HEMATOLOGY & HEMOSTASIS ACADEMY

Section 3

RED BLOOD CELLS

LEARNING OBJECTIVES

When you complete this section, you will be able to:

1. **Recognize how RBCs are formed**
2. **Indicate why some RBCs may be immature**
3. **Recognize conditions that stimulate production of RBCs**
4. **Name two substances needed for RBC maturation**
5. **Recognize the roles of hemoglobin, transferrin, and ferritin**

DESCRIPTION

An erythrocyte (erythro = red) is a fully mature red cell found in the peripheral blood. Although highly specialized, it is little more than a small bag – a membrane surrounding a solution of protein and electrolytes.

In appearance, an erythrocyte is a bi-concave, disc-shaped cell, somewhat like a doughnut that has no hole. Small enough to pass easily through capillaries in single file, RBCs can change shape into almost any configuration – a characteristic that gives them access to all tissue cells.

FORMATION OF RBCS

RBCs are formed continuously, but their number is precisely regulated. Too few cells will not oxygenate tissue; too many cells will impede blood flow. Mature RBCs cannot reproduce themselves, so several million new cells enter the blood daily from blood-forming centers in bone marrow. The term for red blood cell formation is erythropoiesis.

Life Span. When an RBC is about 120 days old, it is trapped and removed from the blood by the spleen or the liver. Its iron atoms, however, are recycled; approximately 25 milligrams of iron become available daily from the breakdown of old RBCs.

Bone Marrow. Virtually all bones in children up to the age of 5 are blood-forming centers. Bone marrow becomes less productive as age increases. In adults (over age 20), RBCs are formed in the marrow of the vertebra, sternum (breastbone), ribs, and the ends of the long bones.

Cell Generations. RBCs develop in a series of cell generations in the bone marrow **(Figure 2).** After several generations, new cells called basophilic erythroblasts emerge. (A note about naming: WBCs are dyed or stained for viewing microscopically. A cell with basophilic staining properties is a cell that stains specifically with basic dyes; a cell with eosinophilic staining properties is a cell that stains with eosin, a red acidic dye. Erythroblast literally means an immature red cell.)

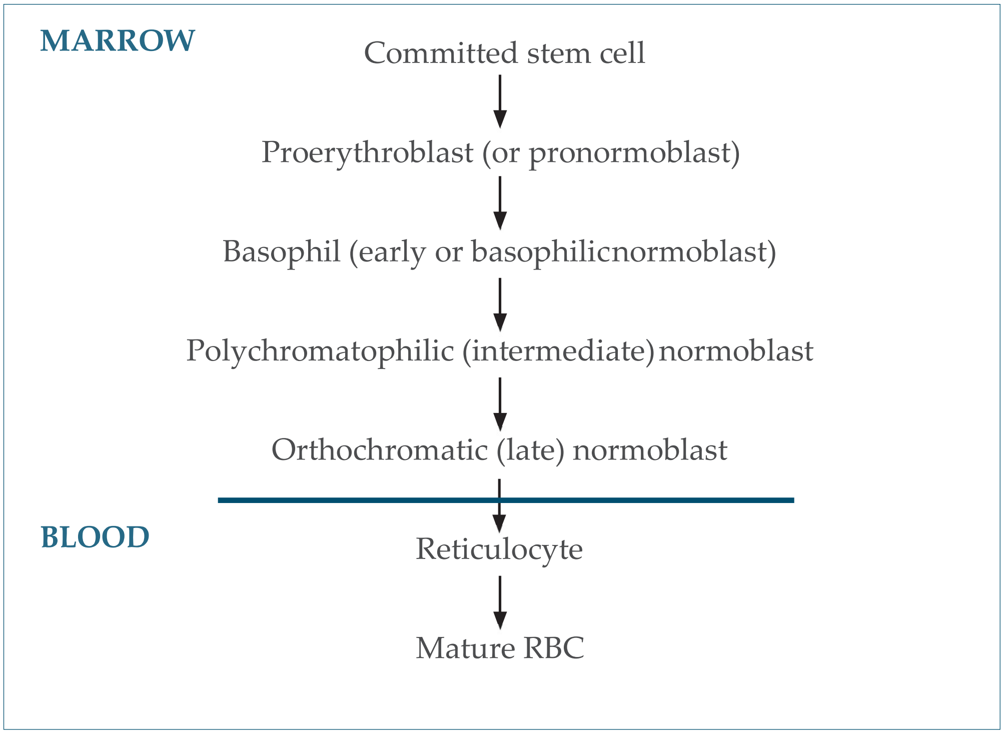


Figure 2. Formation of RBCs.

In the next cell generations, hemoglobin begins to give the cells their typical red color and the nucleus is extruded from the cell. The cell is now called a reticulocyte (reticula = network) because staining causes strands of residual RNA cell content to clump into a network.

Reticulocytes pass into the capillaries by diapedesis (squeezing through the pores of the membrane) and become mature RBCs within one or two days. These cells normally make up about 1% of circulating RBCs.

REGULATION OF RBC PRODUCTION

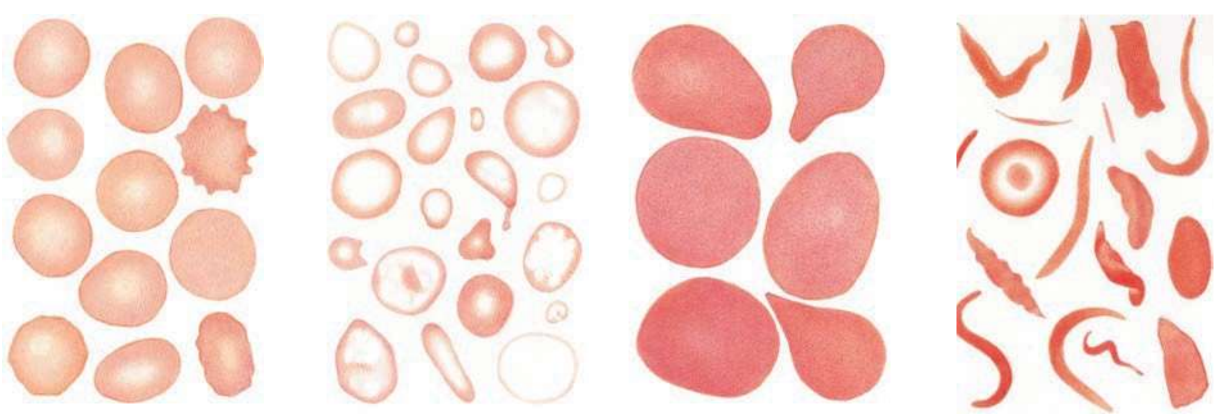
Tissue oxygenation regulates RBC production. If the amount of oxygen transported to the tissues decreases, the rate of RBC production increases **(Table 3)**.

CONDITIONS THAT STIMULATE RBC PRODUCTION
Low blood volume; blood loss due to hemorrhaging
Anemia; low RBC content due to destruction or lack of production of RBCs; low hemoglobin in blood
Destruction of bone marrow as in radiation therapy
Lack of available oxygen due to high altitudes
Poor blood flow due to circulatory diseases such as heart failure
Lung diseases that decrease absorption of oxygen

Table 3. Stimulation of RBC production.

The Feedback Mechanism. Tissue hypoxia (abnormally low oxygen level) triggers the kidneys to increase production of erythropoietin. This hormone stimulates bone marrow to produce stem cells and speeds the passage of newly formed RBCs through the various generations. Bone marrow continues producing RBCs as long as tissue hypoxia is present or until tissue is adequately oxygenated. Feedback signals to bone marrow diminish production of erythropoietin to the level needed to maintain the normal production of RBCs.

RBC production can be judged by counting reticulocytes in the blood and by ferrokinetics, that is, the amount and traffic of iron in the blood.



Normal

Iron-deficient anemia

Megaloblastic anemia

Sickle cell anemia (Hb SS)

Figure 3. Normal compared to several types of abnormal RBCs.

If bone marrow produces many RBCs rapidly, immature cells are released into the blood. The number of reticulocytes can increase to as high as 30%-50% of total circulating RBCs. Erythroblasts (NRBCs – nucleated red blood cells) may also appear in the circulating blood.

Maturation of RBCs depends on the presence of two substances – vitamin B12 (cyanocobalamin) and folic acid (another member of the vitamin B complex). Both are needed for cell synthesis of DNA (deoxyribonucleic acid, the genetic material that controls heredity). Both are obtainable from a normal diet and must pass through the gastrointestinal (GI) tract.

Lack of one or both of these substances inhibits RBC production and causes blood cells forming in the bone marrow to enlarge. Called megaloblasts (literally, large immature cells) in the forming stage and macrocytes (large cells) as adult RBCs, these abnormal cells are irregular in shape, have flimsy membranes, and often contain excess hemoglobin. Macrocytes carry oxygen but have a very short life.

Poor absorption of vitamin B12 is due to lack of secretion of intrinsic factor by the gastric mucosa. Intrinsic factor must be present for absorption and utilization of vitamin B12. Folic acid deficiency may be due to lack of vitamin C. These absorption and deficiency problems can arise in alcoholics, geriatric patients, and in pregnant or lactating women.

HEMOGLOBIN

Hemoglobin, the oxygen-carrying component of RBCs, is composed of two pairs of protein chains called globin and four smaller units called heme, which contain iron. Iron binds and releases oxygen (O_2). Decreases in hemoglobin reduce the amount of O_2 carried by the blood to cells.

The oxygen-carrying capacity of hemoglobin can be affected by the formation of gases that can prevent O_2 from reaching cells and by abnormalities of hemoglobin production and destruction.

IRON

Although iron is important in cellular metabolism and oxidation, the body needs only trace amounts of two types of iron:

- Functional iron, a component of hemoglobin and myoglobin (a pigment in muscles); approximately 70% of body iron
- Iron stored in the forms of ferritin and hemosiderin

Iron that is not part of hemoglobin is bound to the blood protein transferrin, which transports it to storage tissues (liver, bone marrow, and spleen). In storage tissues, iron binds to another protein to form ferritin. Normally about 35% of the circulating transferrin is saturated with iron. The degree to which transferrin is saturated with iron indicates the iron supply for developing RBCs.

To keep hemoglobin and other functional iron levels constant, the body draws iron from storage. Because it is readily mobilized when iron is lost (through hemorrhage) or inadequate (poor diet), ferritin is depleted early in iron deficiency. Accurate ferritin measurement often reveals iron-deficient anemia before other laboratory values change.