BIOLOGY 12 - CHAPTER 11 - BLOOD - CHAPTER NOTES

- Human beings are approximately **70% WATER** by body weight. Where is all this water?
- Most of this water is **within cells**, while a smaller amount is found within:
  - A. **TISSUE FLUID** (surrounds cells
  - B. **LYMPH** (within lymph vessels)
  - C. **BLOOD VESSELS**
- **BLOOD** is required by the body to maintain homeostasis. Blood is a **liquid connective tissue**. Blood functions in a) **TRANSPORT** (of gases, wastes, and nutrients) b) **CLOTTING** (to seal injuries) c) **INFECTION FIGHTING**. Average person has about 5 to 6 liters of blood.
- If blood is allowed to sit in a test tube without clotting, it will divide into **TWO MAIN PARTS:**

A. **PLASMA** (the liquid portion of blood) - makes up about **55% of blood volume**. Contains water and **organic** and **inorganic substances** (***proteins, gases, salts, nutrients, wastes***).

Plasma Constituent	Function	Source
Water	Maintains blood volume and transports molecules	Absorbed from large intestine
Plasma Proteins a. Albumin b. Fibrinogen c. Globulins	All maintain blood osmotic pressure & pH Transport Clotting Fight Infection	 Liver Liver Lymphocytes
Gases a. Oxygen b. CO_2	 Cellular Respiration End product of metabolism	 Lungs Tissues
Nutrients: Fats, glucose, amino acids, etc.	Food for cells	Absorbed from intestinal villi
Salts	Maintain blood osmotic pressure/pH, aid metabolism	Absorbed from intestinal villi
Wastes	End products of metabolism	Tissues
Hormones, vitamins etc.	Aid metabolism	Varied

B. **FORMED ELEMENTS**: the "solid part" of blood, consists of the following parts.

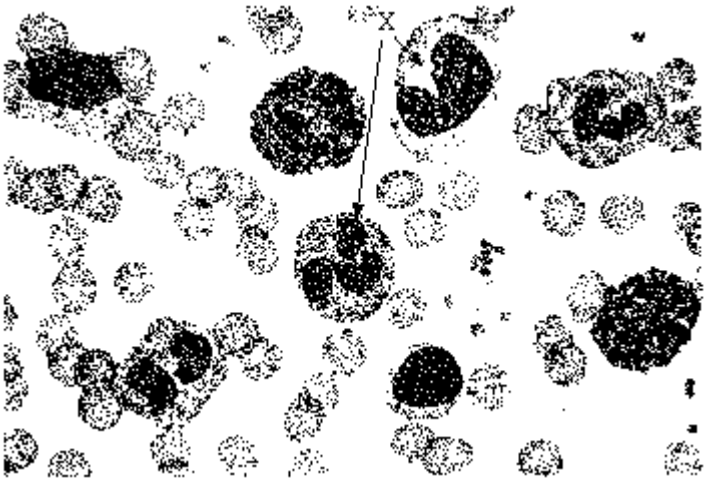
a. **RED BLOOD CELLS (ERYTHROCYTES)**
Transport **oxygen**, formed in **bone marrow**. Over 95% of formed elements are erythrocytes.

b. **WHITE BLOOD CELLS (LEUKOCYTES)**
Fight infection, formed in bone marrow and lymphoid tissue.

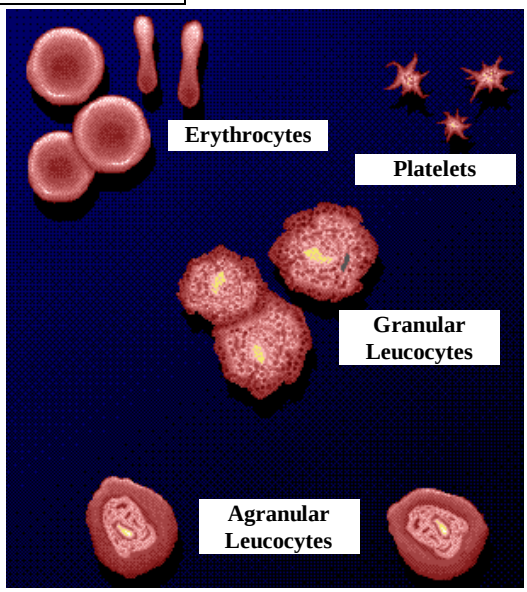
c. **PLATELETS (THROMBOCYTES)**
Function in blood clotting

- The white blood cells can also be classified according to their appearance.

Erythrocytes	Leukocytes		Thrombocytes
Red Blood Cells	White Blood Cells		Platelets
	Granular Leukocytes	Agranular Leukocytes	
	Basophils	Monocytes	
	Eosinophil	Lymphocytes	
	Neutrophil		



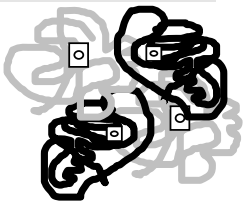
Here is a micrographs showing formed elements in human blood



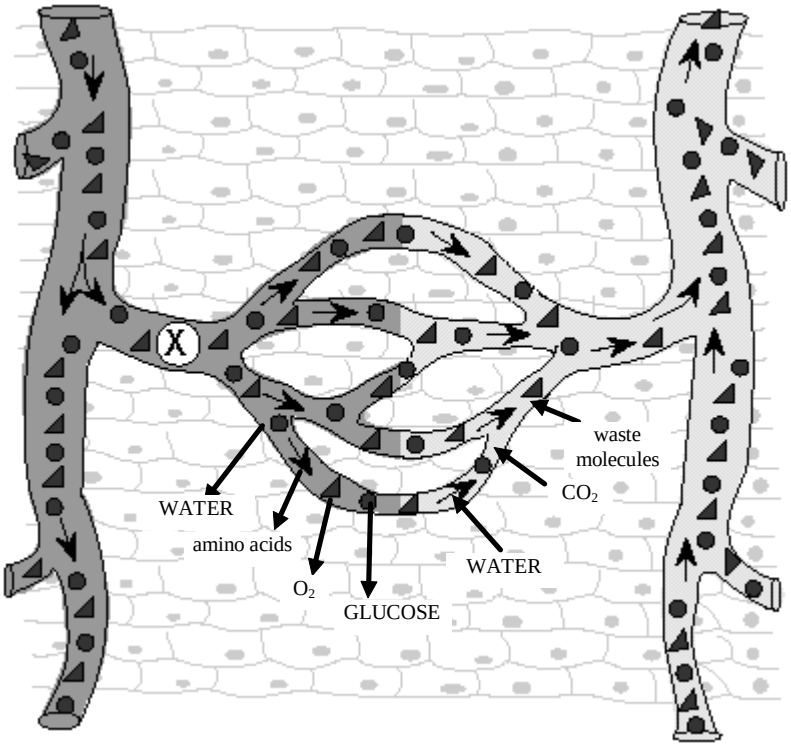
Blood Proteins

- Are required for the **transport** of many molecules. For example, **cholesterol** is a lipid that is insoluble in plasma. It must be carried by proteins.
- HDL (high-density lipoprotein) is "better" than LDL for binding with cholesterol, according to some studies, in the prevention of atherosclerosis.
- Blood proteins also contribute to the **viscosity** of blood ("blood is thicker than water"), which aids in transport.
- Blood proteins also contribute to **osmotic pressure**, which maintains **blood volume**.

Hemoglobin



- O_2 is carried by **Hemoglobin**, which is made of **4 amino acid chains** (2 *alpha* (α) and 2 *beta* (β)). Each chain has **iron-containing heme group** which **attaches to oxygen**.
- Hemoglobin is an excellent carrier of oxygen because it **weakly binds** with **oxygen** in the **cool, neutral conditions** in the **lungs**, and **easily gives O_2** up in the **warmer** and **more acidic tissues**.
- Hemoglobin is always contained **within red blood cells**. Since hemoglobin is a red pigment, red blood cells appear red. This colour can **change** based on what the hemoglobin is attached to.
- **OXYHEMOGLOBIN** (hemoglobin bound to oxygen, abbreviated as **HbO_2**) is **bright red**, while **REDUCED HEMOGLOBIN** (hemoglobin that has lost its oxygen) is **dark purple**.
- **Carbon Monoxide** (**CO**) is a poison found in car exhaust. It binds to Hb better than oxygen, and stays bound for several hours regardless of the environmental conditions. CO poisoning can lead to **death**.



In the diagram above, the blood at point **X** would **likely** contain a relatively high concentration of a) urea b) oxygen c) carbon dioxide d) bicarbonate ions

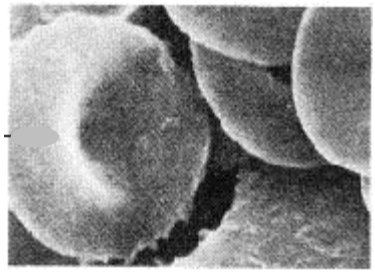
- Hemoglobin picks O_2 up in the lungs and releases O_2 in tissues. Meanwhile, CO_2 and wastes diffuse **out** of cells. What this means is that there are all sorts of diffusing molecules going in and out of the blood and cells. We should understand how this works and what drives the movement of molecules. The main answer lies in battle of blood pressure versus osmotic pressure. The pressure of blood in blood vessel would tend to push molecules out of the blood. Osmotic pressure is the opposing force trying to force molecules into the blood. Osmotic pressure is basically constant, but blood pressure varies considerable around a capillary bed. This causes some natural movement of molecules.
- At the **arterial side** of a capillary, **blood pressure** is **higher** than the osmotic pressure and therefore water, oxygen and glucose tend to **leave the bloodstream**.
- At the **venous end** of a capillary, the **osmotic pressure is higher** than the blood pressure and, therefore, water, ammonia, and carbon dioxide tend to **enter the bloodstream**.
- Reduced hemoglobin can now pick up CO_2 to form **carbaminohemoglobin** ($HbCO_2$).
- However, most CO_2 transported as **BICARBONATE ION** (= **HCO_3^-**), which is formed after CO_2 combines with water, forming carbonic acid which then dissociates. Note the following reaction:

$$CO_2 + H_2O \text{<--->} H_2CO_3 \text{<--->} H^+ + HCO_3^-$$

- The **enzyme CARBONIC ANHYDRASE speeds up this reaction**.

- The H^+ released by the above reaction could wreak havoc on blood pH. To prevent this **H^+ is picked up by** the **<u>globin</u> <u>portion</u> <u>of</u> <u>hemoglobin</u>** (to become **<u>HHb</u>**) so that **<u>pH is maintained</u>.**

Red Blood Cells



- There are close to 30 trillion blood cells in an adult. Each cubic millimeter of blood contains from 4 1/2 to 5 1/2 million red blood cells and an average total of 7,500 white blood cells. In humans, red blood cells are **small**, **biconcave**, **disk-shaped** cells without **nuclei**.
- Red blood cells are made by cells called "**<u>STEM</u> <u>CELLS</u>**" in red bone marrow (over 2 million per second!) of the **skull**, **ribs**, **vertebrae**, and **ends** of the **long bones**. Here, Stem Cells continuously divide. During the maturation process, a red blood cell **<u>loses</u> <u>its</u> <u>nucleus</u>** and gets much **smaller**.
- **Oxygen levels in blood** determine the **rate of RBC formation**. When oxygen tension is low, the kidneys produce a chemical called **<u>renal</u> <u>erythropoietic</u> <u>factor</u>** (REF) that, after combining with globulin from the liver, causes the bone marrow to produce more RBC.
- RBC live for only **120 days** and then are destroyed in the **liver** and **spleen**. The iron is recovered from the hemoglobin and sent to the bones, while the heme portion is chemically degraded and is excreted by the liver in the bile as bile pigments.

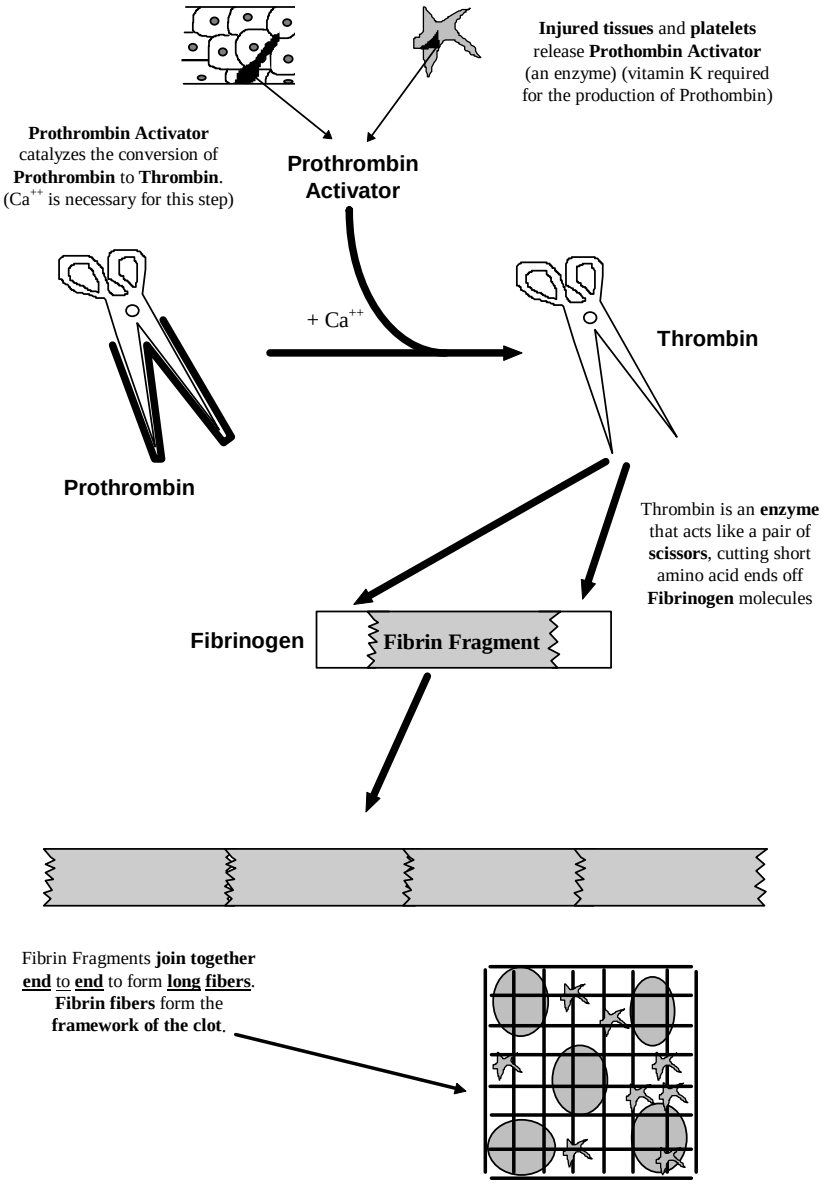
BLOOD CLOTTING

- After an injury, **coagulation** "or **clotting**" takes place to prevent excessive blood loss.
- This requires the action of 1) **platelets** 2) **prothrombin**, and 3) **fibrinogen**.
- Platelets result from fragmentation of large cells called **megakaryocytes** in red bone marrow. You have more than a **trillion** in your blood.

- **Fibrinogen** and **prothrombin** are plasma proteins manufactured and deposited in the blood by the **liver** (**vitamin K** is required for the production of prothrombin)
- Here is a **<u>simplified</u> <u>summary</u>** of the steps involved in clot formation:

1. **Platelets clump** at the site of the puncture and partially seal the leak.
2. Platelets and injured tissues **release** the **enzyme** ***<u>prothrombin activator</u>*** that *activates* **prothrombin** to ***<u>thrombin</u>***. Calcium ions (Ca^{++}) are necessary for this step.
3. **Thrombin** acts as an enzyme and **severs** *two short a.a. chains from each fibrinogen molecule*.
4. These activated chains join end to end to form long ends of **<u>fibrin</u>**.
5. Fibrin threads entangle red cells and platelets in the damaged area and ***form the framework*** of the clot.

- Red cells trapped in the clot give it its red colour.
- Clotting takes place **faster at warmer temperatures** than cold because it is



controlled by enzymes.

- **Serum** is plasma from which the fibrinogen has been removed due to clotting.
- A fibrin clot is only a **temporary repair**. Eventually, an enzyme called **plasmin** destroys the fibrin network and restores the fluidity of plasma.

INFECTION FIGHTING: another major function of blood

- The body's first line of defense against invading pathogens like bacteria and viruses is the **skin**.
- The second line of defense is the blood: specifically, **white blood cells** and **gamma globulins**.

WHITE BLOOD CELLS

- White blood cells are usually larger than RBC (8 - 20 μm), have a nucleus, and appear white (if not stained -- when stained, they appear bluish).
- Much less numerous than RBC (only **7,000 to 8,000 cells per cubic millimeter**). White blood cells, called **leukocytes**, are outnumbered by the red blood cells 600 to 1.

There are two main types of Leukocytes:

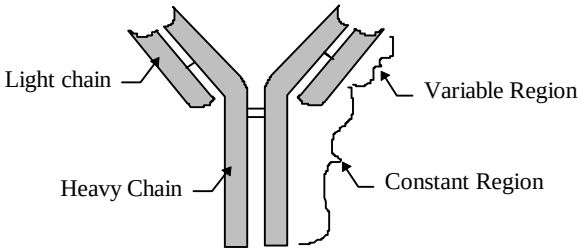
1. **Granulocytes**: have granules in the cytoplasm and a many-lobed nucleus joined by nuclear threads (called "polymorphonuclear"). The granulocytes include **Neutrophils** (phagocytizes primarily bacteria), **Eosinophils** (phagocytizes and destroys antigen-antibody complexes), and **Basophils** (congregates in tissues, releases histamine when stimulated). Formed in the red bone marrow. The granules of a neutrophil are **lysosomes**.
2. **Agranulocytes**: Include **Lymphocytes** and **Monocytes**. They don't have granules, and have a circular (lymphocytes) or indented (monocytes) nucleus. They are produced in **lymphoid tissue** found in the spleen, lymph nodes, and tonsils. Tye B lymphocytes produce **antibodies** in blood and lymph, Type T lymphocytes kill virus-containing cells. Monocytes become **macrophages**.

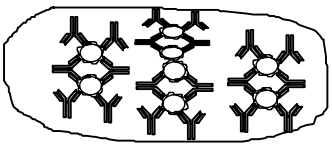
- Infection fighting by white cells is **primarily dependent** on the **neutrophils**, which comprise **60** to **70**% of all leukocytes, and the **lymphocytes** (which make up **25** to **30**%).
- Neutrophils, monocytes, and eosinophils are **phagocytic**. They **engulf** invaders at the site of infection.
- Lymphocytes don't work this way. They secretea class of **gamma globulins** (proteins) called **IMMUNOGLOBULINS** (=**ANTIBODIES**), which combine with foreign substances to inactivate them.
- Lymphocytes are the smallest white blood cells. When microbes invade the body, lymphocytes begin to multiply and they become transformed plasma cells. Each microbe stimulates only one type of lymphocyte to multiply and form one type of plasma cell. The type of plasma cell formed is the type that can make a specific antibody to destroy the particular microbe that has invaded the body.
- Red bone marrow continually produces white blood cells, except lymphocytes and monocytes, and keeps a reserve ready in case of need. Lymphocytes and monocytes are produced by lymphatic tissue located in the lymph nodes and spleen. When a parasite or virus invades and begins to colonize, the reserves of white blood cells are released and the manufacturing of large quantities of the appropriate white cells begins. It is this increased production that causes fever. Because white blood cells are very specific for various illnesses, their count can help doctors diagnose patients.

ANTIBODIES: very specific proteins that attach to invading pathogens

- **Lymphocytes produce antibodies** in response to invading pathogens.
- Each lymphocyte produces **one type** of antibody that is specific for one type of **antigen**. An **antigen** is a foreign substance (usually a **protein**, sometimes a carbohydrate) that **stimulates the release** of antibodies to it. e.g. an antigen could be protein coat of a virus.
- Antibodies combine with antigens in such a way that the antigens are rendered harmless. Each antibody fits its antigen like a lock and key.
- An individual is **immune** to an antigen if he/she has
- antibodies to that particular antigens.
- The blood in the individual contains lymphocytes that can remain in the system for **years**, ready to produce antibodies if that antigen is detected.

STRUCTURE OF AN ANTIBODY





Antibodies binding to antigens (proteins on surface of a cell)

- **Exposure to the antigen**, either naturally or by way of a vaccine, can cause active immunity to develop.
- Diseases will often cause an increase in a particular type of white cell. e.g. **mononucleosis** characterized by greater #'s of dark staining lymphocytes. **Leukemia** is a form of cancer characterized by uncontrolled production of abnormal white cells, which accumulate in the bone marrow, lymph nodes, spleen, and liver, causing them to malfunction. Leukemia patients often have severe anemia, clotting difficulties, and succumb to many infections.

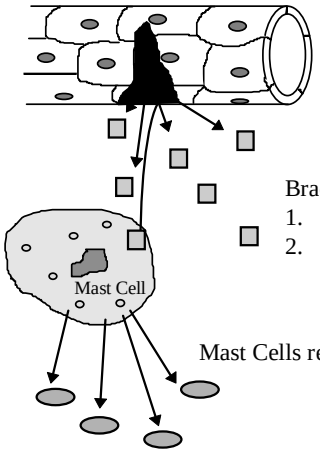
THE INFLAMMATORY REACTION

- Whenever the skin is broken due to a minor injury, a series of events occur that are known as the **inflammatory response** because there is **swelling** and **reddening** at the site of the injury. This response is designed to **get the body's defenses marshaled as quickly as possible at the site where they are needed**.

1. When blood vessels and tissue cells get ruptured by an injury, they **release** precursors of **BRADYKININ**, a chemical with several jobs: 1) it **initiates nerve impulses** ---> this results in **PAIN** 2) bradykinin causes **MAST CELLS** (a type of cell that resides in tissues that is derived from Basophils) to release **histamine**, which together with bradykinin causes a capillary to become enlarged and more permeable.
2. the *enlarged capillary* causes the skin to **redden** and its increased permeability allows *proteins and fluids to escape* so that **swelling** results.
3. Meanwhile, **bacteria** and **viruses** are also entering through the rupture.
4. Lymphocytes release antibodies that attack the invading pathogens, preparing them for **phagocytosis** by neutrophils or monocytes.
5. Once monocytes have arrived on the scene, they swell up to five to ten times their original size and become **macrophages** (large phagocytic cells that are able to devour a hundred invaders and still survive).

- Dead neutrophils plus cells, bacteria, and WBC form **pus**, a **thick yellowish fluid**.

The inflammatory response is a "911 call" to the immune system. It marshalls phagocytic white blood cells to the site of invasion by bacteria

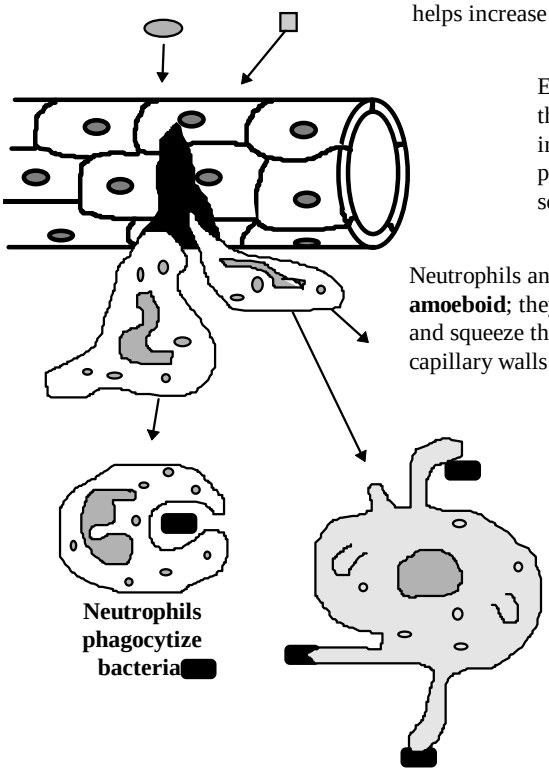


Injured tissues and capillaries release factors that form **BRADYKININ**.

Bradykinin:
1. stimulates nerves ("pain")
2. causes **MAST CELLS** (derived from basophils) to release **HISTAMINE**.

Mast Cells release **histamine**

Histamine causes capilliaries to **dilate**, **enlarge**, and become more **permeable** (bradykinin helps increase this effect).



Enlarged capillaries causes the skin to **redden**, and its increased **permeability** allows proteins and fluids to escape, so that **swelling** results.

Neutrophils and monocytes are **amoeboid**; they can change shape and squeeze through enlarged capillary walls to enter tissue fluid.

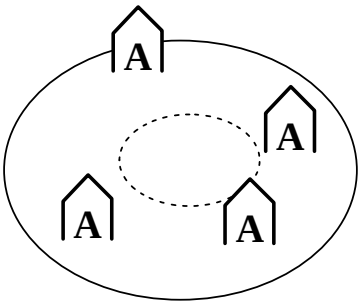
Monocytes become **MACROPHAGES**, which are large cells that are great at phagocytosis and also stimulate the release of other white blood cells from bone marrow. Macrophages eat up old blood cells, bits of dead tissue, bacteria, debris.

The "battlefield debris" called "**pus**" consists of dead and living leukocytes, dead cells, tissue, and bacteria.

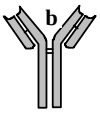
BLOOD TYPING

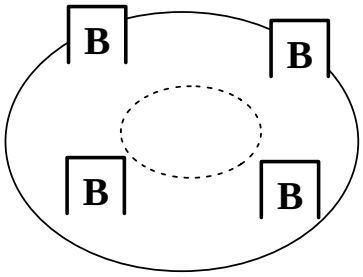
- Human blood is classified according to the **antigens** present on the surface of the red blood cells. The most common blood types belong to the **ABO Grouping**.
- Two antigens that may be present on the red cells are called "A" and "B". An individual may have one of these antigens present (in which case they will have type A or type B blood), or both (type AB) or neither (type O). Therefore, there are four blood types in the ABO Grouping.
- Each individual also carries antibodies in his/her plasma to the antigens ***not*** present on that individual's red cells. e.g. Type A blood has antibody b, Type AB blood has **no** antibodies.
- If the same antigen and antibody are present, **AGGLUTINATION** (or clumping) of red cells will occur (can cause death).
- Blood recipients may only receive donated blood for which they have no antibodies in their plasma.

This test indicates is B^+ blood type.

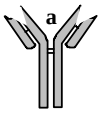


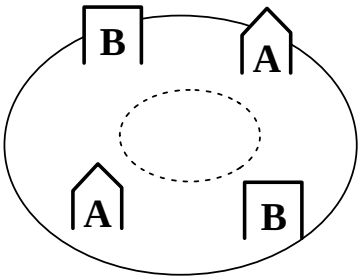
TYPE "A" BLOOD
- has type "A" **antigens**
- makes type b **antibodies** (antibodies that attack B antigens)



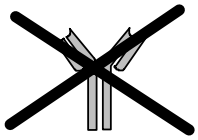


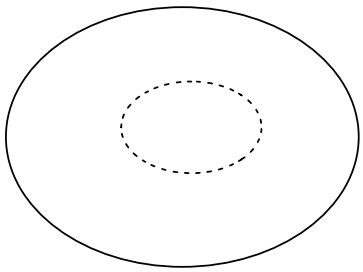
TYPE "B" BLOOD
- has type "B" **antigens**
- makes type a **antibodies** (antibodies that attack A antigens)



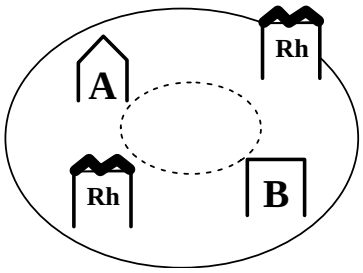


TYPE "AB" BLOOD
- has both "A" & "B" **antigens**
- makes **NO ANTIBODIES** to A or B antigens.





TYPE "O" BLOOD
- has **neither** A nor B **antigens**
- makes both type a and type b **antibodies**



Rhesus Antigen (Rh factor)
- Rh factor is **another antigen** that can be present on RBC.
- Either you have it ("+") or you don't ("-")
- If you are Rh negative, you **don't make antibodies** to Rh unless you have been exposed to it.
- The person above is **Rh**$^+$

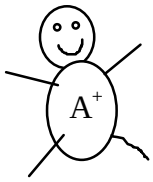
Type	Antigen	Antibody	%U.S. Black	%U.S. Caucasian
A	A	b	25	41
B	B	a	20	7
AB	A,B	none	4	2
O	none	a,b	51	50

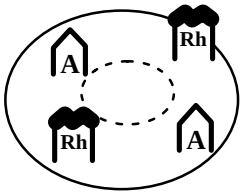
The Rh System

Another important antigen in matching blood types is the Rh factor (another antigen found on red blood cells)

- People with this particular antigen on the red cells are **Rh positive**; those without it are **Rh negative**.
- Rh negative individuals **do not normally make antibodies to the Rh factor**, but they will make them ***when exposed to the Rh factor***. It is possible to extract these antibodies **and use them for blood type testing**, since Rh positive blood will agglutinate when mixed with Rh antibodies.
- The Rh factor is very important during **pregnancy**. If the ***mother is Rh negative*** and the ***father is Rh positive***, the child *may be* Rh positive. During gestation, it is *normal that a few red cells from the child will find their way into the mother's system* -- **she will then produce Rh antibodies**.
- If the **mother becomes pregnant with another Rh positive baby**, Rh antibodies my cross the placenta and destroy the child's red cells. This is called **FETAL ERYTHROBLASTOSIS**.
- Current treatment: give Rh^- women an Rh immune globulin injection (like an injection of antibodies) called **RhoGAM** just **after** the birth of any Rh^+ child. This injection will **DESTROY ANY RED CELLS** left over from the ***baby***, **BEFORE** the mother has a chance to start producing her own antibodies.
- The injection *won't work if the woman has already started to produce her own antibodies*.

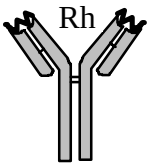
For Example: A^- mother X O^+ father could produce A^+ baby.



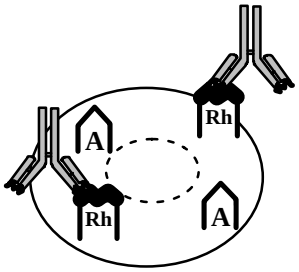


A few of baby's blood cells get into mother just before or during childbirth.

Mom then produces antibodies to the Rh factor



If she gets pregnant with another Rh^+ baby, her anti-Rh antibodies can cross placenta during pregancy and cause agglutination of baby's RBC -- can seriously harm or kill the baby.



Treatment: immediately after birth of Rh^+ baby, give mother injection of RhoGAM. It contains Rh antibodies that **destroy any of the baby's RBC** left in the mother **before she can produce antibodies to Rh factor**.