

Macrocytic and microcytic anaemia

The World Health Organization (WHO) defines anemia as a hemoglobin (Hb) count of less than 13 g/L in men, less than 12 g/L in nonpregnant women, and less than 11 g/L in pregnant women and the elderly.

The cause of anemia varies by age, sex, and geography, and iron deficiency anemia is the most common etiology. For differential diagnosis, it is useful to classify the type of anemia based on the red cell indices of Wintrobe, which is calculated from red blood cell count, hemoglobin concentration, and hematocrit.

The mean corpuscular volume (*MCV*) is calculated from hematocrit (%) $\times 10/\text{RBC count (106/?l)}$, and macrocytic anemias are defined as $\text{MCV} > 98 \text{ fL}$. On the other hand, **Microcytic anemia** is defined as the presence of small, often hypochromic, red blood cells in a peripheral blood smear and is usually characterized by a low MCV (less than 83 fL).

The system of classifying anemia to macrocytic and microcytic anemia is based on red cell size and shape.

Definition of Anemia (WHO Criteria)

- **Men:** Hb < 13 g/dL
- **Non-pregnant women:** Hb < 12 g/dL
- **Pregnant women & elderly:** Hb < 11 g/dL

Classification of Anemia by Red Blood Cell Size (Mean Corpuscular Volume - MCV)

- **MCV:** Average volume of a red blood cell (RBC)

Microcytic Anemia

- **Definition:** $\text{MCV} < 83 \text{ fL}$
- RBCs are smaller than normal (microcytosis), often hypochromic (less hemoglobin).
- **Common causes:**
 - **Iron deficiency anemia (most common)** — due to chronic blood loss or poor intake
 - **Thalassemias** — inherited hemoglobin synthesis disorders
 - **Anemia of chronic disease (ACD)** — inflammatory or chronic illnesses causing impaired iron utilization

Macrocytic Anemia

- **Definition:** $\text{MCV} > 98 \text{ fL}$
- RBCs are larger than normal (macrocytosis).

- Two main categories:
 1. **Megaloblastic anemia** — due to defective DNA synthesis causing abnormal nuclear maturation in erythroblasts
 - Causes:
 - Vitamin B12 deficiency
 - Folic acid deficiency
 - Drugs interfering with DNA synthesis (e.g., methotrexate, chemotherapy)
 2. **Non-megaloblastic anemia** — caused by increased reticulocytes or other causes not related to impaired DNA synthesis
 - Causes:
 - Liver disease
 - Alcoholism
 - Hypothyroidism
 - Bone marrow disorders

Additional Laboratory Parameters

- **Red Cell Distribution Width (RDW):** Measures the variability in RBC size (anisocytosis)
 - Normal range: 10–14%
 - Elevated RDW suggests mixed populations of small and large cells (e.g., early iron deficiency or combined deficiency anemia).
- **Poikilocytosis:** Variation in RBC shape, often seen in anemia.

Pathophysiology Overview

- **Microcytic anemia:**
Caused by impaired hemoglobin synthesis — decreased hemoglobin production leads to smaller RBCs.
- **Macrocytic anemia:**
Results from either
 - **Impaired DNA synthesis** (megaloblastic) causing nuclear-cytoplasmic asynchrony, or
 - **Increased reticulocyte count** (young RBCs are larger than mature RBCs) in response to bleeding or hemolysis.

Mechanisms of Anemia

- **Excessive blood loss** (acute or chronic)
- **Increased red cell destruction (hemolysis)**
- **Decreased red cell production** (nutritional deficiencies, marrow failure, chronic disease)

Compensatory Response to Anemia

- Tissue hypoxia stimulates erythropoietin production by the kidneys.
- Erythropoietin promotes red cell production in bone marrow, increasing reticulocyte count by 5-8 times in healthy marrow.
- Exception: In chronic renal failure, erythropoietin production is reduced, worsening anemia.

