[1st year]

[concise blood physiology]

[by physio-team]

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Formation of blood (haemopoiesis)

- site of blood formation :

1: In the fetus :

(a) The yolk sac is the only site of blood formation in the first 3 month of life . Thereafter, haemopoiesis starts in the liver and spleen and continues until the 7th month of intrauterine life .

(b) Bone marrow. Blood formation in the bone marrow commences in the 4th month of intrauterine life and from 7th month of intrauterine life until birth it becomes the only haemopoietic organ.

2: After delivery and throughout the life.

Red blood cell (erythrocytes) :

- Development :

The development of erythrocytes starts from primitive haemopoietic stem cell, which becomes successively a **proerythroblast; early, intermediate** and **late normoblast; reticulocyte**; and finally an erythrocyte or mature red cell.

- Structure :

The erythrocyte is a non-nucleated cell shaped like a flat biconcave disc.

Destruction and removal of red cells occur in the **reticu-ioendothelial system .**

Nutritional requirement for red cell production:

1-**Amino acid.** Amino acid needed for synthesis of the **globin** of **hemoglobin** .

2-**Iron**. This is dealt with in detail at a later stage in this chapter. Iron deficiency causes **microcytic hypochromic** anemia, i.e. smaller than normal red cells with reduction in the hemoglobin content.

3-Vitamin. There are several vitamins essential for normal heamopoiesis :

a) B12 (**cyanocobalamin**) and **folic acid** play an important role in the synthesis of **nucleoproteins**. The deficiency of either leads to a disturbance of deoxyribonucleic acid (DNA) metabolism in developing nucleated red cell precursors. The result is megaloblastic (mega=large) erythropoiesis and megaloblastic (**macrocytic**) anaemia (**pernicious anaemia**).

b) As a reducing agent, **vitamin C** (ascorbic acid) facilitates iron absorption in the gut by helping to keep iron in the reduced (ferrous, Fe^{2+}) state. Ascorbic acid is also involved in the normal metabolism of cyanocobalamin and folic acid. Diets deficient in vitamin C are likely to be deficient in the folic acid. Both vitamin are presentin vegetable foods and both are heat-labile and therefore deficiency of both vitamins is common. The result can be normocytic, macrocytic or microcytic anaemia with normochromic or hypochromic red cells.

c) Pyridoxine (B_6) .

d) **Riboflavin**, nicotinic acid, pantothenic acid, biotin and thiamine are B vitamin.

e) vitamin E.

4-**Trace elements.** Copper, cobalt, zinc, manganese, nickel and other mineral are present in the erythrocyte.

Control of erythropoiesis :

Oxygen deprivation (hypoxia) or blood loss triggers the formation of the hormone erythropoietin, which acts on the bone marrow to stimulate erythropoiesis.

Chemistry :

Erythropoiesis is a glycoprotein.

Sources :

Most of the hormone erythropoietin (90%) is produced in the peritubular cells of the renal cortex and outer medulla; the rest is secreted by the liver.

Action :

Erythropoietin stimulates the early **stem cell** (otherwise called the erythropoietin-sensitive stem cell or erythrocyte-comitted stem cell) to differentiate into a proerythroblast.

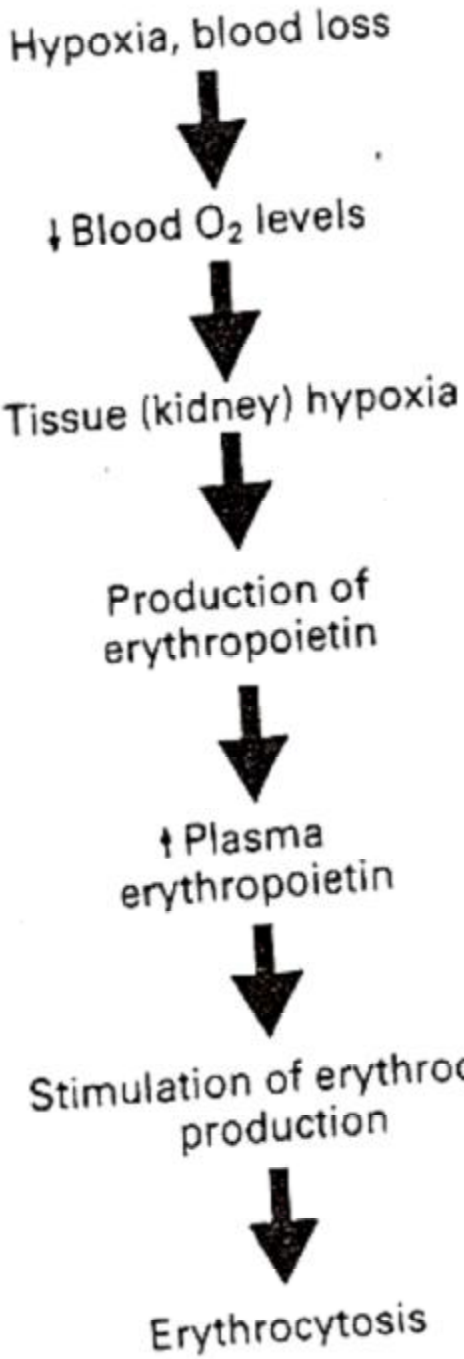


Fig. 2.2 The mechanism of production of erythropoietin.

Iron metabolism

-Distribution of iron in the body

The total amount of iron in the body of healthy adult is 3-5 g distributed as follows:

1- haemoglobin. Most of iron in body(65-75%) is present in hemoglobin

2- storage (available) iron. Twenty per cent of total body iron Is present as the protein-iron compound ferritin in the liver spleen and bone marrow.

3- cellular or tissue (non-available) iron. This is the iron (average 150 mg) which is present in body cell as a major component of oxidative enzyme system, e.g . cytochrome, and as part of myoglobin.

4- transport or plasma iron a very small amount of iron (3-4 mg) is found in the plasma in combination with β-globin, transferrin. measurement of serum ferritin is a reliable indicator of the level of iron stores in the body.

Absorption

Most of the iron in food is in the oxidized ferric (fe^{3+}) state; however it is absorbed better when it is in the reduced ferrous(fe^{2+}). Ferrous ions are carried into the mucosal cell by active transport once iron is inside the cell, it becomes attached to non-ferritin protein carrier . where it is picked up by transferring and carried to the various sites in the body, or it remains within the cell, where it stimulates ferritin formation by combining with an intracellular protein apoferritin to from ferritin , which is deposited in the mucosal cell.

Transferring as a globuiar protein (molecular weight 86 000) and is normally 30-40% saturated with iron; remaining 60-70 % forms the unsaturated latent iron-binding capacity .

Iron is stored in the reticuloendothelial cell in the main storage organs for iron , which are the liver , spleen and bone marrow . iron is stored row forms: ferritin and haemosiderin.

Types of normal hemoglobin

1- Adult hemoglobin (HbA)

HbA composed 98% of the haemoglobin in healthy adults .

2- hemoglobin A2 (HbA2)

In HbA_2 the globin moiety is composed of two α and two δ chains.

3- Haemoglobin F (HbF)

This is the major respiratory pigment during intrauterine life.

- Function:

1- carrige of oxygen

2- carriage of carbon dioxide

3- buffer . Haemoglobin, begin a protein, acts as one of the buffers in blood accounting for about 70% of its buffering power

Anaemia:

Anaemia may occur if the number of red cells (red cell count) falls below normal level.

Causes and classification of anaemia:

1. Blood loss, whether acute, as in hemorrhage following a car accident, or chronic, which occurs in chronic bleeding in the gastrointestinal track, e.g. piles, peptic ulcer or the present of worms, particularly hookworms, in the intestine.
2. Diminished red blood cell production by bone marrow. This may occur in the following situations:

    a. Deficiency of nutritional substance(s)required for erythropoiesis (nutritional anaemia). Iron deficiency causes the bone marrow to produce cells smaller in size than normal (microcytes) and with a small load of haemoglobin, since iron is an integral component of the haemoglobin molecule. The cells therefore have a lighter red color than normal (hypo-chromic). Iron-deficiency anaemia is described as microcytic hypo-chromic anaemia. It is the commonest type of anaemia in the developing countries and is mainly due to deficiency of iron in the diet or blood loss. It is particularly likely to occur in children and adolescents due to demands of growth, and in women of child-bearing age due to blood losses during menstruation and child birth. Deficiencies of vitamin B12 and folic acid case megaloblastic anaemia. Dietary deficiency is almost unknown. However, deficiencies occur as a result of malabsorption (see chapter 8). Folic acid deficiency in diet is also common in tropical countries, where the resulting anaemia is prevalent in malnourished children and in women during pregnancy, when the general body requirements for folic acid increase.

    b. Diminished red cell production may occur when the bone marrow space is occupied by secondary cancer cells or fibrous tissue, as in myelosclerosis, or as a result of destruction by radiation or drug (aplastic anaemia).

3. Excessive destruction of red cells(hemolytic anaemia). The factors causing destruction may be within red cells, e.g. presence of abnormal haemoglobin such as HbS, due to which the cell take a sickle or crescent shape when exposed to low oxygen tension. These sickle cells have a short life span as they are readily broken down and removed by the reticuloendothelial system. Sickle-cell anaemia is very common in the tropics particularly in people of west african origin.

    The cause of haemolysis may come from out side the red blood cells, e.g. blood group incompatibility, where an antibody may react with a blood group antigen present in the red cell

poylcythaemia Classification :

1. **True or absolute poylcythaemia, characterized by an increase in the total number of circulatring red blood cells (red cell mass). it is of two types:**

    a) Primary or poylcythaemia rubra vera , where bone marrow continues to produce red cells with no regard to the normal physiological negative feedback mechanism of the hormone erythropoietin.

    b) Secondary polycythaemia, due to hypoxia, as in high altitudes and chronic respiratory of cardiac disease. This type of polycythaemia is characterized by high levels of **erythropoietin** released in response to hypoxia.

2. **Relative polycythaemia occurs in cases of dehydration due to excessive fluid loss (vomiting of sweating) or decreased water intake . Plasma volume is decreased and consequently the red cells are concentrated (Haemoconcemtration) thus, there is no increase in the red cell mass but the ratio of cells to plasma is high.**

Chemotaxis.

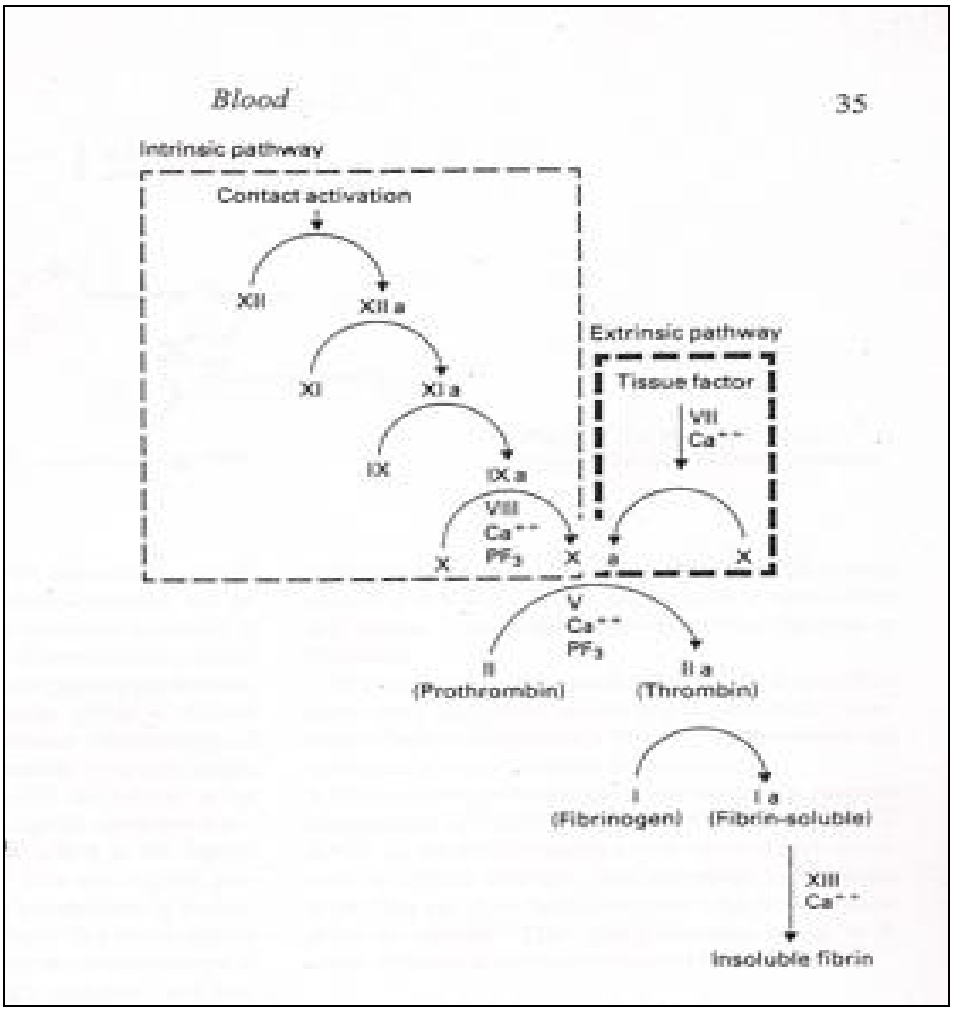
The neutrophils are actively motile cells; they can move more rapidly than any other cell in the body. Their movement is directed towards bacteria in a purposeful manner.

The acquired immune deficiency syndrome (AIDS)

In healthy person the cellular immune responses are performed with a predominance of circulating T-helper lymphocyte (T4 or CD4 cells) over T-suppressor lymphocyte (T8 or CD8 cells); the normal ratio is 2:1.

Rhesus incompatibility between mother and fetus (haemolytic disease of the newborn):

Rhesus incompatibility arises when a Rh-negative woman gets pregnant and the fetus is Rh-Positive , having inherited the D gene form the father . As mentioned earlier, the mother may develop anti-D antibody as a result of such an incompatible pregnancy or if she has received incompatible (D+) blood before pregnancy. The first baby usually escapes the effects. Such immune antibodies, usually of the IgG type, may cross the placenta in future pregnancies. If the second fetus is Rh-positive, the immune anti-D may react with and destroy fetal red cells, Resulting in the disease called haemolytic disease of the newborn. The fetus may be born with haemolytic anaemia , which if severe. May necessitate exchange blood transfusion. Blood group O Rh-negative is infused in the newborn at one point while the haemolysed blood is gradually withdrawn from infant at another point . Haemolytic disease of the newborn has an overall reported incidence of one in 200 of all pregnancies this figure has decreased further with the use of prophylactic anti-D antibody. Which is injected into Rh-positive child. The injected antibody will react with and get rid of fetal Rh-positive cell before they immunize the mother.


Blood
35
Intrinsic pathway
Contact activation
XII
XII a
XI
XI a
IX
IX a
VIII
Ca++
PF3
X
X
Extrinsic pathway
Tissue factor
VII
Ca++
a
X
V
Ca++
PF3
II
(Prothrombin)
II a
(Thrombin)
I
(Fibrinogen)
I a
(Fibrin-soluble)
XIII
Ca++
Insoluble fibrin