diagnosis may require testing the level of the individual clotting factor suspected.
	The treatment often involves giving factor replacement.
	Von Willebrand's Disease
	- this is the most common hereditary clotting disorder.
	Disseminated Intravascular Coagulation (DIC)
	- an excessive stimulus leads to widespread intravasvular clotting
	- this casues two huge problems:
	1. the clots cause micro infarcts that can severely damage organs.
	prone to bleeding
	- this is very serious life threatening condition.
	Leukemia - malignancy of white blood cells
	- there are many types, each behaving differently and needing tailored treatment.
	with pancytopenia leading to anemia, frequent infections, and bleeding,
	enlargement of lymph nodes, spleen and liver, headache, and **CNS involvement:** visual disturbances,
	Early studies may show CBC with pancytopenia and rare leukemic cells.
	Later studies may show elevated white blood cell count with a diff that is mostly leukemic cells.



Normal lymphocyte



Leukemic Blasts