**College of Pharmacy**

**Fourth year. Clinical Pharmacy**

**Hematologic Disorders**

**Anemias**

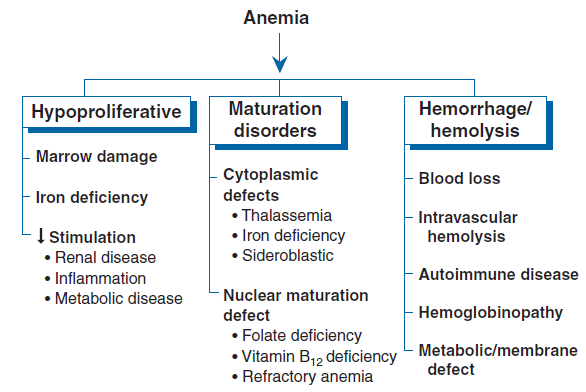
**Introduction**

1-Anemiais a group of diseases characterized by a **decrease in either hemoglobin** (Hb) or the **volume of red blood cells** (RBCs), resulting in **decreased oxygen-carrying capacity** of blood.

2-The World Health Organization defines anemia as Hb **less than 13 g/dL in men** or **less than 12 g/dL in women.**

**Pathophysiology**

1-The functional classification of anemias is found in **Fig. -1**.



**Figure -1. Functional classification of anemia.**

2- **Morphologic classifications** are based on **cell size**.

**A-Macrocytic cells** are larger than normal and are associated with deficiencies of vitamin B12 or folic acid.

**B-Microcytic cells** are smaller than normal and are associated **with iron deficiency**, whereas **normocytic anemia** may be associated with **recent blood loss or chronic disease.**

3**-Iron-deficiency anemia (IDA),** characterized by **decreased levels** of **ferritin** (most sensitive marker) and serum **iron**, and decreased **transferrin saturation**, can be caused by inadequate dietary intake, inadequate gastrointestinal (GI) absorption, increased iron demand (eg, pregnancy), blood loss, and chronic diseases.

**4-Vitamin B12– and folic acid–deficiency** anemias, macrocytic in nature, can be caused by inadequate dietary intake, malabsorption syndromes, and inadequate utilization.

A**-Deficiency of intrinsic factor** causes decreased absorption of **vitamin B12** (ie, **pernicious anemia**).

**B-Folic acid–deficiency** anemia can be caused by hyperutilization due to pregnancy, hemolytic anemia, malignancy, chronic inflammatory disorders, long-term dialysis, or growth spurt.

**C-Drugs can cause anemia** by reducing absorption of folate (eg, phenytoin) or through folate antagonism (eg, methotrexate).

**5-Anemia of inflammation (AI)** is a newer term used to describe both anemia of chronic disease and anemia of critical illness.

**A**-AI is an anemia that traditionally has been associated with malignant, infectious, or inflammatory processes, tissue injury, and conditions associated with release of proinflammatory cytokines.

**B**-**Serum iron is decreased** but in contrast to IDA, the **serum ferritin concentration is normal or increased**.

**Clinical presentation**

1-**Acute-onset anemia** is characterized by **cardiorespiratory symptoms** such as palpitations, angina, orthostatic light-headedness, and breathlessness.

2-**Chronic anemia** is characterized by weakness, fatigue, headache, orthopnea, dyspnea on exertion, vertigo, faintness, cold sensitivity, and pallor.

3-**IDA is characterized by** glossal pain, smooth tongue, reduced salivary flow, **pica** (compulsive eating of nonfood items), and **pagophagia** (compulsive eating of ice).

4-**Neurologic effects** (eg, numbness and paraesthesisas) **of vitamin B12 deficiency** may precede hematologic changes. Psychiatric findings, including irritability, depression, and memory impairment, may also occur with vitamin B12 deficiency. **Anemia with folate deficiency is not associated with neurologic symptoms.**

**Diagnosis**

1-Rapid diagnosis is essential because anemia is often **a sign of underlying pathology.** Severity of symptoms does not always correlate with the degree of anemia.

2-Initial evaluation of anemia involves a **complete blood cell count** (CBC), **reticulocyte index**, and **examination of the stool for occult blood**.

3-The earliest and most sensitive laboratory change for IDA is **decreased serum ferritin** (storage iron).

4-**In macrocytic anemias**, mean corpuscular volume is usually elevated. **Vitamin B12 and folate concentrations can be measured t**o differentiate between the two deficiency anemias.

5-In AI, **serum iron is usually decreased**, but, unlike IDA, **serum ferritin is normal or increased**. The peripheral smear reveals **normocytic anemia**.

**Treatment**

**Goals of Treatment**: The goals are to return hematologic parameters to normal, restore normal function and quality of life, and prevent long-term complications.

**Iron-deficiency anemia**

1-**Oral iron therapy** with soluble ferrous iron salts, which are **not enteric coated** and **not slow or sustained release**, is recommended at a daily dosage of 150–200 mg elemental iron in two or three divided doses.

2-Iron is best absorbed from meat, fish, and poultry. **Administer iron at least 1 hour before meals** because food interferes with absorption, but administration with **food may be needed to improve tolerability.**

3-Consider **parenteral iron for patients with** iron malabsorption, intolerance of oral iron therapy, or nonadherence.

4-**Iron dextran**, sodium ferric gluconate, **iron sucrose**, ferumoxytol, and ferric carboxymaltose are available parenteral iron preparations **with similar efficacy** but different pharmacokinetics, bioavailability, and **adverse effect profiles**.

**Vitamin B12–deficiency anemia**

1-**Oral vitamin B12 supplementation** is as effective as parenteral, even in patients with pernicious anemia, because the alternate vitamin B12 absorption pathway is independent of intrinsic factor.

2-Parenteral therapy acts more rapidly than oral therapy and **is recommended if neurologic symptoms are present**. Initiate daily **oral** cobalamin administration after symptoms resolve.

3-Continue vitamin **B12 for life** in patients with **pernicious anemia**.

**Folate-deficiency anemia**

1-Oral folic acid, 1 mg daily for 4 months, is usually sufficient for treatment of folic acid–deficiency anemia, unless the etiology cannot be corrected.

2-If malabsorption is present, a dose of 1–5 mg daily may be necessary. Parenteral folic acid is available but rarely necessary.

**Anemia of inflammation**

1-Treatment of AI is less specific than that of other anemias and should **focus on correcting reversible causes**. Reserve **iron therapy for an established IDA**; **iron is not effective when inflammation is present**. RBC transfusions are effective but should be

limited to Hb of 7–8 g/dL.

2-**Erythropoiesis-stimulating agents** (ESAs) can be considered, but response can be impaired in patients with AI. Iron, cobalamin, and folic acid supplementation may improve response to ESA treatment.

3-Potential toxicities of exogenous ESA administration include **increases in blood pressure**, nausea, headache, fever, bone pain, and fatigue. Hb must be monitored during ESA therapy. **An increase in Hb greater than 12 g/dL with treatment or a rise of greater than 1 g/dL every 2 weeks has been associated with increased mortality and cardiovascular events**.

4-In patients with anemia of **critical illness**, **parenteral iron** is often used but is associated with **a theoretical risk of infection.**

**Anemia in pediatric populations**

1**-Infants aged 9–12 months:** Administer ferrous sulfate 3–6 mg/kg/day (elemental iron) divided once or twice daily between meals for 4 weeks. Continue for two additional months in responders to replace storage iron pools.

2-The dose and schedule of vitamin B12 should be titrated according to clinical and laboratory response. The daily dose of folic acid is 1 mg.

**Evaluation of therapeutic outcomes**

1-IDA: Positive response to oral iron therapy is characterized by an increase in Hb **seen at 2 weeks**. Hb should return to normal after 2 months; **continue iron therapy until iron stores are replenished and serum ferritin normalized** (up to 12 months).

2-Megaloblastic anemia: Signs and symptoms usually improve within a few days after starting vitamin B12 or folic acid therapy.

**Reference**

**Joseph T. DiPiro, Robert L. Pharmacotherapy: A Pathophysiologic Approach, 12th Edition. 2023.**