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Important Aspects of Etiology And Pathogenesis of Hemolytic Anemias

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Abstract
Hemolytic anemias occur due to the superiority of erythrocyte destruction over formation. Usually, hereditary and acquired forms of hemolytic anemia are distinguished. Under physiological conditions, erythrocytes live 100-120 days. In hemolytic anemia, the life span of erythrocytes is reduced to 12-14 days and pathological hemolysis occurs.
Key words: hemolysis, erythrocyte, membranopathies, enzymopathies, hemoglobinopathies, hemolytic jaundice.

Usually, hereditary and acquired forms of hemolytic anemia are distinguished. Under physiological conditions, erythrocytes live 100-120 days. Then, the pigment free bilirubin, formed as a result of the decomposition of macrophages in the spleen, loses the deformability of erythrocytes, circulates in the blood and goes to the liver, where it is combined with glucuronic acid with the participation of enzymes. Bilirubin glucuronide enters the intestine as part of bile.

According to the mechanism of pathological hemolysis, it is divided into cellular and intravascular type. Intracellular hemolysis of erythrocytes takes place in the cells of the reticuloendothelial system in the spleen, and there is an increase in the amount of free bilirubin in the blood serum, an increase in the excretion of urobilinogen through urine and feces, and a tendency to the formation of stones in the gallbladder and bile ducts.

Intravascular hemolysis of erythrocytes occurs in the blood vessels with the participation of complement, hemoglobin in the plasma increases and is excreted unchanged in the urine or in the form of hemosiderin. In some cases, hemosiderin accumulates in internal organs and causes hemosiderosis. Haptoglobin formed in the plasma can clog the kidney tubules and cause acute kidney failure.

Hereditary hemolytic anemias are divided into 3 groups according to the location of the mutational defect:

1. Membranepathies are associated with structural disorders of the protein and lipid components of the erythrocyte membrane.
2. Fermentopathies are associated with deficiency of enzymes of erythrocyte pentose phosphate cycle, glycolysis ATF and porphyrin synthesis, nucleotides and glutathione metabolism.
3. Hemoglobinopathies - hemoglobin chain synthesis disorder.

Hereditary membranopathies include hereditary microspherocytosis - Minkowski - Shofar disease. This disease is inherited in an autosomal dominant manner. In Minkovsky-Shofar's disease, the membrane defect consists in the high permeability of the erythrocyte shell to Na+ ions.

As soon as the K+- Na+ pump is activated, Na+ increases inside the cell and the osmotic pressure inside the cell increases. As a result, fluid enters erythrocytes and becomes spherical. This mechanism is caused by the absence of spectrin from the proteins on the surface of erythrocytes and the decrease in the amount of lipids. The breakdown of erythrocytes is related to the specificity of blood circulation in the spleen. In the red pulp, part of the blood goes out of the sinuses, that is, into the intersinus space. Here, erythrocytes fall into an environment with low levels of glucose and cholesterol. Such an environment is considered unfavorable for erythrocytes, causes erythrocytes to suffocate and lose their elasticity. Therefore, erythrocytes can pass through the narrow sinuses of the spleen due to their deformability. The erythrocyte membrane can lose a certain part of its surface during the passage through the narrow intersinus slit. If hemolysis does not occur, after the membrane defect disappears, erythrocytes shrink and return to the bloodstream. This is how microcytosis develops. During re-transmission from the splenic sinuses, microspherocytes are engulfed by the macrophage system or disintegrate without their participation. That is why splenectomy helps in this disease.

Also to hereditary membranopathies:

- Hereditary elleptocytosis
- Hereditary poikilocytosis
- Hereditary stomatosis
- Hereditary acanthocytosis
- Hereditary echinocytosis

Fermentopathy is an example of anemia caused by deficiency of glucose-6-phosphate dehydrogenase enzyme. The disease is inherited in a dominant way linked to the X chromosome. Dominant anemia is rarely observed. It is known that the disease manifests itself with hemolytic crises after the use of some drugs: sulfonamides, anti-malarial and anti-tuberculosis preparations. The above-mentioned preparations oxidize hemoglobin and stop its respiratory function. This condition is not observed in healthy people because they have an antioxidant system. The main component of the antioxidant system is the regeneration of glutathione, and the amount of regenerated glutathione decreases in glucose-6-phosphate dehydrogenase deficiency. For this reason, the therapeutic dose of medicinal preparations with oxidizing properties in these patients oxidizes and breaks down hemoglobin. In the hemoglobin molecule, heme is cut off and the globin chain precipitates, which is called a Gains body. These inclusions are eliminated by the spleen. In some cases, hemolytic crises occur when the horse beans plant is used or when flower pollen is smelled, its active factors reduce the power of the antioxidant system by oxidizing regenerated glutathione.

The most common of hemoglobinopathies is sickle cell anemia. In such patients, instead of Hb A, Hb C is synthesized. Hereditary defect occurs due to replacement of glutathione acid with valine at position 6 of beta chain in Hb S. As a result, in hypoxia, the solubility of hemoglobin is sharply reduced. Hb C, which is 100 times less soluble than oxidized Hb and 50 times less soluble than Hb A, precipitates in the form of crystals in an acidic environment, deforms erythrocytes and gives them a sickle shape. The membrane of such erythrocytes loses its resistance and undergoes hemolysis inside the vessel.

Thalassemia is a group of congenital microcytic hemolytic anemias, which occurs due to a defect in the synthesis of the hemoglobin chain. Alpha thalassemia associated with an alpha (α) chain synthesis disorder is relatively common among people of African and South Asian descent. Beta (b) thalassemia is more common in Mediterranean, Middle Eastern and Indian peoples.

A normal mature hemoglobin (Hb A) molecule is composed of 2 pairs of α and β chains. Also, adults keep up to 2.5% of Hb A2 (consisting of 2 alpha and 2 delta chains) and about 2% of Hb F (fetal hemoglobin consists of 2 alpha and 2 gamma chains) in normal blood. Usually, a total of 4 genes are responsible for the synthesis of α-chain, 2 of which are located on paired chromosomes. Thalassemia minor and major differ according to the degree of genetic defects occurring in these 4 genes.

If alpha + allele 1 is defective (alpha/alpha; alpha/-), such patients do not have clinical symptoms and are only carriers. If 2 out of 4 heterozygous genes are defective (alpha/-; alpha/-) or (alpha/alpha;-/-), mild or moderate anemia is observed in such patients, and it is called a thalassemia minor.

If there is a defect in 3 out of 4 genes, an excessive amount of beta chain (gamma chain in babies) tetramers are formed due to a defect in alpha chain synthesis. Hemoglobin with such a defect is called Hb H Bart's hemoglobin.

If there is a defect in the 4th gene, then Hb cannot carry oxygen and the fetus with such a defect will die without development.

Beta thalassemia is also caused by a defect in the genes responsible for β-chain synthesis. Major beta thalassemia or Cooley's anemia occurs in homozygous (beta/0; beta/0) or complex heterozygous (beta/0; beta/+) patients with severe anemia symptoms and iron transfusion and absorption in the 1st and 2nd year of life. Jaundice, trophic ulcers on the legs and cholelithiasis are observed as a result of the load. The disease is characterized by splenomegaly, and the breakdown of even normal donor erythrocytes increases. Due to hyperplasia of the bone marrow, the skull and bones are thickened, and defects occur in the jaw teeth (see the picture). Tubular bones are prone to pathological fractures, and sick children lag behind in growth. Excessive accumulation of iron trace element in the body, if it is in the heart muscles, leads to heart failure, and in internal organs, it often leads to liver hemosiderosis and liver cirrhosis.

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