
Physiology of blood

Red Blood Cells (Erythrocytes)

Erythrocytes : are the most abundant cells of the blood and are necessary for the delivery of oxygen to the tissues.

The major function of red blood cells, also known as erythrocytes, is to transport hemoglobin, which in turn carries oxygen from the lungs to the tissues.

The red blood cells have other functions besides transport of hemoglobin. For instance, they contain a large quantity of carbonic anhydrase, an enzyme that catalyzes the reversible reaction between carbon dioxide (CO₂) and water to form carbonic acid (H₂CO₃), increasing the rate of this reaction several thousand fold.

The rapidity of this reaction makes it possible for the water of the blood to transport enormous quantities of CO₂ in the form of bicarbonate ion (HCO₃⁻) from the tissues to the lungs, where it is reconverted to CO₂ and expelled into the atmosphere as a body waste product.

➤ Shape and Size of Red Blood Cells

Normal red blood cells are biconcave discs having a mean diameter of about 7.8 micrometers and a thickness of 2.5 micrometers at the thickest point and 1 micrometer or less in the center.

The shapes of red blood cells can change remarkably as the cells squeeze through capillaries. Actually, the red blood cell is a “bag” that can be deformed into almost any shape.

Furthermore, because the normal cell has a great excess of cell membrane for the quantity of material inside, deformation **does not** stretch the membrane greatly and, consequently, does not rupture the cell, as would be the case with many other cells.

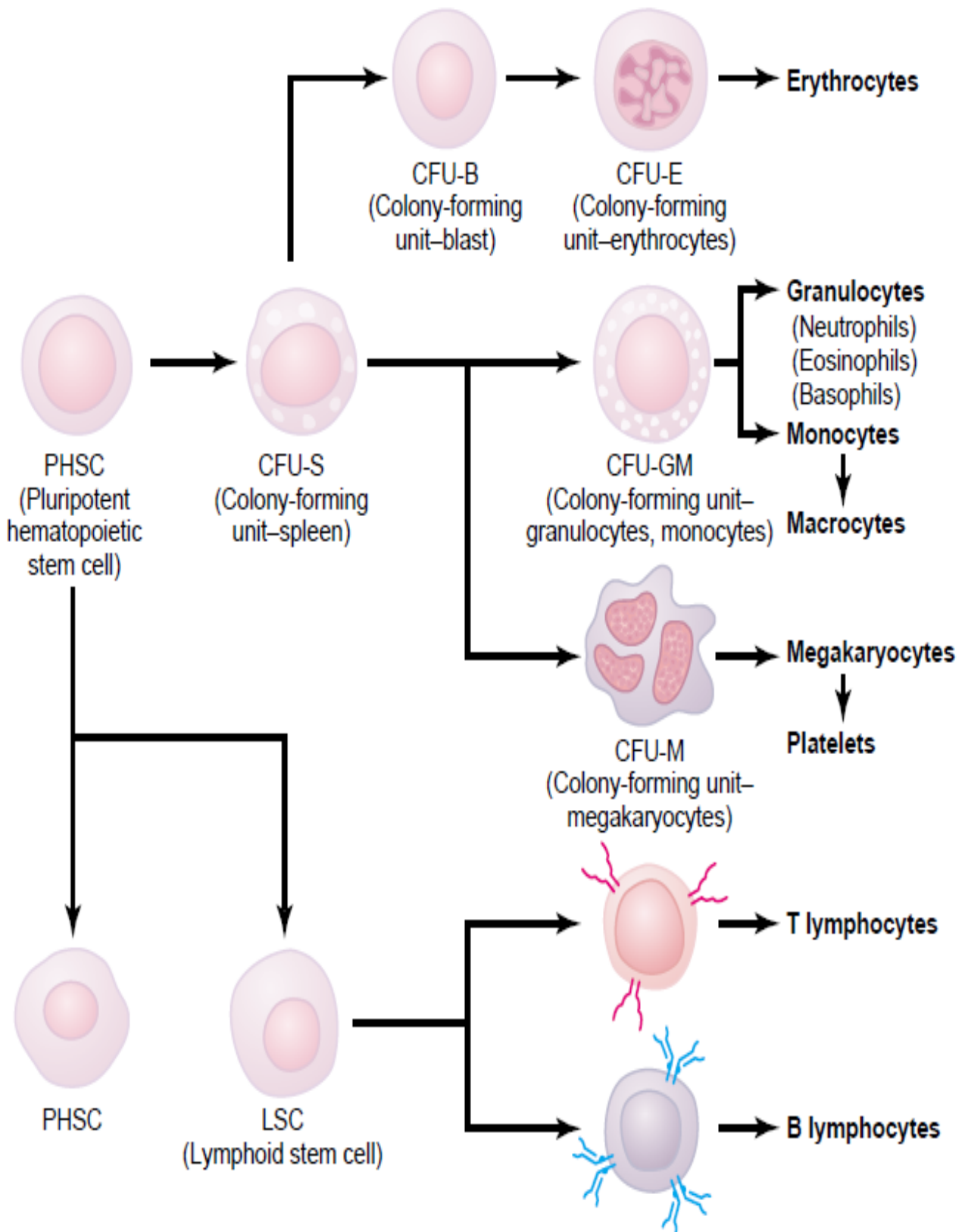
Concentration of Red Blood Cells in the Blood. In normal men, the average number of red blood cells per cubic millimeter is 5,200,000 ($\pm 300,000$); in normal women, it is 4,700,000 ($\pm 300,000$). Persons living at high altitudes have **greater** numbers of red blood cells.

➤ Production of Red Blood Cells

Areas of the Body That Produce Red Blood Cells. In the early weeks of embryonic life, primitive, nucleated red blood cells are produced in the **yolk sac**. During the middle trimester (ثلاث اشهر) فصل of gestation (الحمل), the **liver** is the main organ for production of red blood cells, but reasonable numbers are also produced in the spleen and lymph nodes. Then, during the last month or so of gestation and after birth, red blood cells are produced exclusively in the **bone marrow**.

➤ Genesis of Blood Cells

The blood cells begin their lives in the bone marrow from a single type of cell called the pluripotential hematopoietic **stem cell**, from which all the cells of the circulating blood are eventually derived.



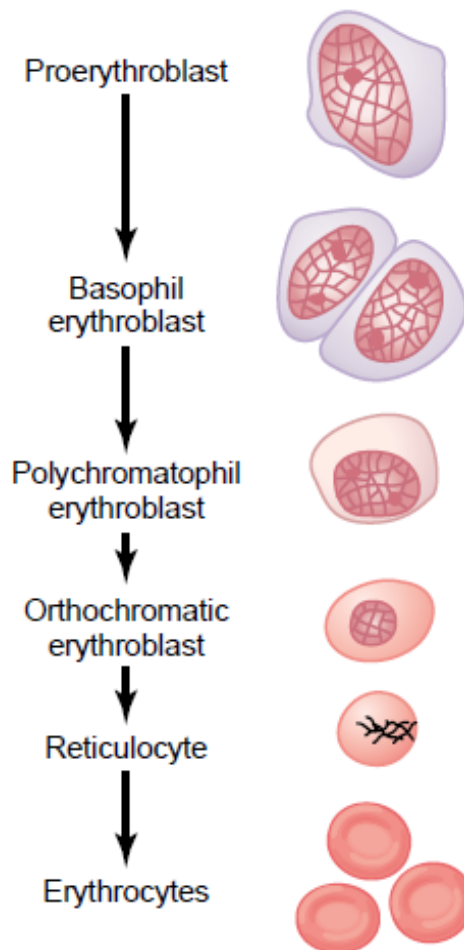
➤ **Stages of Differentiation of Red Blood Cells**

The first cell that can be identified as belonging to the red blood cell series is the **proerythroblast** . Under appropriate stimulation, large numbers of these cells are formed from the CFU-E stem cells.

Once the proerythroblast has been formed, it divides multiple times, eventually forming many mature red blood cells. The first-generation cells are called **basophil** erythroblasts because they stain with basic dyes; the cell at this time has accumulated very little hemoglobin. In the succeeding generations , the cells become filled with hemoglobin to a concentration of about 34 per cent, the nucleus condenses to a small size, and its final remnant is absorbed or extruded from the cell. At the same time, the endoplasmic reticulum is also reabsorbed. The cell at this stage is called a **reticulocyte** because it still contains a small amount of basophilic material, consisting of remnants of the Golgi apparatus, mitochondria, and a few other cytoplasmic organelles. During this reticulocyte stage, the cells pass from the bone marrow into the blood capillaries by diapedesis (squeezing through the pores of the capillary membrane) .

The remaining basophilic material in the reticulocyte normally disappears within 1 to 2 days, and the cell is then a mature erythrocyte. Because of the short life of the reticulocytes, their concentration among all the red cells of the blood is normally slightly less than 1 per cent.

GENESIS OF RBC



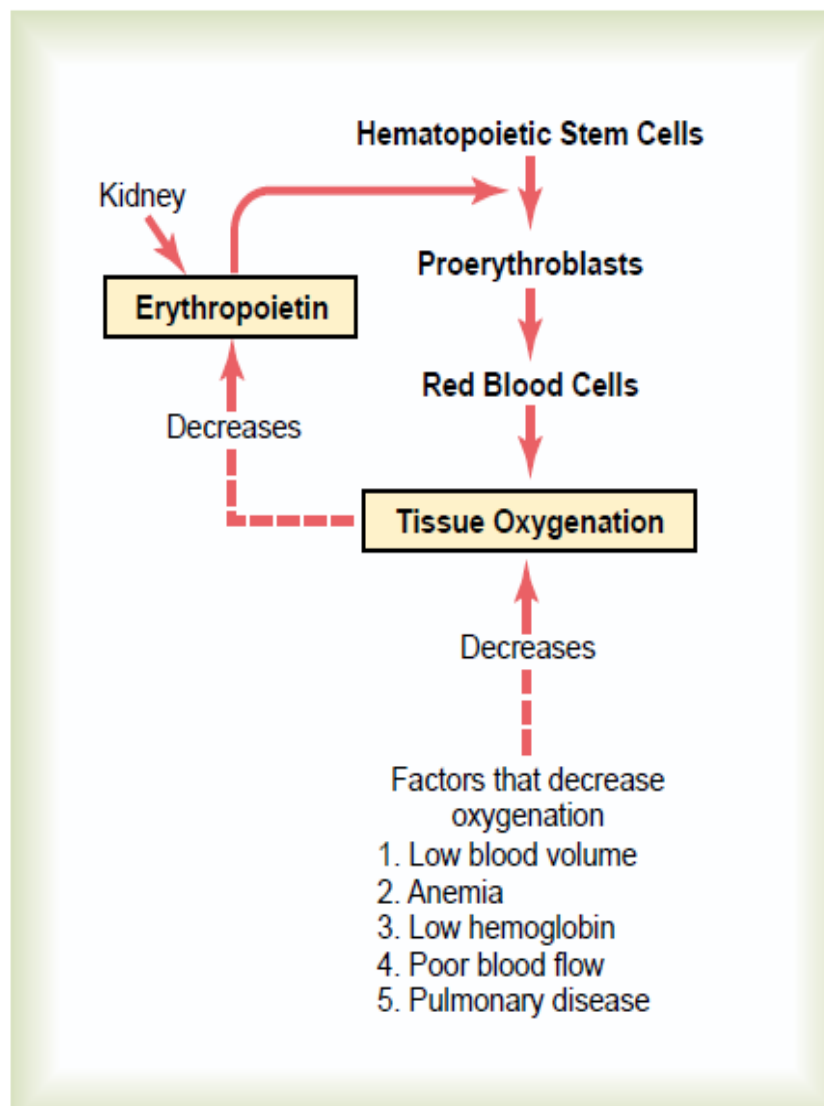
➤ Regulation of Red Blood Cell Production

The total mass of red blood cells in the circulatory system is regulated within narrow limits, so that (1) an adequate number of red cells is always available to provide sufficient transport of oxygen from the lungs to the tissues, yet (2) the cells do not become so numerous that they impede blood flow.

Tissue Oxygenation Is the Most Essential Regulator of Red Blood Cell Production. Any condition that causes the quantity of oxygen transported to the tissues to decrease ordinarily increases the rate of red blood cell production. Thus, when a person becomes extremely anemic as a result of hemorrhage or any other

condition, the bone marrow immediately begins to produce large quantities of red blood cells. Also, destruction of major portions of the bone marrow by any means, especially by x-ray therapy, causes hyperplasia of the remaining bone marrow, thereby attempting to supply the demand for red blood cells in the body.

At very high altitudes, where the quantity of oxygen in the air is greatly decreased, insufficient oxygen is transported to the tissues, and red cell production is greatly increased. In this case, it is not the concentration of red blood cells in the blood that controls red cell production but the amount of oxygen transported to the tissues in relation to tissue demand for oxygen.



✓ The principal stimulus for red blood cell production in low oxygen states is a circulating hormone called **erythropoietin** . In the absence of erythropoietin, **hypoxia** has little or no effect in stimulating red blood cell production. But when the erythropoietin system is functional, hypoxia causes a marked increase in erythropoietin production, and the erythropoietin in turn enhances red blood cell production until the hypoxia is relieved.

In the normal person, about 90 per cent of all erythropoietin is formed in the **kidneys**; the remainder is formed mainly in the liver.

Hemoglobin (Hb) :

Is the red coloring pigment and the O₂ binding protein of RBC . It forms 95% of the dry weight of RBC . The function of hemoglobin is to carry O₂ and CO₂ .

If Hb is found in plasma as free hemoglobin it leads to the following problems :

- 1- Increases the viscosity of blood leading to an increase in blood pressure .
- 2- Increase in the osmotic pressure of blood .
- 3- Free Hb will be filtered & excreted by the kidneys leading to hemoglobinuria , renal failure and anemia .

Quantity of Hemoglobin in the Cells:

Red blood cells have the ability to concentrate hemoglobin in the cell fluid up to about 34 grams in each 100 milliliters of cells. whole blood of men contains an average of 15 grams of hemoglobin per 100 milliliters of cells; for women, it contains an average of 14 grams per 100 milliliters.

Life Span and Destruction of Red Blood Cells

When red blood cells are delivered from the bone marrow into the circulatory system, they normally circulate an average of 120 days before being destroyed.

Even though mature red cells do not have a nucleus, mitochondria, or endoplasmic reticulum, they do have cytoplasmic enzymes that are capable of metabolizing glucose and forming small amounts of adenosine triphosphate.

These enzymes also (1) maintain pliability ليونة of the cell membrane, (2) maintain membrane transport of ions, (3) keep the iron of the cells' hemoglobin in the ferrous form rather than ferric form, and (4) prevent oxidation of the proteins in the red cells.

Even so, the metabolic systems of old red cells become progressively less active, and the cells become more and more fragile, presumably because their life processes wear out.

Once the red cell membrane becomes fragile, the cell ruptures during passage through some tight spot of the circulation. Many of the red cells self-destruct in the spleen, where they squeeze through the red pulp of the spleen.

When the spleen is removed, the number of old abnormal red cells circulating in the blood increases considerably.

Destruction of Hemoglobin.

When red blood cells burst and release their hemoglobin, the hemoglobin is phagocytized almost immediately by macrophages in many parts of the body, but especially by the **Kupffer** cells of the liver and macrophages of the spleen and bone marrow. During the next few hours to days, the macrophages release iron from the hemoglobin and pass it back into the blood, to be carried by transferring either to the bone marrow for the production of new red blood cells or to the liver and other tissues for storage in the form of ferritin.

Anemias

Anemia means deficiency of hemoglobin in the blood, which can be caused by either too few red blood cells or too little hemoglobin in the cells. Some types of anemia and their physiologic causes are the following.

1- Blood Loss Anemia : After rapid hemorrhage, the body replaces the fluid portion of the plasma in 1 to 3 days, but this leaves a low concentration of red blood cells. If a second hemorrhage does not occur, the red blood cell concentration usually returns to normal within 3 to 6 weeks.

In chronic blood loss, a person frequently cannot absorb enough iron from the intestines to form hemoglobin as rapidly as it is lost. Red cells are then produced that are much smaller than normal and have too little hemoglobin inside them, giving rise to microcytic hypochromic anemia .

2- Aplastic Anemia : Bone marrow aplasia means lack of functioning bone marrow. For instance, a person exposed to gamma ray radiation from a nuclear bomb blast can sustain complete destruction of bone marrow, followed in a few weeks by lethal anemia.

Likewise, excessive x-ray treatment, certain industrial chemicals, and even drugs to which the person might be sensitive can cause the same effect.

3- Megaloblastic Anemi : loss of any one of vitamin B12, folic acid, and intrinsic factor from the stomach mucosa, can lead to slow reproduction of erythroblasts in the bone marrow. As a result, the red cells grow too large, with odd shapes, and are called megaloblasts , those red cells that are formed are mostly oversized, have bizarre shapes, and have fragile membranes. These cells rupture easily, leaving the person in dire need of an adequate number of red cells.

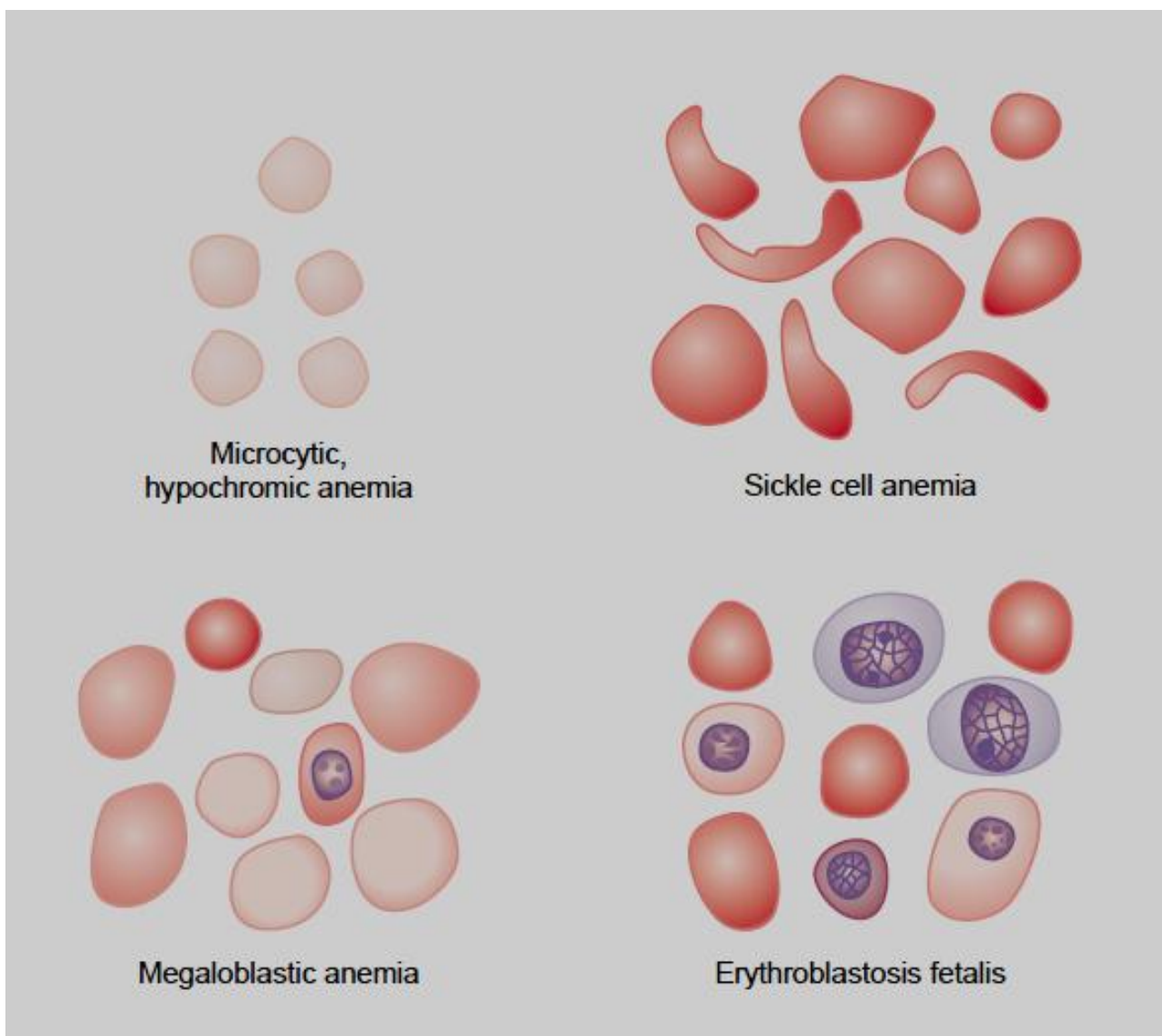
4- Hemolytic Anemia : Different abnormalities of the red blood cells, many of which are hereditarily acquired, make the cells fragile, so that they rupture easily as they go through the capillaries, especially through the spleen. Even though the number of red blood cells formed may be normal, or even much greater than normal in some hemolytic diseases, the life span of the fragile red cell is so short that the cells are destroyed faster than they can be formed, and serious anemia results. Some of these types of anemia are the following : -

a- In hereditary spherocytosis, the red cells are very small and spherical rather than being biconcave discs.

These cells cannot withstand تصدق compression forces because they do not have the normal loose, baglike cell membrane structure of the biconcave discs. On passing through the splenic pulp and some other tight vascular beds, they are easily ruptured by even slight compression.

b- In sickle cell anemia, which is present in 0.3 to 1.0 per cent of West African and American blacks, the cells have an abnormal type of hemoglobin called *hemoglobin S* . When this hemoglobin is exposed to low concentrations of oxygen, it precipitates into long crystals inside the red blood cell .These crystals elongate the cell and give it the appearance of a sickle rather than a biconcave disc. The precipitated hemoglobin also damages the cell membrane, so that the cells become highly fragile, leading to serious anemia. Once the process starts, it progresses rapidly, eventuating in a serious decrease in red blood cells within a few hours and, often, death.

c- In **erythroblastosis fetalis**, Rh-positive red blood cells in the fetus are attacked by antibodies from an Rh-negative mother. These antibodies make the Rh-positive cells fragile, leading to rapid rupture and causing the child to be born with serious anemia. The extremely rapid formation of new red cells to make up for the destroyed cells in erythroblastosis fetalis causes a large number of early blast forms of red cells to be released from the bone marrow into the blood.



Polycythemia

1-Secondary Polycythemia. Whenever the tissues become hypoxic because of too little oxygen in the breathed air, such as at high altitudes, or because of failure of oxygen delivery to the tissues, such as in cardiac failure, the blood-forming organs automatically produce large quantities of extra red blood cells. This condition is called secondary polycythemia, and the red cell count commonly rises to 6 to 7 million/mm³, about 30 per cent above normal.

A common type of secondary polycythemia, called physiologic polycythemia, occurs in natives who live at altitudes of 14,000 to 17,000 feet, where the atmospheric oxygen is very low .

2- Polycythemia Vera (Erythremia) : It a pathological condition, in which the red blood cell count may be 7 to 8 million/mm³ and the hematocrit may be 60 to 70 per cent instead of the normal 40 to 45 per cent. Polycythemia vera is caused by a **genetic** aberration in the hemocytoblastic cells that produce the blood cells. The blast cells no longer stop producing red cells when too many cells are already present. In polycythemia vera, not only does the hematocrit increase, but the total blood volume also increases, on some occasions to almost twice normal.