Hematology

Assist proff.Dina Saadoon

Body fluids

Body fluids, Body fluids, are liquids within the human body. In lean healthy adult men, the total body water is about (60–67%) of the total body weight; it is usually slightly lower in women (52-55%).
The total body of water is divided into fluid compartments, between the intracellular fluid (ICF) compartment (also called space, or volume) and the extracellular fluid (ECF) compartment (space, volume) in a two-to-one ratio: (28–32) liters are inside cells and (14–15) liters are outside cells.

A- The **Extra cellular fluids (ECF) compartment** is divided into the interstitial fluid volume – the fluid outside both the cells and the blood vessels – and the intravascular volume (also called the vascular volume and blood plasma volume) – the fluid inside the blood vessels – in a three-to-one ratio: the interstitial fluid volume is about 12 liters, the vascular volume is about 4 liters.

1-The interstitial fluid compartment is divided into the lymphatic fluid compartment – about 2/3's, or (6–10) liters; the transcellular fluid compartment is the remaining 1/3, or about 4 liters.

2-The vascular volume is divided into the venous volume and the arterial volume; and the arterial volume has a conceptually useful but un measurable sub compartment called the effective arterial blood volume Intracellular compartment

Interstitial compartment

The interstitial compartment (also called "tissue space") surrounds tissue cells. It is filled with interstitial fluid, including lymph. Interstitial fluid provides the immediate microenvironment that allows for movement of ions, proteins and nutrients across the cell barrier. This fluid is not static, but is continually being refreshed by the blood capillaries and recollected by lymphatic capillaries.

3-Trans cellular compartment

The third extracellular compartment, the trans cellular, consists of those spaces in the body where fluid does not normally collect in larger amounts, or where any significant fluid collection is physiologically non functional. Examples of transcellular spaces include the eye, the central nervous system, the peritoneal and pleural cavities, and the joint capsules. A small amount of fluid, called transcellular fluid, does exist normally in such spaces. For example, the aqueous humor, the vitreous humor, the cerebrospinal fluid, the serous fluid produced by the serous membranes, and the synovial fluid produced by the synovial membranes are all transcellular fluids. They are all very important. For example, there is only about 150 milliliters of cerebrospinal fluid in the entire central nervous system at any moment. All of the above mentioned fluids are produced by active cellular processes working with blood plasma as the raw material, and they are all more or less similar to blood plasma except for certain modifications tailored to their function. For example, the **cerebrospinal fluid** is made by various cells of the CNS, mostly the ependymal cells, from blood plasma.

Extracellular compartment

The interstitial, intravascular and transcellular compartments comprise the extracellular compartment. Its extracellular fluid (ECF) contains about one-third of total body water.

Intravascular compartment

The main intravascular fluid in mammals is blood, a complex mixture with elements of a suspension (blood cells), colloid (globulins), and solutes (glucose and ions). The blood represents both the intracellular compartment (the fluid inside the blood cells) and the extracellular compartment (the blood plasma). The average volume of plasma in the average (70-kilogram or 150-pound) male is approximately 3.5 liters . The volume of the intravascular compartment is regulated in part by hydrostatic pressure gradients, and by reabsorption by the kidneys.

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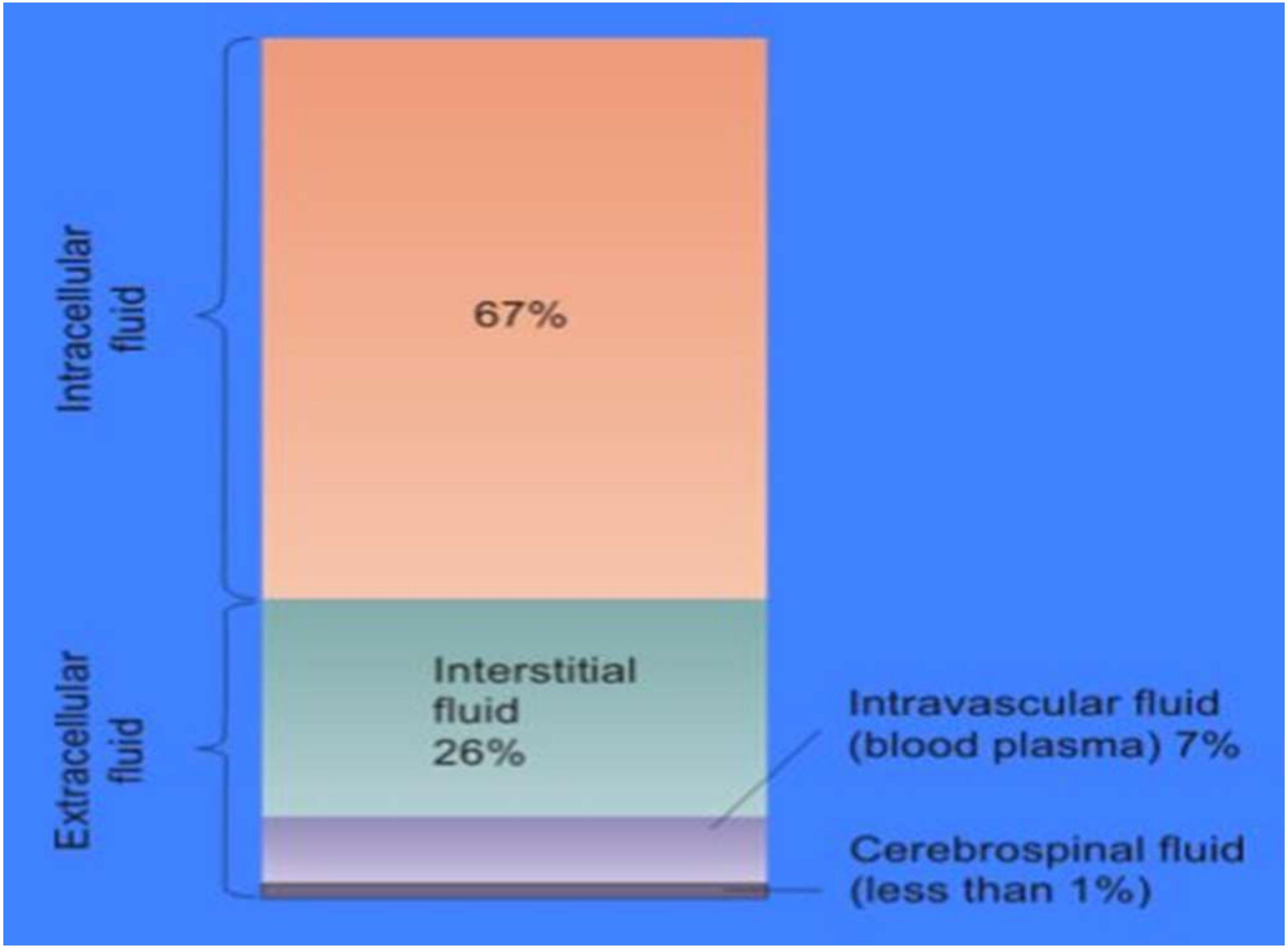
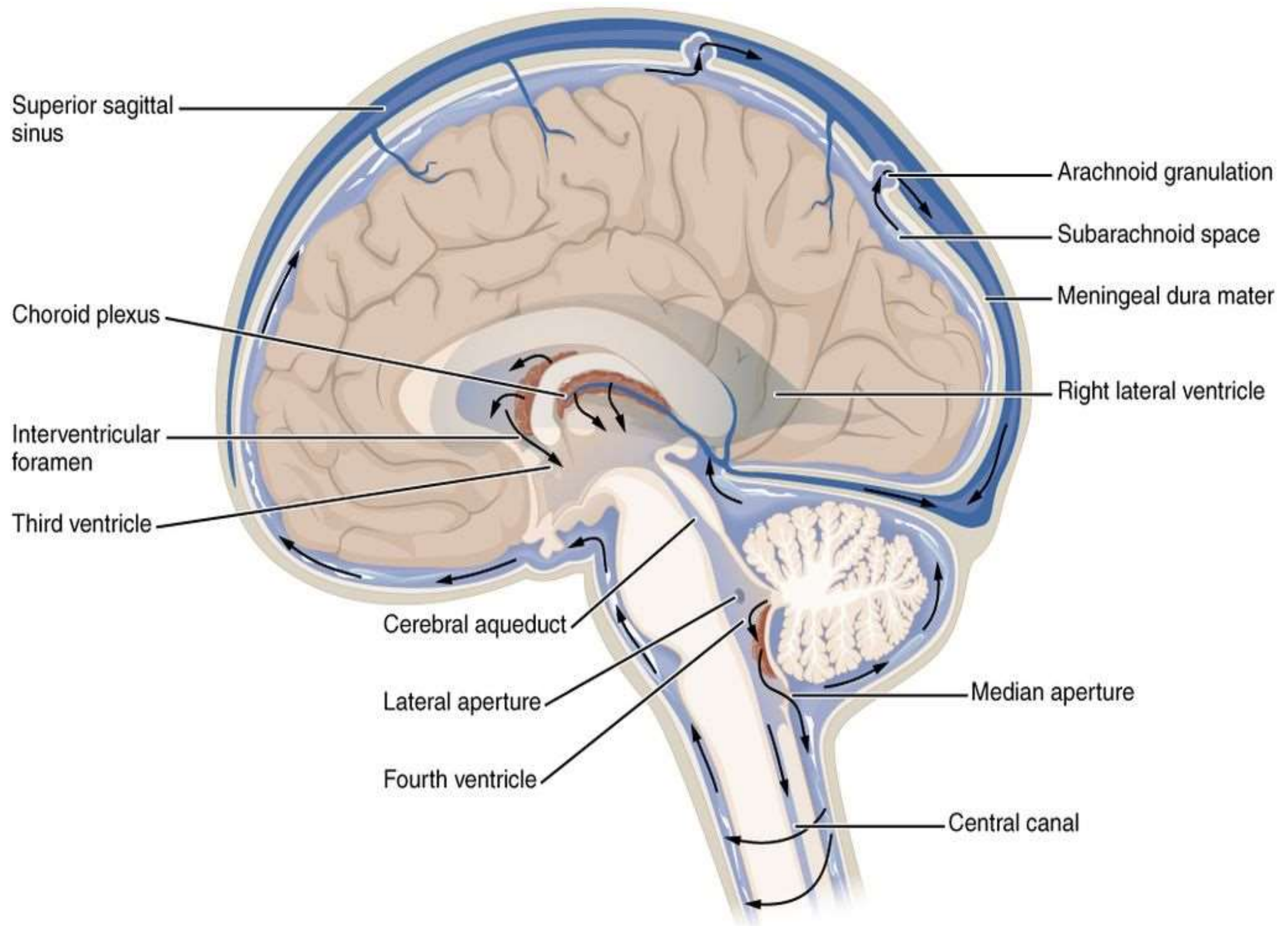

Intracellular fluid
67%
Extracellular fluid
Interstitial fluid 26%
Intravascular fluid (blood plasma) 7%
Cerebrospinal fluid (less than 1%)

B-The intracellular fluid (ICF) is all fluids contained inside the cells, which consists of cytosol and fluid in the cell nucleus. The cytosol is the matrix in which cellular organelles are suspended. The cytosol and organelles together compose the cytoplasm. The cell membranes are the outer barrier. In humans, the intracellular compartment contains on average about 28 liters of fluid, and under ordinary circumstances remains in osmotic equilibrium. It contains moderate quantities of magnesium and sulfate ions.

In the cell nucleus the fluid component of the nucleoplasm is called the nucleosol

CEREBROSPINAL FLUID FORMATION & ABSORPTION

CSF fills the ventricles and subarachnoid space. In humans, the volume of CSF is about 150 mL and the rate of CSF production is about 550 mL/d. Thus the CSF turns over about 3.7 times a day. In experiments on animals, it has been estimated that 50– 70% of the CSF is formed in the choroid plexuses and the remainder is formed around blood vessels and along ventricular walls. Presumably, the situation in humans is similar. The CSF in the ventricles flows through the foramens of Magendie and Luschka to the subarachnoid space and is absorbed through the arachnoid villi into veins, primarily the cerebral venous sinuses. The villi consist of projections of the fused arachnoid membrane and endothelium of the sinuses into the venous sinuses. Similar, smaller villi project into veins around spinal nerve routes.



Superior sagittal sinus
Arachnoid granulation
Subarachnoid space
Meningeal dura mater
Choroid plexus
Right lateral ventricle
Interventricular foramen
Third ventricle
Cerebral aqueduct
Lateral aperture
Median aperture
Fourth ventricle
Central canal

At least in animals, a more important route for CSF reabsorption into the bloodstream in health is via the cribriform plate above the nose and thence into the cervical lymphatics. The composition of CSF is essentially the same as that of brain extracellular fluid (ECF), which in living humans makes up 15% of the brain volume. In adults, free communication appears to take place between the brain interstitial fluid and CSF, although the diffusion distances from some parts of the brain to the CSF are appreciable. Lumbar CSF pressure is normally 70 to 180 mm H2O. Up to pressures well above this range, the rate of CSF formation is independent of intraventricular pressure. However, absorption is proportional to the pressure . At a pressure of 112 mm H2O, which is the average normal CSF pressure, **filtration and absorption** are equal. Below a pressure of approximately 68 mm H2O, absorption stops

BLOOD AS A CIRCULATORY FLUID

Blood consists of a protein-rich fluid known **as plasma**, in which are suspended cellular elements: **white blood cells, red blood cells, and platelets**. The normal total circulating blood volume is about 8% of the body weight (5600 mL in a 70-kg man). About 55% of this volume is plasma.

BONE MARROW In the adult, red blood cells, many white blood cells, and platelets are formed in the bone marrow. In the fetus, blood cells are also formed in the liver and spleen, and in adults such extramedullary hematopoiesis may occur in diseases in which the bone marrow becomes destroyed or fibrosed. In children, blood cells are actively produced in the marrow cavities of all the bones. By age 20, the marrow in the cavities of the long bones, except for the upper humerus and femur, has become inactive .Active cellular marrow is called red marrow; inactive marrow that is infiltrated with fat is called yellow marrow. The bone marrow is actually one of the largest organs in the body, approaching the size and weight of the liver. It is also one of the most active. Normally, 75% of the cells in the marrow belong to the white blood cell-producing myeloid series and only 25% are maturing red cells

Blood is consist from :

1-cellular parts

A-WBCs(granulocyte and agranulocyte)

B-RBCs

C-thrombocyte

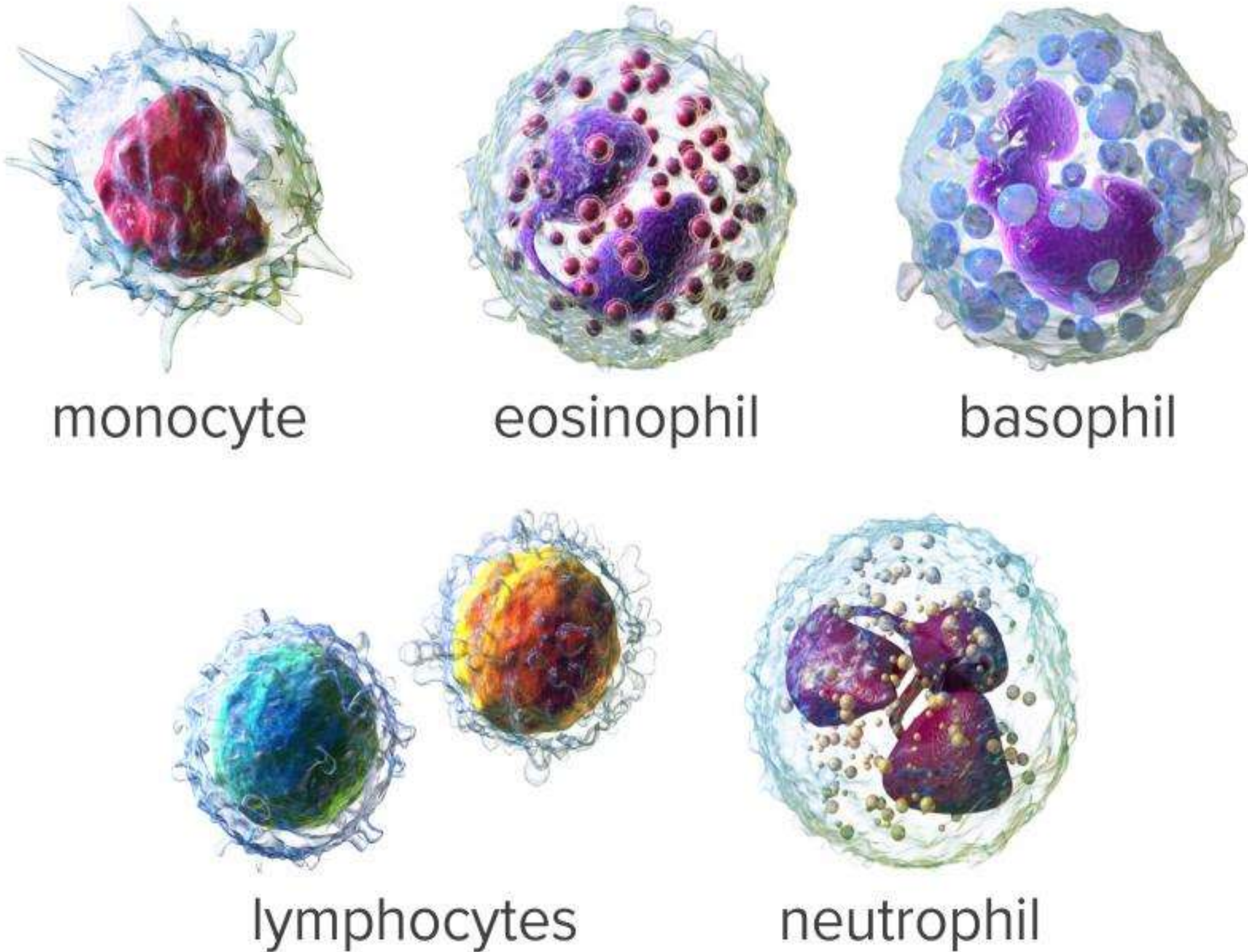
2-fluid parts

A-plasma

B-serum

WHITE BLOOD CELLS Normally, human blood contains 4000 to 11,000 white blood cells per microliter .Of these, the granulocytes (polymorph nuclear leukocytes, PMNs) are the most numerous. Young granulocytes have horseshoe-shaped nuclei. that become multilobed as the cells grow older Most of them contain neutrophil granules (neutrophils), but a few contain granules that stain with acidic dyes (eosinophil), and some have basophilic granules (basophils). The other two cell types found normally in peripheral blood are lymphocytes, which have large round nuclei and scanty cytoplasm, and monocytes, which have abundant granular cytoplasm and kidney-shaped nuclei. Acting together, these cells provide the body with powerful defenses against tumors and viral, bacterial, and parasitic infections.

White Blood Cells



Types of WBCs

1-Graulocyte consist from :

Neutrophils

Are the most abundant white blood cell, constituting 60-70% of the circulating leukocytes. They defend against bacterial or fungal infection. They are usually first responders to microbial infection; their activity and death in large numbers form pus. They are commonly referred to as poly morph nuclear (PMN) leukocytes, although, in the technical sense, PMN refers to all granulocytes. They have a multi-lobed nucleus, which consists of three to five lobes connected by slender strands. This gives the neutrophils the appearance of having multiple nuclei, hence the name polymorph nuclear leukocyte.

The cytoplasm may look transparent because of fine granules that are pale lilac when stained. Neutrophils are active in phagocytosing bacteria and are present in large amount in the pus of wounds. These cells are not able to renew their lysosomes (used in digesting microbes) and die after having phagocytized a few pathogens. Neutrophils are the most common cell type seen in the early stages of acute inflammation. The average lifespan of inactivated human neutrophils in the circulation has been reported by different approaches to be between 5 and 135 hours

Eosinophils compose about 2-4% of white blood cells in circulating blood. This count fluctuates throughout the day, seasonally, and during menstruation. It rises in response to allergies, parasitic infections, collagen diseases, and disease of the spleen and central nervous system. They are rare in the blood, but numerous in the mucous membranes of the respiratory, digestive, and lower urinary tracts.

They primarily deal with parasitic infections. Eosinophils are also the predominant inflammatory cells in allergic reactions. The most important causes of eosinophilia include allergies such as asthma, hay fever, and hives; and parasitic infections. They secrete chemicals that destroy large parasites, such as hookworms and tapeworms, that are too big for any one white blood cell to phagocytize. In general, their nuclei are bi-lobed. The lobes are connected by a thin strand. The cytoplasm is full of granules that assume a characteristic pink-orange color with eosin staining.

Basophils are chiefly responsible for allergic and antigen response by releasing the chemical histamine causing the dilation of blood vessels. Because they are the rarest of the white blood cells (less than 0.5% of the total count) and share physicochemical properties with other blood cells, they are difficult to study. They can be recognized by several coarse, dark violet granules, giving them a blue hue. The nucleus is bi- or tri-lobed, but it is hard to see because of the number of coarse granules that hide it.

They excrete two chemicals that aid in the body's defenses: histamine and heparin. Histamine is responsible for widening blood vessels and increasing the flow of blood to injured tissue. It also makes blood vessels more permeable so neutrophils and clotting proteins can get into connective tissue more easily. Heparin is an anticoagulant that inhibits blood clotting and promotes the movement of white blood cells into an area. Basophils can also release chemical signals that attract eosinophils and neutrophils to an infection site.

2-Agranulocyte consist from:

Lymphocytes are much more common in the lymphatic system than in blood. Lymphocytes are distinguished by having a deeply staining nucleus that may be eccentric in location, and a relatively small amount of cytoplasm. Lymphocytes include:

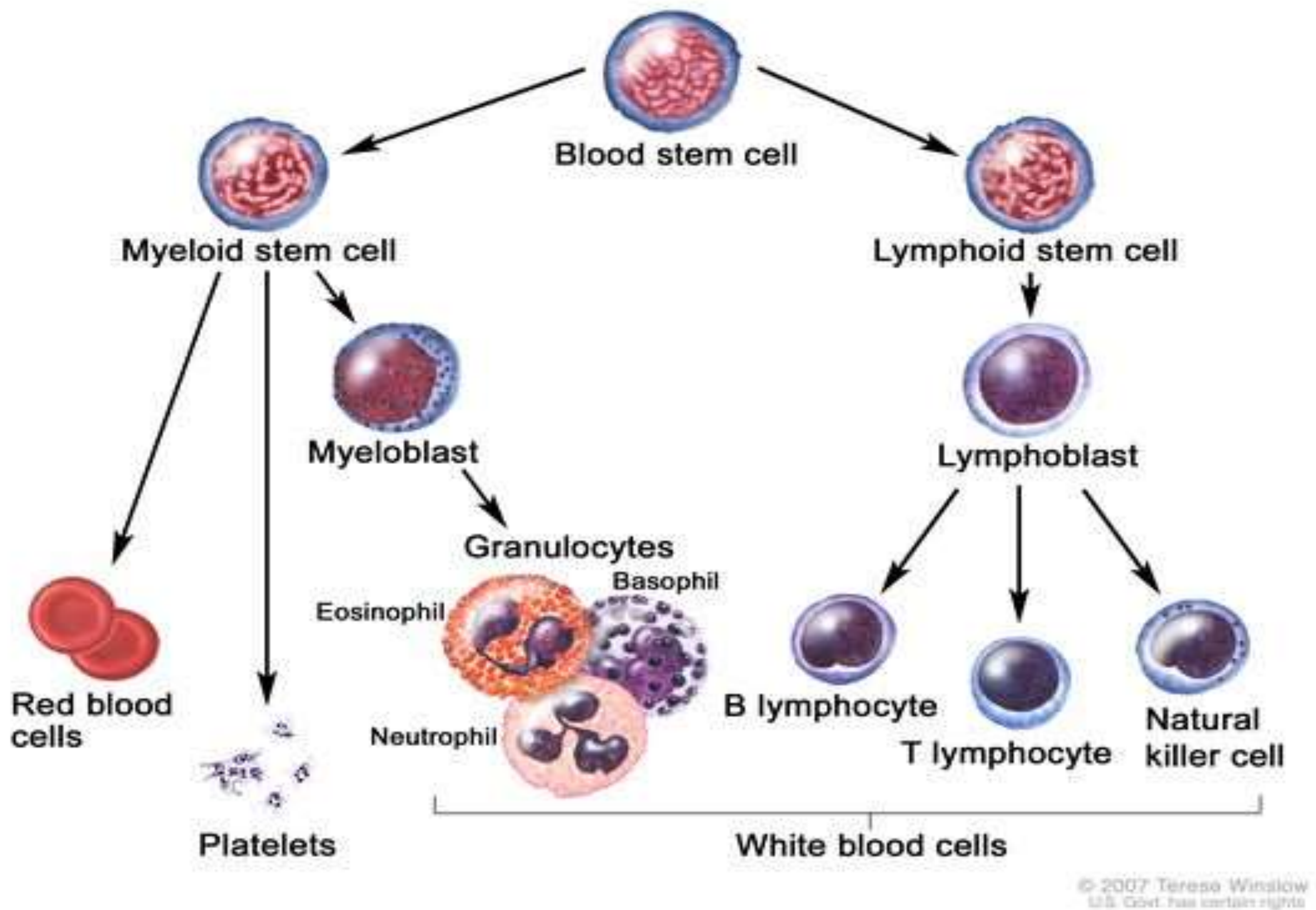
B cells make antibodies that can bind to pathogens, block pathogen invasion, activate the complement system, and enhance pathogen destruction.

T cells

CD4+ helper T cells: T cells displaying co-receptor CD4 are known as CD4+ T cells. These cells have T-cell receptors and CD4 molecules that, in combination, bind antigenic peptides presented on major histocompatibility complex (MHC) class II molecules on antigen-presenting cells. Helper T cells make cytokines and perform other functions that help coordinate the immune response. In HIV infection, these T cells are the main index to identify the individual's immune system integrity.

CD8+ cytotoxic T cells: T cells displaying co-receptor CD8 are known as CD8+ T cells. These cells bind antigens presented on MHC I complex of virus-infected or tumor cells and kill them.

Monocytes, the largest type of white blood cell, share the "vacuum cleaner" (phagocytosis) function of neutrophils, but are much longer lived as they have an extra role: they present pieces of pathogens to T cells so that the pathogens may be recognized again and killed. This causes an antibody response to be mounted. Monocytes eventually leave the bloodstream and become tissue macrophages, which remove dead cell debris as well as attack microorganisms. Neither dead cell debris nor attacking microorganisms can be dealt with effectively by the neutrophils. They have the kidney-shaped nucleus and are typically not granulated.



Blood stem cell
Myeloid stem cell
Lymphoid stem cell
Myeloblast
Lymphoblast
Granulocytes
Basophil
Eosinophil
Neutrophil
Red blood cells
Platelets
B lymphocyte
T lymphocyte
Natural killer cell
White blood cells
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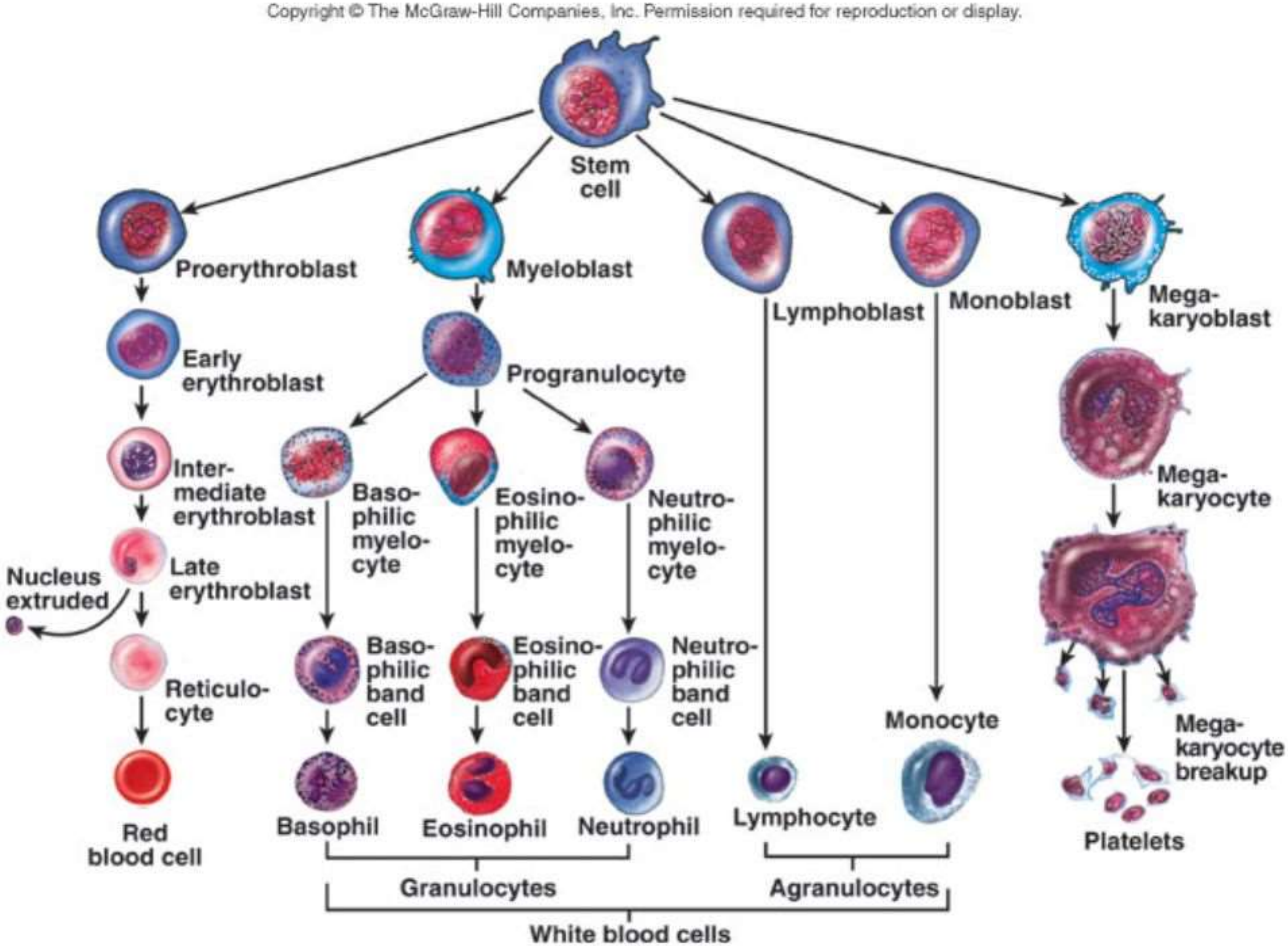
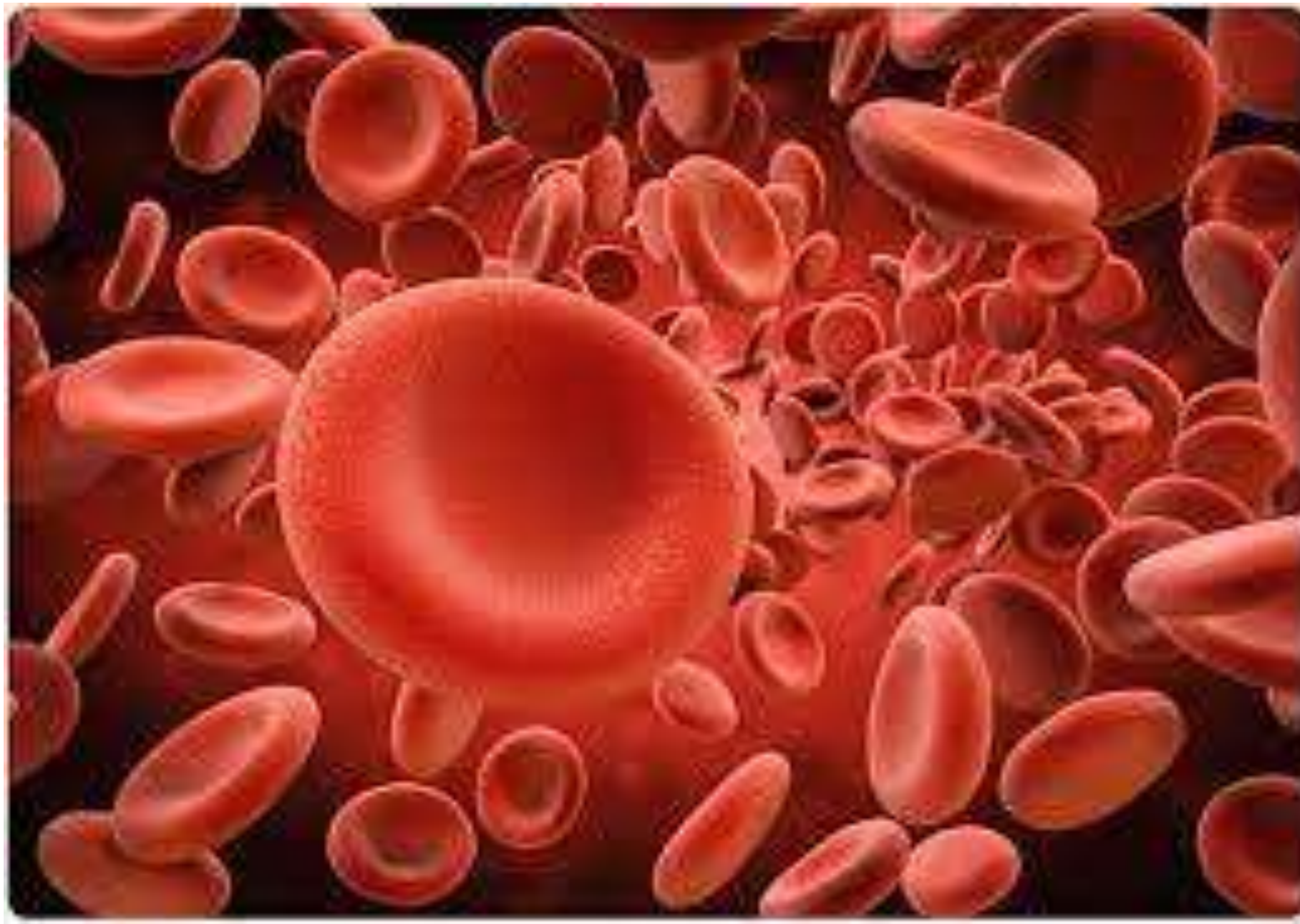


Hematopoiesis مهم

RED BLOOD CELLS

The red blood cells (erythrocytes) carry hemoglobin in the circulation. They are biconcave disks .that are manufactured in the bone marrow. In mammals, they lose their nuclei before entering the circulation. In humans, they survive in the circulation for an average of 120 day. The average normal red blood cell count is 5.4 million/μL in men and 4.8 million/μL in women. Each human red blood cell is about 7.5 μm in diameter and 2 μm thick, and each contains approximately 29 pg of hemoglobin .There are thus about 3 × 1013 red blood cells and about 900 g of hemoglobin in the circulating blood of an adult man.



The red cell develops in bone marrow in several stages: from a hemocytoblast, a multipotential cell in the mesenchyme, it becomes an erythroblast (normoblast); during two to five days of development, the erythroblast gradually fills with hemoglobin, and its nucleus and mitochondria (particles in the cytoplasm that provide energy for the cell) disappear. In a late stage the cell is called a reticulocyte, which ultimately becomes a fully mature red cell. The average red cell in humans lives 100–120 days; there are some 5.2 million red cells per cubic millimetre of blood in the adult human. Some diseases also display red cells of abnormal shape—e.g., oval in pernicious anemia, crescent-shaped in sickle cell anemia, and with projections giving a thorny appearance in the hereditary disorder acanthocytosis. The number of red cells and the amount of hemoglobin vary among different individuals and under different conditions; the number is higher, for example, in persons who live at high altitudes and in the disease polycythemia. At birth the red cell count is high; it falls shortly after birth and gradually rises to the adult level at puberty.

Normal human red blood cells have an average life span of about 120 days in the circulation after which they are engulfed by macrophages. This is an extremely efficient process as macrophages phagocytose about 5 million erythrocytes every second without any significant release of hemoglobin in the circulation.
Old or damaged RBCs are removed from the circulation by macrophages in the spleen and liver, and the hemoglobin they contain is broken down into heme and globin. The globin protein may be recycled, or broken down further to its constituent amino acids, which may be recycled or metabolized.

Bilirubin (bil-ih-ROO-bin) is a yellowish pigment that is made during the normal breakdown of red blood cells. Bilirubin passes through the liver and is eventually excreted out of the body.

Production of red blood cells (erythropoiesis)

Red cells are produced continuously in the marrow of certain bones. As stated above, in adults the principal sites of red cell production, called erythropoiesis, are the marrow spaces of the vertebrae, ribs, breastbone, and pelvis. Within the bone marrow the red cell is derived from a primitive precursor, or erythroblast, a nucleated cell in which there is no hemoglobin. Proliferation occurs as a result of several successive cell divisions. During maturation, hemoglobin appears in the cell, and the nucleus becomes progressively smaller. After a few days the cell loses its nucleus and is then introduced into the bloodstream in the vascular channels of the marrow. Almost 1 percent of the red cells are generated each day, and the balance between red cell production and the removal of aging red cells from the circulation is precisely maintained. When blood is lost from the circulation, the erythropoietic activity of marrow increases until the normal number of circulating cells has been restored. Erythropoietin (EPO) acts as the primary stimulus for erythropoiesis, being mostly produced by the kidneys in response to decreased tissue oxygenation

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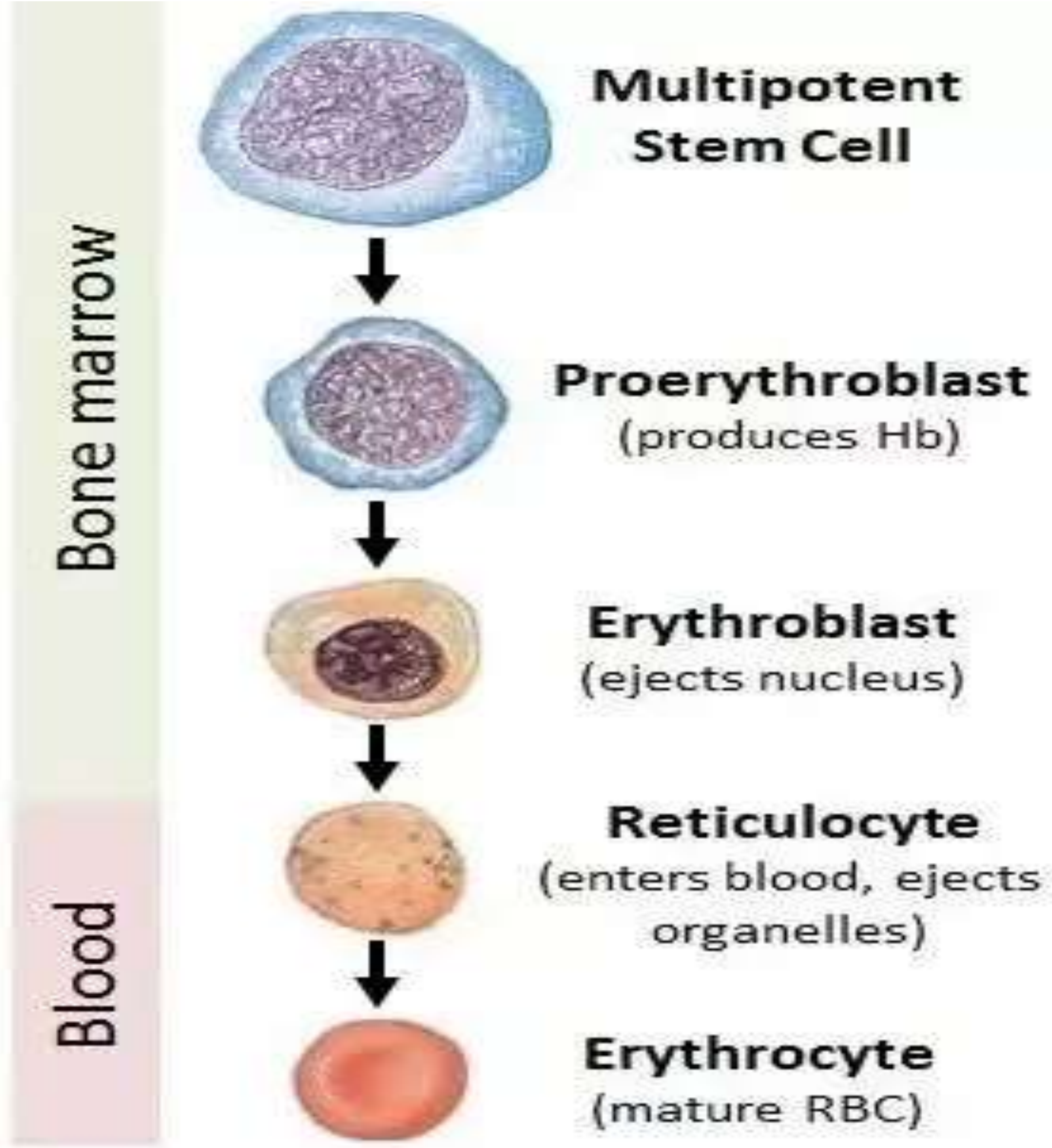
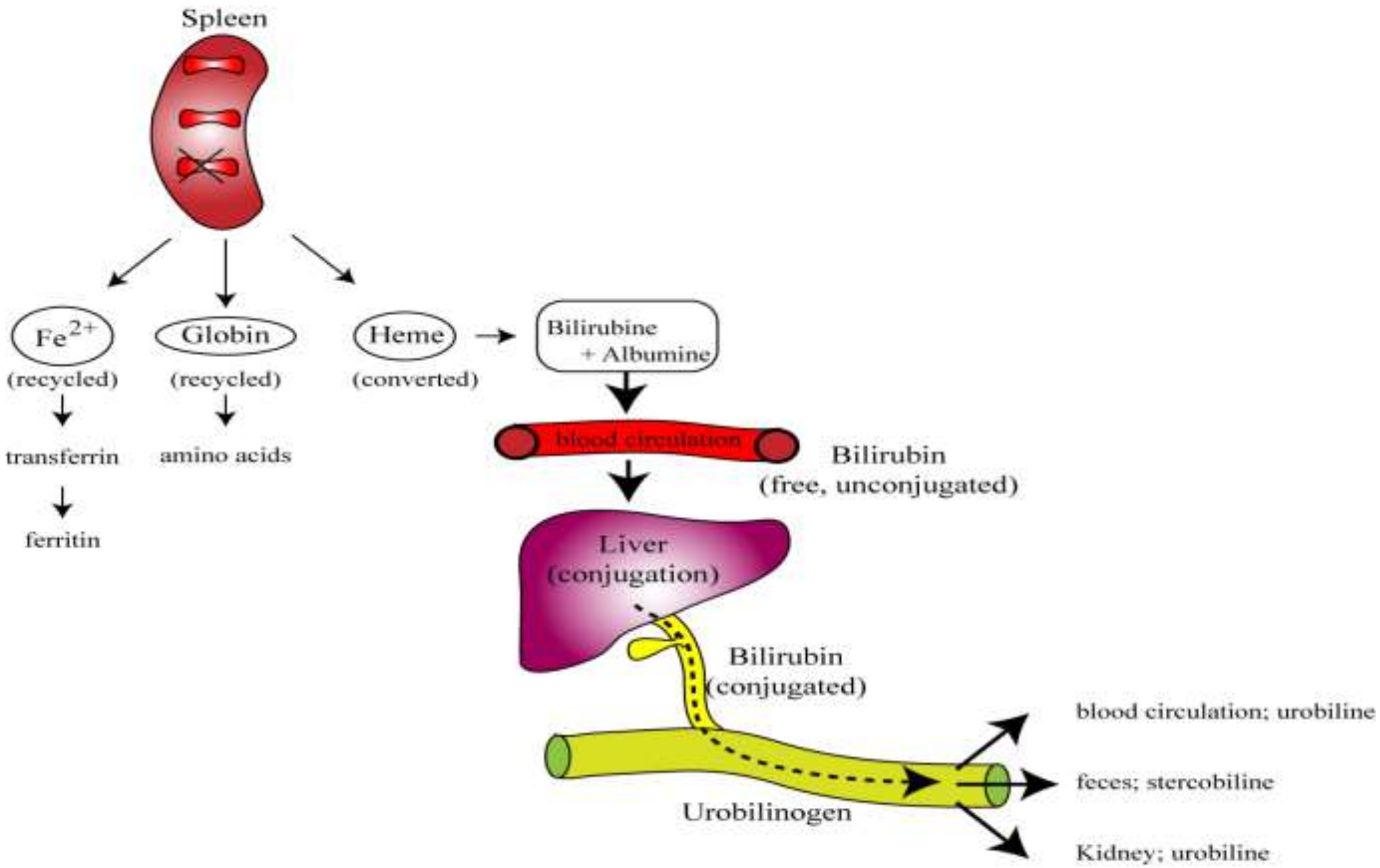

Bone marrow
Blood
Multipotent Stem Cell
Proerythroblast
(produces Hb)
Erythroblast
(ejects nucleus)
Reticulocyte
(enters blood, ejects organelles)
Erythrocyte
(mature RBC)

Destruction of RBCs

In a normal adult the red cells of about half a litre (almost one pint) of blood are produced by the bone marrow every week. A number of nutrient substances are required for this process. Some nutrients are the building blocks of which the red cells are composed For example, amino acids are needed in abundance for the construction of the proteins of the red cell, in particular of hemoglobin. Iron also is a necessary component of hemoglobin. Important among these are several vitamins such as riboflavin, vitamin B12, and folic acid, necessary for the maturation of the developing red cell; and vitamin B6 (pyridoxine), required for the synthesis of hemoglobin. The male sex hormone, testosterone, stimulates red cell production; for this reason, red cell counts of men are higher than those of women. Red cells have an average life span of 120 days. Because red cells cannot synthesize protein, reparative processes are not possible. As red cells age, wear and tear leads to loss of some of their protein, and the activity of some of their essential enzymes decreases. Phagocytic cells form a part of the lining of blood vessels, particularly in the spleen, liver, and bone marrow.

These cells, called macrophages, are constituents of the reticuloendothelial system and are found in the lymph nodes, in the intestinal tract, and as free-wandering and fixed cells. Protein, including that of the hemoglobin, is broken down, and the component amino acids are transported through the plasma to be used in the synthesis of new proteins. The iron removed from hemoglobin passes back into the plasma and is transported to the bone marrow, where it may be used in the synthesis of hemoglobin in newly forming red cells. Iron not necessary for this purpose is stored within the reticuloendothelial cells but is available for release and reuse whenever iIn contrast, the porphyrin ring structure of hemoglobin, to which iron was attached, undergoes a chemical change that enables its excretion from the body. This reaction converts porphyrin, a red pigment, into bilirubin, a yellow pigment. Bilirubin released from reticuloendothelial cells after the destruction of erythrocytes is conveyed through the plasma to the liver, where it undergoes further changes that prepare it for secretion into the bile. The amount of bilirubin produced and secreted into the bile is determined by the amount of hemoglobin destroyed.



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Destruction of RBCs diagram

jaundice

excess accumulation of bile pigments in the bloodstream and bodily tissues that causes a yellow to orange and sometimes even greenish discoloration of the skin, the whites of the eyes, and the mucous membranes. Jaundice is best seen in natural daylight and may not be apparent under artificial lighting. The degree of coloration depends on the concentration of bile pigment (bilirubin) in the blood, its rate of tissue diffusion, and the absorption and binding of bilirubin by the tissue. Bilirubin enters the tissue fluids and is absorbed more readily at sites of inflammation and edema (abnormal accumulation of fluids in the tissues).

The most common mechanisms causing jaundice are an overproduction of bile by the liver, so that more is produced than can be readily excreted; congenital defects, which may impair the removal of bile pigments or cause overproduction; inability of liver cells to remove bile pigments from the blood because of liver disease; leakage of bilirubin removed by the liver back into the bloodstream (regurgitation); or obstruction of the bile ducts. A healthy newborn may develop jaundice because the liver has not fully matured.

Platelets, also called thrombocytes are a component of blood whose function (along with the coagulation factors) is to react to bleeding from blood vessel injury by clumping, thereby initiating a blood clot.Platelets have no cell nucleus; they are fragments of cytoplasm that are derived from the megakaryocytes of the bone marrow or lung,which then enter the circulation. Platelets are found only in mammals, whereas in other vertebrates (e.g. birds, amphibians), thrombocytes circulate as intact mononuclear cells. ShapeCirculating inactivated platelets are biconvex discoid (lens-shaped) structures 2–3 µm in greatest diameter.Activated platelets have cell membrane projections covering their surface.normal value 15,000-400,000 cell/mm3.

Low platelet concentration is called thrombocytopenia, and is due to either decreased production or increased destruction. Elevated platelet concentration is called thrombocytosis, and is either congenital, reactive (to cytokines), or due to unregulated production: one of the myeloproliferative neoplasms or certain other myeloid neoplasms. A disorder of platelet function is called a thrombocytopathy or a platelet function disorder.

Normal platelets can respond to an abnormality on the vessel wall rather than to hemorrhage, resulting in inappropriate platelet adhesion/activation and thrombosis: the formation of a clot within an intact vessel. This type of thrombosis arises by mechanisms different from those of a normal clot: namely, extending the fibrin of venous thrombosis; extending an unstable or ruptured arterial plaque, causing arterial thrombosis; and microcirculatory thrombosis. An arterial thrombus may partially obstruct blood flow, causing downstream ischemia, or may completely obstruct it, causing downstream tissue death.