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Anaemia

is defined as decreased red cell count or haemoglobin content of blood.

Detection of anaemia is usually performed by estimating haemoglobin content of blood.

It can also be done by performing either total RBC count of blood or by estimating packed cell volume (haematocrit).

Clinically, anaemia is detected by assessing the degree of paleness usually by looking at the lower palpebral conjunctiva or nail beds.

Detection of morphological type of anaemia depends on various blood indices

Classification

Anemia's can be classified either **morphologically or etiologically**.

Common causes of anemia are:

1. Inadequate supply of nutrients resulting in deficiency anemia's (deficiency of iron, vitamins and proteins)

2. Aplasia of bone marrow.

3. Anemia associated with chronic diseases

4. Anemia associated with renal failure

5. Anemia due to inherited diseases (e.g. thalassemia)

6. Anemia due to blood loss

Morphological Classification

Morphologically, anemia are classified into three types:

Hypochromic microcytic,

Normochromic normocytic and

Macrocytic normochromic

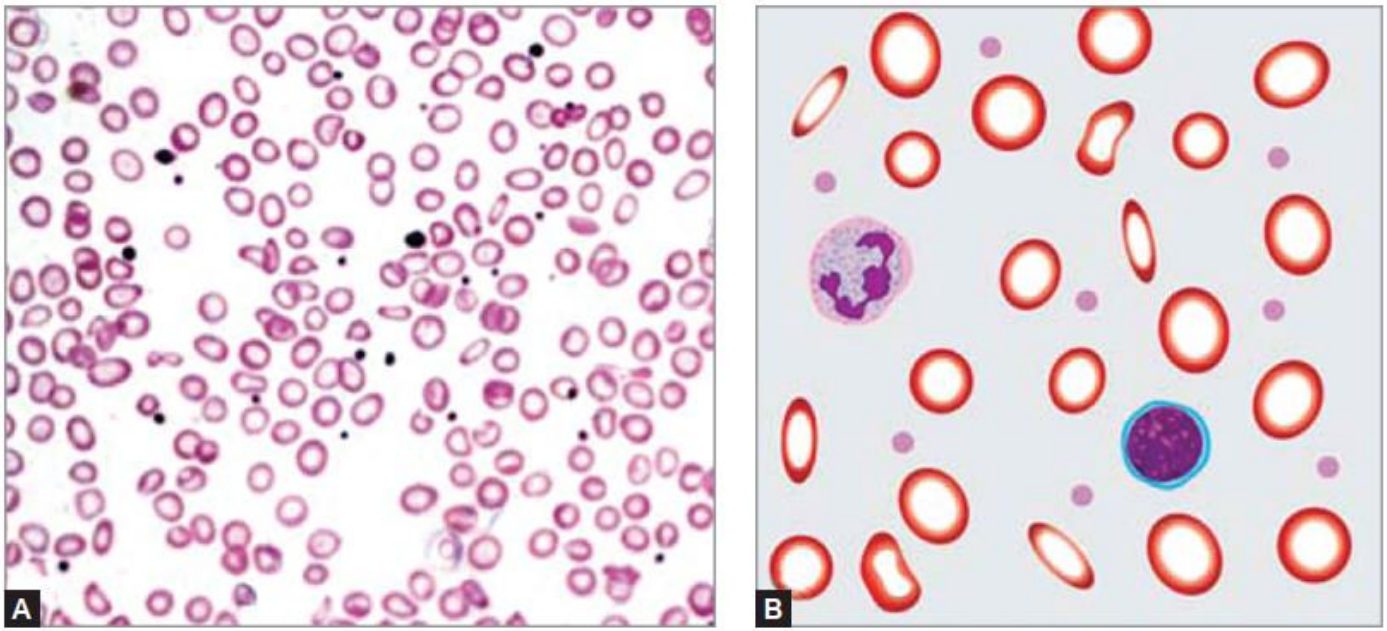
Hypochromic Microcytic Anemia

MCV, MCH, and MCHC are below normal. Such subnormal red cell indices correspond to **microcytosis** and **hypochromia** of red cells in the blood film

Micronormoblasts are seen in bone marrow examination.
This occurs due to the result of a **defect in red cell formation** in which ***hemoglobin synthesis is impaired*** to a great extent.
The common examples are:

i) ***Iron deficiency anemia*** in which there is inadequate iron for formation of the heme component of the hemoglobin, and

ii) ***Thalassemia*** in which the formation of the globin component of hemoglobin is defective.



Figs. 15.1A and B: Microcytic hypochromic anemia. (A) Peripheral blood smear (note microcytosis); (B) Schematic picture of the smear (note presence of microcytes with hypochromia).

Normochromic Normocytic Anemia

MCV, MCH, and MCHC are within the normal range. Size and hemoglobin concentration of the red cells are normal in the blood film.

It usually occurs in following conditions:

i) Substantial blood loss (***blood loss anemia***),

ii) Hemolysis (***hemolytic anemia***) and

iii) Impairment of red cell production by bone marrow failure or chronic renal failure (***aplastic anemia***

Macrocytic Normochromic Anemia

The MCV is above the upper limit of the normal. It corresponds to **macrocytosis** of red cells in the blood film.

The red cells are usually normochromic, though they are macrocytic.

Megaloblasts are seen in bone marrow examination.

Howell-Jolly body, hyper segmentation of neutrophils, basophilic stippling are also seen

The typical example of this type of anemia is ***megaloblastic anemia*** that occurs due to deficiency of vitamin B12 or folic acid

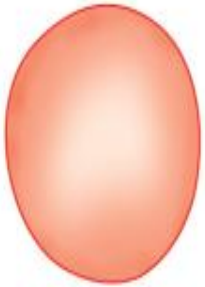
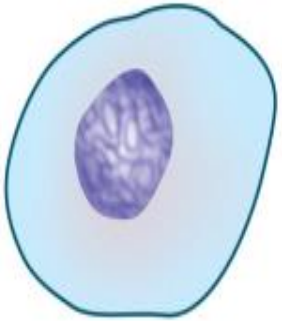
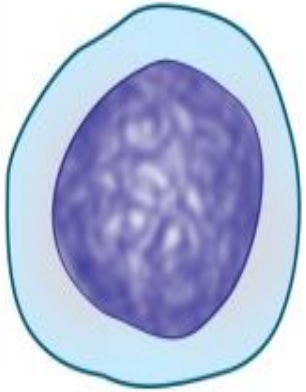
	Laboratory findings	Normal	Megaloblastic anemia
Blood	Red cell morphology	 Normal red cell	 Macrocytic red cell
	Red cell indices	MCV, MCH, MCHC—all normal	MCV ↑, MCH ↑, MCHC—Normal or ↓
Bone marrow	Marrow erythropoiesis	 Normoblastic	 Megaloblastic
	Marrow iron stores	 Normal	 Increased

Fig. 15.2: General laboratory findings in macrocytic anemia, compared with the normal report.

A. Decreased red cell production

1. *Stem cell failure*
   - Aplastic anemia
   - Anemia of leukemia

2. *Progenitor cell failure*
   - Pure red cell aplasia
   - Chronic renal failure
   - Chronic diseases

3. *Precursor cell failure*
   - Megaloblastic anemia
   - Iron deficiency anemia
   - Thalassemia
   - Hemoglobinopathies

B. Increased red cell destruction or loss

1. *Acquired causes*
   - Acute blood loss
   - Hypersplenism
   - Micro- and macroangiopathic
   - Antibody-mediated

2. *Hereditary causes*
   - Membrane defects
   - Enzyme defects
   - Globin defect

Etiological classification :

Blood Loss Anemia

Anemia due to blood loss mainly occurs due to acute hemorrhage or chronic hemorrhage.

Acute Hemorrhage:

Anemia due to acute hemorrhage depends on the extent of blood loss and the time that has lapsed since bleeding.

In acute blood loss, usually there is a reduction in the total blood volume. Therefore, hemoglobin in the residual blood is normal.

However, when the compensatory mechanisms set in to expand the blood volume, hemodilution decreases hemoglobin content.

Therefore, estimation of hemoglobin after few hours of acute blood loss does not assesses the actual degree of anemia.

Chronic Hemorrhage:

Chronic hemorrhage occurs mainly in gastrointestinal, genitourinary and respiratory tract diseases.

Gastrointestinal blood loss:

Peptic ulcer, hemorrhoids, hiatus hernia, carcinoma of the stomach and colon, esophageal verises, chronic aspirin ingestion, ulcerative colitis, hookworm infestation etc.

Respiratory diseases:

Respiratory diseases that produce epistaxis, hemoptysis as occurs in pulmonary tuberculosis or bronchogenic carcinoma produce anemia

Genitourinary disease:

Diseases that cause hematuria and hemoglobinuria produce anemia.

Diseases of genital tract:

In females, loss of blood from genital tract like menstrual disorders (menorrhagia, metrorrhagia) and uterine pathologies produce anemia

Aplastic Anemia

Aplastic anemia is the anemia due to **impaired red cell production**. Marrow examination shows a near ***absence of hematopoietic precursor cells***.

Hemolytic Anemia

Hemolytic anemia results from increase in the rate of red cell destruction.
Defects causing premature red cell destruction may be divided into two broad categories:

Intracorpuscular, and
Extracorpuscular

1. Acquired conditions

i. Chemicals: Benzene, DDT, and pentachlorophenol

ii. Drugs:

- Anticancer drugs (cyclophosphamide, busulfan, methotrexate, 5-flurouracil, daunorubicin),
- Antibiotics (chloramphenicol)
- Diuretics (acetazolamide)
- Anti-inflammatory (phenylbutazone)
- Anticonvulsant (carbamazepine, hydantoin)

iii. Radiation of bone marrow

iv. Viral infections: Epstein-Barr virus, hepatitis (non-A, non-B)

2. Hereditary conditions

i. Fanconi anemia

ii. Schwachman syndrome

3. Idiopathic (most common, 65% of all causes)

Classification of aplastic anemia:

Iron Deficiency Anemia (IDA)

This is the commonest form of anemia in the developing countries. It usually occurs due to deficiency of iron in the diet. There are **three major factors** in the pathogenesis of IDA.

Increased physiological demand for iron as occurs in pregnancy, lactation, growing children. Therefore, in these groups, extra iron should be available in the diet; otherwise IDA occurs.

Inadequate iron intake, as occurs due to deficiency in the diet.

Pathological blood loss like bleeding peptic ulcer, piles, worm infestations, epistaxis, hemoptysis etc.

Hereditary Spherocytosis

This is a hemolytic anemia in which the fundamental abnormality is the increased defect of red cell membrane (due to decreased quantity of spectrin) that results in spherocytic shape of the cell.

Spherocytes have a decreased surface area to volume ratio and the cells are more rigid (less deformable).
Therefore, when cells pass through the splenic pulp, they are destroyed.

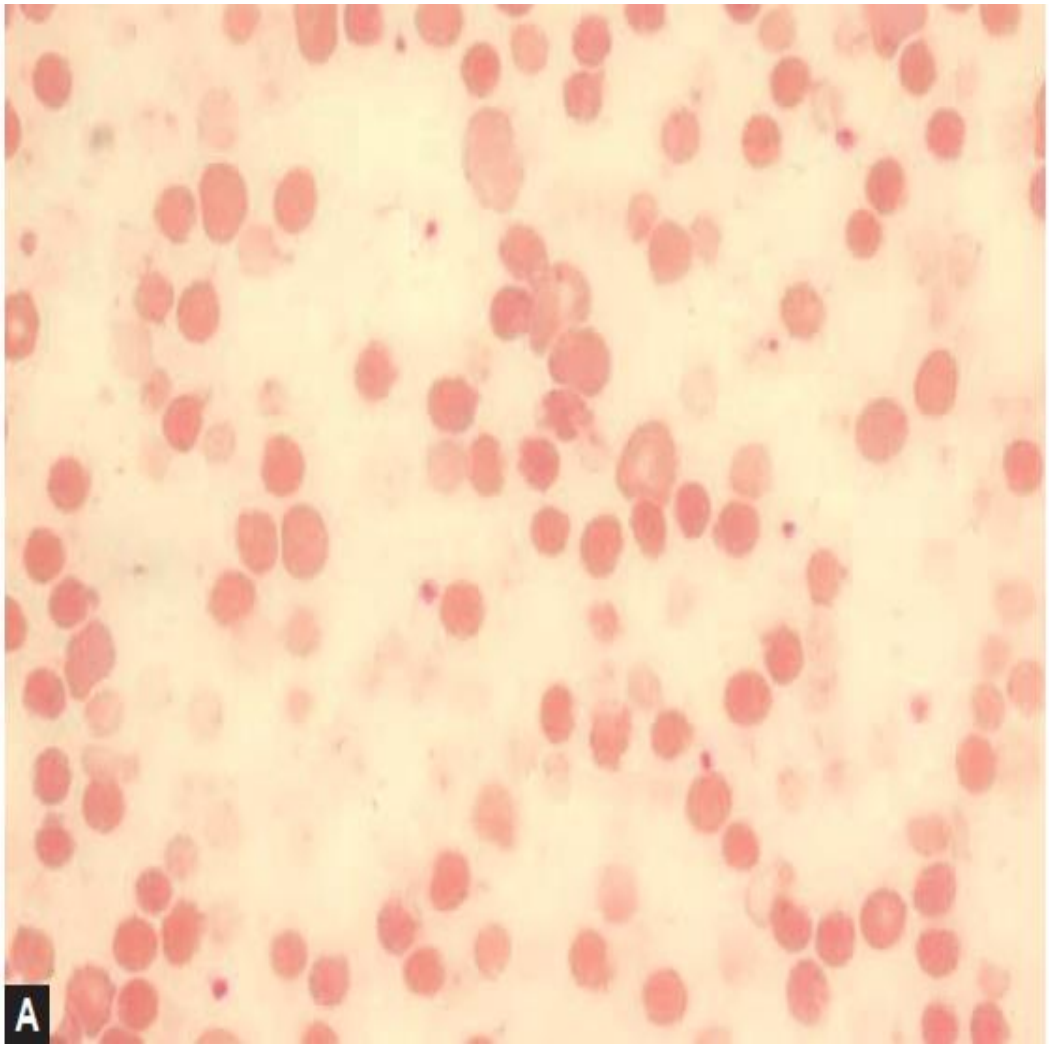
This is an ***autosomal dominant disorder*** which affects males and females equally

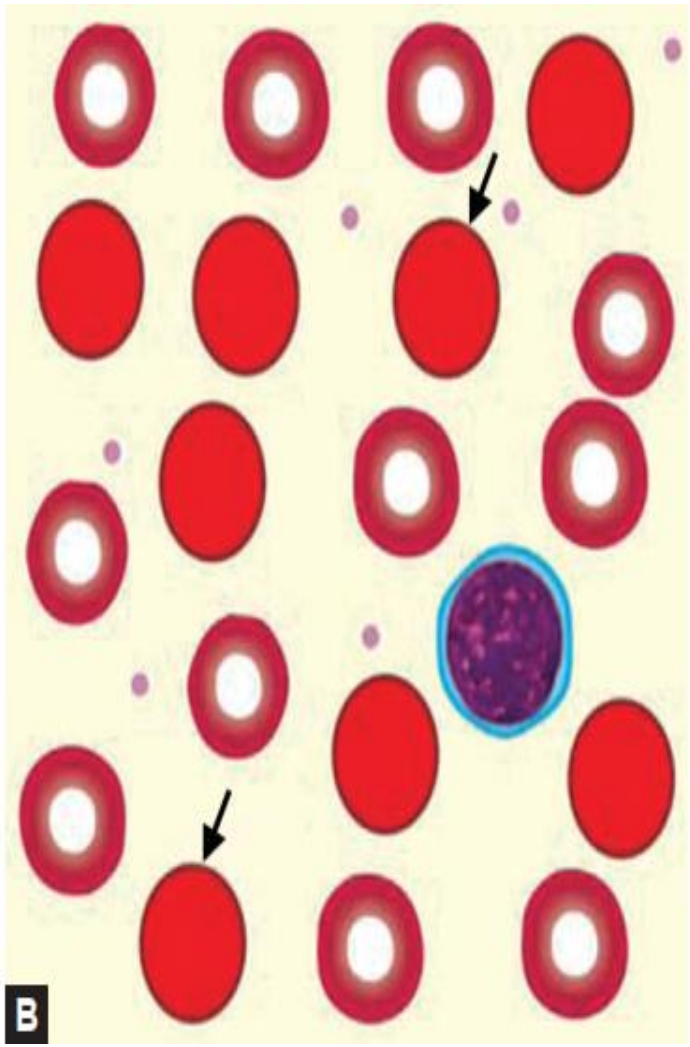
The usual features are anemia, jaundice, enlarged spleen, and may present with gall stone.

The blood picture typically shows **anemia with spherocytosis,** increased osmotic fragility, hyper bilirubinemia, and reticulocytosis.

Usually, anemia is **normocytic and normochromic**.

Splenectomy helps in improving the condition





A} peripheral smear showing numerous spherocytes in hereditary spherocytosis .

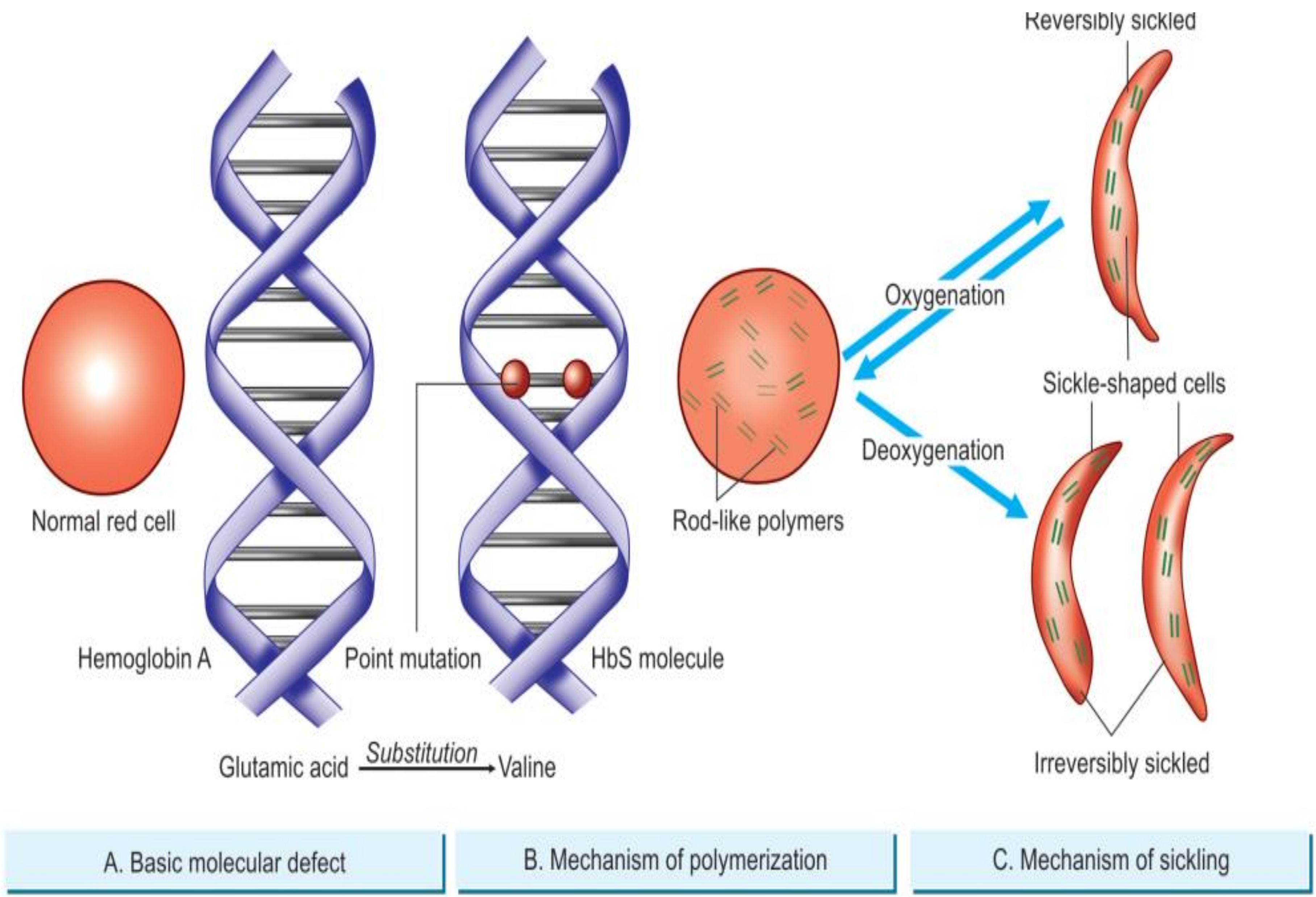
B} note presence of many spherical red cells indicated by arrow

Sickle Cell Anemia

This is a hereditary disorder in which red cells contain an abnormal hemoglobin called **Hb S**.

Hb S is the hemoglobin in which *glutamic acid is replaced by **valine** at the 6th position of beta chain*.
In the deoxygenated state, conformational changes induced by Hb S makes the cell more rigid and deformed to take the shape of a sickle.

Therefore, cells undergo **intravascular hemolysis**.



Pathogenesis of sickle cell anemia.. Note sickling occurs on deoxygenation .

Diagnosis is usually made by

- **sickle test**

(demonstrating sickling of red cells when the blood is mixed with freshly prepared solution of a reducing agent like sodium meta-bisulphite),

- **hemoglobin solubility test**

(relative insolubility of reduced Hb S in phosphate buffer), and **hemoglobin electrophoresis**.

- **Hyposplenism** is usually associated, due to micro-infarctions in spleen. ***Autosplenectomy*** may occur.

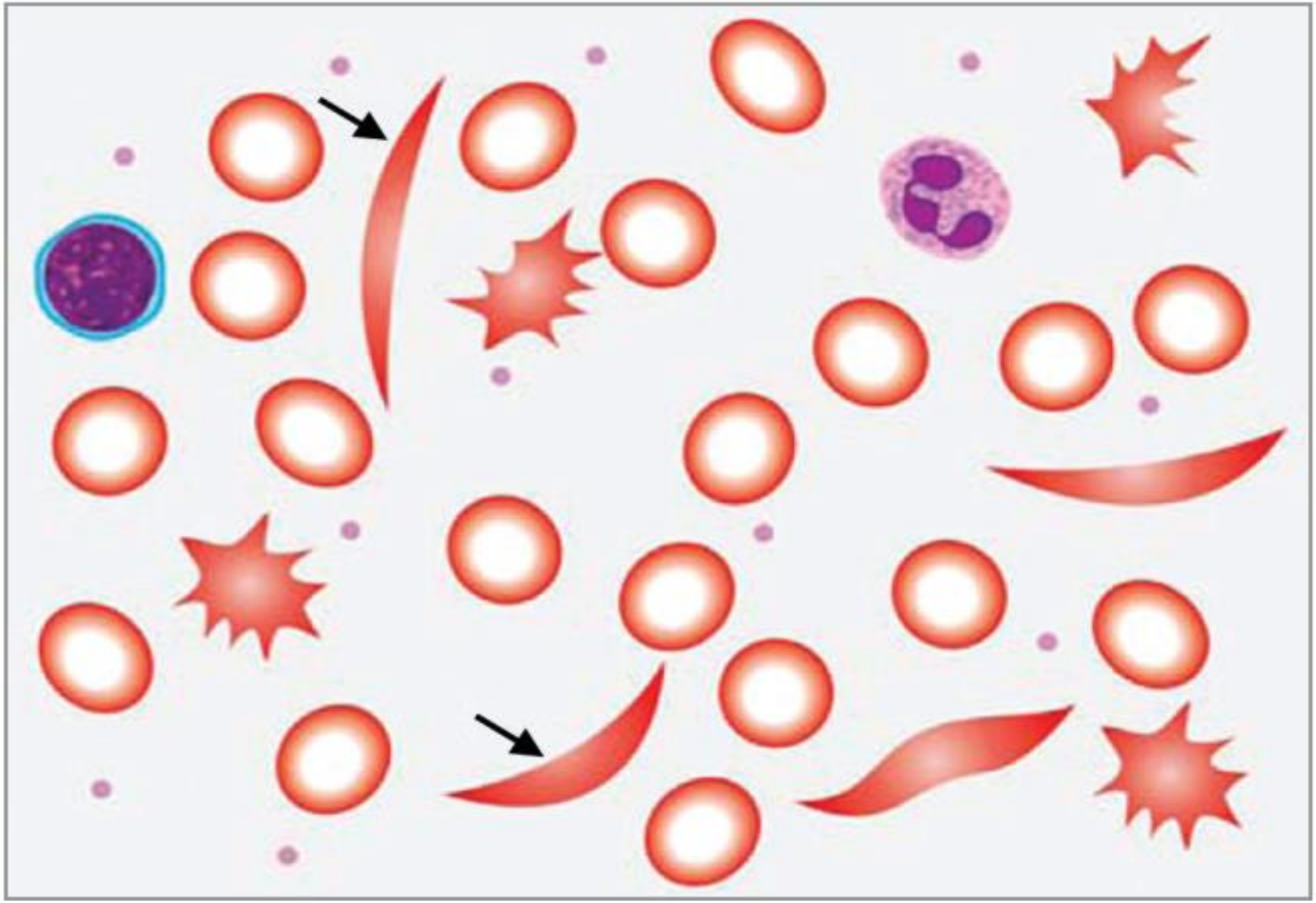
The anemia is usually **normochromic and normocytic**

Thalassemia:

Thalassemia is a genetically determined heterogeneous group of commonest *monogenic disorder* in which the rate of **synthesis of one or more types of hemoglobin polypeptide chain is decreased**. Thus, there are two major classes of thalassemia:
α thalassemia and β thalassemia, in which α and β globin genes are involved respectively.
This causes decrease in the respective polypeptide chain of hemoglobin

Types of thalassemia:

1. ***β thalassemia***
2. ***α thalassemia***

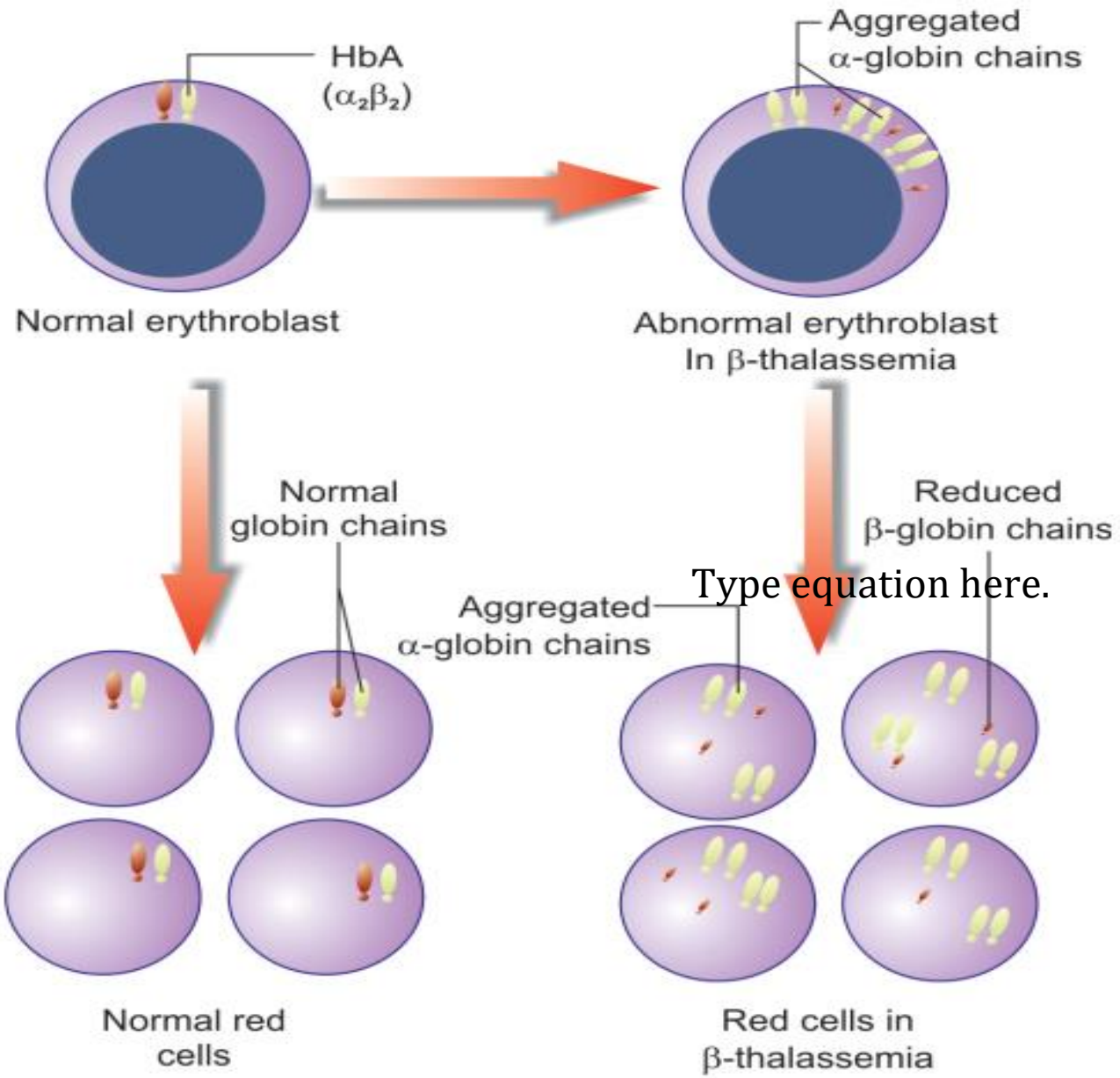


Examination of peripheral blood smear in sickle cell anemia.
Note the red cells in sickle shape

β thalassemia

In β thalassemia (failure to synthesize β chain), which is more common, there is excess α chain production that damages red cell precursor and red cells.
There are many homozygous and heterozygous, and major and minor forms of the disease.

In **β thalassemia major**, anemia develops in first few months of life and becomes progressively severe.
Splenomegaly, hepatomegaly and skeletal deformities are common.
Though anemia is usually *microcytic and hypochromic*, all forms and combinations are not uncommon



Pathogenesis of β - thalasssemia major

α thalassemia

Anemia of **α thalassemia** (failure to synthesize α chain) is more *hemolytic* than dyserythropoietic.
The thalassemias are **diagnosed** by:
Hemoglobin electrophoresis

Demonstration of **Hb-H inclusions** (in the absence of sufficient alpha chains, excess of beta or gamma chains aggregate to form Hb-H)
Study of rate of globin chain synthesis
Alkali denaturation test
Acid elution test

Polycythemia

Though, polycythemia strictly denotes increase in all cell types of blood, traditionally it represents increase in number of red cells. It exists in two main forms.

The ***primary form***, also called **polycythemia Vera** is a clonal neoplastic disorder of hematopoietic stem cells.

The ***secondary forms*** are conditions of increased red cell production that usually occur due to appropriate or inappropriate increase in secretion of erythropoietin

A. Primary polycythemia
- Polycythemia vera
B. Secondary polycythemia (secondary erythrocytosis)
1. Appropriate increase in erythropoietin secretion (proportionate to the degree of tissue hypoxia) – High altitude – Congenital heart disease with right to left shunt – Chronic pulmonary diseases – Chronic smokers – Enzyme deficiency in red cells
2. Inappropriate increase in erythropoietin secretion – Renal tumors, renal cyst, hydronephrosis – Liver tumors (mainly hepatocarcinoma) – Brain tumors (cerebellar hemangioma) – Endocrine disorders (pheochromocytoma, virilizing ovarian tumors, Batter syndrome)
C. Apparent (relative) polycythemia
– Dehydration – Redistribution of body fluid

Types of polycythemia

In primary form, the cause of the disease is the ***abnormality of Haemopoietic stem cells*** characterized by uncontrolled proliferation of cells of erytroid, granulocytic and megakaryocytic series, resulting in increased of all forms of formed elements of blood.

Thus, "***primary polycythemia***" is appropriate for the primary form

In secondary forms, the cause of the disease is ***excess erythropoietin secretion*** that results in increase in red cell production (mostly without increase in granulocytes and platelets).

Thus, "***secondary erythrocytosis***" is more appropriate than secondary polycythemia for the secondary forms

Types of Polycythemia

Polycythemia is broadly divided into ***three forms*** .
The **primary form** is the *polycythemia vera*.

The **secondary forms** are secondary to other conditions or diseases.

The ***relative or apparent polycythemia*** is not true polycythemia, but a spurious increase in red cells due to dehydration

Polycythaemia Vera

Polycythaemia Vera is an abnormality of hematopoietic stem cell in which a single stem cell is transformed into a cell that has a selective growth advantage that gradually becomes the major source of marrow precursors.

Disease commonly starts in 6th decade of life, and usually presents with headache, plethora (a ruddy complexion), pruritus, thrombosis and GI bleeding.

For plethoric appearance of patients, the disease is also called Polycythaemia Rubra Vera