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 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 (Which causes the formation of methemoglobin that will not carry oxygen)
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. There, the spaces between the structural trabeculae of the red pulp only 3 micrometers wide, in comparison with the 8-micrometer diameter of the red cell.

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 (figure 1). The porphyrin portion of the hemoglobin molecule is converted by the macrophages, through a series of stages, into the bile pigment bilirubin, which is released into the blood and later removed from the body by secretion through the liver into the bile.

![Fig.(1): Destruction of Hemoglobin](image-url)
Disorder of Red Blood Cells:

**Anemia**

Anemia, which is a deficiency of red blood cells, is probably the most common human pathological state worldwide. The condition is not a disease, but is instead the manifestation of an underlying pathological process. Anemia is a sign and not a diagnosis. Once recognized, however, the sign can serve as a road marker in the quest of cause. Although not a primary disease process, anemia can produce severe morbidity and occasionally even death. Chronic severe anemia strains the heart, for instance, and can produce high-output cardiac failure. Consequently, steps to correct the anemia should accompany the diagnostic evaluation.

Anemia can be caused either by too rapid loss or too slow production red blood cells. Some types of anemia and their physiological 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, which is shown in Figure 2–1.

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 Anemia**
   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 (figure 2-3). Thus, atrophy of the stomach mucosa, as occurs in *pernicious anemia*, or loss of the entire stomach after surgical total gastrectomy can lead to megaloblastic anemia. Also, patients who have intestinal sprue, in which folic acid, vitamin B12, and other vitamin B compounds are poorly absorbed, often develop megaloblastic anemia. Because in these states the erythroblasts cannot proliferate rapidly enough to form normal numbers of red blood cells, 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- Hereditary Spherocytosis**

In *hereditary spherocytosis*, the red cells are very small and *spherical* rather than being biconcave discs. These cells cannot withstand 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- Sickle Cell Anemia**

In *sickle cell anemia*, the cells have an abnormal type of hemoglobin called *hemoglobin S*, caused by abnormal composition of beta chains in the hemoglobin molecule. 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 called a sickle cell disease (figure 2-2), in which low oxygen tension in the tissues causes sickling, which leads to ruptured red cells, which causes a further decrease in oxygen tension and still more sickling and red cell destruction. Once the process starts, it progresses rapidly, eventuating in a serious decrease in red blood cells within a few hours and, often, death.

**c- Erythroblastosis Fetalis**

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 (figure 2-4).

Hemolysis also occasionally results from transfusion reactions, from malaria, from reactions to certain drugs, and as an autoimmune process.
Effects of Anemia on Function of the Circulatory System

The viscosity of the blood depends almost entirely on the blood concentration of red blood cells. In severe anemia, the blood viscosity may fall to as low as 1.5 times that of water rather than the normal value of about 3. This decreases the resistance to blood flow in the peripheral blood vessels, and great quantities of blood flow through the tissues and return to the heart, thereby greatly increasing cardiac output. Moreover, hypoxia causes the peripheral tissue blood vessels to dilate, allowing a further increase in the return of blood to the heart and increasing the cardiac output. Thus, one of the major effects of anemia is greatly increased cardiac output, as well as increased pumping workload on the heart.

However, when a person with anemia begins to exercise, the heart is not capable of pumping much greater quantities of blood than it is already pumping. Consequently, during exercise, which greatly increases tissue demand for oxygen, extreme tissue hypoxia results, and acute cardiac failure ensues.
Polycythemia

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 8 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.

Polycythemia Vera (Erythremia)
In people who have a pathological condition known as polycythemia vera, the red blood cell count may be 7 to 8 million/mm³ and the hematocrit may be 60 to 70 percent instead of the normal 40 to 45 per cent. Polycythemia vera is a timorous condition of the organs that produce blood cells. This causes excess production of red blood cells, white blood cells and platelets. In polycythemia vera, not only does the hematocrit increase, but the total blood volume also increases the viscosity of the blood in polycythemia vera sometimes increases from the normal of 3 times the viscosity of water to 10 times that of water.

Effect of Polycythemia on Function of the Circulatory System
Because of the greatly increased viscosity of the blood in polycythemia, blood flow through the peripheral blood vessels is often very sluggish and decreases the rate of venous return to the heart. So the blood volume is greatly increased in polycythemia, which tends to increase venous return. The arterial pressure in about one third of people with polycythemia is elevated.
In polycythemia vera, the quantity of blood in this plexus is greatly increased. Further, because the blood passes sluggishly through the skin capillaries before entering the venous plexus, a larger than normal quantity of hemoglobin is deoxygenated. The blue color of all this deoxygenated hemoglobin masks the red color of the oxygenated hemoglobin. Therefore, a person with polycythemia vera ordinarily has a ruddy complexion with a bluish (cyanotic) tint to the skin.