Baida almusawy **Human Physiology/Blood physiology**

lecture (4)

Overview of Blood

Blood is circulated around the body within the cardiovascular system. function of blood is to supply transportation of dissolved gases, nutrients, hormones, & metabolic wastes regulation of pH & electrolyte composition of interstitial fluids throughout body, blood absorbs & neutralizes acids generated by active tissues, needs to get rid of protons, restriction of fluid losses through damaged vessels or at other injury sites, defense against toxins & pathogens, stabilization of body temperature.

The blood is circulated through the lungs and body by the pumping action of the heart. The right ventricle pressurizes the blood to send it through the capillaries of the lungs, while the left ventricle repressurizes the blood to send it throughout the body. Pressure is essentially lost in the capillaries, hence gravity and especially the actions of skeletal muscles are needed to return the blood to the heart.

Gas Exchange

Oxygen (O2) is the most immediate need of every cell and is carried throughout the body by the blood circulation. Oxygen is used at the cellular level as the final electron acceptor in the electron transport chain (the primary method of generating ATP for cellular reactions). Oxygen is carried in the blood bound to hemoglobin molecules within red blood cells. Hemoglobin binds oxygen when passing through the alveoli of the lungs and releases oxygen in the warmer, more acidic environment of bodily tissues, via simple diffusion.

Carbon dioxide (CO2)

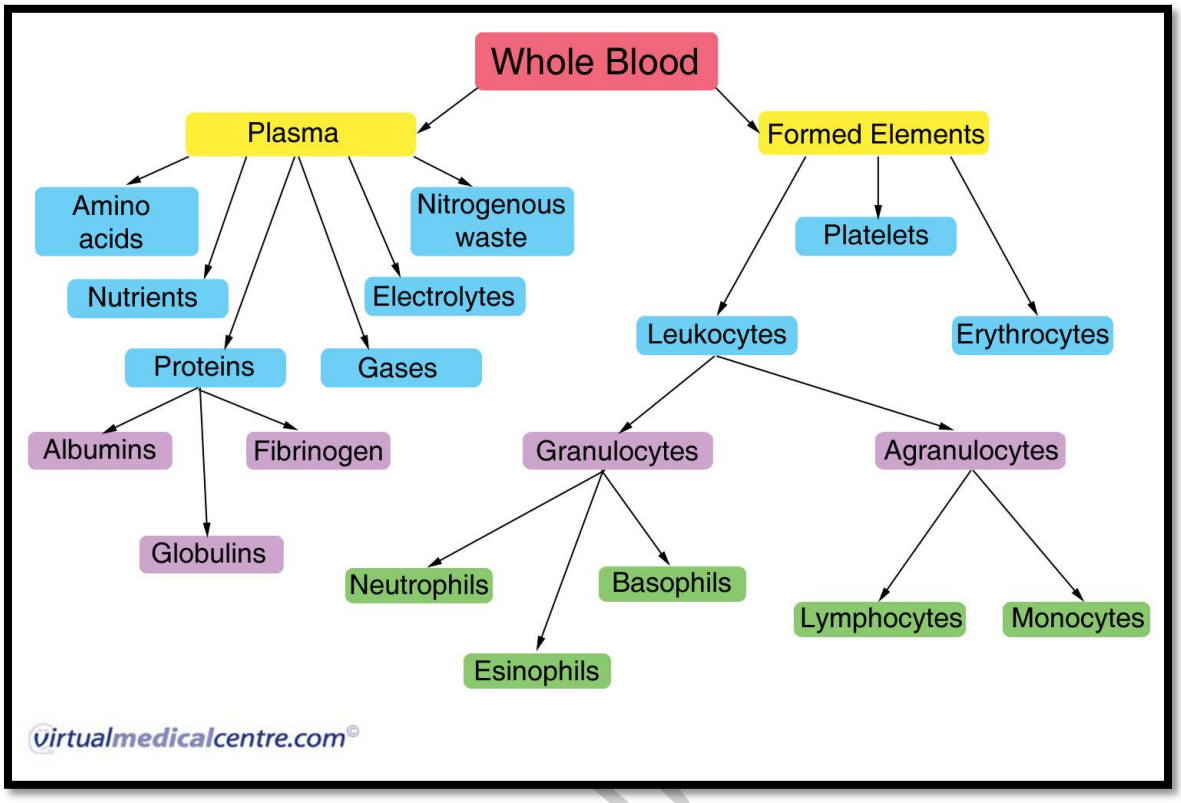
is removed from tissues by blood and released into the air via the lungs. Carbon dioxide is produced by cells as they undergo the processes of cellular respiration (particularly the Kreb's Cycle). The molecules are produced from carbons that were originally part of glucose. Most of the carbon dioxide combines with water and is carried in the plasma as bicarbonate ions. An excess of carbon dioxide (through exercise, or from holding ones breath) quickly shifts the blood pH to being more acidic (acidosis). Chemoreceptors in the brain and major blood vessels detect this shift and stimulate the breathing center of the brain (the medulla oblongata). Hence, as CO2 levels build up and the blood becomes more acidic, we involuntarily breathe faster, thus lowering CO2 levels and stabilizing blood pH. In contrast, a person who is hyperventilating (such as during a panic attack) will expire more CO2 than being produced in the body and the blood will become too alkaline (alkalosis).

Blood Composition

Blood is a circulating tissue composed of fluid plasma and cells (red blood cells, white blood cells, platelets). Anatomically, blood is considered a connective tissue, due to its origin in the bones and its function. Blood is the means and transport system of the body used in carrying elements (e.g. nutrition, waste, heat) from one location in the body to another, by way of blood vessels. Blood is made of two parts:

1. Plasma which makes up 55% of blood volume.

2. Formed cellular elements (red and white blood cells, and platelets) which combine to make the remaining 45% of blood volume.



Plasma makeup

Plasma is made up of 90% water, 7-8% soluble proteins (albumin maintains bloods osmotic integrity, others clot, etc), 1% electrolytes, and 1% elements in transit. One percent of the plasma is salt, which helps with the pH of the blood. The largest group of solutes in plasma contains three important proteins to be discussed. There are: albumins, globulins, and clotting proteins.

Albumins are the most common group of proteins in plasma and consist of nearly two-thirds of them (60-80%). They are produced in the liver. The main function of albumins is to maintain the osmotic balance between the blood and tissue fluids and is called colloid osmotic pressure. In addition, albumins assist in transport of different materials, such as vitamins and certain molecules and drugs (e.g. bilirubin, fatty acids, and penicillin).

Globulins are a diverse group of proteins, designated into three groups: gamma, alpha, and beta. Their main function is to transport various

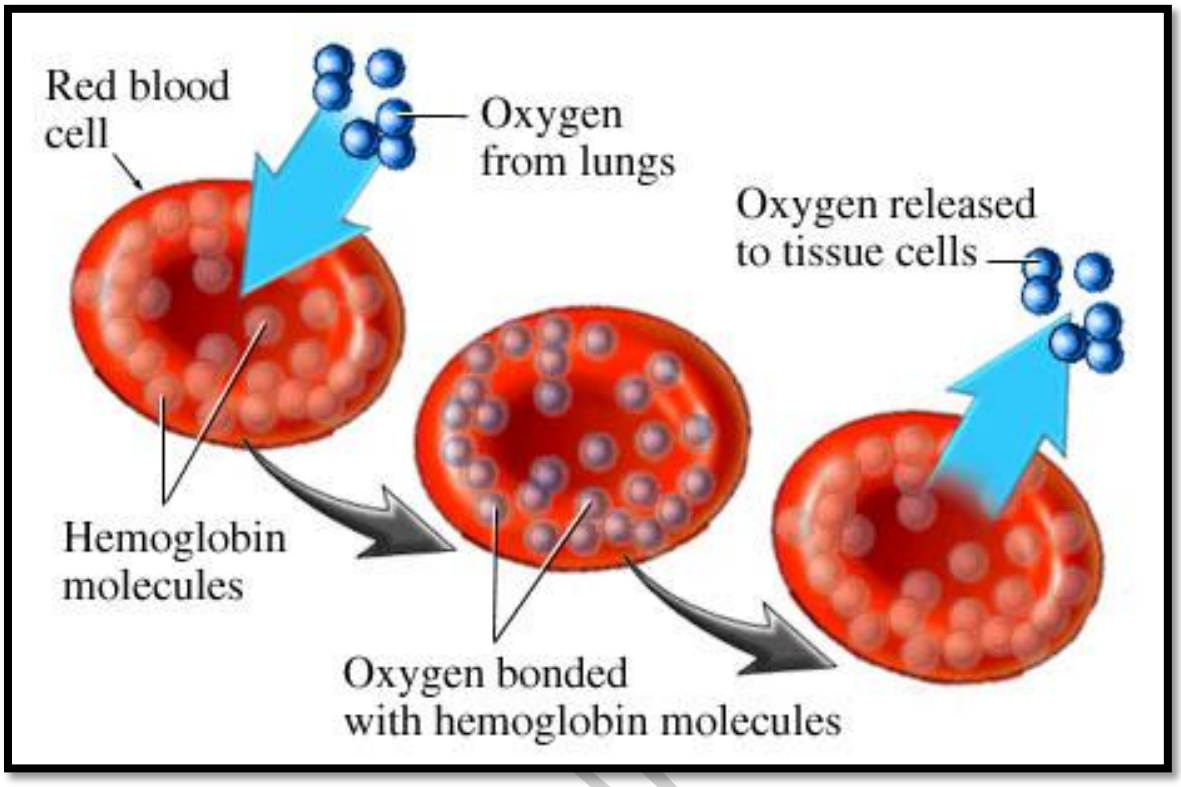
substances in the blood. Gamma globulins assist the body's immune system in defense against infections and illness.

Clotting proteins are mainly produced in the liver as well. There are at least 12 substances, known as "clotting factors" that participate in the clotting process. One important clotting protein that is part of this group is fibrinogen, one of the main components in the formation of blood clots. In response to tissue damage, fibrinogen makes fibrin threads, which serve as adhesive in binding platelets, red blood cells, and other molecules together, to stop the blood flow.

Plasma also carries Respiratory gases; CO2 in large amounts(about 97%) and O2 in small amounts(about 3%), various nutrients(glucose, fats), wastes of metabolic exchange(urea, ammonia), hormones, and vitamins. Picture of red blood cells.

Red Blood Cells

Red blood cell (erythrocyte) also known as "RBC's". RBC’s are formed in the myeloid tissue or most commonly known as red bone marrow, although when the body is under severe conditions the yellow bone marrow, which is also in the fatty places of the marrow in the body will also make RBC The formation of RBC’s is called erythropoiesis (erythro / red; poiesis / formation). Red blood cells lose nuclei upon maturation, and take on a biconcave, dimpled, shape. They are about 7-8 micrometers in diameter. There are about 1000x more red blood cells than white blood cells. RBC's live about 120 days and do not self repair. RBC's contain hemoglobin which transports oxygen from the lungs to the rest of the body, such as to the muscles, where it releases the oxygen load.The hemoglobin gets it's red color from their respiratory pigments.



Shape

RBC'S have a shape of a disk that appears to be "caved in" or almost flattened in the middle; this is called bi-concave. This bi-concave shape allows the RBC to carry oxygen and pass through even the smallest capillaries in the lungs. This shape also allows RBCs to stack like dinner plates and bend as they flow smoothly through the narrow blood vessels in the body. RBC's lack a nucleus (no DNA) and no organelles, meaning that these cells cannot divide or replicate themselves like the cells in our skin and muscles. RBC's have a short life span of about 120 days, however, as long as our myeloid tissue is working correctly, we will produce about 2-3 million RBC's per second. That is about 200 billion a day! This allows us to have more to replace the ones we lose.

Destruction

Red blood cells are broken down and hemoglobin is released. The globin part of the hemoglobin is broken down into amino acid components,

which in turn are recycled by the body. The iron is recovered and returned to the bone marrow to be reused. The heme portion of the molecule experiences a chemical change and then gets excreted as bile pigment (bilirubin) by the liver. Heme portion after being broken down contributes to the color of feces and your skin color changing after being bruised.

Control of erythrocyte production

Erythropoiesis is controlled by the kidney, which releases a hormone known as erythropoietin if the delivery of O2 to renal cells falls below normal. This will occur if the concentration of circulating hemoglobin is reduced, during anemia. The bone marrow responds by increasing red cell production, thus increasing the hemoglobin content back to normal.

White Blood Cells

Shape

White blood cells are different from red cells in the fact that they are usually larger in size 10-14 micrometers in diameter. White blood cells do not contain hemoglobin which in turn makes them translucent. Many times in diagrams or pictures white blood cells are represented in a blue color, mainly because blue is the color of the stain used to see the cells. White blood cells also have nucleii, that are some what segmented and are surrounded by electrons inside the membrane.

Functions

White blood cells (leukocytes) are also known as "WBC's". White blood cells are made in the bone marrow but they also divide in the blood and lymphatic systems. They are commonly amoeboid (cells that move or feed by means of temporary projections, called pseudopods (false feet), and escape the circulatory system through the capillary beds. The different types of WBC's are Basophils, Eosinophils, Neutrophils, Monocytes, B- and T-cell lymphocytes. Neutrophils, Eosinophils, and Basophils are all granular

leukocytes. Lymphocytes and Monocytes are agranular leukocytes. **Basophils** store and synthesize histamine which is important in allergic reactions. They enter the tissues and become "mast cells" which help blood flow to injured tissues by the release of histamine. **Eosinophils** are chemotoxic and kill parasites**. Neutrophils** are the first to act when there is an infection and are also the most abundant white blood cells. Neutrophils fight bacteria and viruses by phagocytosis which mean they engulf pathogens that may cause infection. The life span of a of Neutrophil is only about 12-48 hours. **Monocytes** are the biggest of the white blood cells and are responsible for rallying the cells to defend the body. Monocytes carry out phagocytosis and are also called macrophages. Lymphocytes help with our immune response. There are two Lymphocytes: **the B- and T- cell. B-Lymphocytes** produce antibodies that find and mark pathogens for destruction. **T-Lymphocytes** kill anything that they deem abnormal to the body. WBCs are classified by phenotype which can be identified by looking at the WBCs under a microscope. The Granular phenotype are able to stain blue. The Agranular phenotype are able to stain red. Neutrophils make up 50-70% of Granular cells Eosinophils make up 2-4%, and Basophils 0-1%. Monocytes make up 2-8% of Agranular cells. B and T Lymphocytes make up 20-30%. As you can see, there is a great deal of differentiation between WBCs. These special cells help our bodies defend themselves against pathogens. Not only do they help our immune system but they remove toxins, wastes, and abnormal or damaged cells. Thus, we can say that WBCs' main function is being Phagocytic which means to engulf or swallow cells.

Leucocyte production

Leucocytes originate from the pluripotential stem cells in the bone marrow, which divide and mature giving two separate leucocyte stem cell lines.

1- The myeloid line

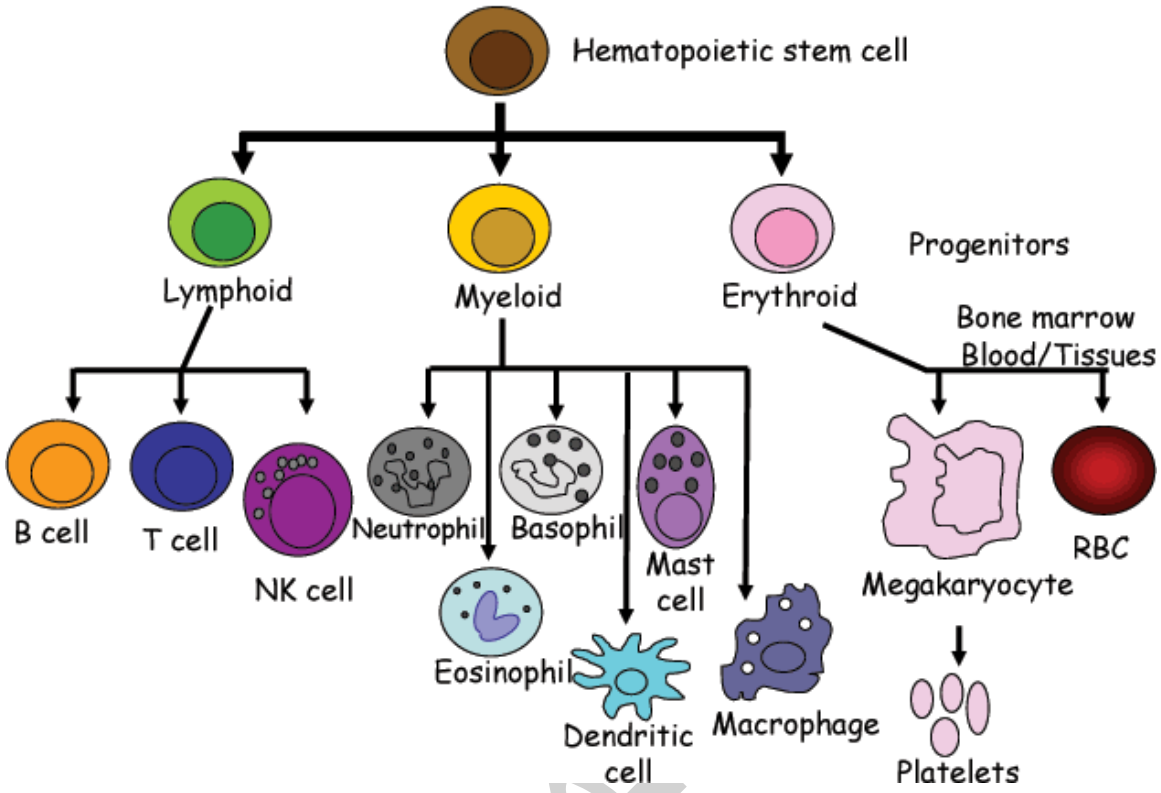
This gives rise to the three types of granulocyte as well as monocytes and macrophages. These cells all have important phagocytic roles. The myeloid stem cell line also produces megakaryocytes from which platelets are derived.

2- The lymphoid line

From this stem cell line the lymphocytes are produce. **B cells mature** in the marrow before being distributed to the lymphoid tissues of the body, i.e. the lymph nodes, spleen, thymus and Peyer's patches in the intestinal submucosa. **T lymphocyte** where they mature fully before being redistributed to other lymphoid sites. Lymphocytes can replicate and develop further within the lymphoid tissues of the body and there is a continuous recirculation of lymphocytes from blood to lymph and back again.

Platelets

Platelets, also called thrombocytes, are membrane-bound cell fragments. Platelets have no nucleus,they are between one to two micrometers in diameter, and are about 1/10th to 1/20th as abundant as white blood cells. Less than 1% of whole blood consists of platelets. They result from fragmentation of large cells called Megakaryocytes - which are cells derived from stem cells in the bone marrow. Platelets are produced at a rate of 200 billion per day. Their production is regulated by the hormone called Thrombopoietin. The circulating life of a platelet is 8‑10 days. The sticky surface of the platelets allow them to accumulate at the site of broken blood vessels to form a clot. This aids in the process of hemostasis ("blood stopping"). Platelets secrete factors that increase local platelet aggregation (e.g., Thromboxane A), enhance vasoconstriction (e.g., Serotonin), and promote blood coagulation (e.g., Thromboplastin).



Hemostasis (Coagulation or Clotting)

when blood vessels are cut or damaged, the loss of blood from the system must be stopped before shock and possible death occur, a process called coagulation or clotting.

• **Prothrombin**: When blood vessels are damaged, vessels and nearby platelets are stimulated to release a substance called prothrombin activator, which in turn activates the conversion of prothrombin, a plasma protein, into an enzyme called thrombin. This reaction requires calcium ions.

• **Thrombin**: Thrombin facilitates the conversion of a soluble plasma protein called fibrinogen into long insoluble fibers or threads of the protein fibrin.

• **Fibrin**: Fibrin threads wind around the platelet plug at the damaged area of the blood vessel, forming an interlocking network of fibers and a framework for the clot. This net of fibers traps and helps hold platelets, blood cells and

other molecules tight to the site of injury, functioning as the initial clot. This temporary fibrin clot can form in less than a minute, and usually does a good job of reducing the blood flow. Next, platelets in the clot begin to shrink, tightening the clot and drawing together the vessel walls. Usually, this whole process of clot formation and tightening takes less than a half hour.

Table for some clotting factors

Factor	name
I	Fibrinogen
II	Prothrombin
III	Thromboplastin or tissue factor
IV	Calcium
VII	Proconvertin (Stable factor)
VIII	Antihaemophilic factor A
IX	Antihaemophilic factor B (Christmas factor)
XII	Hageman factor

ABO Group System

The ABO blood group is represented by substances on the surface of red blood cells (RBCs). These substances are important because they contain specific sequences of amino acid and carbohydrates which are antigenic. As well as being on the surface of RBCs, some of these antigens are also present on the cells of other tissues. A complete blood type describes the set of 29 substances on the surface of RBCs, and an individual's blood type is one of the many possible combinations of blood group antigens. Usually only the ABO blood group system and the presence or absence of the Rhesus

D antigen (also known as the Rhesus factor or RH factor) are determined and used to describe the blood type.

Blood Group AB individuals have both A and B antigens on the surface of their RBCs, and their blood serum does not contain any antibodies against either A or B antigen. Therefore, a individual with type AB blood can receive blood from any group (with AB being preferable), but can only donate blood to another group AB individual. AB blood is also known as "Universal receiver."

Blood Group A individuals have the A antigen on the surface of their RBCs, and blood serum containing IgM antibodies against the B antigen. Therefore, a group A individual can only receive blood from individuals of groups A or O (with A being preferable), and can donate blood to individuals of groups A or AB.

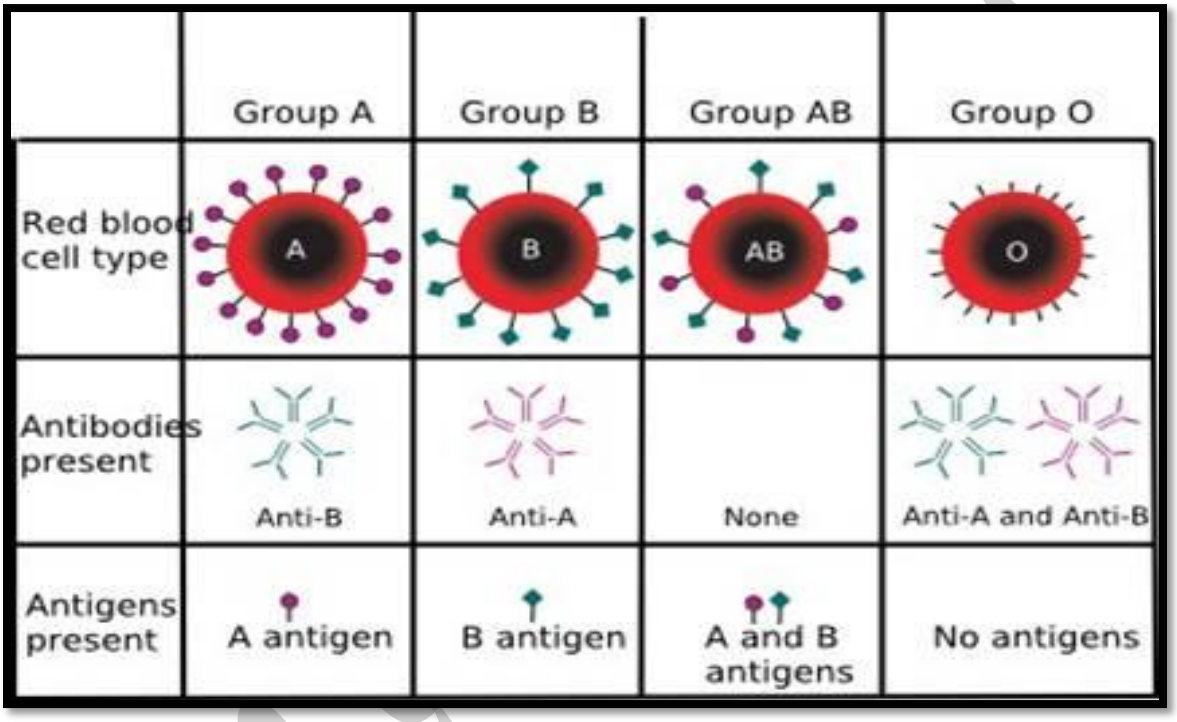
Blood Group B individuals have the B antigen on their surface of their RBCs, and blood serum containing IgM antibodies against the A antigen. Therefore, a group B individual can only receive blood from individuals of groups B or O (with B being preferabe), and can donate blood to individuals of groups B or AB.

Blood group O individuals do not have either A or B antigens on the surface of their RBCs, but their blood serum contains IgM antibodies against both A and B antigens. Therefore, a group O individual can only receive blood from a group O individual, but they can donate blood to individuals of any ABO blood group (ie A, B, O or AB). O blood is also know as "Universal donor."

Rh Factor

Blood is either Rh positive or Rh negative depending on whether red cells carry one of the Rh antigens or not.

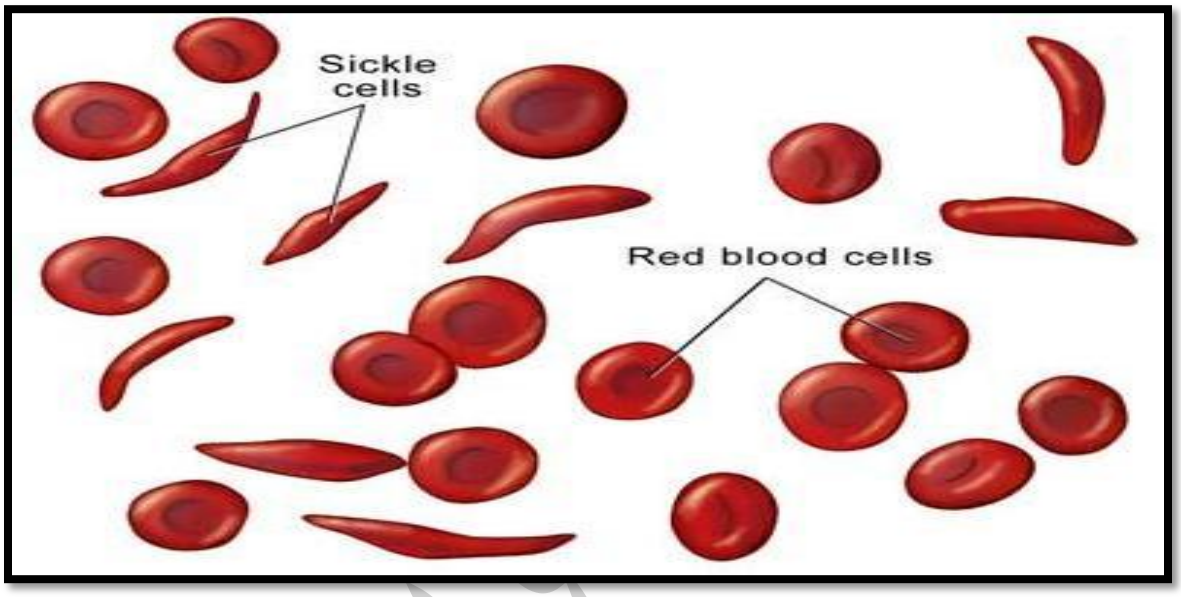
Many people have the Rh Factor on the red blood cell. Rh carriers do not have the antibodies for the Rh Factor, but can make them if exposed to Rh. Most commonly Rh is seen when anti-Rh antibodies cross from the mothers placenta into the child before birth. The Rh Factor enters the child destroying the child's red blood cells. This is called Hemolytic Disease.



Sickle cell

Sickle-cell disease is a general term for a group of genetic disorders caused by sickle hemoglobin (Hgb S or Hb S). In many forms of the disease, the red blood cells change shape upon deoxygenation because of polymerization of the abnormal sickle hemoglobin. This process damages the red blood cell membrane, and can cause the cells to become stuck in blood vessels. This deprives the downstream tissues of oxygen and causes ischemia and infarction. The disease is chronic and lifelong. Individuals are

most often well, but their lives are punctuated by periodic painful attacks. In addition to periodic pain, there may be damage of internal organs, and/or stroke. Lifespan is often shortened with sufferers living to an average of 40 years. It is common in people from parts of the world where malaria is or was common, especially in sub-Saharan Africa or in descendants of those peoples.



Polycythemia

Polycythemia is a condition in which there is a net increase in the total circulating erythrocyte (red blood cell) mass of the body. There are several types of polycythemia.

Primary Polycythemia

In primary polycythemia, there may be 8 to 9 million and occasionally 11 million erythrocytes per cubic millimeter of blood (a normal range for adults is 4-5 million), and the hematocrit may be as high as 70 to 80%. In addition, the total blood volume can increase to as much as twice as normal. The entire vascular system can become markedly engorged with blood, and circulation times for blood throughout the body can increase up to twice the normal value. The increased numbers of erythrocytes can increase of the

viscosity of the blood to as much as five times normal. Capillaries can become plugged by the very viscous blood, and the flow of blood through the vessels tends to be extremely sluggish.

As a consequence of the above, people with untreated Polycythemia are at a risk of various thrombotic events (deep venous thrombosis, pulmonary embolism), heart attack and stroke, and have a substantial risk of Budd-Chiari syndrome (hepatic vein thrombosis). The condition is considered chronic; no cure exists. Symptomatic treatment (see below) can normalize the blood count and most patients can live a normal life for years.

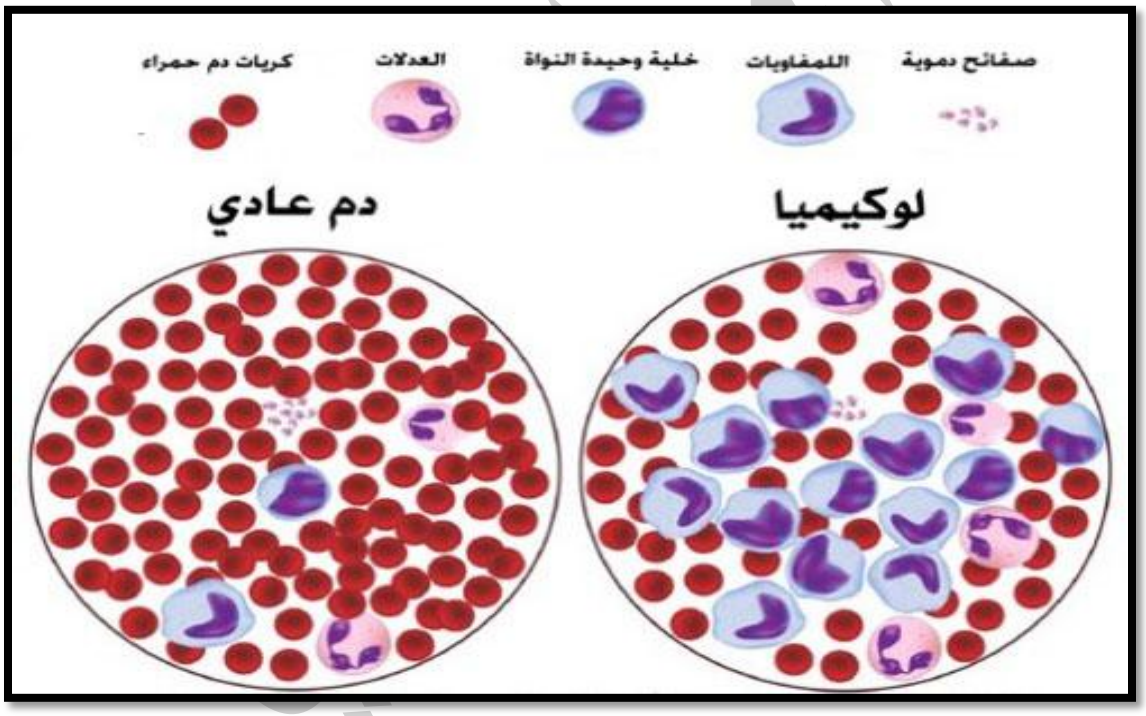
Secondary polycythemia

Secondary polycythemia is caused by either appropriate or inappropriate increases in the production of erythropoietin that result in an increased production of erythrocytes. In secondary polycythemia, there may be 6 to 8 million and occasionally 9 million erythrocytes per cubic millimeter of blood. A type of secondary polycythemia in which the production of erythropoietin increases appropriately is called physiologic polycythemia. Physiologic polycythemia occurs in individuals living at high altitudes (4275 to 5200 meters), where oxygen availability is less than at sea level. Many athletes train at higher altitudes to take advantage of this effect — a legal form of blood doping. Actual polychthemia sufferers have been known to use their condition as an athletic advantage for greater stamina.

Other causes of secondary polycythemia include smoking, renal or liver tumors, or heart or lung diseases that result in hypoxia. Endocrine abnormalities, prominently including pheochromocytoma and adrenal adenoma with Cushing's Syndrome, are also secondary causes. Athletes and bodybuilders who abuse anabolic steroids or erythropoietin may develop secondary polycythemia.

Leukemia

Leukemia is a cancer of the blood or bone marrow characterized by an abnormal proliferation of blood cells, usually white blood cells (leukocytes). It is part of the broad group of diseases called hematological neoplasms. Damage to the bone marrow, by way of displacing the normal marrow cells with increasing numbers of malignant cells, results in a lack of blood platelets, Large numbers of these cells in the blood and bone marrow does not give area for the mature cells of normal white blood cells, red blood cells and platelets which are important in the blood clotting process. This means people with leukemia may become bruised, , or develop.



Hemophilia

Hemophilia is a disease where there is low or no blood protein, causing an inability to produce blood clots. There are two types of Hemophilia: Type A, which is a deficiency in factor VIII and Type B, (Christmas disease) a deficiency on factor IX. Because people with hemophilia do not have the ability to make blood clots, even a little cut may

kill them, or the smallest bump or jar to the body could cause severe bruising that doesn't get better for months.

Hemophilia is passed down from mothers to their sons. Hemophilia is sometimes known as the "Royal Disease". This is because Queen Victoria, Queen of England (1837-1901), was a carrier of hemophilia.