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PATHOPHYSIOLOGICAL AND HEMATOLOGICAL MECHANISMS OF ANEMIA: MORPHOLOGICAL CHANGES, DIAGNOSTIC APPROACHES, AND CLINICAL SIGNIFICANCE

Mirzayeva Nigora Alijonovna
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Abstract: Anemia is a common hematological condition characterized by reduced hemoglobin concentration and impaired oxygen transport. This narrative review examines the pathophysiological and morphological mechanisms of iron deficiency, megaloblastic, inflammatory, and hemolytic anemia. Established hematological literature was evaluated through descriptive and comparative analysis. Alterations in erythropoiesis, iron metabolism, red blood cell morphology, and marrow function provide important diagnostic information. Integrating erythrocyte indices, reticulocyte counts, iron studies, and clinical assessment is essential for identifying the underlying cause and selecting appropriate management.

Keywords: anemia, erythropoiesis, iron deficiency, hemoglobin, erythrocytes, megaloblastic anemia, hemolysis, iron metabolism.

Introduction

Anemia is one of the most frequent hematological abnormalities and may arise from nutritional deficiency, systemic disease, blood loss, or premature erythrocyte destruction. Hemoglobin transports oxygen from the lungs to peripheral tissues, and reduced hemoglobin concentrations impair the oxygen-carrying capacity of blood. Compensatory cardiovascular responses may develop, but the consequences depend on anemia severity, duration, and physiological reserve.

Iron deficiency commonly produces microcytic hypochromic erythrocytes. Vitamin B12 and folate deficiencies impair DNA synthesis and may cause megaloblastic anemia. Chronic inflammation alters iron distribution and erythropoiesis, whereas hemolytic disorders shorten red blood cell survival. This review analyzes the morphological and pathophysiological mechanisms of anemia and their diagnostic implications.

Materials and Methods

This article is a narrative review based on established hematological, physiological, and clinical literature. Descriptive analysis was used to characterize erythrocyte morphology and mechanisms of anemia; comparative analysis was used to distinguish microcytic, normocytic, and macrocytic patterns. Laboratory parameters considered included hemoglobin, mean corpuscular volume, reticulocyte count, ferritin, transferrin saturation, vitamin B12, folate, and markers of hemolysis. No original patient data, laboratory experiments, or statistical analyses were performed.

Results

Erythropoiesis occurs primarily in adult red bone marrow and proceeds from hematopoietic progenitors through erythroblast stages to reticulocytes and mature erythrocytes. Erythropoietin,

produced predominantly by the kidneys in response to reduced oxygen availability, promotes erythroid cell survival and differentiation. Iron, folate, and vitamin B12 are essential for effective erythrocyte production.

Iron deficiency anemia results from inadequate intake, reduced absorption, increased requirements, or chronic blood loss. The liver-derived hormone hepcidin regulates systemic iron availability through ferroportin. In absolute iron deficiency, hepcidin is generally suppressed, but inadequate iron still impairs hemoglobin synthesis. Erythrocytes become small and pale, often accompanied by anisocytosis and increased red cell distribution width. Low ferritin and transferrin saturation support iron deficiency, although ferritin may rise during inflammation.

Megaloblastic anemia results from impaired DNA synthesis, most commonly due to vitamin B12 or folate deficiency. Nuclear-cytoplasmic asynchrony in erythroid precursors produces macro-ovalocytes and hypersegmented neutrophils. Vitamin B12 deficiency can also cause neurological dysfunction, which folate replacement alone does not treat.

Anemia of chronic inflammation develops through inflammatory cytokine signaling, increased hepcidin production, iron restriction, and reduced erythropoietic responsiveness. It is often normocytic but may be microcytic. Serum iron and transferrin saturation are frequently low, whereas ferritin can be normal or elevated.

Hemolytic anemia occurs when red blood cell destruction exceeds compensatory marrow production. Causes include inherited membrane or enzyme abnormalities, hemoglobin disorders, immune destruction, and mechanical injury. Laboratory findings may include elevated reticulocytes, indirect bilirubin and lactate dehydrogenase, with reduced haptoglobin. Peripheral blood smears may show spherocytes or schistocytes depending on the cause.

Diagnostic evaluation requires confirmation of low hemoglobin using population-appropriate thresholds, assessment of red blood cell indices, reticulocyte response, peripheral smear, and targeted investigations for iron deficiency, nutritional deficiency, renal dysfunction, inflammation, or hemolysis. Mean corpuscular volume is useful for initial classification but does not independently establish etiology.

Discussion

Anemia represents a heterogeneous group of conditions rather than a single disease. Although reduced hemoglobin concentration is a common feature, the mechanisms of impaired erythrocyte production, increased destruction, and blood loss differ considerably. Iron deficiency reflects inadequate substrate for hemoglobin synthesis; megaloblastic anemia reflects defective DNA synthesis; and inflammatory anemia reflects disturbed iron distribution and marrow response.

Hepcidin provides a mechanistic link between inflammation and iron availability. Elevated hepcidin during inflammation limits iron export from enterocytes and macrophages, whereas suppression of hepcidin during absolute iron deficiency facilitates iron absorption and mobilization. This distinction is clinically important because ferritin is an acute-phase reactant.

Morphological examination is valuable, but mixed deficiencies may mask typical erythrocyte indices. Accurate diagnosis therefore requires clinical history and integrated laboratory interpretation. Treatment must address the underlying cause, including iron replacement for

confirmed deficiency, vitamin B12 replacement when indicated, and appropriate management of chronic inflammatory or renal disease. The narrative nature of this review limits quantitative conclusions.

Conclusion

Anemia develops through multiple mechanisms involving iron deficiency, impaired DNA synthesis, inflammation, inadequate erythropoiesis, blood loss, or hemolysis. Erythrocyte morphology and laboratory indices offer important diagnostic clues but must be interpreted with clinical findings. Understanding hepcidin regulation, erythropoietin signaling, and marrow physiology supports accurate classification and cause-directed treatment. Further research into molecular markers may improve individualized diagnosis and management.

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