Composition Of Blood & RBC

WEB LECTURE BY

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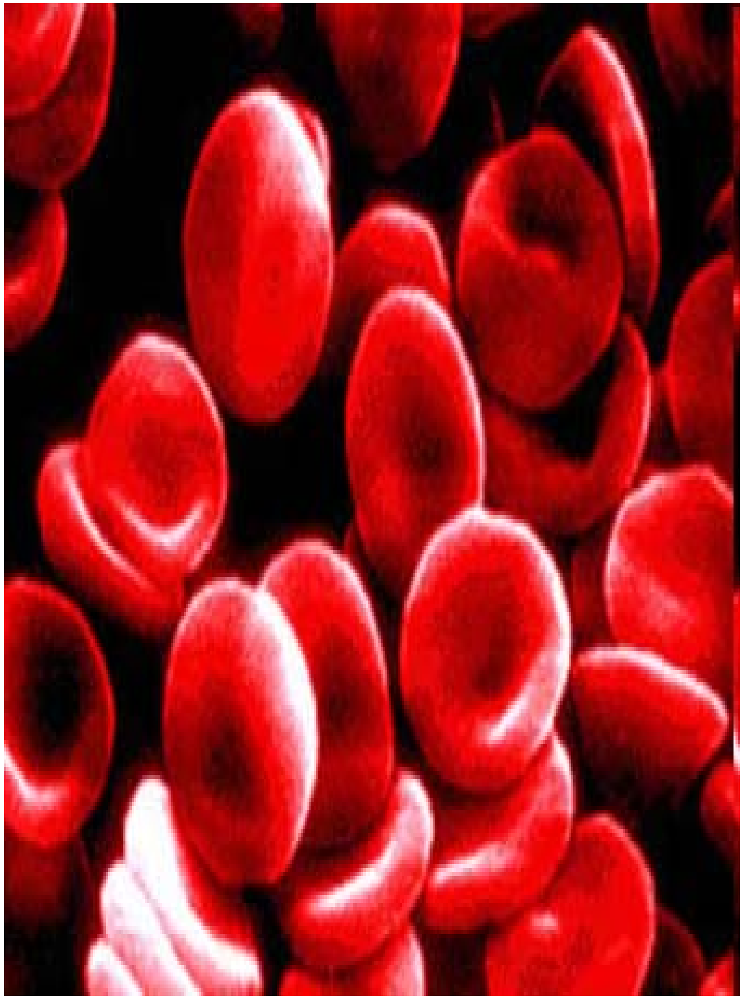
(A) Blood

(B) RBC

(C) Erythropoiesis

(A) Blood

- Introduction Of Blood
- Properties Of Blood
- Composition Of Blood
- Types Of Blood Cells
- Functions Of Blood



Composition of blood plasma

Plasma

Plasma is the straw-colored liquid in which the blood cells are suspended.

Component	**Percent**
Water	~92
Proteins	6–8
Salts	0.8
Lipids	0.6
Glucose (blood sugar)	0.1

Introduction Of Blood

Blood Is a connective tissue in fluid form.

It is called as:-

1. **Fluid of life** -because it carries Oxygen from lungs to all parts of body & vice-versa.
2. **Fluid of growth** -because it carries nutritive substances from the digestive system & hormones from endocrine gland to all the tissues.
3. **Fluid of health** -because it protects the body against the diseases & gets rid of waste products by transporting them to the excretory organs.

Properties Of Blood

1. Color :Blood is red in color. Arterial blood is scarlet red because it contains more oxygen & venous blood is purple red because more of carbon dioxide.
2. Volume :The average volume of blood in normal adult is 5 L. In new born it is 450ml. It increases during growth & reaches 5L at the time of Puberty. In females it is 4.5L

3. Reaction and pH :Blood is slightly Alkaline and its pH in normal conditions is 7.4.

4. Specific Gravity :The specific gravity are as follows:-

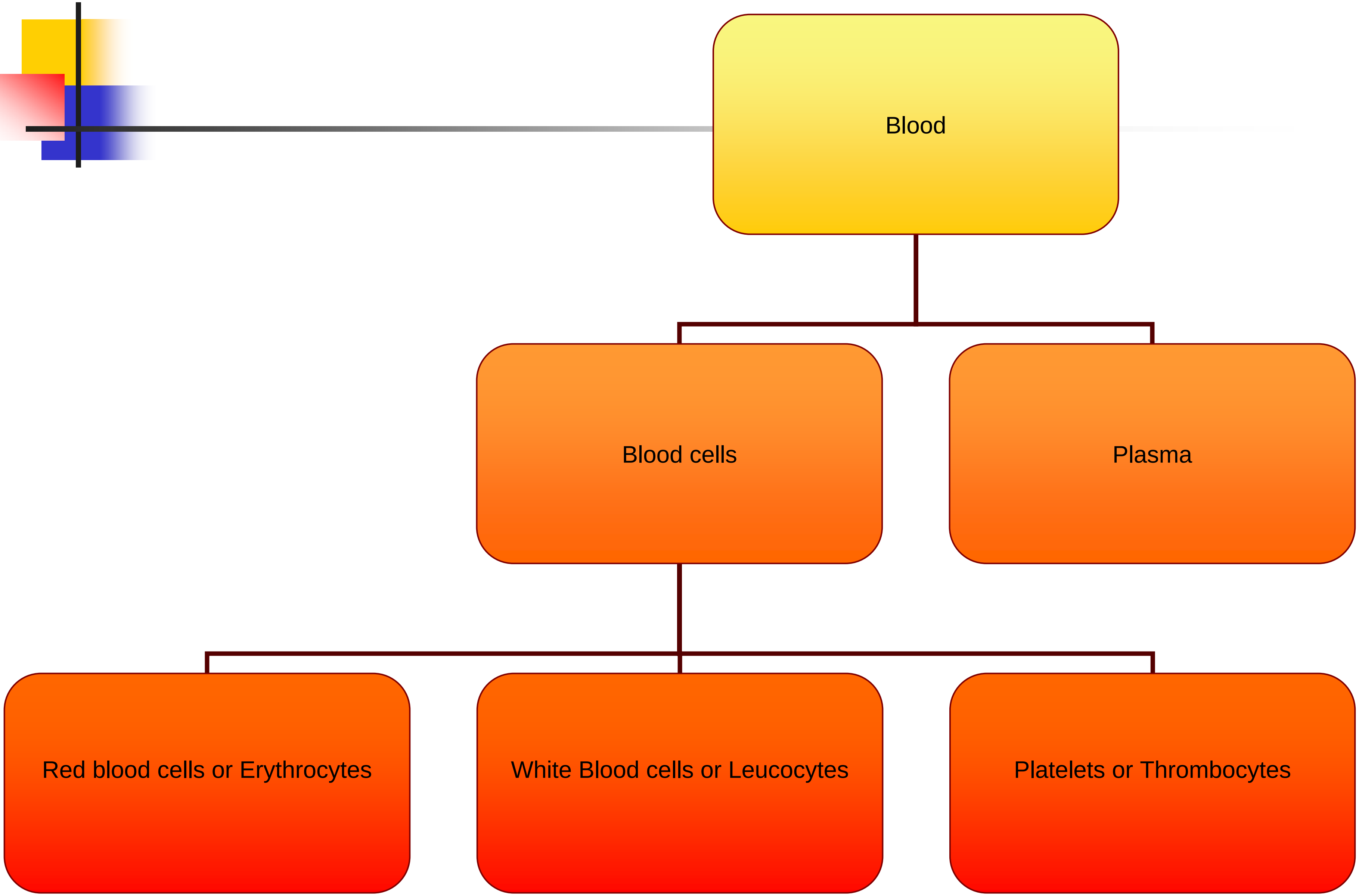
Of total Blood	:1.052 to 1.061
Of Blood cells	:1.092 to 1.101
Of Plasma	:1.022 to 1.026

5. Viscosity :Blood is five times more viscous than water. It is mainly due to red blood cells and plasma proteins.

Composition Of Blood

Blood contains the blood cells which are called formed elements and liquid portion known as plasma. Blood cells are further divided as:-

Composition Of Blood



Functions Of Blood

1. <u>Nutrient Function</u>

   Nutritive substances like glucose, amino acids, lipids and vitamins derived from digested food are absorbed from gastrointestinal tract and carried by blood to different parts of the body for growth & production of energy.

2. **Respiratory Function**

Transport of respiratory gases is done by the blood. It carries oxygen from alveoli of lungs to different tissues and carbon dioxide from tissues to alveoli.

3. **Excretory Function**

Waste products formed in the tissues during various metabolic activities are removed by the blood and carried to the excretory organs like kidney,skin,etc for excretion.

4. **Transport Of Hormones & Enzymes**

   The hormones which are secreted by ductless(endocrine) gland are released directly into the blood. The blood transports these hormones to their target organs/tissues. Blood also transports enzymes.

5. **Regulation Of Water Balance**

   Water content of blood is freely interchangeable with interstitial fluid. This helps in regulation of water content in the body.

6. **Regulation Of Acid Base Balance**

The plasma proteins and hemoglobin act as buffers and help in regulation of acid base balance.

7. **Regulation Of Body Temperature**

Because of the high specific heat of blood, it is not responsible for maintaining the thermoregulatory mechanism in the body, i.e. the balance between heat loss and heat gain in the body

8. **Storage Function**

Water and some important substances like proteins,glucose,sodium and potassium are constantly required by the tissues. Blood serves as readymade source for these substances. These substances are taken from blood during the conditions like starvation, fluid loss, electrolyte loss, etc.

9. **Defensive Function**

Blood plays important role in defense of the body. The white blood cells are responsible for this function. Neutrophils and monocytes engulf the bacteria by phagocytosis. Lymphocytes ase involved in development of immunity. Eosinophils are responsible for detoxification,disintergration and removal of foreign proteins

(B) RBC

- Introduction Of RBC
- Morphology Of RBC
- Properties Of RBC
- Variations Of RBC

  -In number (Physiological & Pathological)

  -In Size

  -In Shape

  -In structure
- Functions Of RBC

Introduction Of RBC

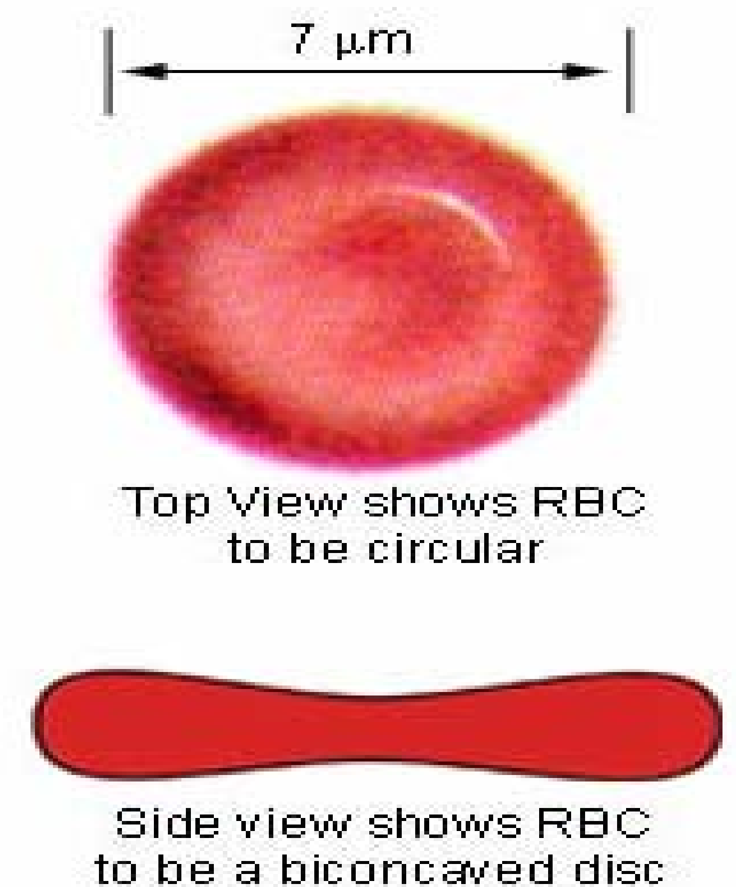
Red Blood Cells(RBC) are also known as erythrocytes(erythros=red). The red color of RBC is due to the presence of the coloring pigment called hemoglobin. RBCs play a vital role in transport of respiratory gases.

The RBC count ranges between 4-5.5 millions per cu mm of blood. In adult males it is 5 millions/cu mm and in adult females it is 4.5 millions/cu mm.

Morphology Of RBC

- **Normal shape**

  Normally, the RBC are disk shaped and biconcave(dumb-belled shaped)



The biconcave contour of RBCs has following mechanical advantages:

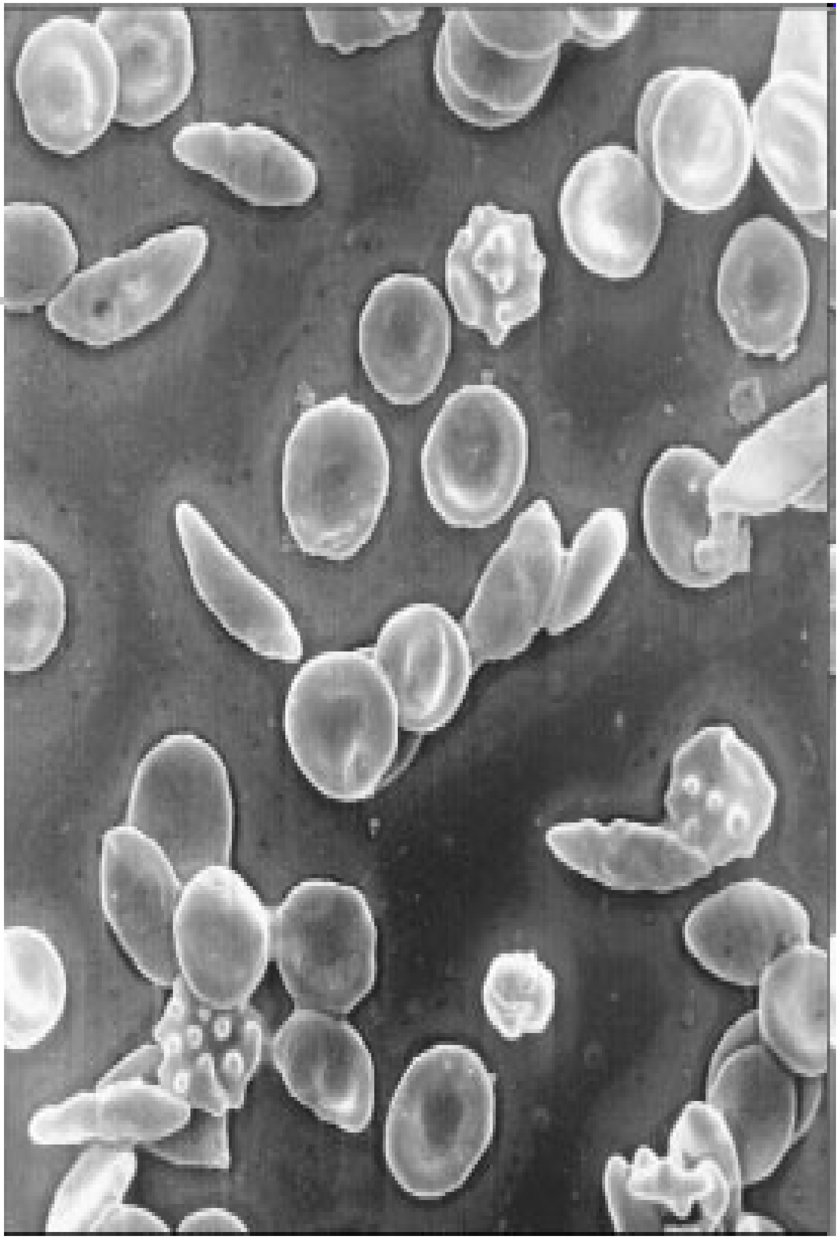
1. It helps in equal and rapid diffusion of oxygen and other substances into the interior of the cell.
2. Large surface area is provided for absorption or removal of different substances.
3. Minimal tension is offered on the membrane when the volume of the cell alters.
4. While passing through minute capillaries, these cells can squeeze through capillaries very easily.

Normal Size

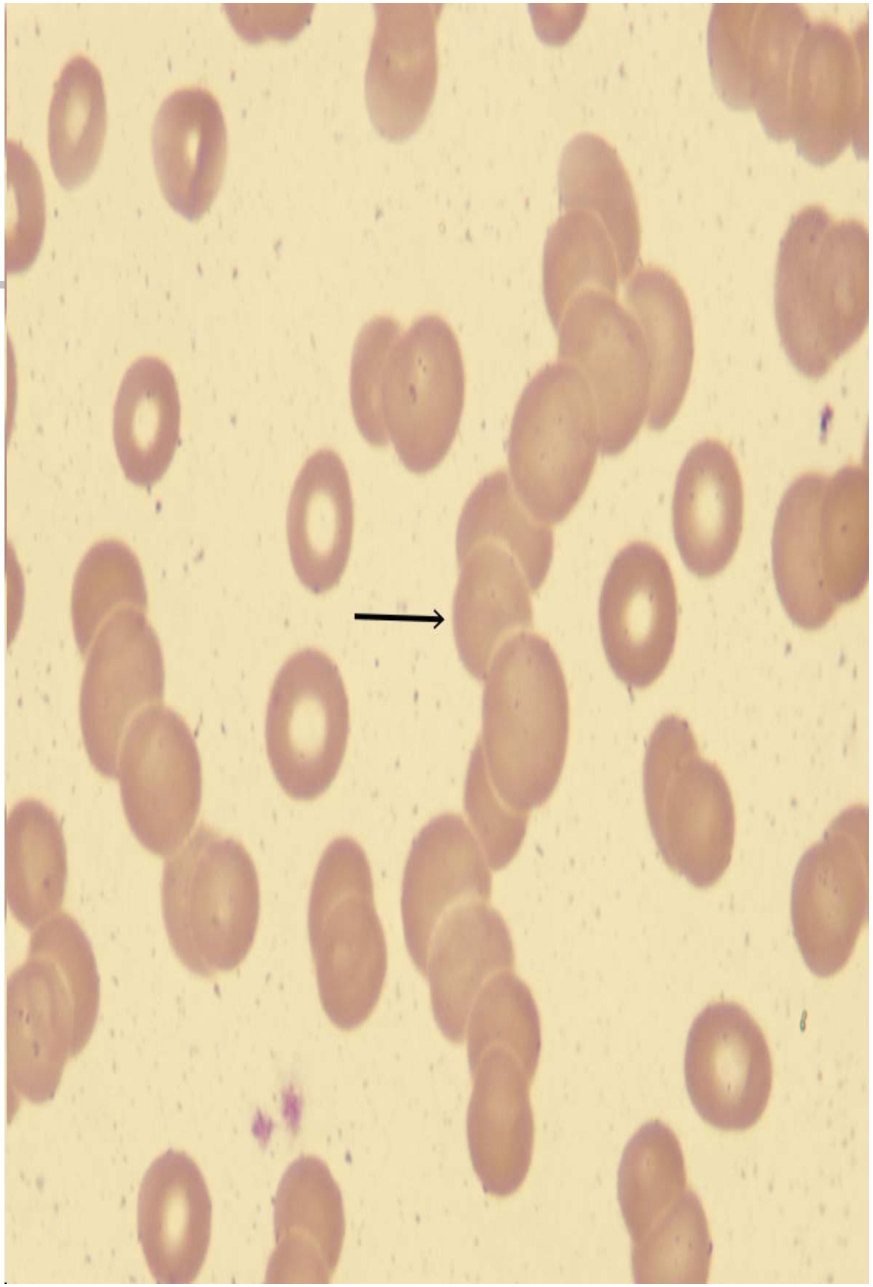
Diameter	: 7.2micron(6.9-7.4micron)
Thickness	: At the periphery it is thicker with 2.2micron & at center it is thinner with 1micron
Surface area	: 120 sq m.
Volume	: 85-90 cu m.

- **Normal Structure**

The RBC is non-nucleated formed elements in the blood. So,DNA is absent mitochondria also are absent and energy is produced from glycolytic process. Golgi apparatus are also absent in RBC. Red cell does not have any insulin receptor and so the glucose uptake by this cell is not controlled by insulin



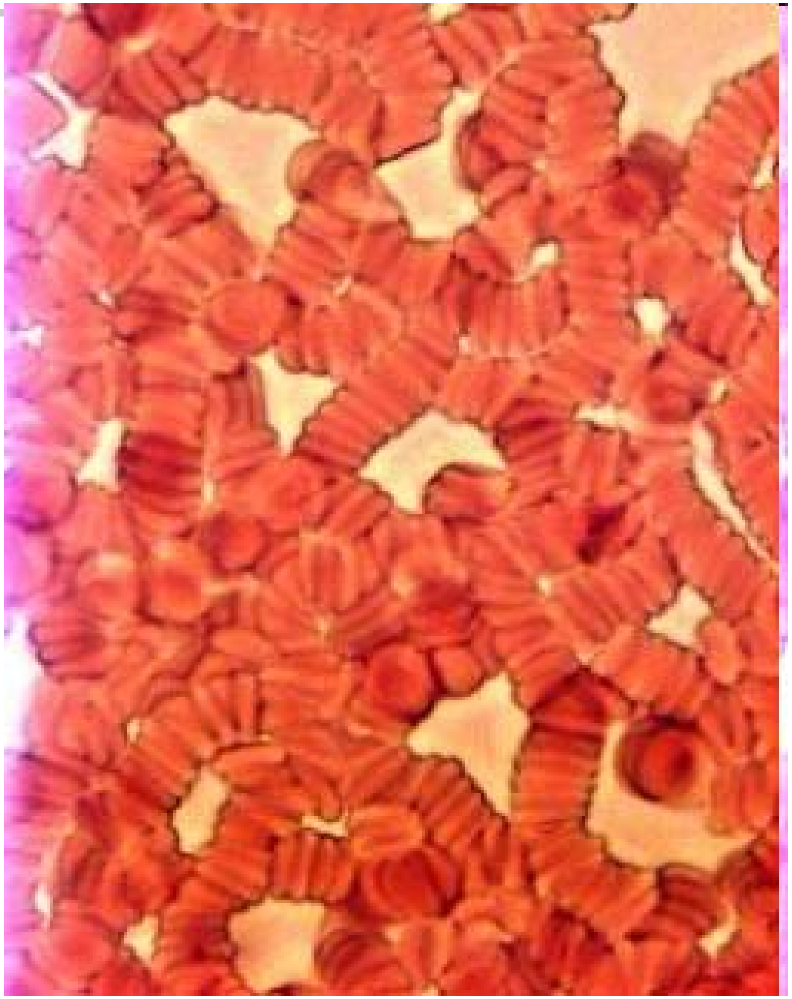
RBC has a special type of cytoskeleton which is made up of actin and spectrin. Both the proteins are anchored to Transmembrane proteins but means of another proteins called ankyrin. The absence of spectrin results in Hereditary Spherocytosis.



Properties Of Red Blood Cells

1. **Rouleaux formation**

When blood is taken out of the blood vessel, the RBCs pile up one above the other like the pile of coins. This property of RBC is called as Rouleaux formation

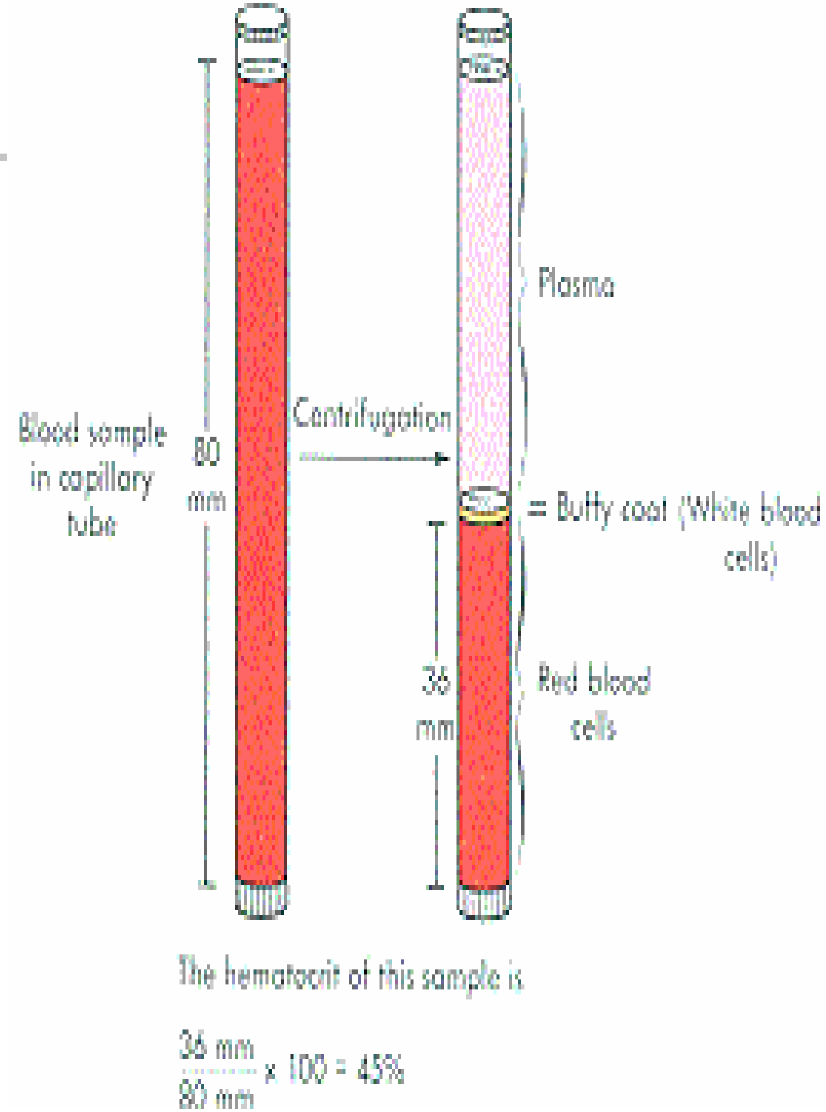


2. Specific Gravity

The specific gravity of RBC is 1.092 to 1.101

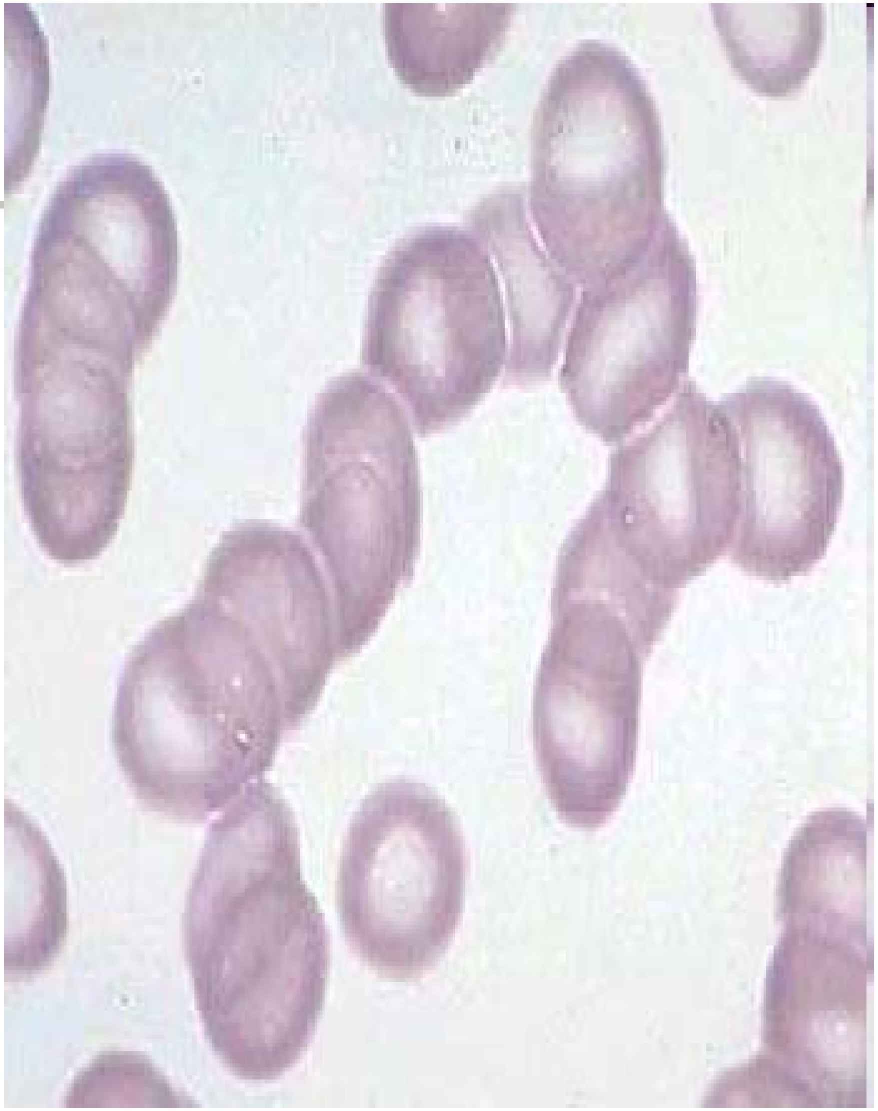
3. Packed cell volume

When the blood is collected in the centrifuge tube along with proper anticoagulant and centrifuged for the period of 30 minutes at the speed of 3000 rpm, the RBCs settle at the bottom of the tube leaving behind clear plasma at the top. The RBCs form 45% of the total blood. This is called as packed cell volume or hematocrit



4. **Suspension Stability**

During circulation, the RBC remain suspended uniformly in the blood. This property is called as suspension stability



Variations Of RBC

- In Number

  -Physiological Variations (Increase & Decrease)

  -Pathological Variations

- Increase in RBC count due to physiological variations are as follows:-

1. Age

At birth the RBC count is 8-10 millions/cu mm of blood. The count decreases within 10 days after birth due to destruction of RBCs causing physiological jaundice in some infants. However in infants and growing children the cell count is more than the value in adults.

2. <u>Sex</u>

Before puberty and after menopause in females the RBC count is similar to that in males. During reproductive period in females, the count is less than in males (4.5 millions/cu mm).

3. High Altitude

The inhabitants of mountains (above 10,000 feet from mean sea level) have an increased RBC count of more than 7 millions/cu mm. It is due to hypoxia (decreased oxygen supply in the tissues) in high altitude. During hypoxia, a hormone called erythropoietin is released from the kidneys. The erythropoietin in turn stimulates the bone marrow to produce RBCs.

4. <u>Muscular Exercise</u>

There is a temporary increase in RBC count after exercise. It is because of mild hypoxia and contraction of spleen. Spleen stores small quantity of blood and so it is called as reservoir of blood.

5. <u>Emotional Conditions</u>

The RBC count is increased during emotional conditions like anxiety, because of sympathetic stimulation.

6. Increased Environmental Temperature

The increase in the atmospheric pressure increases the RBC count.

7. After Meals

There is a slight increase in RBC count after taking meals

Decrease in RBC count due to physiological variations are as follows:-

1. <u>High Barometric Pressures</u>

   At high barometric pressures as in deep sea, when the oxygen tension of blood is higher, the RBC count decreases.

2. <u>During Sleep</u>

The RBC count slightly decreases during sleep and immediately after getting up from sleep.

3. <u>Pregnancy</u>

In Pregnancy, the RBC count decreases. It is because of increases in ECF volume. Increase in ECF volume, increases in plasma volume also resulting in hemodilution. So, there is relative reduction in RBC count.

Pathological Variations

- Pathological Polycythemia

The abnormal increase in the RBC count is called pathological Polycythemia. The red cell count increases above 7 millions/cu mm of the blood. Polycythemia is of 2 types:-

1. Primary Polycythemia
2. Secondary Polycythemia

1.Primary Polycythemia

Primary Polycythemia is also known as Polycythemia Vera. Its is a disease with Persistent increase in RBC count above 14 millions/cu mm of blood. This is always associated with increased white blood cell count above 24,000/cu mm of blood. Polycythemia Vera occurs in Myeloproliferative disorders like malignancy of red bone marrow

2.Secondary Polycythemia

This is secondary to some of the pathological conditions such as:

1. Respiratory disorders like emphysema
2. Congenital disease
3. Ayerza’s disease-associated with hypertrophy of R.ventricle & obstruction of blood flow to lungs
4. Chronic carbon monoxide poisoning
5. Poisoning by chemicals like phosphorus and arsenic
6. Repeated mild hemorrhages

Variations in size of RBC

Under physiological conditions, the size of RBC in venous blood is slightly larger then those in arterial blood. The variations in size of RBC are:-

1. Microcytes – decrease in size
2. Macrocytes – increase in size
3. Anisocytosis – cells without uniform size

1. <u>Microcytes</u>

Microcytes are present in:

i. Iron deficiency anemia

ii. Prolonged forced breathing

iii. Increased osmotic pressure in blood

2. <u>Macrocytes</u>

Macrocytes are present in:

i. Megaloblastic anemia

ii. Muscular exercise

iii. Decreased osmotic pressure in blood

3. <u>Anisocytes</u>

Anisocytes occur in pernicious anemia.

Variations in shape of RBC

The shape of RBC is altered in many conditions including different types of anemia

1. Crenation: shrinkage as in hypertonic solution
2. Spherocytosis: globular form as in hypotonic solution
3. Elliptocytosis: elliptical shape as in certain types of anemia
4. Sickle cell: crescentic shape as in sickle cell anemia
5. Poikilocytosis: unequal shapes due to deformed cell membrane. Shapes can be flask, hammer or any other unusual shape

- Variations in structure of RBC

1. Punctate Basophilism

   The striated appearance of RBCs by the presence of dots of basophilic materials is called as Punctate Basophilism. It occurs in condition like lead poisoning.

2. Ring

   Ring or twisted strands of basophilic materials appear in the periphery of RBCs. This is also called as Goblet ring. It appears in RBC in certain types of anemia.

3. Howell-Jolly Bodies

   In certain types of anemia, some nuclear fragments are present in the ectoplasm of the RBCs. These nuclear fragments are called as Howell-Jolly Bodies

Functions Of RBC

1. **Transport of oxygen from the lungs to the tissues**

   Hemoglobin in RBC combines with oxygen to form oxyhemoglobin. About 97% of oxygen is transported in the blood in the form of oxyhemoglobin.

2. **Transport of carbon dioxide from the tissues to the lungs**

Hemoglobin combines with carbon dioxide and form carbhemoglobin. About 30% of carbon dioxide is transported in this form.

RBCs contain a large amount of the carbonic anhydrase. This enzyme is necessary for the formation of bicarbonate from water & carbon dioxide. Thus it helps to transport carbon dioxide in the from of bicarbonate from tissues to lungs. About 63% of carbon dioxide is transported in this form.

3. **Buffering action in blood**

Hemoglobin functions as good buffer. By this action it regulates the hydrogen ion concentration and thereby plays an important role in the maintenance of acid base balance.

4. **Blood group determination**

RBCs carry the blood group antigens like A agglutinogen, B agglutinogen and Rh factor. This helps in determining the blood group and enables to prevent reactions due to incompatible blood transfusion.

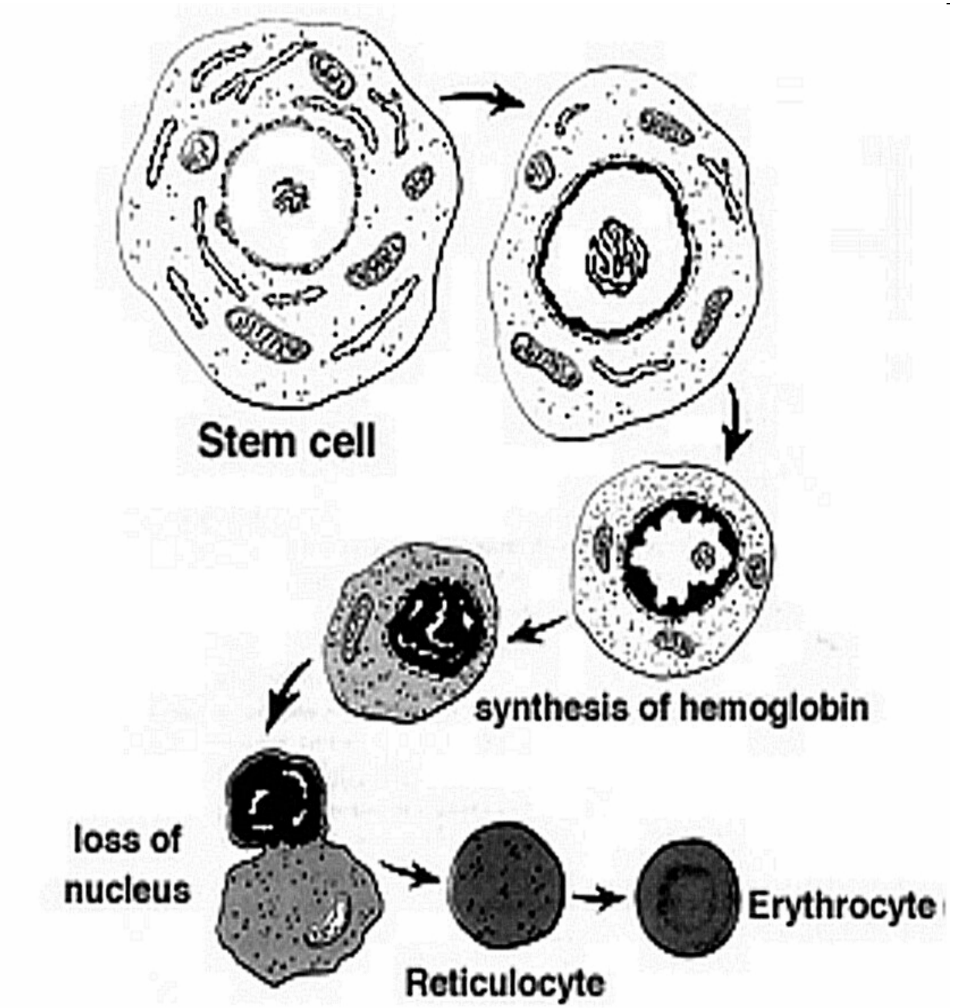
(C) Erythropoiesis

- Introduction Of Erythropoiesis
- Site Of Erythropoiesis
- Process Of Erythropoiesis
- Changes During Erythropoiesis
- Stages Of Erythropoiesis
- Factors Necessary for Erythropoiesis

Introduction Of Erythropoiesis

Definition

Erythropoiesis is the process which involves the origin, development and maturation of erythrocytes. Hemopoiesis of Hematopoiesis is the process which includes origin, development and maturation of all the blood cells



Site Of Erythropoiesis

(i) IN FETAL LIFE

In fetal life, the erythropoiesis occurs in three stages

1. Mesoblastic Stage
2. Hepatic Stage
3. Myeloid Stage

(ii) IN NEWBORN BABIES AND ADULTS

(i) IN FETAL LIFE

1. **Mesoblastic Stage**

   During the first two months of interuterine life, the RBCs are produced from mesenchyme of the yolk sac

2. **Hepatic Stage**

   From the third month of interuterine life, liver is the main organ that produces red blood cells. Spleen and lymphoid organs also produce some erythrocytes.

3. **Myeloid Stage**

   During the last three months of interuterine life, the RBCs are produced from red bone marrow and liver

(ii) IN NEWBORN BABIES AND ADULTS

In this stage the RBCs are produced from red bone marrow.

1. Up to the age of 5 to 6 years- from red bone marrow of all bones.
2. From the age of 6 years to 20 years- from red bone marrow of long bone and all membranous flat) bones.
3. After the age of 20 years- from membranous bones like vertebra, sternum, ribs, scapula, iliac bones and skull bones and from the ends of long bones. The shaft of long bones becomes yellow bone marrow because of fat deposition and looses the erythropoietic function.

During bone disorders, the RBCs are produced in spleen.

Process Of Erythropoiesis

- Stem Cells

The stem cells are primitive cells in the bone marrow, which give rise to all blood cells. Stem cells is defined as a cell which is capable of both self-renewal and differentiation.

Pluripotent Hemopoietic stem cell (PHSC) are derived from the stem cells. It is defined as the cell that can give rise to cells of all groups of Hemopoietic cells like myeloid cells and lymphoid cells. In early stages, the PHSC are not designed from a particular type of blood cell. So at this stage, the PHSC are called as uncommitted Pluripotent Hemopoietic stem cell (uncommitted PHSC).

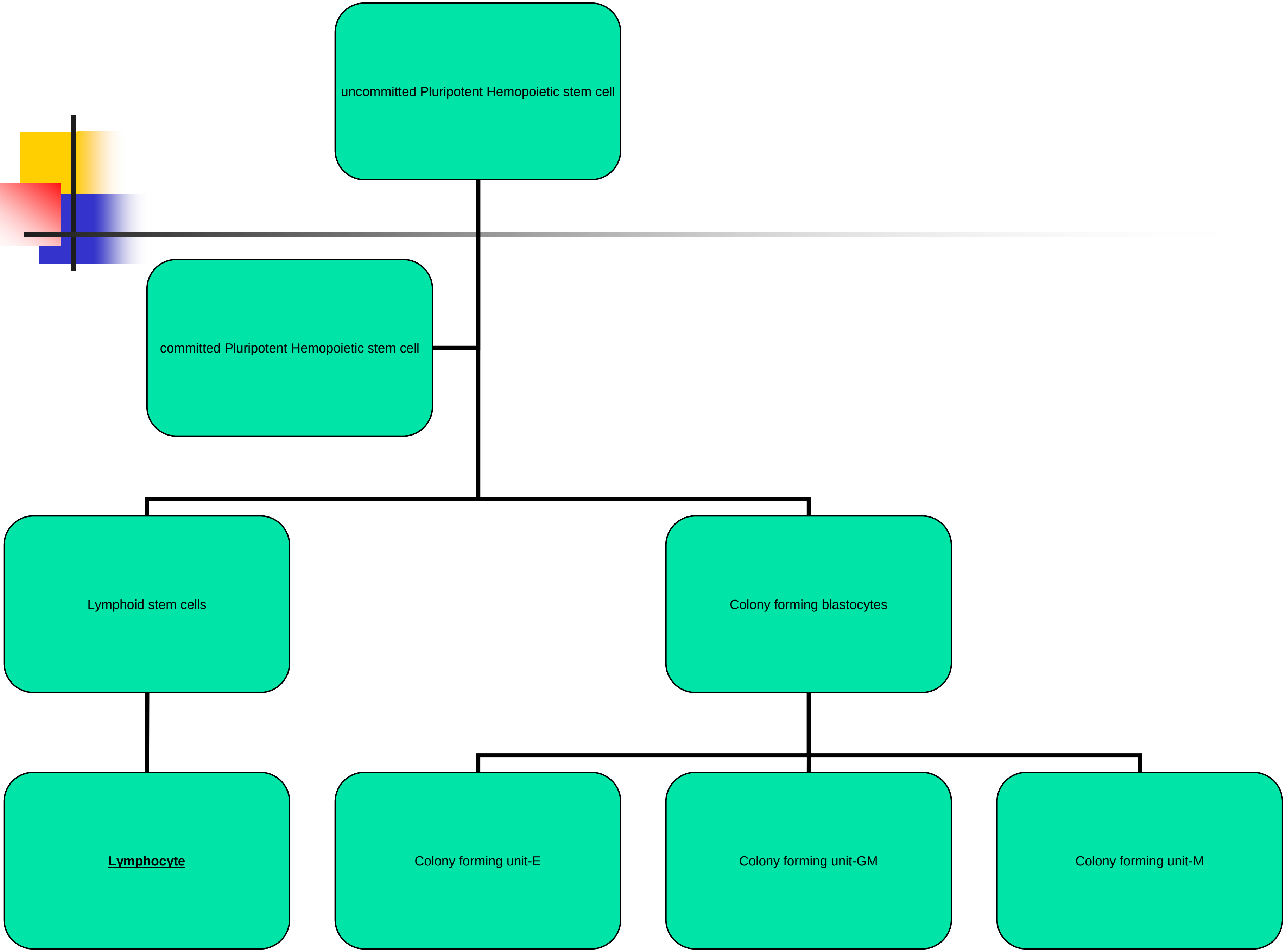
When the cells are designed from a particular type of blood cell, the uncommitted PHSC are called as committed Pluripotent Hemopoietic stem cell (committed PHSC). Committed PHSC is defined as a cell which is restricted to give rise to one group of Hemopoietic cells.

The committed PHSC cells are of two types:

1. Lymphoid stem cells (LSC) which give rise to lymphocytes and natural killer (NK) cells
2. Colony forming blastocytes which give rise to myeloid cells, blood cells other than lymphocytes. When grow in cultures, these cells form colonies hence the name colony forming blastocytes.

The different units of colony forming cells are:-

- Colony forming unit–erythrocytes (CFU-E). The stem cells develop into erythrocytes.
- Colony forming unit–granulocytes/monocytes (CFU-GM). These cells give rise to granulocytes (Neutrophils, basophils and eosinophils) or Monocytes.
- Colony forming unit–megakaryocytes (CFU-M) Platelets develop from these cells.


uncommitted Pluripotent Hemopoietic stem cell
committed Pluripotent Hemopoietic stem cell
Lymphoid stem cells
Colony forming blastocytes
Lymphocyte
Colony forming unit-E
Colony forming unit-GM
Colony forming unit-M

Changes During Erythropoiesis

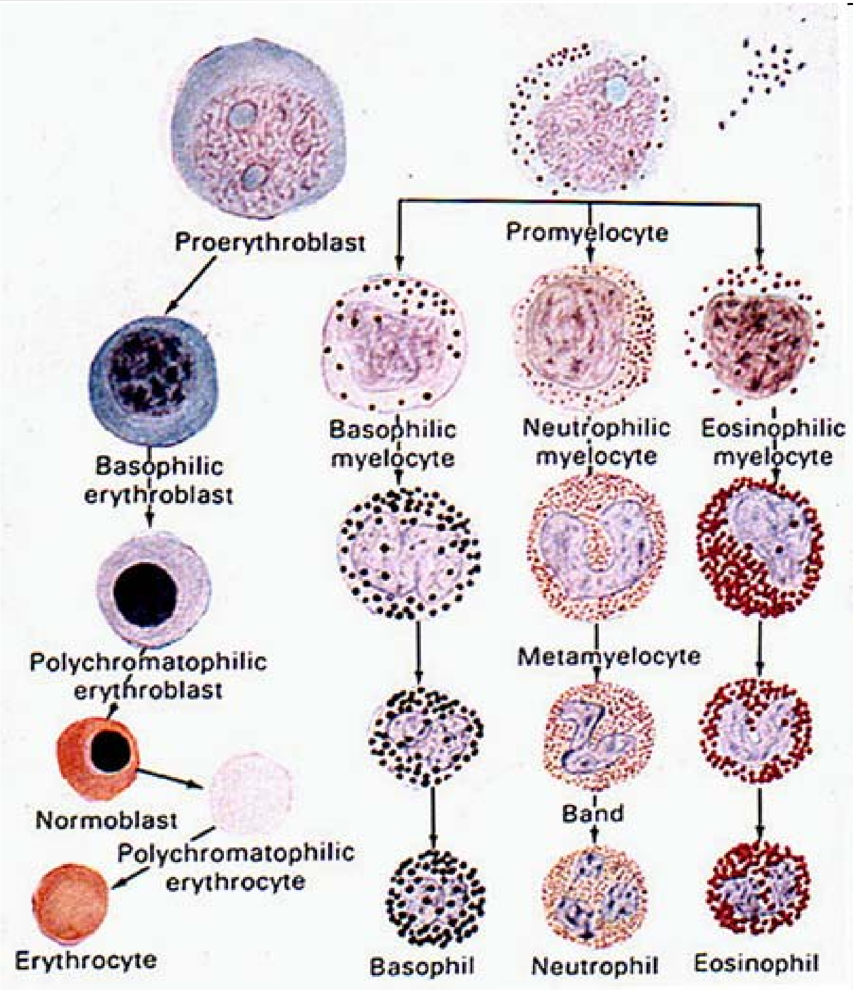
The stem cells of the colony forming unit-E (CFU-E) pass through different stages and finally becomes mature RBCs. During these stages four important stages are noticed.

1. Reduction in size of the cell
2. Disappearance of nucleoli and nucleus
3. Appearance of hemoglobin
4. Change in staining properties of cytoplasm

Stages Of Erythropoiesis

The various stages between stem cell and matured RBC are

1. Proerythroblast
2. Early Normoblast
3. Intermediate Normoblast
4. Late Normoblast
5. Reticulocyte
6. Matured erythrocyte



1. Proerythroblast

Proerythroblast or megaloblast is the first cell derived from stem cell (CFU-E). It is very large in size with a diameter of 20 micron. Its nucleus is large and occupies the cell almost completely. The nucleus has two more nucleoli and a reticular network. The Proerythroblast does not contain hemoglobin. The cytoplasm is basophilic in nature. The Proerythroblast multiplies several times and finally forms the cell of next stage called as Early Normoblast

2. Early Normoblast

It is little smaller with a diameter of about 15 micron. 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 as basophilic erythroblast. This cell develops into Intermediate Normoblast

3. Intermediate Normoblast

This cell is smaller than the early normoblast with a diameter of 10-12 micron. The nucleus is still present. But, the chromatin network shows further condensation. The hemoglobin starts appearing.

The 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 as polychromophilic erythroblast. This cell develops into Late Normoblast

4. Late Normoblast

The diameter of the cell decreases further to about 8-10 micron. 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 as orthochromic erythroblast. In late normoblast, 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 reticulocyte.

5. Reticulocyte

It is also know as immature RBC. It is slightly larger then immature 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 as Reticulocyte. The reticulum of Reticulocyte stains with supravital stain.

In new born babies, the Reticulocyte count is 2-6% of RBCs, i.e. 2-6 Reticulocytes are present for every 100% of RBCs. The number of Reticulocytes decreases during the first week after birth. Later, the Reticulocyte count remains constant at or below 1% of RBCs. The number increases whenever production and release of RBCs increase.

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

6. Matured erythrocyte

Now, the reticular network disappears and the cell becomes matured RBC. The matured RBC is biconcave and it is smaller in size with a diameter of 7.2 micron attaining biconcave shape. It is with hemoglobin and without nucleus.

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

Factors Necessary for Erythropoiesis

Development and maturation of Erythrocytes require variety of factored which are classified into 3 categories:-

1. General factors
2. Maturation factors
3. Factors necessary for hemoglobin formation

1. General factors

General factors necessary for Erythropoiesis are:-

a. Erythropoietin

b. Thyroxin

c. Hemopoietic growth factors

d. Vitamins

a. Erythropoietin

The most important general factor for Erythropoiesis is hormone Erythropoietin. It is also called Hemopoietic or erythrocyte stimulating factors. Erythropoietin is a glycoprotein. It is secreted by peritubular capillaries of kidney. Hypoxia is the stimulant for the secretion of Erythropoiesis.

- Actions of Erythropoietin

Erythropoietin causes formation and release of new RBCs into circulation. After secretion, it takes 4 to 5 days to show the action.

Erythropoietin promotes following processes:

(i). Production of proerythroblasts from the stem cells in CFU-E of the bone marrow.

(ii). Development of proerythroblasts into matured RBCs through normoblastic stages

(iii). Released of matured erythrocytes into blood. Even some Reticulocytes are released along with matured RBCs

b. Thyroxin

Being a general metabolic hormone thyroxine accelerates the processes of Erythropoiesis at many levels. So, polycythemia is common in hyperthyroidism.

c. Hemopoietic growth factors

Hemopoietic growth factors or growth inducers are the interleukins and stem cell factor. These factors induce the proliferation of pluripotent stem cells.

Interluekins are glycoproteins. The Interluekins in Erythropoiesis are:-

i. Interluekin-3 (IL-3) secreted by T cells
ii. Interluekin-6 (IL-6) secreted by T cells, endothelial cells and macrophages
iii. Interluekin-11 (IL-11) secreted by Osteoblast

d. Vitamins

Some vitamins are also necessary for process of Erythropoiesis the deficiency of these vitamins cause anemia associated with other disorders. The vitamins which are necessary for Erythropoiesis are:

i. Vitamin B: its deficiency causes anemia and pellagra

ii. Vitamin C: its deficiency causes anemia and scurvy

iii. Vitamin D: its deficiency causes anemia and rickets

iv. Vitamin E: its deficiency leads to anemia and malnutrition

2. Maturation factors

Vitamin B12, intrinsic factor and folic acid are necessary for maturation of RBCs

1. Vitamin B12 (cyanocobalamin)

This is essential for maturation of erythrocytes. The deficiency of Vitamin B12 causes pernicious anemia. So, Vitamin B12 is called antipernicious factor.

Source of Vitamin B12

Vitamin B12 is called extrinsic factor because it is obtained mostly from diet. Its absorption from the intestine requires the presence of intrinsic factor of Castle. Vitamin B12 is stored mostly in liver and in small quantity in muscle.

When necessary, Vitamin B12 is transported to the bone marrow to promote malnutrition of RBCs. It is produced in large quantities in intestinal flora

Action of Vitamin B12

Vitamin B12 is essential for synthesis of DNA. Its deficiency leads to failure in malnutrition of the cell and reduction in cell division. Also the cells are larger with fragile weak cell membrane

2. Intrinsic factor of Castle

It is produced from gastric mucosa and it is essential for absorption of Vitamin B12 from intestine into the blood. In the absence of intrinsic factor, Vitamin B12 is not absorbed. This happens to severe gastritis, ulcers and gastrectomy. The deficiency of intrinsic factor also causes pernicious anemia. Since vitamin B12 is not absorbed. The extrinsic and intrinsic factors are together called as Hematinic principle

3. Folic Acid

Folic Acid is also essential for maturation. It is required for synthesis of DNA. In the absence of Folic Acid, the synthesis of DNA decreases causing failure of maturation. This leads to anemia which, the cells are larger and appear in megaloblastic stage. And the anemia due to folic acid deficiency is called as megaloblastic anemia

3. <u>Factors necessary for hemoglobin formation</u>

Various materials are essential for the formation of hemoglobin in the RBCs. The deficiency of these Substances decreases the production of hemoglobin leading to anemia. Such factors are:-

1. <u>First class proteins & amino acids:</u> proteins of high biological value are essential for formation of hemoglobin. Amino acids derived from these proteins are required for the synthesis of protein part of hemoglobin.
2. <u>Iron:</u> it is necessary for the formation of heme part of the hemoglobin
3. <u>Copper:</u> it is necessary for the absorption of iron from gastrointestinal tract.
4. <u>Cobalt & nickel:</u> it is essential for the utilization of iron during hemoglobin formation
5. <u>Vitamins:</u> VitaminC, Riboflavin, nicotic acid & pyridoxine are essential for the formation of hemoglobin.

THANK YOU…