Name of Unit	Body Fluids and Blood, Lymphatic System
Course/Subject Name:	Human Anatomy and Physiology-I
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Learning Outcome of Module 03

LO	Learning Outcome (LO)	Course Outcome Code
LO1	Explore composition and function of blood	BP101.4
LO2	To understand hemopoiesis process.	BP101.4
LO3	To understand formation of hemoglobin, mechanism of coagulation.	BP101.4
LO4	To understand blood grouping, Rh factors, transfusion and its significance.	BP101.4
LO5	To understand lymphatic System and its parts	BP101.4
LO6	To understand lymph circulation and function of lymphatic system	BP101.4

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Body Fluids And Blood • Body Fluids • Composition and Function of Blood • Hemopoiesis and Formation of Hemoglobin • Mechanisms of Coagulations, Blood Grouping and Rh factor • Transfusion and its significance • Anemia & disorder of blood. • Reticuloendothelial system
Lymphatic System • Lymphatic organs and tissue • Lymphatic vessels • Lymph Circulation and Function of Lymphatic System

BODY FLUIDS AND BLOOD

Most cells of a multicellular organism cannot move around to obtain oxygen and nutrients or eliminate carbon dioxide and other wastes. Instead, these needs are met by two fluids: blood and interstitial fluid.

Blood is a connective tissue composed of a liquid extracellular matrix called blood plasma that dissolves and suspends various cells and cell fragments.

Interstitial fluid is the fluid that bathes body cells and is constantly renewed by the blood.

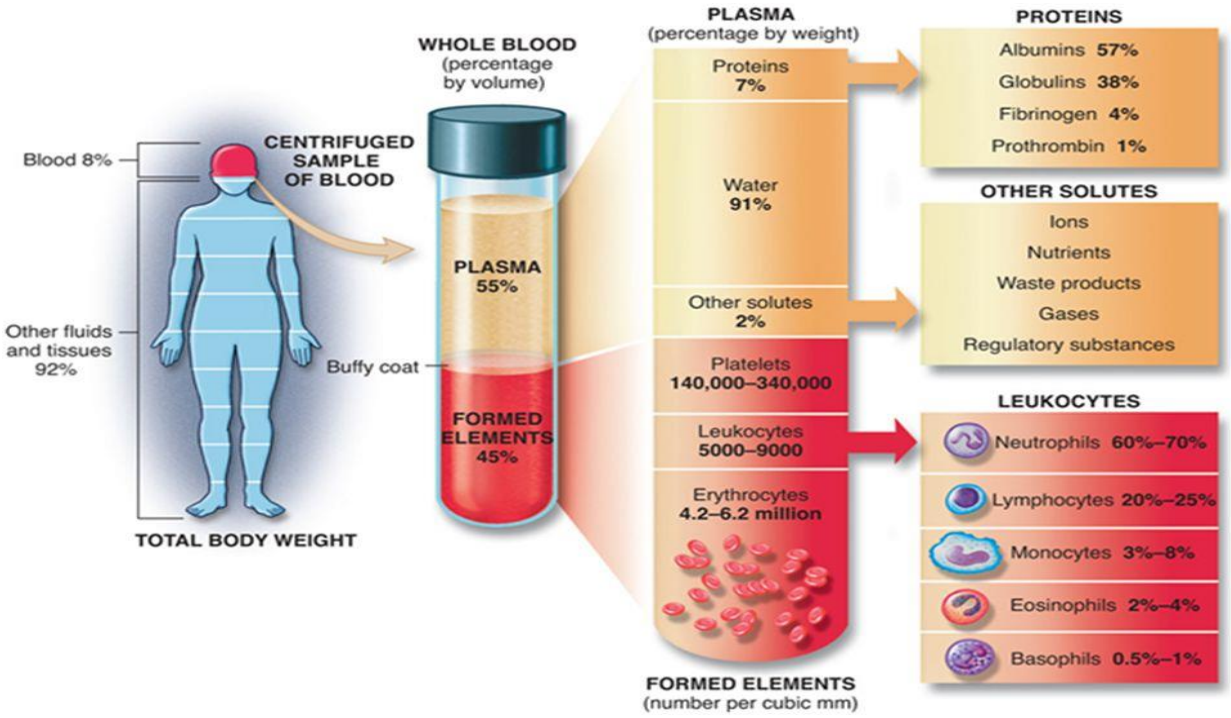
The branch of science concerned with the study of blood, blood-forming tissues, and the disorders associated with them is **haematology.**

COMPONENTS OF BLOOD:

Blood has two components:

1. Blood plasma: A watery liquid extracellular matrix that contains dissolved substances.

2. Formed elements: cells and cell fragments.



Blood is about 45% formed elements and 55% blood plasma. Normally, more than 99% of the formed elements are cells named for their red colour—red blood cells (RBCs). Pale, colourless white blood cells (WBCs) and platelets occupy less than 1% of the formed elements.

1. Blood Plasma:

When the formed elements are removed from blood, a straw-coloured liquid called **blood plasma** (or simply **plasma**) is left. Blood plasma is about 91.5% water and 8.5% solutes, most of which (7% by weight) are proteins (**called as Plasma proteins**).

Chemical composition of blood plasma:

CONSTITUENT	FUNCTIONS
Water (91.5%)	Liquid portion of blood. Acts as solvent and suspending medium for components of blood; absorbs, transports, and releases heat.
Plasma Proteins (7.0%): Albumins Globulins Fibrinogen	Exert colloid osmotic pressure, which helps maintain water balance between blood and tissues and regulates blood volume. Function as transport proteins for several steroid hormones and for fatty acids. Antibodies (immunoglobulins) help attack viruses and bacteria. Alpha and beta globulins transport iron, lipids, and fat-soluble vitamins. Plays essential role in blood clotting.
Other Solutes (1.5%): Electrolytes Nutrients	Help maintain osmotic pressure and play essential roles in the function of cells. Include amino acids (from proteins), glucose (from carbohydrates), fatty acids and glycerol (from triglycerides), vitamins, and minerals.

2. Formed Elements:

The **formed elements** of the blood include three principal components:

I. Red blood cells or Erythrocytes

II. White blood cells or Leucocytes

A. Granular leukocytes (contain conspicuous granules that are visible under a light microscope after staining)

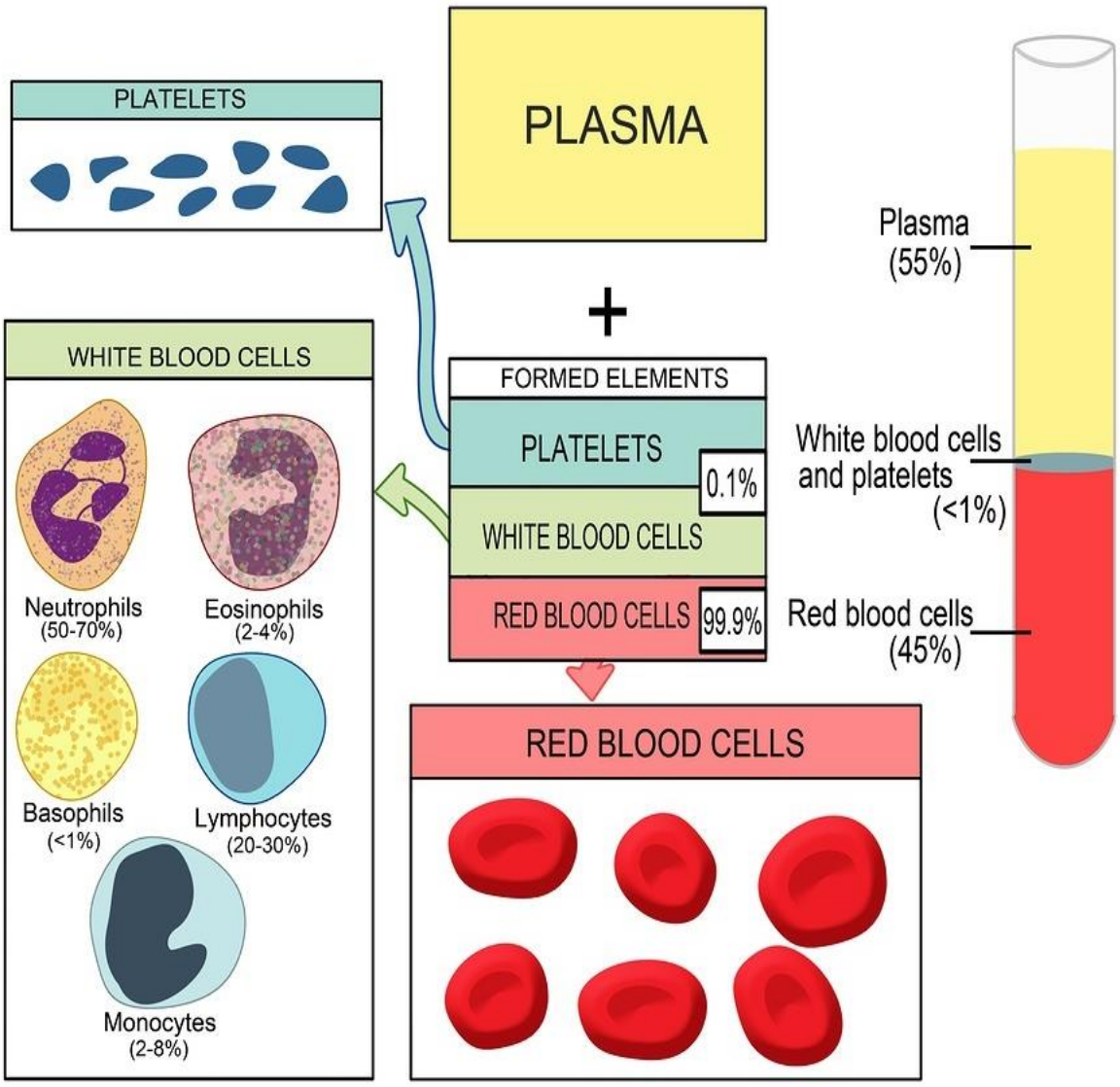
- Neutrophils
- Eosinophils
- Basophils

B. Agranular leukocytes (no granules are visible under a light microscope after staining)

- T and B lymphocytes and natural killer (NK) cells
- Monocytes

III. Platelets

RBCs and WBCs are whole cells; platelets are cell fragments.



Elements of the blood

I.RED BLOOD CELLS (RBC's) or ERYTHROCYTES:

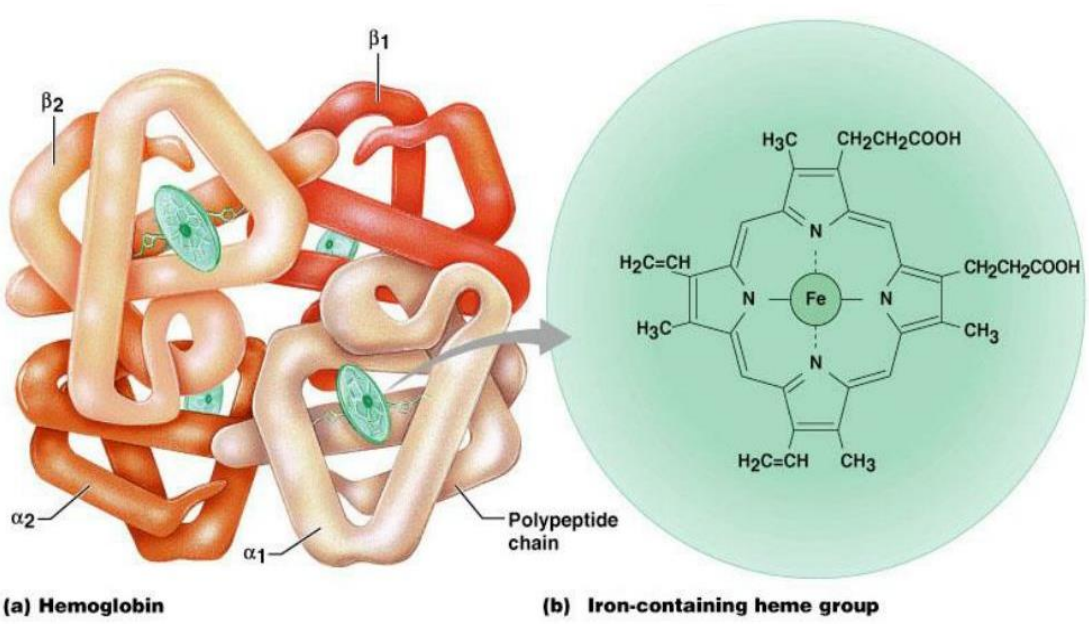
- Red blood cells (RBCs) or erythrocytes contain the oxygen-carrying protein haemoglobin, which is a pigment that gives whole blood its red colour.
- Life span: 120 Days
- Normal range:
  - Adult Male: 5.4 million per microliter (μL) of blood
  - Adult female: 4.8 million per microliter (μL) of blood

RBC Anatomy:

RBCs are biconcave discs with a diameter of 7–8 μm. Mature red blood cells have a simple structure. Their plasma membrane is both strong and flexible, which allows them to deform without rupturing as they squeeze through narrow capillaries.

RBC Functions:

RBCs lack a nucleus and other organelles and can neither reproduce nor carry on extensive metabolic activities. Red blood cells are highly specialized for their oxygen transport function. Because mature RBCs have no nucleus, all their internal space is available for oxygen transport. Even the shape of an RBC facilitates its function. A biconcave disc has a much greater surface area for the diffusion of gas molecules into and out of the RBC than would, say, a sphere or a cube.



(a) Hemoglobin (b) Iron-containing heme group

Structure of Hemoglobin

Each RBC contains about 280 million hemoglobin molecules. A hemoglobin molecule consists of a protein called globin, composed of four polypeptide chains (two alpha and two beta chains); a ring like non-protein pigment called a heme is bound to each of the four chains. At the center of each heme ring is an iron ion (Fe^{2+}) that can combine reversibly with one oxygen molecule, allowing each hemoglobin molecule to bind four oxygen molecules.

Characteristics of RBCs:

✓ Count: 5.4 millions RBCs per microliter (ul) of blood in male and 4.8 millions RBCs per ul of blood in female.

✓ Shape: Biconcave disc shaped.

✔ Size: Diameter 7-8 µm and thickness 2 µm.

✓ Contains: Haemoglobin.

Haemoglobin is the iron-containing oxygen transport metalloprotein in the red blood cells. Haemoglobin transports oxygen from the lungs to the body tissues. When the oxygen concentration is high in the alveoli, the haemoglobin combines with oxygen to form oxyhaemoglobin. When the blood reaches the tissue with a low concentration of oxygen, the haemoglobin dissociates with the oxygen releasing the oxygen into the body tissues. RBCs contain no nucleus, endoplasmic reticulum, ribosomes and mitochondria. RBCS contain larger surface area because of biconcavity for oxygen diffusion. They can easily squeeze through the capillaries. Their life span is about 120 days.

Erythropoiesis:

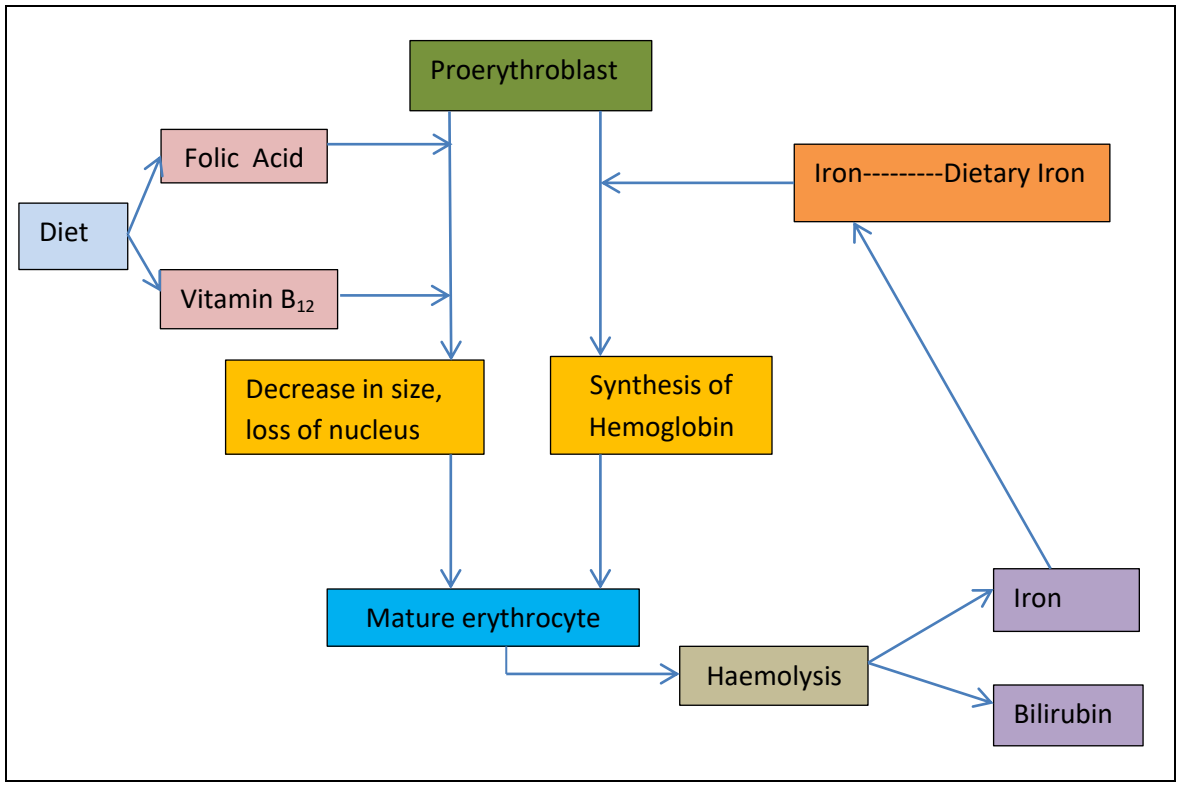
The process of development of red blood cells from pluripotent stem cells called as erythropoiesis. Erythrocytes are produced in red bone marrow present at the ends of long bones. The immature cells are released into blood stream as reticulocytes and then mature into erythrocytes in one or two days within circulation. During this time they lose their nucleus and therefore become incapable of division. The erythropoiesis is characterized by two main features:

✓Maturation of the cell

✓ Formation of hemoglobin inside the cell

Maturation of Cell:

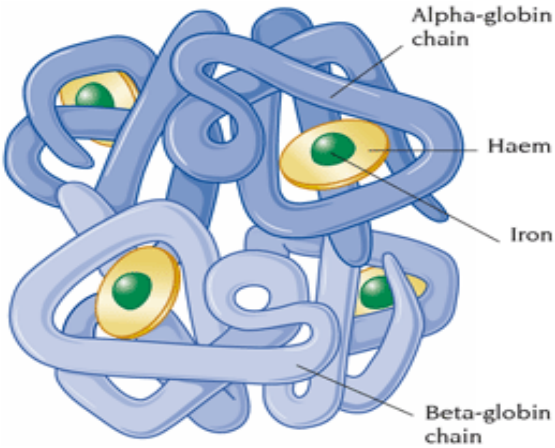
During this process the cell decreases in size and loses its nucleus. These changes depend on presence of vitamin B_{12} and folic acid. These are present in a normal diet containing dairy products, meat and green vegetables Absorption of vitamin B_{12} depends on a glycoprotein called as intrinsic factor secreted by parietal cells in the gastric glands. Together they form intrinsic factor-vitamin B_{12} complex (IF-B12). During its passage through intestine, the bound vitamin is protected from enzymatic digestion and is absorbed in the terminal ileum. Folic acid is absorbed in the duodenum and jejunum where it undergoes change before entering the blood. Deficiency of either vitamin B_{12} or folic acid leads to impaired red cell production.



Maturation of erythrocytes

FORMATION OF HAEMOGLOBIN

Haemoglobin is a complex protein, consisting of globin and an iron containing haem, and is synthesised inside developing erythrocytes in red bone marrow. Haemoglobin in mature erythrocytes combines with oxygen to form oxyhaemoglobin giving blood its characteristic red colour. Haemoglobin is also involved in the transport of carbon dioxide from the body cells to the lungs for excretion. Each haemoglobin molecule contains four atoms of iron. Each atom can carry one molecule of oxygen and therefore one haemoglobin molecule can carry up to four molecules of oxygen.



Haemoglobin

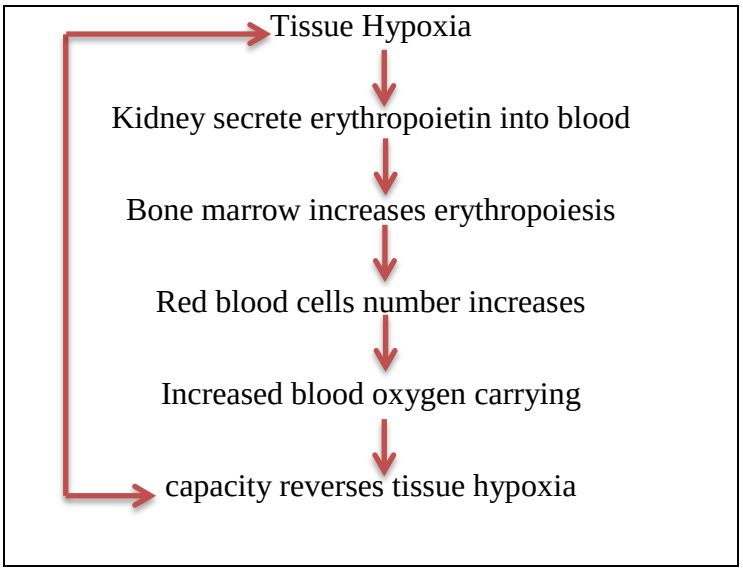
Control of Erythropoiesis:

The number of red cells remains fairly constant, which means that the bone marrow produces erythrocytes at the rate at which they are destroyed. This is due to a homeostatic negative feedback mechanism. The primary stimulus to increase erythropoiesis is hypoxia, i.e. deficient oxygen supply to body cells.

This occurs when:

✓ The oxygen carrying power of blood is reduced by haemorrhage or excessive erythrocyte breakdown (haemolysis) due to disease.

✓ The oxygen tension in the air is reduced.



Control of erythropoiesis

Hypoxia increases erythrocyte formation by stimulating the production of the erythropoietin hormone by the kidneys. Erythropoietin stimulates the production of proerythroblasts and the release of increased numbers of reticulocytes into the blood. These changes increase the oxygen carrying capacity of the blood and reverse tissue hypoxia. When the tissue hypoxia is overcome, erythropoietin production declines. When erythropoietin levels are low, red cell formation does not take place even in the presence of hypoxia, and anaemia develops

Destruction of Erythrocytes:

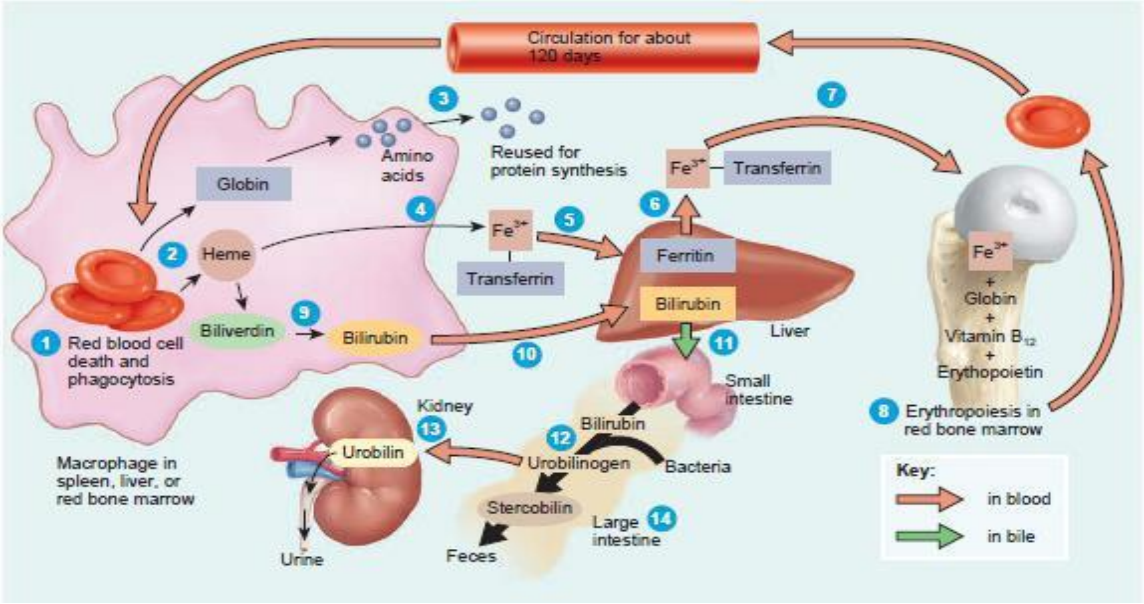
The life span of erythrocytes is about 120 days and haemolysis is carried out by phagocytic reticulo endothelial cells. The main sites of reticulo endothelial cells are the spleen, bone marrow

and liver. As erythrocytes undergo ageing, changes in cell membranes make them more susceptible to haemolysis. Iron released by haemolysis is retained in the body and reused in the bone marrow to form haemoglobin. Biliverdinis formed from the protein part of the erythrocytes. It is reduced to the yellow pigment bilirubin and transported to the liver. In the liver it is changed from a fat-soluble to a water-soluble form as a constituent of bile.

Ruptured red blood cells are removed from circulation and destroyed by fixed phagocytic macrophages in the spleen and liver, and the breakdown products are recycled, as follows;

1. Macrophages in the spleen, liver, or red bone marrow phagocytize ruptured and worn-out red blood cells.
2. The globin and heme portions of haemoglobin are split apart.
3. Globin is broken down into amino acids, which can be reused to synthesize other proteins.
4. Iron is removed from the heme portion in the form of Fe^{3+} which associates with the plasma protein transferrin.
5. In muscle fibres, liver cells, and macrophages of the spleen and liver, Fe^{3+} detaches from transferrin and attaches to an iron-storage protein called ferritin.
6. Upon release from a storage site or absorption from the gastrointestinal tract, reattaches to transferrin.
7. The Fe^{3+} transferrin complex is then carried to red bone marrow, where RBC precursor cells are used in haemoglobin synthesis. Iron is needed for the heme portion of the haemoglobin molecule, and amino acids are needed for the globin portion. Vitamin B12 is also needed for the synthesis of haemoglobin.
8. Erythropoiesis in red bone marrow results in the production of red blood cells, which enter the circulation.
9. When iron is removed from heme, the non-iron portion of heme is converted to biliverdin, a green pigment, and then into bilirubin, a yellow orange pigment.
10. Bilirubin enters the blood and is transported to the liver.
11. Within the liver, bilirubin is released by liver cells into bile, which passes into the small intestine and then into the large intestine.
12. In the large intestine, bacteria convert bilirubin into urobilinogen.
13. Some of the urobilinogen is absorbed back into the blood, converted to a yellow pigment called urobilin and excreted in urine.

14. Most urobilinogen is eliminated in faeces in the form of a brown pigment called stercobilin which gives faeces its characteristic colour.



Formation and destruction of red blood cells

II. WHITE BLOOD CELLS (WBC's) or LEUCOCYTES:

White blood cells or **leukocytes** have nuclei and do not contain hemoglobin. WBCs are classified as either granular or agranular, depending on whether they contain conspicuous chemical-filled cytoplasmic granules (vesicles) that are made visible by staining when viewed through a light microscope.

1. Granular leukocytes: Neutrophils, Eosinophils, and Basophils

2. Agranular leukocytes: Lymphocytes and Monocytes.

Life Span: Few hours to few days

Normal Count: 5000-10000 cells / micro litre

Granular leukocytes (polymorphonuclear leukocytes):

All granulocytes have multilobed nuclei in their cytoplasm. Their names represent the dyes they take up when stained in the laboratory.

A. Eosinophiles: Eosinophils take up the orange-red acid dye, eosin. They have large, uniform sized granules. The nucleus often has two lobes connected by a thick strand of chromatin.

Functions: Combat the effects of histamine in allergic reactions phagocytize antigen–antibody and destroy certain parasitic worms.

B. Basophiles: Basophils take up alkaline methylene blue. The granules commonly obscure the nucleus, which has two lobes.

Functions: Liberate heparin, histamine, and serotonin in allergic reactions that intensify the overall inflammatory response.

C. Neutrophiles: Neutrophils are puple because they take up both dyes. The nucleus has two to five lobes, connected by very thin strands of chromatin.

Functions: Phagocytosis. Destruction of bacteria with lysozyme, defensins, and strong oxidants, cytoplasm has very such as superoxide anion, hydrogen peroxide, fine, and hypochlorite anion.

AGRANULAR LEUKOCYTES:

Even though so-called agranular leukocytes possess cytoplasmic granules, the granules are not visible under a light microscope because of their small size and poor staining qualities.

Lymphocytes: The nucleus of a lymphocyte is round or slightly indented and stains darkly. The cytoplasm stains sky blue and forms a rim around the nucleus.

There are three types of lymphocytes: T lymphocytes (T cells), B lymphocytes (B cells), and natural killer (NK) cells.

T lymphocytes (T cells): T cells attack viruses, fungi, transplanted cells, cancer cells, some bacteria and are responsible for transfusion reactions, allergies and the rejection of transplanted organs.

B lymphocytes (B cells): B cells develop into plasma cells, which secrete antibodies. Immune responses carried out by both B cells and T cells help combat infection and provide protection against some diseases.

Natural killer (NK) cells: Natural killer cells attack a wide variety of infectious microbes and certain spontaneously arising tumour cells.

Functions: Mediate immune responses, including antigen–antibody reactions. B cells develop into plasma cells, which secrete antibodies; T cells attack invading viruses, cancer cells, Natural killer cells attack a wide variety of infectious microbes and certain spontaneously arising tumour cells.

Monocytes: The nucleus of a monocyte is usually kidney shaped or horseshoe shaped, and the cytoplasm is blue-gray and has a foamy appearance. The colour and appearance are due to very fine azurophilic granules which are lysosomes.

Functions: Phagocytosis (after transforming into fixed or wandering macrophages).

III. PLATELETS OR THROMBOCYTES:

These are very small discs, 2–4 μm in diameter, derived from the cytoplasm of megakaryocytes in red bone marrow. Although they have no nucleus, their cytoplasm is packed with granules containing a variety of substances that promote blood clotting, which causes haemostasis (cessation of bleeding).

The normal blood platelet count is between 1,50,000–4,00,000/ cubic mm. The mechanisms that regulate platelet numbers are not fully understood, but the hormone thrombopoietin from the liver stimulates platelet production. The life span of platelets is between 8 and 11 days and those not used in haemostasis are destroyed by macrophages mainly in the spleen.

PHYSICAL CHARACTERISTICS OF BLOOD:

- Blood is denser and more viscous (thicker) than water and feels slightly sticky.
- The temperature of blood is 38°C (100.4°F), about 1°C higher than oral or rectal body temperature, and it has blood varies with its oxygen content. When it has high oxygen content, it is bright red. When it has low oxygen content, it is dark red.
- Blood constitutes about 20% of extracellular fluid, amounting to 8% of the total body mass.
- The blood volume is 5 to 6 liters in an average-sized adult male and 4 to 5 liters in an average-sized adult female. The difference in volume is due to differences in body size.

FUNCTIONS OF BLOOD:

Blood, which is a liquid connective tissue, has three general functions:

1. Transportation:

- Blood transports oxygen from the lungs to the cells of the body and carbon dioxide from the body cells to the lungs for exhalation.
- It carries nutrients from the gastrointestinal tract to body cells and hormones from endocrine glands to other body cells.

- Blood also transports heat and waste products to various organs for elimination from the body.

2. Regulation:

- Circulating blood helps maintain homeostasis of all body fluids.
- Blood helps regulate pH through the use of buffers.
- It also helps adjust body temperature through the heat absorbing and coolant properties of the water in blood plasma and its variable rate of flow through the skin, where excess heat can be lost from the blood to the environment.
- In addition, blood osmotic pressure influences the water content of cells, mainly through interactions of dissolved ions and proteins.

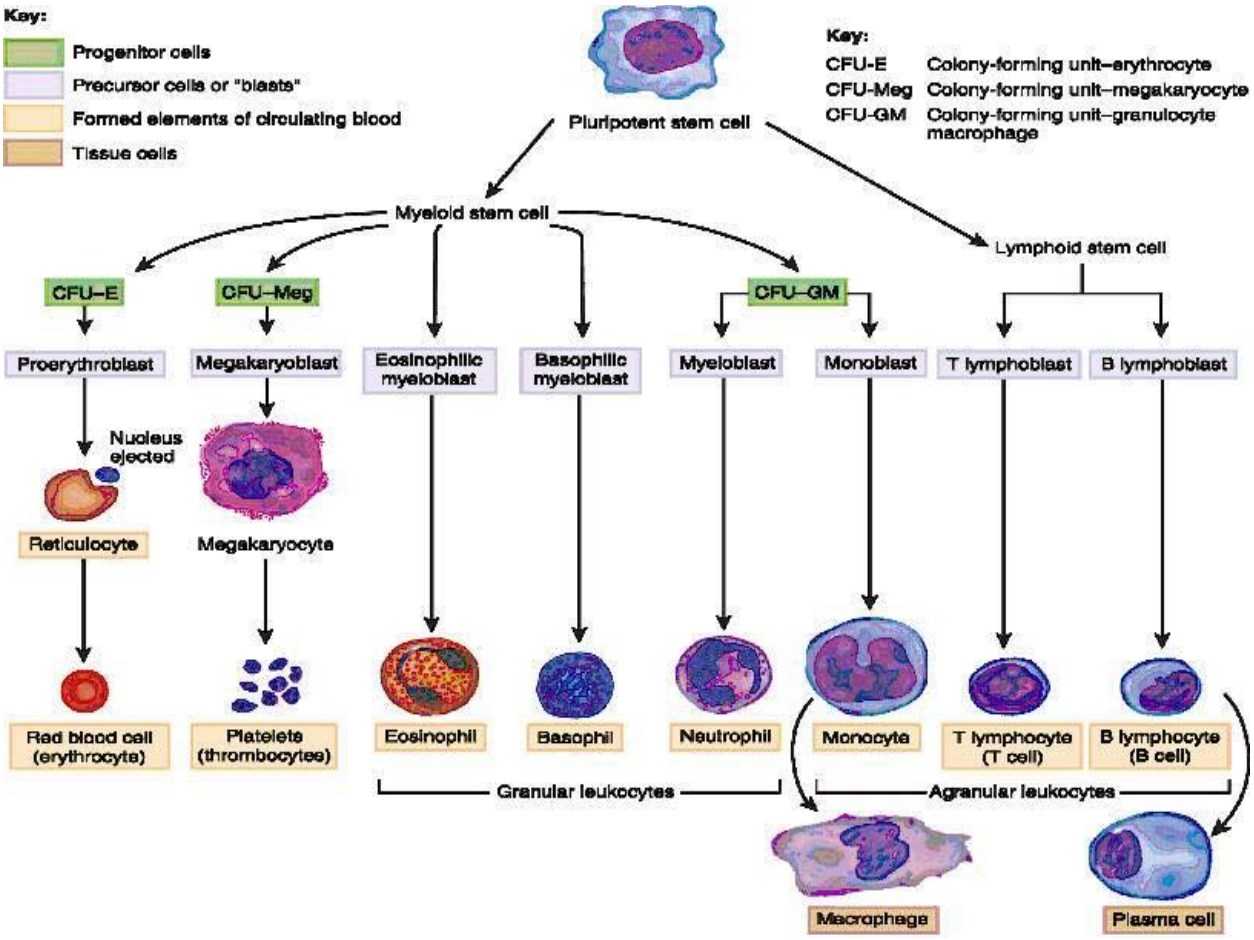
3. Protection:

- Blood can clot, which protects against its excessive loss from the cardiovascular system after an injury.
- White blood cells protect against disease by carrying on phagocytosis.
- Several types of blood proteins, including antibodies, interferons, and complement, help protect against disease in a variety of ways.

FORMATION OF BLOOD CELLS OR HAEMOPOESIS:

- The process by which the formed elements of blood develop is called hemopoiesis or haematopoiesis.
- Before birth, hemopoiesis first occurs in the yolk sac of an embryo and later in the liver, spleen, thymus, and lymph nodes of a foetus. Red bone marrow becomes the primary site of hemopoiesis in the last three months before birth, and continues as the source of blood cells after birth and throughout life.
- About 0.05–0.1% of red bone marrow cells are derived from mesenchyme and are called pluripotent stem cells or hemocytoblasts. These cells have the capacity to develop into many different types of cells.

- In order to form blood cells, pluripotent stem cells in red bone marrow produce two further types of stem cells, which have the capacity to develop into several types of cells. These stem cells are called myeloid stem cells and lymphoid stem cells.
- Myeloid stem cells begin their development in red bone marrow and give rise to red blood cells, platelets, monocytes, neutrophils, eosinophils, and basophils. Lymphoid stem cells begin their development in red bone marrow but complete it in lymphatic tissues; they give rise to lymphocytes.
- During hemopoiesis, some of the myeloid stem cells differentiate into progenitor cells. Other myeloid stem cells and the lymphoid stem cells develop directly into precursor cells. Progenitor cells are no longer capable of reproducing themselves and are committed to giving rise to more specific elements of blood. Some progenitor cells are known as colony-forming units (CFUs). CFU–E ultimately produces erythrocytes (red blood cells), CFU–Meg produces megakaryocytes, the source of platelets, and CFU–GM ultimately produces granulocytes (specifically, neutrophils) and monocytes.
- Progenitor cells, like stem cells, resemble lymphocytes and cannot be distinguished by their microscopic appearance alone. In the next generation, the cells are called precursor cells, also known as blasts.
- Over several cell divisions they develop into the actual formed elements of blood. For example, monoblasts develop into monocytes, eosinophilic myeloblasts develop into eosinophils, and so on. Precursor cells have recognizable microscopic appearances.
- Several hormones called hemopoietic growth factors regulate the differentiation and proliferation of particular progenitor cells.
- **Erythropoietin or EPO** increases the number of red blood cell precursors. **Thrombopoietin or TPO** is a hormone produced by the liver that stimulates the formation of platelets (thrombocytes) from megakaryocytes. Several different cytokines regulate development of different blood cell types. Two important families of cytokines that stimulate white blood cell formation are **colony-stimulating factors (CSFs)** and **interleukins.**



ERYTHROPOIESIS

DEFINITION: Erythropoiesis is the process of the origin, development and maturation of erythrocytes.

PROCESS OF ERYTHROPOIESIS:

Cells of CFU-E pass through different stages and finally become the matured RBCs. During these stages four important changes are noticed.

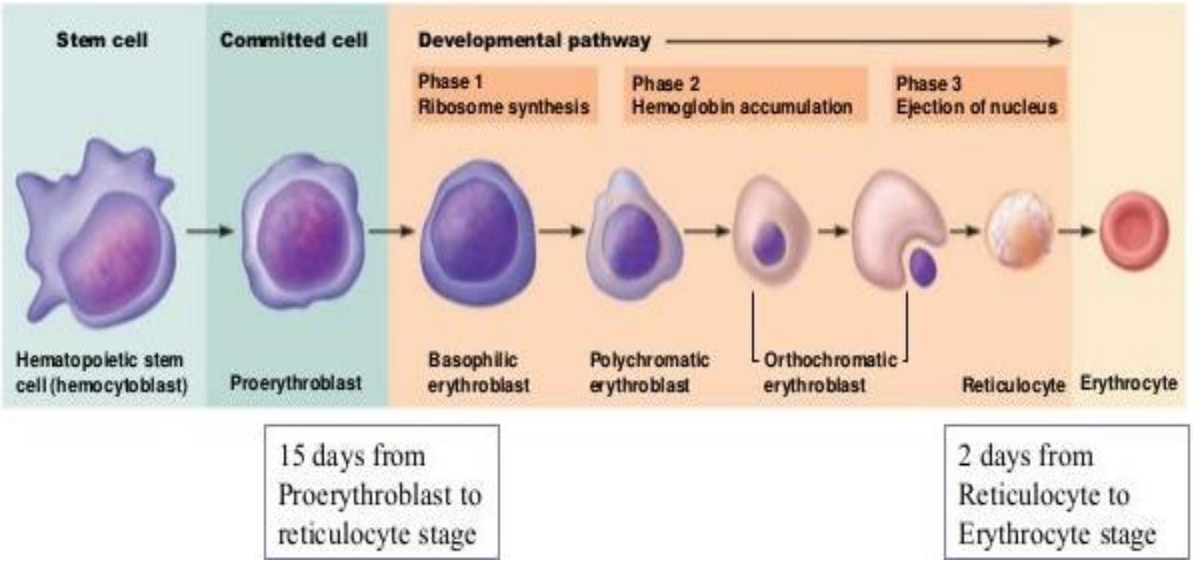
- Reduction in size of the cell (from the diameter of 25 to 7.2 μ)
- Disappearance of nucleoli and nucleus
- Appearance of haemoglobin
- Change in the staining properties of the cytoplasm.

STAGES OF ERYTHROPOIESIS

Various stages between CFU-E cells and matured RBCs are:

1. Proerythroblast
2. Early normoblast
3. Intermediate normoblast.

4. Late normoblast
5. Reticulocyte
6. Matured erythrocyte.



1. Proerythroblast (Megaloblast): Proerythroblast or megaloblast is the first cell derived from CFU-E. It is very large in size with a diameter of about 20 µ. Its nucleus is large and occupies the cell almost completely. The nucleus has two or more nucleoli and a reticular network. Proerythroblast does not contain hemoglobin. The cytoplasm is basophilic in nature. Proerythroblast multiplies several times and finally forms the cell of next stage called early normoblast. Synthesis of hemoglobin starts in this stage. However, appearance of hemoglobin occurs only in intermediate normoblast.

2. Early Normoblast: The early normoblast is little smaller than proerythroblast with a diameter of about 15 µ. In the nucleus, the nucleoli disappear. Condensation of chromatin network occurs. The condensed network becomes dense. The cytoplasm is basophilic in nature. So, this cell is also called basophilic erythroblast. This cell develops into next stage called intermediate normoblast.

3. Intermediate Normoblast: Cell is smaller than the early normoblast with a diameter of 10 to 12 µ. The nucleus is still present. But, the chromatin network shows further condensation. The hemoglobin starts appearing. Cytoplasm is already basophilic. Now, because of the presence of hemoglobin, it stains with both acidic as well as basic stains. So this cell is called polychromophilic or polychromatic erythroblast. This cell develops into next stage called late normoblast.

4. Late Normoblast: Diameter of the cell decreases further to about 8 to 10 µ. Nucleus becomes very small with very much condensed chromatin network and it is known as ink-spot nucleus. Quantity of hemoglobin increases. And the cytoplasm becomes almost acidophilic. So, the cell is now called orthochromic erythroblast. In the final stage of late normoblast just before it passes to next stage, the nucleus disintegrates and disappears. The process by which nucleus disappears is called pyknosis. The final remnant is extruded from the cell. Late normoblast develops into the next stage called reticulocyte.

5. Reticulocyte: Reticulocyte is otherwise known as immature RBC. It is slightly larger than matured RBC. The cytoplasm contains the reticular network or reticulum, which is formed by remnants of disintegrated organelles. Due to the reticular network, the cell is called reticulocyte.

Reticulocyte is basophilic due to the presence of remnants of disintegrated Golgi apparatus, mitochondria and other organelles of cytoplasm. During this stage, the cells enter the blood capillaries through capillary membrane from site of production by diapedesis.

6. Matured Erythrocyte: Reticular network disappears and the cell becomes the matured RBC and attains the biconcave shape. The cell decreases in size to 7.2 µ diameter. The matured RBC is with hemoglobin but without nucleus.

It requires 7 days for the development and maturation of RBC from proerythroblast. It requires 5 days up to the stage of reticulocyte. Reticulocyte takes 2 more days to become the matured RBC.

IMPORTANT EVENTS DURING ERYTHROPOIESIS:

Stages of Erythropoiesis	Important Events
Proerythroblast	Synthesis of hemoglobin starts
Early normoblast	Nucleoli disappear
Intermediate normoblast	Hemoglobin starts appearing
Late normoblast	Nucleus disappears
Reticulocyte	Reticulum is formed. Cell enters capillary from site of production
Matured RBC	Reticulum disappears, Cell attains biconcavity

FACTORS NECESSARY FOR ERYTHROPOIESIS:

Development and maturation of erythrocytes require variety of factors, which are classified into three categories:

1. General factors
    i. Erythropoietin
    ii. Thyroxine
    iii. Hemopoietic growth factors: Interleukins
    iv. Vitamins: Vit. B, Vit. C, Vit. D, Vit E.
2. Maturation factors: Vit B 12, Folic acid, Intrinsic factor of Castle
3. Factors necessary for hemoglobin formation: Iron, Copper, Cobalt, Nickel, Proteins and amino acids.

HAEMOSTASIS

Haemostasis is the instinctive response for the body to stop bleeding and loss of blood. Haemostasis occurs when blood is present outside of the body or blood vessels.

Three mechanisms reduce blood loss:

Vascular spasm: It is the first response as the blood vessels constrict to allow le blood to be lost.

Platelets plug formation: Platelets stick together to form a temporary seal to cover the break in the vessel wall.

Blood clotting: Coagulation reinforces the platelet plug with fibrin threads that act as a molecular glue.

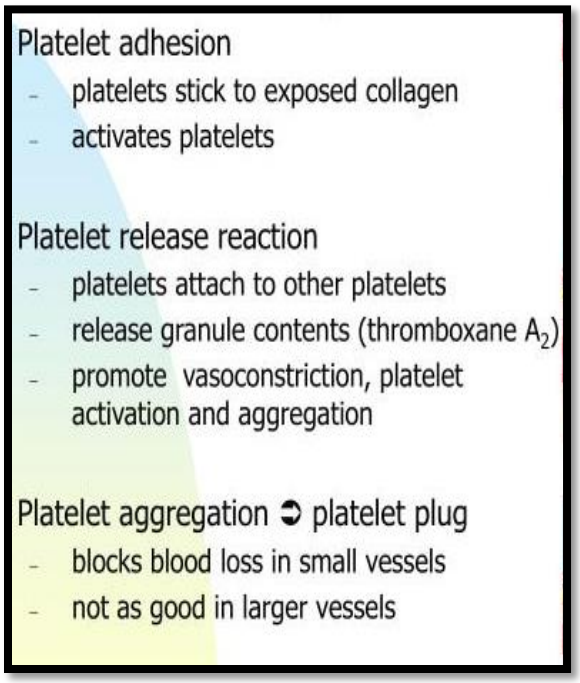
Vascular Spasm:

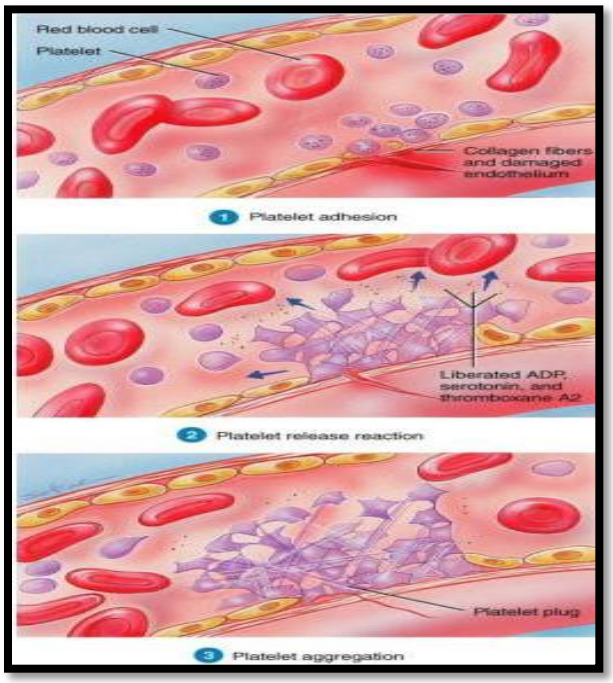
Vascular spasm is the blood vessels' first response to injuy. When arteries or arterioles are damaged, the circularly arranged smooth muscle in their walls contracts immediately, a reaction called vascular spasm.The damaged vessels constrict which reduces the amount of blood flow through the area and limits the amount of blood loss. This reduces blood loss for several minutes to several hours.This response is triggered by factors such as a direct injury to vascular smooth muscle, chemicals released by endothelial cells and activated platelets, and reflexes initiated by local pain receptors.

Platelet Plug Formation:

Platelets play an important role in haemostatic process. Platelets sticks together to form a plug that temporarily seals the break in the vessel wall called as platelet adhesion. As they adhere to

the collagen fibres of a wound they become spiked and much stickier.Then they release chemical messengers such as adenosine diphosphate (ADP) serotonin and thromboxane A2.





Process of homeostasis

This phase is called as platelet release reaction. These chemicals are released to cause more platelets to stick to the area and release their contents and enhance vascular spasms. This phase is called platelet aggregation. As more chemicals are released, more platelets stick and release their chemicals; creating a platelet plug. Platelets contains Platelet-Derived Growth Factor (PDGF), a hormone that can cause proliferation of vascular endothelial cells, vascular smooth muscle fibres, and fibroblasts to help repair damaged blood vessel walls. The platelet plug formation is activated by a glycoprotein called the Von Willebrand factor (VWE), found in the blood plasma. A platelet plug is very effective in preventing blood loss in a small vessel.

BLOOD CLOTTING:

Clotting is the process by which blood forms clots. It is a series of chemical reaction that culminates in the formation of fibrin threads. It is a complex cascade of enzymatic reaction in which each factor activates many molecules of the next one in a fixed series.

Clotting can be divided into three stages

Intrinsic pathway: It leads to the formation of prothrombinase with fewer steps which occur rapidly.

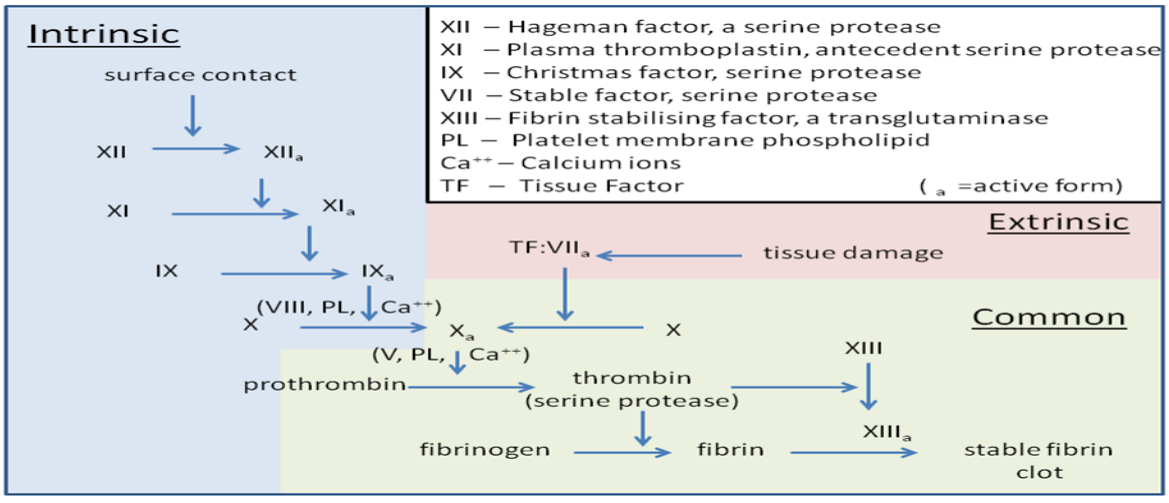
Extrinsic pathway: It leads to the formation of prothrombinase with more number of steps which occur more slowly.

NUMBER*	NAME(S)	SOURCE
I	Fibrinogen.	Liver.
II	Prothrombin.	Liver.
III	Tissue factor (thromboplastin).	Damaged tissues and activated platelets.
IV	Calcium ions (Ca^{2+}).	Diet, bones, and platelets.
V	Proaccelerin, labile factor, or accelerator globulin (AcG).	Liver and platelets.
VII	Serum prothrombin conversion accelerator (SPCA), stable factor, or proconvertin.	Liver.
VIII	Antihemophilic factor (AHF), antihemophilic factor A, or antihemophilic globulin (AHG).	Liver.
IX	Christmas factor, plasma thromboplastin component (PTC), or antihemophilic factor B.	Liver.
X	Stuart factor, Prower factor, or thrombokinase.	Liver.
XI	Plasma thromboplastin antecedent (PTA) or antihemophilic factor C.	Liver.
XII	Hageman factor, glass factor, contact factor, or antihemophilic factor D.	Liver.
XIII	Fibrin-stabilizing factor (FSF).	Liver and platelets.

Clotting factors

Intrinsic Pathway

The pathway is more complex and occurs more slowly, usually in several minutes. The activators are either in direct contact With blood or contained within the blood vessel. If endothelial cells are damaged, blood comes in direct contact with collagen fibres in the Connective tissue around the endothelium of blood vessel. Injury to endothelial cells causes damage to platelets, resulting in release of phospholipids by the platelets. Contact with collagen fibres activates clotting factor XII, which activates clotting factor. Platelet phospholipids and Ca^{2+}, participates in the activation of factor X. Once factor X is activated, t com Dines with factor V to form the active enzyme prothrombinase, completing the intrinsic pathway.



Common clotting pathway

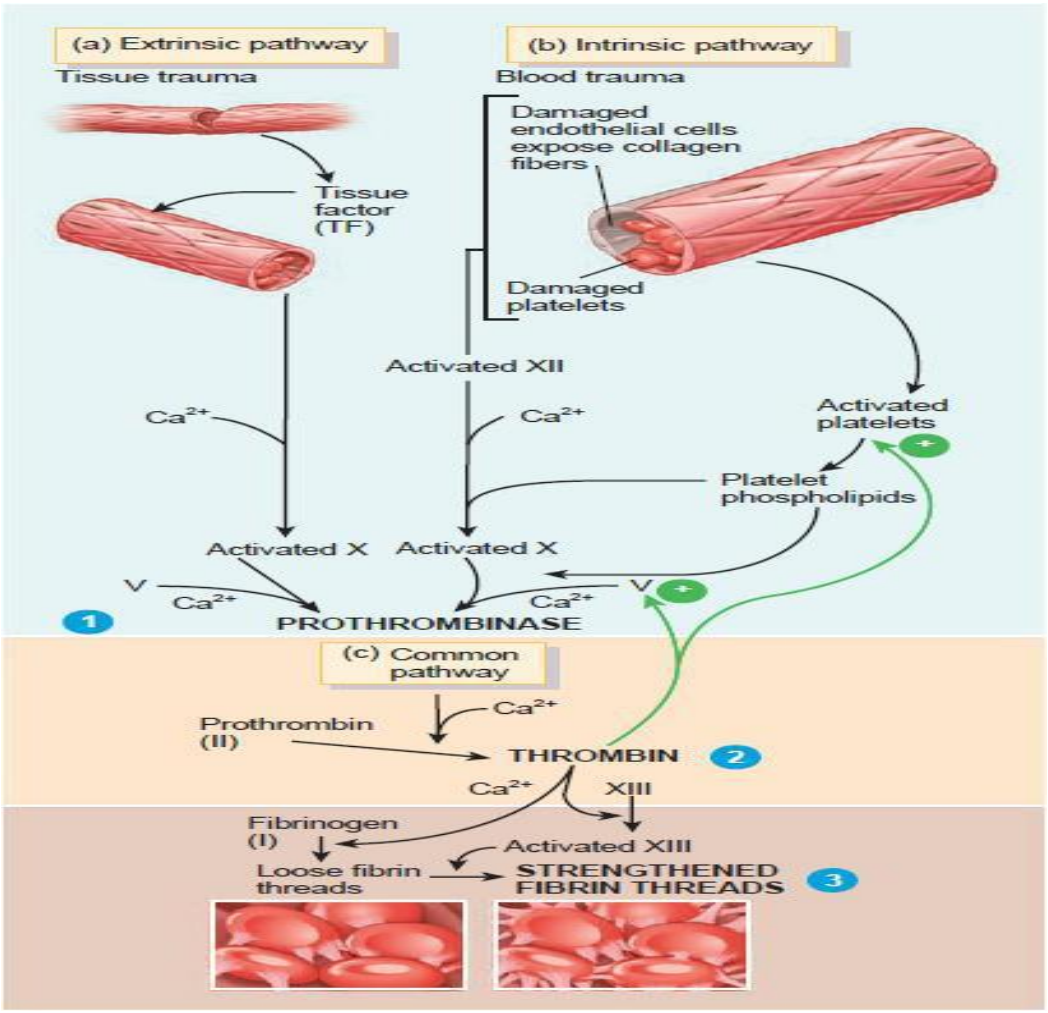
Extrinsic Pathway:

It consists of fewer steps and occurs rapidly within a second. In this pathway a tissue protein called tissue. Factor (TF) leaks into the blood from cells outside the blood vessels and initiates the formation of prothrombinase. TF is a complex mixture of lipoproteins and phospholipids released from the surfaces of damaged cells. In the presence of Ca^{2+}, TF activates factor X. Once factor X is activated, it combines with factor v, in the presence of Ca^{2+} to form the active enzyme prothrombinase, completing the extrinsic pathway.

Common Pathway:

The formation of prothrombinase is the starting point of common pathway. In the second stage of blood clotting, prothrombinase and Ca^{2+} catalyze the conversion of prothrombin to thrombin.

In the third stage, thrombin in presence of Ca^{2+}, converts fibrinogen (soluble) to loose fibrin threads (insoluble). Thrombin also activates factor XII (fibrin stabilizing factor), which strengthens and stabilizes the fibrin threads into a sturdy clot.



Blood Clotting

BLOOD GROUPS

The blood groups are decided by the presence or absence of certain red cell antigen which are called antigens and present on the surface of RBC membrane The antigens are lipoprotein or glycoprotein.

Transfusion: A transfusion is the transfer of whole blood or blood components (Red blood cells only or blood plasma only) into the bloodstream or directly into the red bone marrow.

Donor: The person who donates the blood is called as donor.

Recipient: The person who receives the blood is called as recipient. In a haemoagglutination reaction;

(a) The red cell antigen is called as agglutinogen.

(b) The antibody involved in reaction is called as agglutinin.

There are two main blood group systems:

A-B-O System

Rh System

A-B-O System:

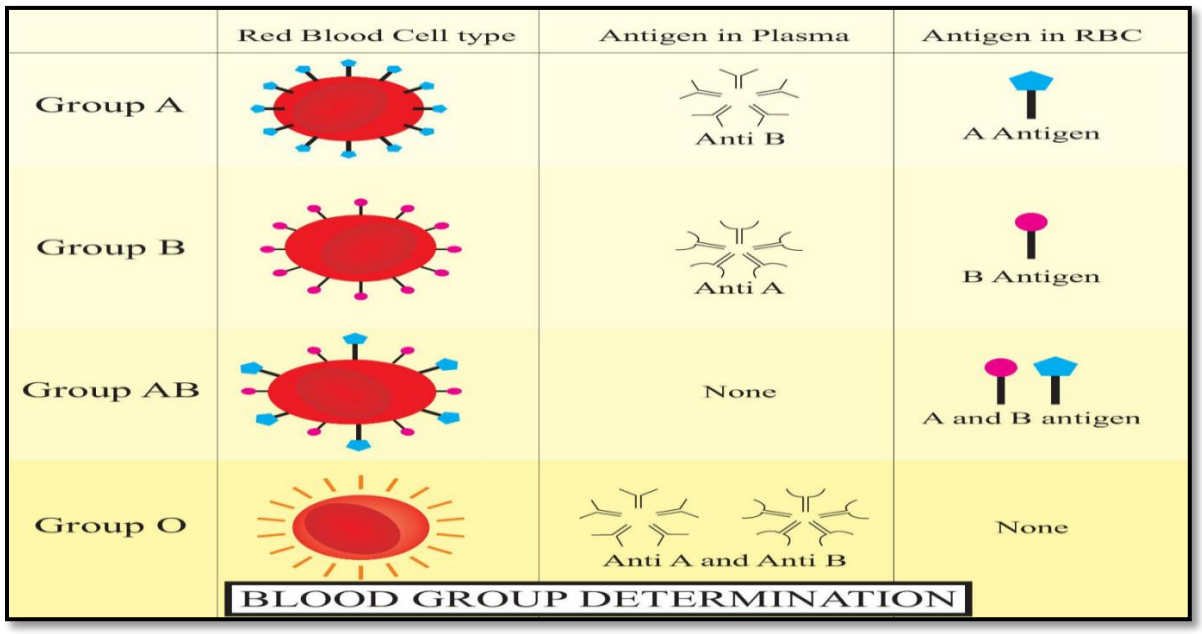
The ABO blood group is based on two glycolipid antigens called as A and B antigens.

A person whose RBCs displays only antigen A has type A blood.

A person whose RBCs displays only antigen B has type B blood.

A person whose RBCs displays both antigen A and B have type AB blood.

A person whose RBCs displays neither antigen A nor B have type O blood.



Hence, there are mainly four blood groups.

A Group

B Group

AB Group

O Group

This depends on the reaction obtained by mixing the RBCS with two different reagent Known as Anti-A and Anti-B serum.

Blood	Anti- A serum.	Agglutination	A BLOOD GROUP
Blood	Anti-B serum.	No Agglutination	
Blood	Anti-A serum.	No Agglutination	B BLOOD GROUP
Blood	Anti-B serum.	Agglutination	
Blood	Anti-A serum.	Agglutination	AB BLOOD GROUP
Blood	Anti-B serum.	Agglutination	
Blood	Anti-A serum.	No Agglutination	O BLOOD GROUP
Blood	Anti-B serum.	No Agglutination	

A-B-O system of blood group

Blood Group A:

When RBCs are mixed with Anti-A and Anti-B serum and if agglutination is observed with Anti-A then blood group is A. This indicates that antigen-A is present on RBCs and the serum contains Anti-B antibodies. Blood group A is compatible with Group A and Group O. It is incompatible with Group B and Group AB.

Blood Group B:

When RBCs are mixed with Anti-A and Anti-B serum and if agglutination is observed with Anti-B the blood group is B. This indicates that antigen-B is present on RBCs and the serum contains Anti-A antibodies. Blood group B is compatible with Group B and Group O. It is incompatible with Group A and Group AB.

Blood Group AB:

When RBCs are mixed with Anti-A and Anti-B serum, agglutination is observed with both Anti-A and Anti-B, the blood group is supposed to be AB. This indicates that presence of antigen-A and B on RBCs and the serum does not have any Anti-A and Anti-B antibodies AB blood group

is compatible with Group A. B. AB and Group O and therefore people with blood group AB are called as universal recipients because they do not have A aid B to attack on the donated RBCs.

Blood Group O:

When RBCs are mixed with Anti-A and Anti-B serum, and if agglutination is not observed with either of them then blood group is O. This indicates that absence of antigen-A and B on RBCs and the serum contains both Anti-A and Anti-B antibodies. Hence, people with blood group O are referred to as universal donors. Type O people can receive only type O blood. They cannot receive blood of type-A, B and AB.

Rhesus blood group system (Rh factor):

The Rh blood group is so named because the antigen was discovered in the blood of the Rhesus monkey. People whose RBCs have Rh antigens are designated Rh (Rh positive); those who lack Rh antigens are designated Rh- (Rh negative). Normally, blood plasma does not contain anti-Rh antibodies. If an Rh- person receives an Rh' blood transfusion, however, the immune system starts to make anti-Rh antibodies that will remain in the blood. If a second transfusion of Rh+ blood is given later, the previously formed anti-Rh antibodies will cause agglutination and hemolysis of the RBCs in the donated blood, and a severe reaction may occur.

RETICULO ENDOTHELIAL SYSTEM (RES)

It is also called as macrophage system or the mononuclear phagocyte system. It is a network of cells located throughout the body that help to filter out dead and toxic particles and also work to identity foreign substances in both the blood and tissues. It is part of the immune system of human body and consists of phagocytic cells. .It is closely related to lymphatic system because the two are independent structurally and functionally. This system is made up of highly phagocytic cells which are widely distributed in the body

Cellular component of RES:

Monocytes

Macrophage present in tissues such as skin (Histocytes), liver (Kupffer), spleen, bone marrow, lymph nodes and lung. Endothelial cells present as an antigen (bone marrow, spleen, lymph node).

Macrophages:

These remain fixed to their organs. The mostly filter and destroy objects which are foreign to the body, such as Bacteria, viruses. Some macrophages are mobile, and they can group together to become one big phagocytic cell in order to ingest larger foreign particles.

Types of Macrophages: (same function but different names according to the location)

- ✓ Macrophage differs depending on the organs in which they reside.
- ✓ Kupffer cells present in the liver.
- ✓ Microglia present in the brain.
- ✓ Reticular cells present in the lymph nodes, bone marrow, spleen.
- ✓ Tissue histocytes present in the subcutaneous tissues (fixed macrophages).
- ✓ Alveolar cells present in the lungs.

Formation of macrophages:

Origin: Stem cell in bone marrow proliferates to monoblast maturing to promonocyte and mature monocytes released into blood. Remain for 10-20 hours in circulation as monocytes Then leave blood to tissues transforming into larger cells known as macrophage. Macrophage life span is longer up to few months in tissues.

Transformation of monocytes to macrophages:

They are characterized by an increase in:

- ✓ Cell size
- ✓ Number and complexity of intracellular organelles golgi complex, mitochondria and lysosomes
- ✓ Intracellular digestive enzymes

Functions:

- ✓ ***Phagocytosis:*** Bacterial, dead cells, foreign particles is the basic component of immune system, and it also helps the lymphocytes.
- ✓ Indirect immune function: Processing and presenting antigen to lymphocytes. le
- ✓ Breakdown of aging RBC.
- ✓ Storage and circulation of iron.

DISORDERS OF HEAMOPOETIC SYSTEM

ANAEMIAS

Anaemia is a condition in which the oxygen carrying capacity of blood is reduced or is less than the normal quantity of haemoglobin in the blood. This condition results in pallid complexion, loss of vigour and lack of energy.

Symptoms of Anaemia:

Weakness

Tiredness

Pale skin, gums and nail beds

Fast heartbeat

Shortness of breath

Fainting

Fatigue

Chest pain

Types of Anaemia:

Impaired RBCs production: RBC production could be impaired due to the following reasons:

Iron deficiency anaemia

Megaloblastic anaemia

Pernicious anaemia

Hypoplastic anaemia

Increased RBCs loss:

Haemolytic anaemia

Haemorrhagic anaemia

Iron deficiency anaemia:

It is a common type of anaemia results due to inadequate absorption of iron, excessive loss of iron, increased iron requirement, or insufficient intake of iron. Women are at a greater risk for iron-deficiency anemia due to menstrual blood loss and increased iron demands of the growing foetus during pregnancy.

This can result if:

- ✓ The body does not make enough red blood cells.
- ✓ Bleeding causes loss of red blood cells more quickly than they can be replaced.

- ✓ The common cause of iron deficiency anaemia is infestation due to parasitic worms hookworms, whipworms and roundworms

Malaria and vitamin-A deficiency are also common causes of anaemia.

In women over 50 years of age, the most common causes is chronic gastrointestinal bleeding from non-parasitic causes such as gastric ulcers, duodenal ulcers o gastrointestinal cancer.

Megaloblastic Anaemia:

Inadequate intake of vitamin B12 Or folic acid causes megaloblastic anaemia in which the red bone marrow proauces large, abnormal red blood cells (megaloblasts). It may also be causes by drugs that alter gastric secretion or are used to treat cancer.

Pernicious Anaemia:

It occurs due to insufticient haemopojesis resulting from an inability of the stomach to produce intrinsic factor which Is needed for absorption of vitamin B12 in the small intestine. It can develop due to loss of gastric parietal cell of intrinsic tactor, a protein essential for subsequent a responsible for the secretion intrinsic factor, a protein essential for subsequent absorption of vitamin B12 in ileum

Aplastic Anaemia:

Destruction of red bone marrow results in aplastic anaemia. It is caused by toxins, gamma radiation, and certain medication needed for haemopoiesis.

Haemolytic Anaemia:

It is a form of anemia due to haemolysis, the abnormal breakdown (RBCS), either in the blood vessels (intravascular haemolysis) or elsevwhere in human body (extravascular haemolysis) This is also caused due to parasites, toxins and antibody from incompatible blood.

Haemorrhagic Anaemia:

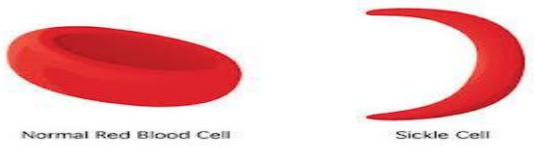
Excessive loss of RBCs through resulting from large wounds, stomach ulcers and heavy menstruation leads to haemorrhagic anaemia.

Sickle Cell Anaemia (SCA):

SCA is a serious disorder in which the body makes sickle-shaped red blood cells. Sickle shaped means that the red blood cells are shaped like a crescent. Normal red blood cells are disc-shaped and move easily through blood vessels. Red blood cells contain an iron-rich protein called hemoglobin. This protein carries oxygen from the lungs to the rest of the body. Sickle cells contain abnormal haemoglobin called sickle haemoglobin or haemoglobin S.Sickle haemoglobin causes the cells to develop a sickle, or crescent shape. Sickle cels are stiff and sticky. They tend

to block blood flow in the blood vessels of the limbs and organs. It is due to genetic mutation that causes substitution of wrong amino acid in a particular portion of globin. At low oxygen concentration in many capillaries, haemoglobin molecules combine witheach other to form fibre like structures which distort that RBCs membrane to form sickle shape.Such a sickle shaped RBCs Occlude and burst in capillaries leading to anaemic conditions.

(a) Normal red blood cell (b) Sickled red blood cell



Sickle cell RBC

Thrombocytopenia

Very low platelet counts that result in a tendency to bleed from capillaries.

Pernicious anemia

Insufficient hemopoiesis resulting from an inability of the stomach to produce intrinsic factor, which is needed for absorption of vitamin B12 in the small intestine, causes pernicious anemia.

Iron-deficiency anemia

It is the most common type of anemia. Women are at greater risk for iron-deficiency anemia due to menstrual blood losses and increased iron demands of the growing fetus during pregnancy. Gastrointestinal losses, such as those that occur with malignancy or ulceration, also contribute to this type of anemia.

Megaloblastic anemia

Inadequate intake of vitamin B12 or folic acid causes megaloblastic anemia, in which red bone marrow produces large, abnormal red (megaloblasts). It may also be caused by drugs that alter gastric secretion or are used to treat cancer.

Leukaemia

It refers to a group of red bone marrow cancers in which abnormal white blood cells multiply uncontrollably.

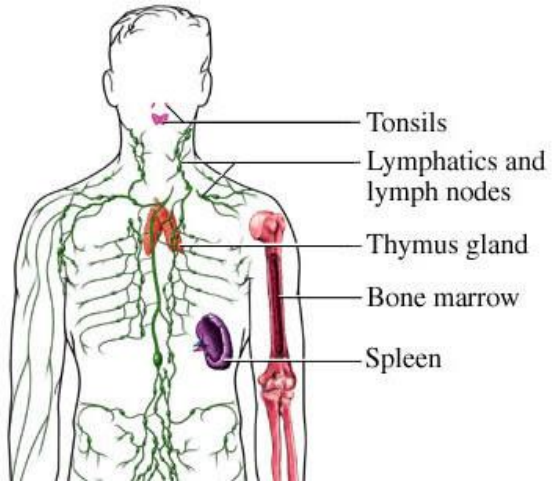
Haemolytic disease of the Newborn (HDN)

When the immune system of the mother sees a baby's RBCs as foreign. Antibodies then develop against the baby's RBCs. These antibodies attack the RBCs in the baby's blood and cause them to break down too early.

LYMPHATIC SYSTEM

The lymphatic system is a major part of the body's immune system. The lymphatic system is a subset of the circulatory system, with a number of actions. The lymphatic system is a network of organs, lymph nodes, lymph ducts and lymph vessels that make and move lymph from tissues of the blood stream. Lymphatic system is a specialized form of reticular connective tissue that consists or tissues and organs that produce, mature and store lymphocytes and macrophages, 1or the body's defence purposes. It acts as a transport channel that carries white blood cells to and from the lymph nodes into the bones and antigen presenting cells to the lymph nodes. Lymphatic capillaries reabsorb excessive tissue fluid and transport the fluid through the lymphatic pathway, and ultimately dispose it into the blood. Lymphatic vessels carry lipid and lipid soluble vitamins absorbed by the gastrointestinal tract to blood.

PARTS OF LYMPHATIG SYSTEM

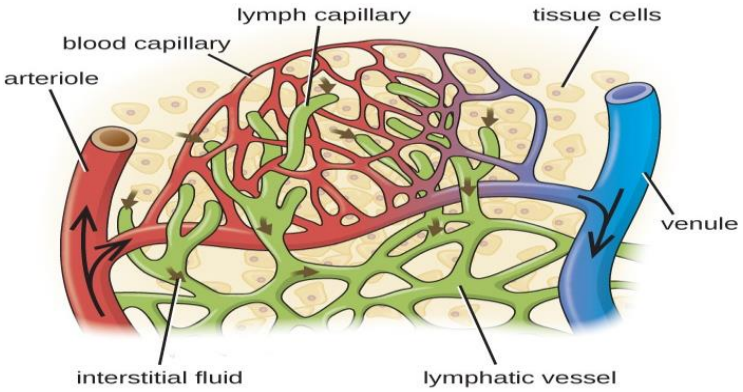


- Lymph
- Lymphatic vessels
  - Lymph trunks and ducts
  - Thoracic (Left lymphatic) duct
  - Right lymphatic duct
- Lymphatic tissue
  - Lymph nodes
  - Tonsils
  - Spleen
  - Thymus gland

Lymphatic system

LYMPH

The excess interstitial fluid which drains into the lymphatic capillaries is called as lymph. Lymph is a clear watery fluid, Similar in composition to plasma, with the exception of plasma proteins. Lymph transports the plasma proteins that seep out of the capillary beds back to the blood stream. It also carries away bacteria and cell debris from damaged tissues, which then filtered out and destroyed by the lymph nodes. Lymph contains lymphocytes, which circulate in the lymphatic system allowing them to patrol the different regions of the body. In the small intestine, fats absorbed from the lymphatic's capillaries called as lacteals give the lymph, a milky appearance.



Lymphatic vessels and capillaries

Chemical composition:

Proteins (g/100 m): 2.6.

Chloride (m.eq/lit);: 116.

Calcium (m.eq/lit); 4.6.

Urea (mg/100 ml);: 23.5.

Flow of Lymph:

The sequence of lymph flow:

Blood capillaries (blood)

↓

Interstitial spaces (interstitial fluid)

↓

Lymphatic capillaries (lymph)

↓

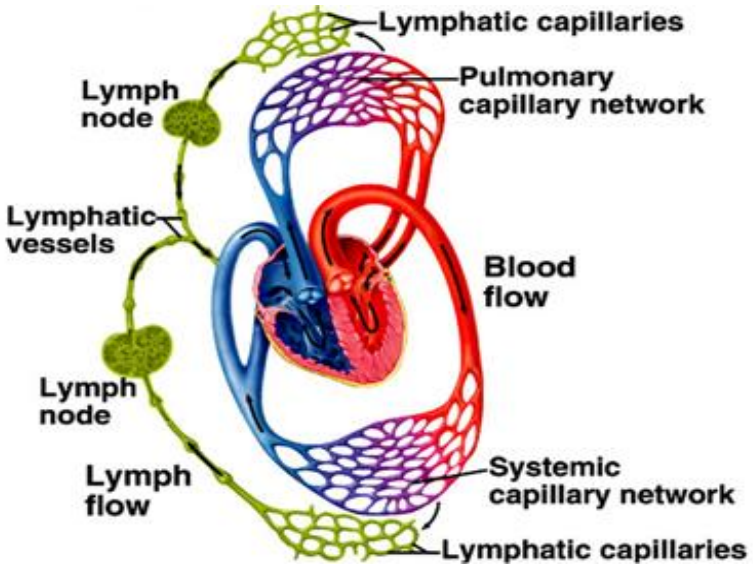
Lymphatic vessels (lymph)

↓

Lymphatic ducts (lymph)

↓

Junction of the internal jugular and subclavian veins (blood)

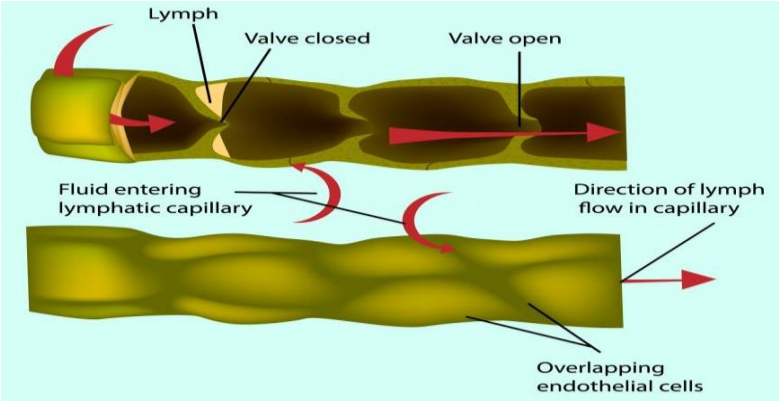


Flow of lymph

The lymphatic flow is regulated by means of movements of skeletal muscles and through the breathing movements. This movement compresses the lymphatic vessels and forces the lymph flow towards the subclavian veins. Lymphatic vessels contain one way valve that prevents back flow of lymph

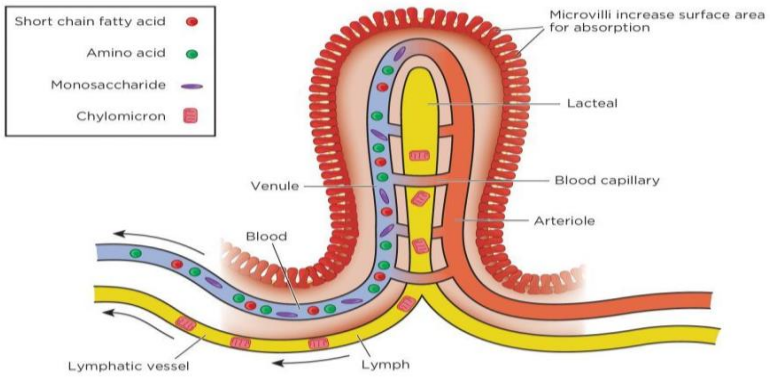
LYMPHATIC VESSELS

These are tiny thin-walled vessels. These are closed at one end. The main purpose is to drain excess interstitial fluid from around the cell to venous circulation. The wall of lymphatic capillaries is made up of endothelium These are larger in diameter.The anchoring filaments hold endothelial cells to the nearby tissues.



Lymphatic vessels

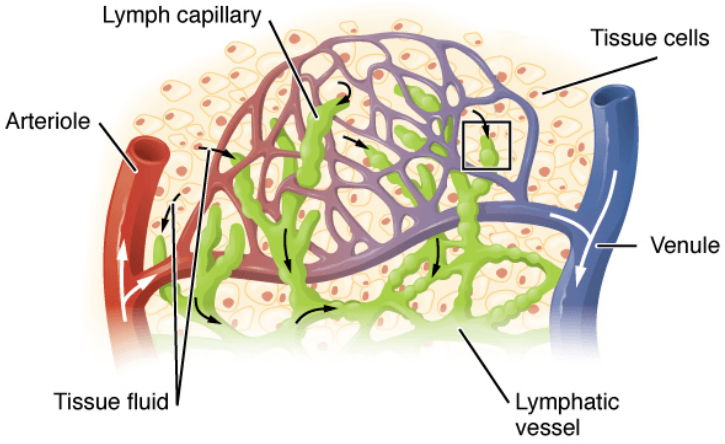
A lacteal isa lymphatic capillary present in mucosa of small intestine It absorbs dietary fats and lipid-soluble vitamins from the small intestine. A special type of lymph, known as chyle, is produced in the digestive system as lymph absorbs triglycerides from the intestinal villi. The chyle has a milky while colouration due to the presence of triglycerides.



Lacteal

LYMPHATIC CAPILLARIES

Lymphatic capillaries combine together to form lymphatic vessels.These are thin-walled structures that carry lymph. Lymph vessels are lined by endothelial cells.A lymph vessel pushes lymph from lymph capillaries to the lymphatic trunk and ducts. Lymphatic vessels resemble small veins.



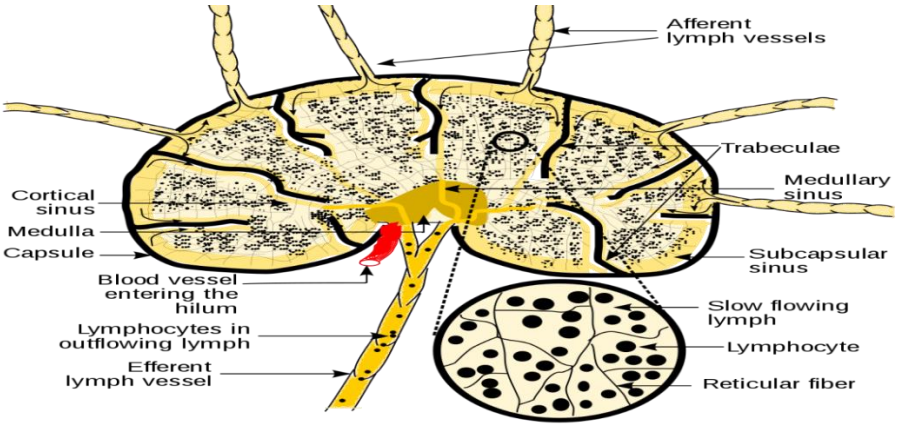
Lymphatic capillaries

LYMPH NODES

The oval or bean shaped organs located along the length or lymphatic vessels called a lymph nodes. They range from 1 to 25 mm in length. They are greyish pink in colour. Lymph nodes are scattered throughout the body, usually in groups. These groups are arranged in two sets; superficial and deep. Each node is covered by a dense connective tissue called as capsule. The capsular extensions are called as trabeculae internally node has two parts: the outer cortex and inner medulla.The outer cortex contains densely packed lymphocytes arranged in masses called as follicles. The outer rim of each follicle contains T-lymphocytes and macrophages. In the medulla, the lymphocytes are arranged in strands called as medullary rays. Internal to the capsule is a supporting network of reticular fibres and fibroblasts. Along with capsule, trabeculae, reticular fibres and fibroblasts constitute the stroma of lymph node. Each node has a concave surface called as hilum. Four or five afferent lymph vessels may enter a lymph node while only one efferent vessel carries lymph away from the node.

Functions:

- The lymph node filter foreign substances from lymph as it moves back to the cardiovascular system.
- These substances along with microbes are trapped by the reticular fibres within the node
- Then lymphocytes and macrophages destroy the foreign substance by phagocytosis



Lymph node

SPLEEN

It is a flattened oval organ located in the upper part of abdomen, under the diaphragm and behind the stomach. It is covered by dense connective tissue called as capsule. The capsular extensions are called as trabeculae. Internal to the capsule is a supporting network of reticular fibres and fibroblast. Along with capsule, trabeculae, reticular fibres and fibroblast forms the stroma (Supporting network) of the spleen. The spleen consists of two different kinds of tissue

White pulp: It consists of masses of lymphocytes and macrophages

Red pulp: It consists of blood sinuses.

Spleen has a concave surface called as hilum. The structure entering and leaving the spleen at the hilum are:

Splenic artery

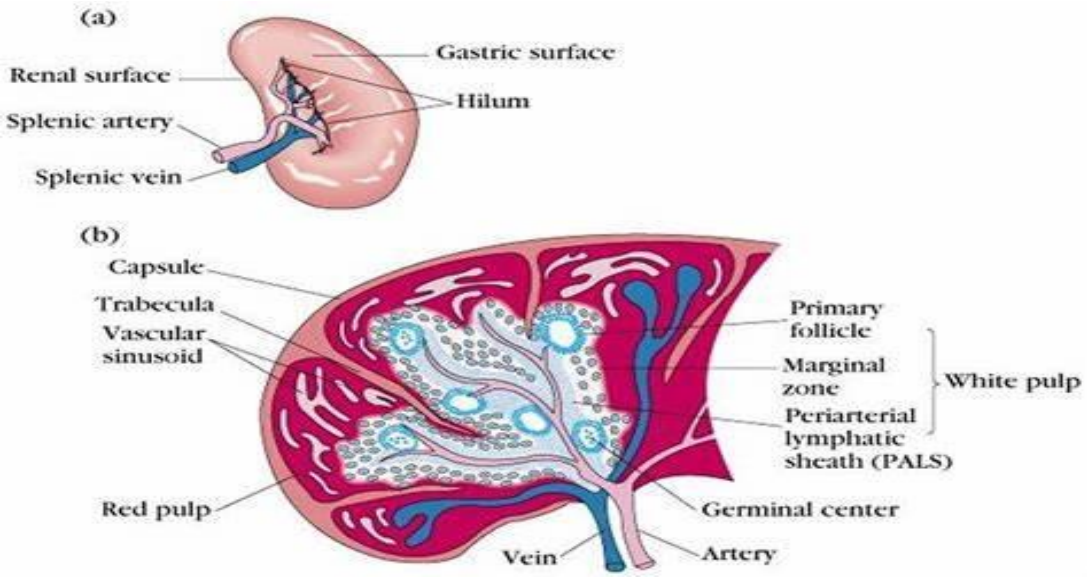
Splenic vein

Lymph vessels

Nerves

Functions:

- It plays an important role in phagocytosis of bacteria damaged RBCS and platelets.
- During early fetal devolvement the spleen participates in blood cell formation.
- Spleen stores and releases blood in times of demands such as during haemorrhage
- The spleen contains T and B-lymphocytes which are activated by presence or antigen to fight off infection.



(a) Spleen *(b) Internal structure of spleen*

Long Answer Questions:

1. Explain the mechanism of blood clotting or write a note on blood clotting.
2. Give Functions of blood and explain platelet plug formation and blood clotting mechanism.
3. Explain in detail mechanism of blood clotting and add a note on haemolytic release of new born.

Short Answer Questions:

1. What is blood clotting and enlist different clotting factors.
2. Write a note on;
   (a) A-B-0-system of blood grouping
   (b) Rh system of blood grouping
3. Explain RBCs life span.
4. Write a note on destruction of erythrocytes.
5. Write a note on blood plasma.
6. What is red bone marrow?
7. Note on platelet plug formation.
8. Note on haemolytic disease of new born.
9. Note on platelet plug formation.
10. Explain functions of blood.
11. Write a note on WBCs.

12. Define blood and give its different functions.

13. Give the composition of blood.

14. Define anaemia and explain its different types.

15. Explain haemopoiesis process.

16. Classify WBCs and explain structure and function of each type.

17. Give definitions of the following disorders.

(a) Leukopenia

(b) Leukocytosis

(c) Thrombocytopenia

(d) Polycythemia

(e) Anemia

(f) Angina Pectoris

(g) Hypertension

(h) Arteriosclerosis

(i) Bronchitis

(j)Haemophilia

18. Explain platelet plug formation.

19. Explain mechanism of blood clotting.

20. Write a note on blood groups.