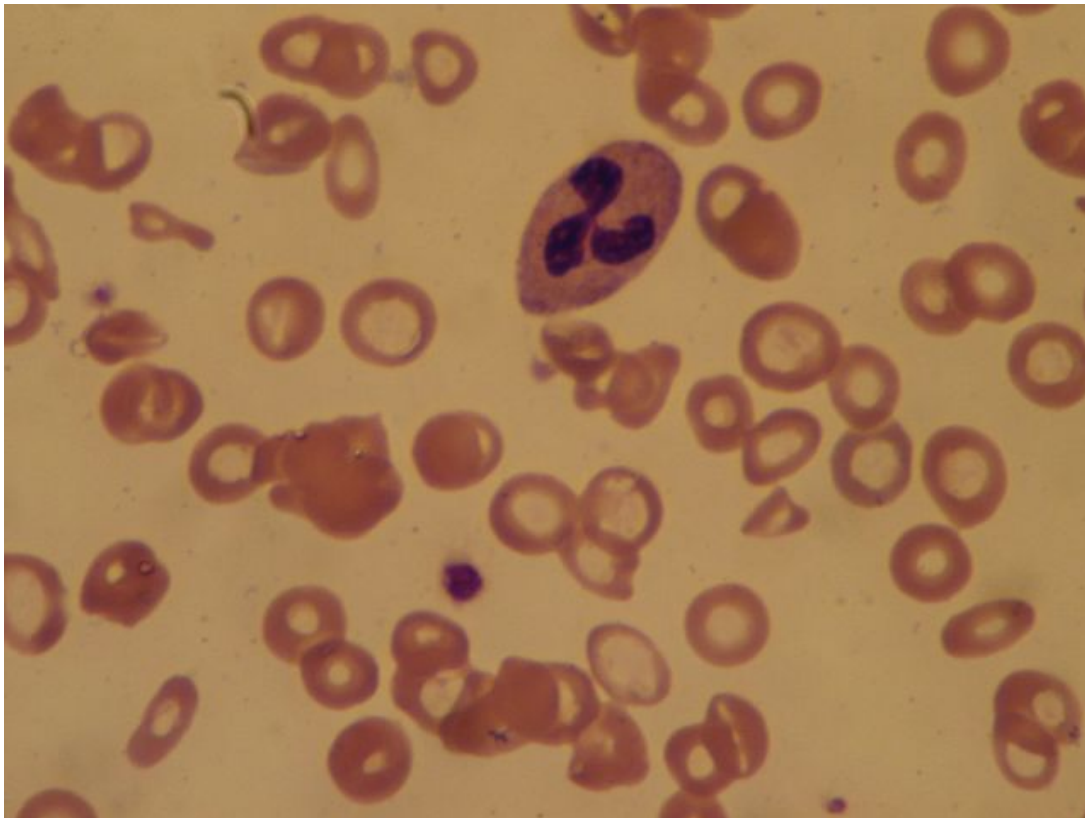


## Classification of Anemias in Children — Clinical Features and Management

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**Anemia is a medical condition that results from a shortage in the oxygen-carrying capacity of the blood due to a decrease in hemoglobin or number of red blood cells (RBCs). Anemia may be caused by excessive blood loss, inefficient production of RBCs, chronic disease or excessive destruction of RBCs. The type, cause, severity and background health problems are the determinants of the signs and symptoms of anemia. Anemia can be effectively managed through nutritional and medical interventions.**



### Definition

**Anemia** is defined as a decrease in the oxygen-carrying capacity of the blood due to decreased hemoglobin concentration or decreased number of red blood cells.

### Etiology and Classification of Anemia

The broad categories of anemia include:

- Anemia caused by excessive blood loss
- Inefficient production of red blood cells
- Anemia that results from a chronic disease
- Anemia caused by excessive destruction of red blood cells

## Anemia due to excessive blood loss

Excessive blood loss leads to anemia through several mechanisms. It is well-known that acute severe bleeding results in anemia but it is easy to overlook the chronic blood loss as a cause of anemia because they are difficult to identify.

The common culprits for chronic blood loss include bleeding ulcers, hemorrhoids, colon cancer, parasitic infections, menstruation, pregnancy, or chronic use of nonsteroidal anti-inflammatory drugs (NSAIDs), among others.

## Inefficient production of red blood cells

Red blood cells require iron, multiple vitamins, and hormones for their optimum production from their stem cells.

Multiple conditions can inhibit the body's ability to produce enough red blood cells. For instance, **poor eating habits** (deficiency of iron, folic acid, Vitamin B12), **inconsistent hormone quantities** (erythropoietin), **chronic illnesses**, and **pregnancy**. An acquired or inherited a condition that can inhibit the production of optimal values of red blood cells is Aplastic anemia. Patients with chronic kidney disease have anemia due to decreased production of erythropoietin.

## Anemia resulting from chronic disease

Several chronic medical disorders lead to anemia. For instance, cancer, rheumatoid arthritis, chronic kidney disease, and tuberculosis. In fact, sometimes anemia can be a pointer to these disorders.

## Anemia caused by excessive destruction of red blood cells

Hemolytic anemia results from the self-destruction of the red blood cells owing to pressure from the circulatory system.

- There are some inherited conditions that may result in hemolytic anemia (Glucose 6-phosphate dehydrogenase deficiency, hereditary spherocytosis), while others, such as infections, medications, etc., are acquired.
- In some rare cases, autoimmune disorders can cause hemolytic anemia.
- **Enlargement of the spleen** (splenomegaly) due to any cause may result in excessive destruction of red blood cells.

## Impaired red cell production

Red cell aplasia	Ineffective erythropoiesis
<ul style="list-style-type: none"> <li>• Parvovirus B19</li> <li>• Blackfan-Diamond anemia</li> <li>• Transient erythroblastopenia of childhood</li> </ul> <p><b>Rare:</b> Aplastic anemia, Fanconi anemia, leukemia</p>	<ul style="list-style-type: none"> <li>• Iron deficiency</li> <li>• Folate/B12 deficiency</li> <li>• Chronic inflammation (e.g., JIA)</li> <li>• Chronic renal failure</li> <li>• Lead poisoning</li> </ul> <p><b>Rare:</b> Myelodysplasia</p>

## Increased destruction

<b>Red cell membrane disorders</b>	<b>Red cell enzyme disorders</b>	<b>Hemoglobinopathy</b>	<b>Immune</b>
<ul style="list-style-type: none"><li>• Hereditary spherocytosis</li><li>• Hereditary elliptocytosis</li></ul>	<ul style="list-style-type: none"><li>• G6PD</li></ul>	<ul style="list-style-type: none"><li>• Thalassemia</li><li>• Sickle cell disease</li></ul>	<ul style="list-style-type: none"><li>• Autoimmune hemolytic anemia</li><li>• Hemolytic anemia of the newborn</li></ul>

## Blood loss

<b>Peripartum</b>	<b>GI bleed</b>	<b>Other</b>
<ul style="list-style-type: none"><li>• Fetal blood loss at birth</li></ul>	<ul style="list-style-type: none"><li>• Polyp disease</li><li>• Meckel's diverticulum</li></ul>	<ul style="list-style-type: none"><li>• Von Willebrand disease</li><li>• Hemophilia</li><li>• Trauma</li></ul>

## Clinical features

The clinical features depend on the type of anemia, its etiology, severity, and background health problems (co-morbidities).

## Symptoms

The general symptoms may include:

- Tiredness, fatigability, and generalized weakness
- Shortness of breath
- Increased heartbeat
- Dizziness and/or a headache
- Tinnitus (feelings of ringing in the ears)
- Mood swings
- Paleness of the skin
- Loss of libido (sexual drive).

## Signs

### 1. Musculoskeletal disorder and weight gain:

- Effort capacity is decreased
- Exercise limitation

### 2. Cardiovascular signs:

- Increased cardiac output
- Tachycardia
- Cardiomegaly
- Congestive Cardiac Failure

### 3. Immune system dysfunction:

- Decreased resistance against infections
- T-lymphocyte and polymorphonuclear leukocyte dysfunction

### 4. Gastrointestinal system signs:

- Splenomegaly
- Hepatomegaly
- Loss of appetite
- Dysphagia
- Pica

### 5. Neurological signs:

- Papilledema
- Sleep disturbance
- Attention-deficit
- Behavioral disorder
- Restless leg syndrome

Physical examination is paramount to ascertain if the individual is presenting with any symptoms of anemia along with any complications. **Since anemia may be the initial symptom of a debilitating condition, evaluating the cause is imperative.** This may not be easy to do when the patient is elderly, malnourished, suffering from a chronic disease or whose anemia is a result of several illnesses. It is essential for the physician to carry out an **in-depth medical, personal and dietary history**. This should include:

- Family or previous personal history of anemia
- Previous history of gallbladder disease, jaundice or enlarged spleen
- History or present heavy menstruation in women
- Bloody stool or signs of internal bleeding
- Dietary history in the elderly and poor, or both

Clue	Diagnosis
<b>8–12 weeks old</b> <ul style="list-style-type: none"> <li>• Pica with anemia only</li> <li>• Pica before anemia               <ul style="list-style-type: none"> <li>• Cows milk diet</li> <li>• Goats milk diet</li> <li>• Weight loss</li> </ul> </li> <li>• Lead in environment</li> </ul>	<b>Physiologic nadir</b> <ul style="list-style-type: none"> <li>• Iron deficiency</li> <li>• Lead poisoning</li> <li>• Iron deficiency</li> <li>• Folate deficiency</li> <li>• Systemic illness</li> </ul>

## Investigations

While there are several means of diagnosing anemia, the most readily available diagnostic test is a **Complete Blood Count (CBC)**. A complete blood count (CBC) is a cocktail of tests that are meant to provide information about the size, quantity, and shape of red blood cells. It also informs us about hemoglobin, hematocrit, and mean corpuscular volume.

Apart from red blood cells, a CBC also provides information on the volume of white blood cells and platelets.

The MCV and the RDW give important clues about the type of anemia.

Microcytic (MVC < 70)	Normocytic (MCV 70–85)	Macrocytic (MCV > 85)
<b>Iron deficiency</b>	Blood loss	<b>Folate deficiency</b>
<b>Lead poisoning</b>	Anemia of chronic disease	<b>Vitamin B12 deficiency</b>

## Hemoglobin

Hemoglobin is the iron-containing oxygen-carrying constituent of blood. The normal value of hemoglobin depends on the **age and gender** of the child.

Anemia is diagnosed when the amount of hemoglobin falls below 12 g/dL for non-pregnant women and 13 g/dL for men. To determine the severity of anemia, the concentration of hemoglobin is categorized as follows:

- Mild anemia is queried when hemoglobin is between 9.5–13.0 g/dL.
- Moderate anemia is suspected when hemoglobin is between 8.0–9.5 g/dL.
- Severe anemia is diagnosed when the concentration of hemoglobin is below 8.0 g/dL.

## Hematocrit

Hematocrit is the **proportion of red blood cells** in the blood. A child with a normal blood count and a high plasma volume may still be anemic because of the high volume of blood cells that have been diluted. The normal hematocrit value depends on the child's age and gender. The range of hematocrit that is used to determine the severity of anemia is:

- Children aged 6 months – 5 years: Below 33 %
- Children aged 5 years –12 years: Below 35 %
- Children aged 12 years –15 years: Below 36 %

## Mean corpuscular volume

Mean corpuscular volume (MCV) measures the **mean size of red blood cells** and is based on the premise that larger red blood cells (macrocytic) are a sign of anemia resulting from a deficiency of Vitamin B12, while microcytic (or smaller red blood cells) result from an iron deficiency or a chronic disease.

## Iron Profile

Iron deficiency is the most common cause of anemia. The iron studies are needed to confirm the diagnosis in patients with microcytic anemia.

## Hemoglobin Electrophoresis

Hemoglobin electrophoresis is required to diagnose the anemia caused by qualitative problems in the production of hemoglobin chains, for instance, thalassemia and sickle cell disease.

## Direct and indirect Coombs test

The Coombs test is used as part of the diagnosis of anemia. A Coombs test will also reveal if the body's antibodies are attacking its own red blood cells, as this can result in hemolytic anemia.

It is also used to check for any issues during blood transfusions as well as screen expectant mothers for the risk of their fetus developing hemolytic disease of the newborn.

# Management

The management of anemia is determined by the **etiology, type, and severity** of the anemia.

Before starting a specific therapy for the correction of anemia, the exact cause of anemia should be confirmed. For instance, corticosteroids are more effective in the treatment of autoimmune hemolytic anemia than other medications. Iron is replaced in cases of iron deficiency anemia and the successful treatment of chronic illnesses correct the underlying anemia.

The medical management of different types of hereditary disorders also varies greatly. For example, while splenectomy is effective in managing hereditary spherocytosis and hereditary elliptocytosis, it is not advantageous in treating other hereditary hemolytic disorders.

For patients with anemia resulting from leukemia, lymphoma, Hodgkin lymphoma, multiple myeloma, myelofibrosis and aplastic diseases, bone marrow, and stem cell transplantation have been used effectively and with excellent outcomes.

## Complications

**Prognosis of anemia is good** in most cases. However, complications may arise in some cases due to multiple organ dysfunctions. Possible complications might include:

- Congestive Cardiac Failure (CCF)
- High risk of infection
- Attention-deficit
- Developmental disorders
- Intellectual Disability (ID)
- Pica syndrome
- Plummer-Vinson syndrome (a triad of iron-deficiency anemia, glossitis, and esophageal webs).

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