

# Anemia



## ■ INTRODUCTION

Anemia is the blood disorder, characterized by the reduction in:

1. Red blood cell (RBC) count
2. Hemoglobin content
3. Packed cell volume (PCV).

Generally, reduction in RBC count, hemoglobin content and PCV occurs because of:

1. Decreased production of RBC
2. Increased destruction of RBC
3. Excess loss of blood from the body.

All these incidents are caused either by inherited disorders or environmental influences such as nutritional problem, infection and exposure to drugs or toxins.

## ■ CLASSIFICATION OF ANEMIA

Anemia is classified by two methods:

1. Morphological classification
2. Etiological classification.

### ■ MORPHOLOGICAL CLASSIFICATION

Morphological classification depends upon the size and color of RBC. Size of RBC is determined by mean corpuscular volume (MCV). Color is determined by mean corpuscular hemoglobin concentration (MCHC). By this method, the anemia is classified into four types (Table 14.1):

#### 1. Normocytic Normochromic Anemia

Size (MCV) and color (MCHC) of RBCs are normal. But the number of RBC is less.

#### 2. Macrocytic Normochromic Anemia

RBCs are larger in size with normal color. RBC count is less.

#### 3. Macrocytic Hypochromic Anemia

RBCs are larger in size. MCHC is less, so the cells are pale (less colored).

#### 4. Microcytic Hypochromic Anemia

RBCs are smaller in size with less color.

## ■ ETIOLOGICAL CLASSIFICATION

On the basis of etiology (study of cause or origin), anemia is divided into five types (Table 14.2):

1. Hemorrhagic anemia
2. Hemolytic anemia
3. Nutrition deficiency anemia
4. Aplastic anemia
5. Anemia of chronic diseases.

**TABLE 14.1: Morphological classification of anemia**

Type of anemia	Size of RBC (MCV)	Color of RBC (MCHC)
Normocytic normochromic	Normal	Normal
Normocytic hypochromic	Normal	Less
Macrocytic hypochromic	Large	Less
Microcytic hypochromic	Small	Less

## 1. Hemorrhagic Anemia

Hemorrhage refers to excessive loss of blood (Chapter 115). Anemia due to hemorrhage is known as hemorrhagic anemia. It occurs both in acute and chronic hemorrhagic conditions.

### Acute hemorrhage

Acute hemorrhage refers to sudden loss of a large quantity of blood as in the case of accident. Within about 24 hours after the hemorrhage, the plasma portion of blood is replaced. However, the replacement of RBCs does not occur quickly and it takes at least 4 to 6 weeks. So with less number of RBCs, hemodilution occurs. However, morphologically the RBCs are normocytic and normochromic.

Decreased RBC count causes hypoxia, which stimulates the bone marrow to produce more number of RBCs. So, the condition is corrected within 4 to 6 weeks.

### Chronic hemorrhage

It refers to loss of blood by internal or external bleeding, over a long period of time. It occurs in conditions like peptic ulcer, purpura, hemophilia and menorrhagia.

Due to continuous loss of blood, lot of iron is lost from the body causing iron deficiency. This affects the synthesis of hemoglobin resulting in less hemoglobin content in the cells. The cells also become small. Hence, the RBCs are microcytic and hypochromic (Table 14.2).

## 2. Hemolytic Anemia

Hemolysis means destruction of RBCs. Anemia due to excessive hemolysis which is not compensated by increased RBC production is called hemolytic anemia. It is classified into two types:

- A. Extrinsic hemolytic anemia.
- B. Intrinsic hemolytic anemia.

A. *Extrinsic hemolytic anemia*: It is the type of anemia caused by destruction of RBCs by external factors. Healthy RBCs are hemolyzed by factors outside the blood cells such as antibodies, chemicals and drugs. Extrinsic hemolytic anemia is also called **autoimmune hemolytic anemia**.

Common causes of external hemolytic anemia:

- i. Liver failure
- ii. Renal disorder

**TABLE 14.2: Etiological classification of anemia**

Type of anemia	Causes	Morphology of RBC
Hemorrhagic anemia	Acute loss of blood	Normocytic, normochromic
	Chronic loss of blood	Microcytic, hypochromic
Hemolytic anemia	Extrinsic hemolytic anemia: <ol style="list-style-type: none"> <li>i. Liver failure</li> <li>ii. Renal disorder</li> <li>iii. Hypersplenism</li> <li>iv. Burns</li> <li>v. Infections – hepatitis, malaria and septicemia</li> <li>vi. Drugs – Penicillin, antimalarial drugs and sulfa drugs</li> <li>vii. Poisoning by lead, coal and tar</li> <li>viii. Presence of isoagglutinins like anti Rh</li> <li>ix. Autoimmune diseases – rheumatoid arthritis and ulcerative colitis</li> </ol>	Normocytic normochromic
	Intrinsic hemolytic anemia: Hereditary disorders	Sickle cell anemia: Sickle shape Thalassemia: Small and irregular
Nutrition deficiency anemia	Iron deficiency	Microcytic, hypochromic
	Protein deficiency	Macrocytic, hypochromic
	Vitamin B12	Macrocytic, normochromic/hypochromic
	Folic acid	Megaloblastic, hypochromic
Aplastic anemia	Bone marrow disorder	Normocytic, normochromic
Anemia of chronic diseases	<ol style="list-style-type: none"> <li>i. Non-infectious inflammatory diseases – rheumatoid arthritis</li> <li>ii. Chronic infections – tuberculosis</li> <li>iii. Chronic renal failure</li> <li>iv. Neoplastic disorders – Hodgkin's disease</li> </ol>	Normocytic, normochromic

- iii. Hypersplenism
- iv. Burns
- v. Infections like hepatitis, malaria and septicemia
- vi. Drugs such as penicillin, antimalarial drugs and sulfa drugs
- vii. Poisoning by chemical substances like lead, coal and tar
- viii. Presence of isoagglutinins like anti-Rh
- ix. Autoimmune diseases such as rheumatoid arthritis and ulcerative colitis.

**B. Intrinsic hemolytic anemia:** It is the type of anemia caused by destruction of RBCs because of the defective RBCs. There is production of unhealthy RBCs, which are short lived and are destroyed soon. Intrinsic hemolytic anemia is often inherited and it includes sickle cell anemia and thalassemia.

Because of the abnormal shape in sickle cell anemia and thalassemia, the RBCs become more fragile and susceptible for hemolysis.

#### *Sickle cell anemia*

Sickle cell anemia is an inherited blood disorder, characterized by sickle-shaped red blood cells. It is also called **hemoglobin SS disease** or **sickle cell disease**. It is common in people of African origin.

Sickle cell anemia is due to the abnormal hemoglobin called hemoglobin S (sickle cell hemoglobin). In this,  $\alpha$ -chains are normal and  $\beta$ -chains are abnormal. The molecules of hemoglobin S polymerize into long chains and precipitate inside the cells. Because of this, the RBCs attain sickle (crescent) shape and become more fragile leading to hemolysis (Fig. 14.1). Sickle cell anemia occurs when a person inherits two abnormal genes (one from each parent).

In children, hemolyzed sickle cells aggregate and block the blood vessels, leading to infarction (stoppage of blood supply). The infarction is common in small bones. The infarcted small bones in hand and foot results in varying length in the digits. This condition is known as **hand and foot syndrome**. Jaundice also occurs in these children.

#### *Thalassemia*

Thalassemia is an inherited disorder, characterized by abnormal hemoglobin. It is also known as **Cooley's anemia** or **Mediterranean anemia**. It is more common in Thailand and to some extent in Mediterranean countries.

Thalassemia is of two types:

- i.  $\alpha$ -thalassemia
- ii.  $\beta$ -thalassemia.

The  $\beta$ -thalassemia is very common among these two.

In normal hemoglobin, number of  $\alpha$  and  $\beta$  polypeptide chains is equal. In thalassemia, the production of these chains become imbalanced because of defective synthesis of globin genes. This causes the precipitation of the polypeptide chains in the immature RBCs, leading to disturbance in erythropoiesis. The precipitation also occurs in mature red cells, resulting in hemolysis.

#### *$\alpha$ -Thalassemia*

$\alpha$ -thalassemia occurs in fetal life or infancy. In this  $\alpha$ -chains are less, absent or abnormal. In adults,  $\beta$ -chains are in excess and in children,  $\gamma$ -chains are in excess. This leads to defective erythropoiesis and hemolysis. The infants may be stillborn or may die immediately after birth.

#### *$\beta$ -Thalassemia*

In  $\beta$ -thalassemia,  $\beta$ -chains are less in number, absent or abnormal with an excess of  $\alpha$ -chains. The  $\alpha$ -chains precipitate causing defective erythropoiesis and hemolysis.

### **3. Nutrition Deficiency Anemia**

Anemia that occurs due to deficiency of a nutritive substance necessary for erythropoiesis is called nutrition deficiency anemia. The substances which are necessary for erythropoiesis are iron, proteins and vitamins like C, B12 and folic acid. The types of nutrition deficiency anemia are:

#### *Iron deficiency anemia*

Iron deficiency anemia is the most common type of anemia. It develops due to inadequate availability of iron for hemoglobin synthesis. RBCs are microcytic and hypochromic.

Causes of iron deficiency anemia:

- i. Loss of blood
- ii. Decreased intake of iron
- iii. Poor absorption of iron from intestine
- iv. Increased demand for iron in conditions like growth and pregnancy.

Features of iron deficiency anemia: Features of iron deficiency anemia are brittle nails, spoon-shaped nails (**koilonychias**), brittle hair, atrophy of papilla in tongue and **dysphagia** (difficulty in swallowing).

#### *Protein deficiency anemia*

Due to deficiency of proteins, the synthesis of hemoglobin is reduced. The RBCs are macrocytic and hypochromic.

### *Pernicious anemia or Addison's anemia*

Pernicious anemia is the anemia due to deficiency of vitamin B12. It is also called Addison's anemia. It is due to atrophy of the gastric mucosa because of autoimmune destruction of parietal cells. The gastric atrophy results in decreased production of intrinsic factor and poor absorption of vitamin B12, which is the maturation factor for RBC. RBCs are larger and immature with almost normal or slightly low hemoglobin level. Synthesis of hemoglobin is almost normal in this type of anemia. So, cells are macrocytic and normochromic/hypochromic.

Before knowing the cause of this anemia, it was very difficult to treat the patients and the disease was considered to be fatal. So, it was called pernicious anemia.

Pernicious anemia is common in old age and it is more common in females than in males. It is associated with other autoimmune diseases like disorders of thyroid gland, Addison's disease, etc. Characteristic features of this type of anemia are lemon yellow color of skin (due to anemic paleness and mild jaundice) and red sore tongue. Neurological disorders such as **paresthesia** (abnormal sensations like numbness, tingling, burning, etc.), **progressive weakness** and **ataxia** (muscular incoordination) are also observed in extreme conditions.

### *Megaloblastic anemia*

Megaloblastic anemia is due to the deficiency of another maturation factor called folic acid. Here, the RBCs are not matured. The DNA synthesis is also defective, so the nucleus remains immature. The RBCs are megaloblastic and hypochromic.

Features of pernicious anemia appear in megaloblastic anemia also. However, neurological disorders may not develop.

### **4. Aplastic Anemia**

Aplastic anemia is due to the disorder of red bone marrow. Red bone marrow is reduced and replaced by fatty tissues. Bone marrow disorder occurs in the following conditions:

- i. Repeated exposure to X-ray or gamma ray radiation.
- ii. Presence of bacterial toxins, quinine, gold salts, benzene, radium, etc.
- iii. Tuberculosis.
- iv. Viral infections like hepatitis and HIV infections.

In aplastic anemia, the RBCs are normocytic and normochromic.

### **5. Anemia of Chronic Diseases**

Anemia of chronic diseases is the second common type of anemia (next to iron deficiency anemia). It is characterized by short lifespan of RBCs, caused by disturbance in iron metabolism or resistance to erythropoietin action. Anemia develops after few months of sustained disease. RBCs are normocytic and normochromic.

Common causes anemia of chronic diseases:

- i. Non-infectious inflammatory diseases such as **rheumatoid arthritis** (chronic inflammatory autoimmune disorder affecting joints).
- ii. Chronic infections like tuberculosis (infection caused by *Mycobacterium tuberculosis*) and abscess (collection of pus in the infected tissue) in lungs.
- iii. Chronic renal failure, in which the erythropoietin secretion decreases (since erythropoietin is necessary for the stimulation of bone marrow to produce RBCs, its deficiency causes anemia).
- iv. Neoplastic disorders (abnormal and disorganized growth in tissue or organ) such as **Hodgkin's disease** (malignancy involving lymphocytes) and cancer of lung and breast.

RBCs are generally normocytic and normochromic in this type of anemia. However, in progressive disease associated with iron deficiency the cells become microcytic and hypochromic.

## ■ SIGNS AND SYMPTOMS OF ANEMIA

### ■ SKIN AND MUCOUS MEMBRANE

Color of the skin and mucous membrane becomes pale. Paleness is more constant and prominent in buccal and pharyngeal mucous membrane, conjunctivae, lips, ear lobes, palm and nail bed. Skin loses the elasticity and becomes thin and dry. Thinning, loss and early grayness of hair occur. The nails become brittle and easily breakable.

### ■ CARDIOVASCULAR SYSTEM

There is an increase in heart rate (tachycardia) and cardiac output. Heart is dilated and cardiac murmurs are produced. The velocity of blood flow is increased.

### ■ RESPIRATION

There is an increase in rate and force of respiration. Sometimes, it leads to breathlessness and dyspnea (difficulty in breathing). Oxygen-hemoglobin dissociation curve is shifted to right.

### ■ DIGESTION

Anorexia, nausea, vomiting, abdominal discomfort and constipation are common. In pernicious anemia, there is atrophy of papillae in tongue. In aplastic anemia, necrotic lesions appear in mouth and pharynx.

### ■ METABOLISM

Basal metabolic rate increases in severe anemia.

### ■ KIDNEY

Renal function is disturbed. Albuminuria is common.

### ■ REPRODUCTIVE SYSTEM

In females, the menstrual cycle is disturbed. There may be menorrhagia, oligomenorrhea or amenorrhea (Chapter 80).

### ■ NEUROMUSCULAR SYSTEM

Common neuromuscular symptoms are increased sensitivity to cold, headache, lack of concentration, restlessness, irritability, drowsiness, dizziness or vertigo (especially while standing) and fainting. Muscles become weak and the patient feels lack of energy and fatigued quite often and quite easily.