HAEMOGLOBIN
&
ANEMIA

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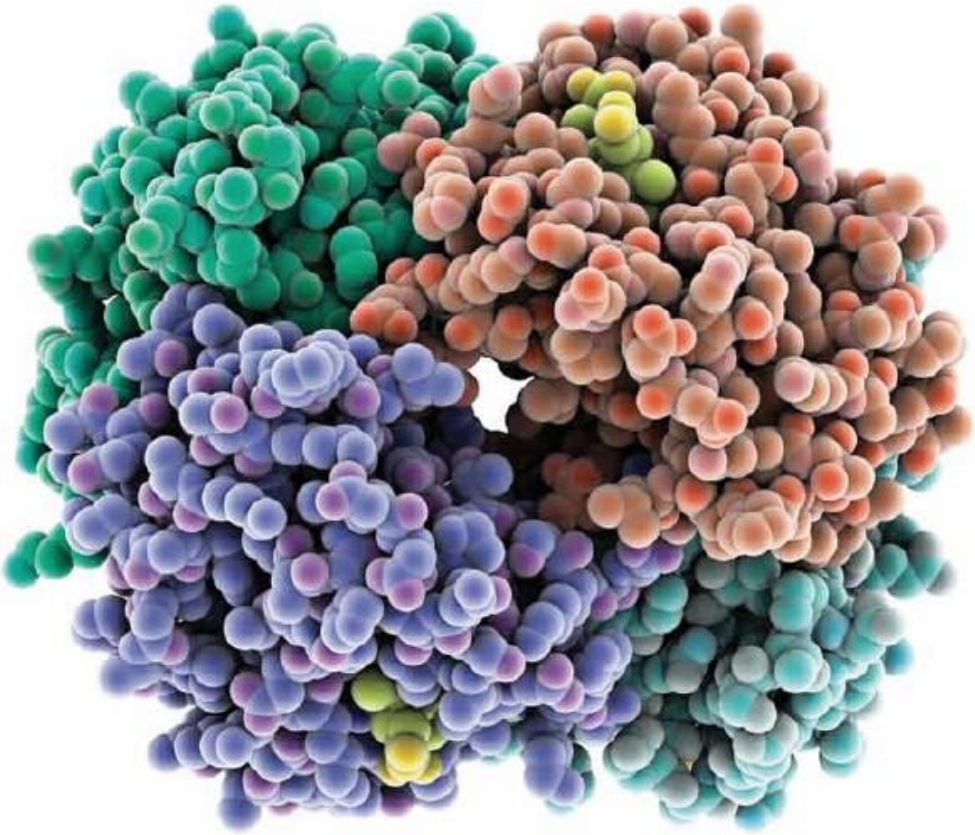
HEMOGLOBIN



INTRODUCTION

- Hemoglobin (Hb) is the iron containing coloring matter of red blood cell (RBC).
- It is a chromoprotein forming 95% of dry weight of RBC and 30% to 34% of wet weight.
- Function of hemoglobin is to carry the respiratory gases, oxygen and carbon dioxide.
- It also acts as a buffer.
- Molecular weight of hemoglobin is 68,000.

NORMAL HEMOGLOBIN CONTENT

- Average hemoglobin (Hb) content in blood is 14 to 16 g/dL.
- However, the value varies depending upon the age and sex of the individual.

AGE

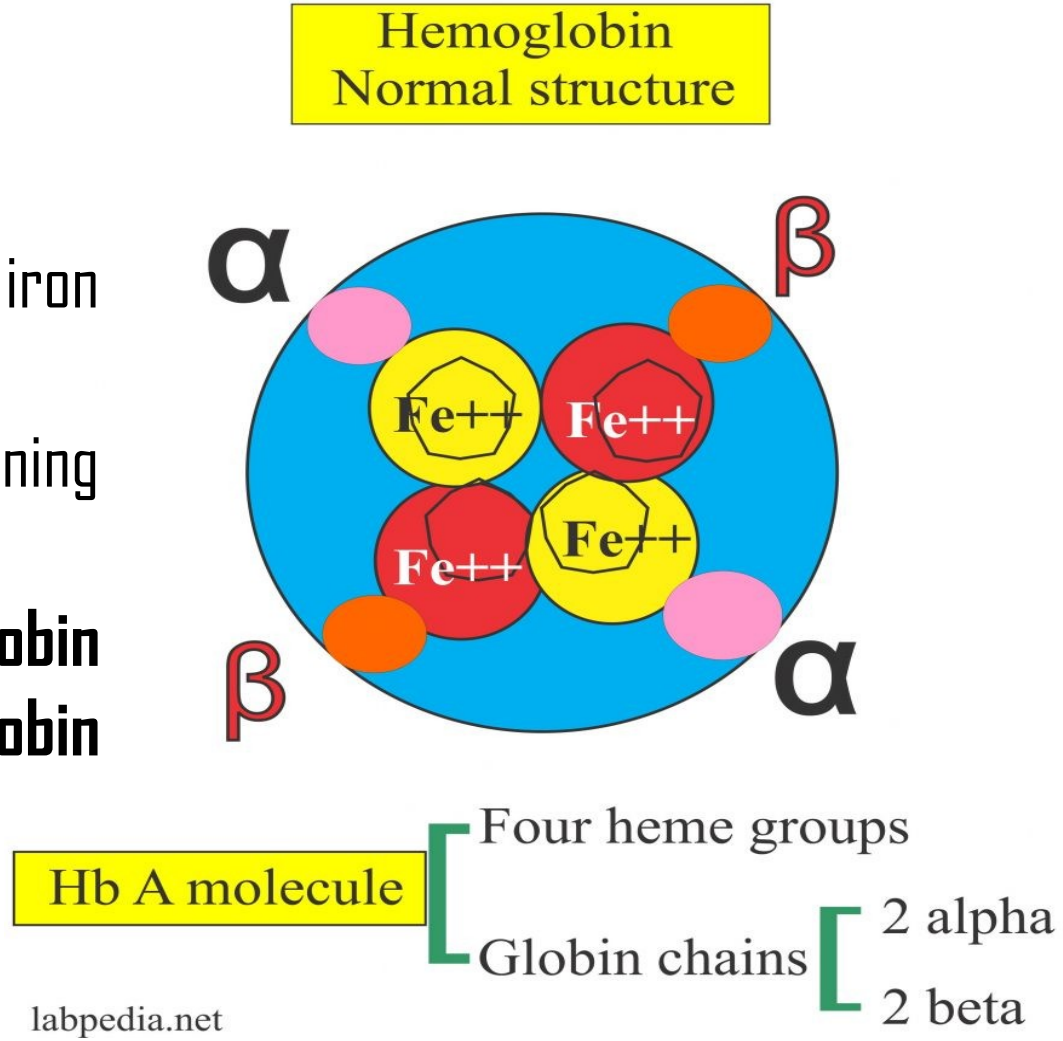
- At birth : 25 g/dL
- After 3rd month : 20 g/dL
- After 1 year : 17 g/dL
- From puberty onwards : 14 to 16 g/dL.

SEX

- In adult males : 15 g/dL
- In adult females : 14.5 g/dL

STRUCTURE OF HEMOGLOBIN

- Hemoglobin is a conjugated protein.
- It consists of a protein combined with an iron containing pigment.
- The protein part is globin and the iron containing pigment is **heme.**
- Heme also forms a part of the structure of **myoglobin** (oxygenbinding pigment in muscles) and **neuroglobin** (oxygenbinding pigment in brain).



IRON

- Normally, it is present in ferrous (Fe2+) form.
- It is in unstable or loose form.
- In some abnormal conditions, the iron is converted into ferric (Fe3+) state, which is a stable form.

PORPHYRIN

- The pigment part of heme is called porphyrin.
- It is formed by four pyrrole rings (tetrapyrrole) called, I, II, III and IV.
- The **pyrrole rings** are attached to one another by methane (CH4) bridges.
- The iron is attached to 'N' of each pyrrole ring and 'N' of globin molecule.

GLOBIN

- Globin contains four polypeptide chains.
- Among the four polypeptide chains, two are chains and two are α-chains.

Polypeptide chain	Molecular weight	Amino acids
α-chain	15,126	141
β-chain	15,866	146

TYPES OF NORMAL HEMOGLOBIN

- Hemoglobin is of two types:

1. Adult hemoglobin – HbA
2. Fetal hemoglobin – HbF

- Replacement of fetal hemoglobin by adult hemoglobin starts immediately after birth. It is completed at about 10th to 12th week after birth.
- Both the types of hemoglobin differ from each other structurally and functionally.

Structural Difference

- In adult hemoglobin, the globin contains two α-chains and two β-chains.
- In fetal hemoglobin, there are two α chains and two γ-chains instead of β-chains.

Functional Difference

- Functionally, fetal hemoglobin has more affinity for oxygen than that of adult hemoglobin.

ABNORMAL HEMOGLOBIN

- Abnormal types of hemoglobin or hemoglobin variants are the pathologic mutant forms of hemoglobin.
- These variants are produced because of structural changes in the polypeptide chains caused by mutation in the genes of the globin chains.
- Most of the mutations do not produce any serious problem.
- Occasionally, few mutations result in some disorders.
- There are two categories of abnormal hemoglobin:

1. **Hemoglobinopathies:** It is a genetic disorder caused by abnormal polypeptide chains of hemoglobin. Like Hemoglobin S, Hemoglobin C and Hemoglobin M etc.
2. **Hemoglobin in thalassemia and related disorders:** In thalassemia, different types of abnormal hemoglobins are present. The polypeptide chains are decreased, absent or abnormal. Like hemoglobin G, H, I, Bart's and Kenya etc.

ABNORMAL HEMOGLOBIN DERIVATIVES

- Hemoglobin is the only carrier for transport of oxygen, without which tissue death occurs within few minutes.
- When hemoglobin is altered, its oxygen carrying capacity is decreased resulting in lack of oxygen. So, it is important to know about the causes and the effects of abnormal hemoglobin derivatives.
- Abnormal hemoglobin derivatives are formed by carbon monoxide (CO) poisoning or due to some drugs like nitrites, nitrates and sulphanamides.
- Abnormal hemoglobin derivatives are:

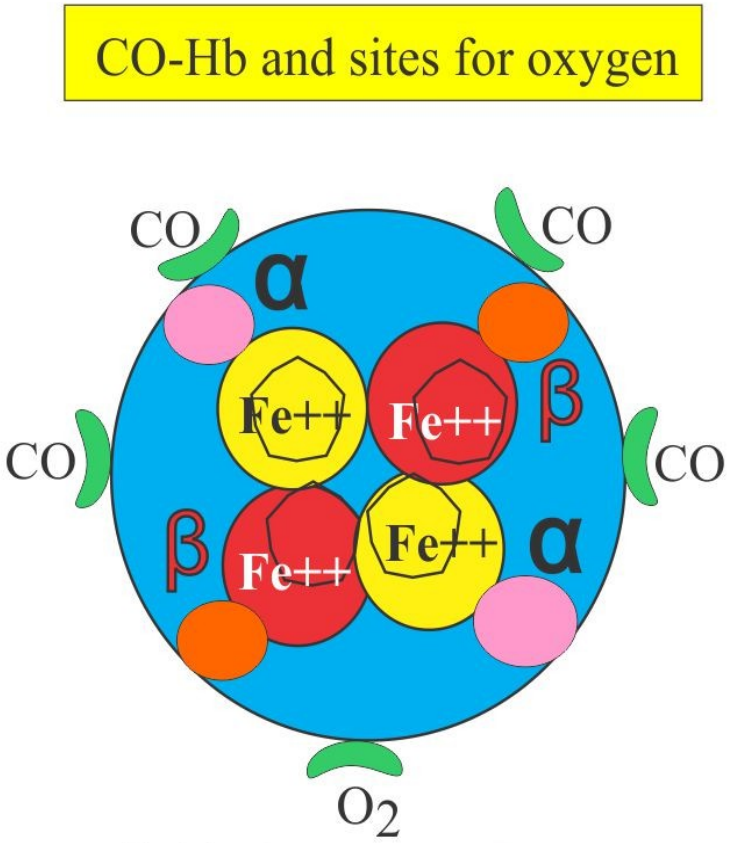
1. **Carboxyhemoglobin**
2. **Methemoglobin**
3. **Sulfhemoglobin.**

CARBOXYHEMOGLOBIN

- Carboxyhemoglobin or carbon monoxyhemoglobin is the abnormal hemoglobin derivative formed by the combination of carbon monoxide with hemoglobin.
- Carbon monoxide is a colorless and odorless gas.
- Since hemoglobin has 200 times more affinity for carbon monoxide than oxygen, it hinders the transport of oxygen resulting in tissue hypoxia.

Sources of Carbon Monoxide

1. Charcoal burning
2. Deep wells & Underground drainage system
3. Exhaust of gasoline engines
4. Heating system with poor or improper ventilation
5. Smoke from fire



Signs and Symptoms of Carbon Monoxide Poisoning

1. While breathing air with less than 1% of CO, the Hb saturation is 15% to 20% and mild symptoms like headache and nausea appear
2. While breathing air with more than 1% CO, the Hb saturation is 30% to 40%. It causes severe symptoms like:
    I. **Convulsions**
    II. **Cardiorespiratory arrest**
    III. **Unconsciousness and coma.**
3. When Hb saturation increases above 50%, **death** occurs.

METHEMOGLOBIN

- Methemoglobin is the abnormal hemoglobin derivative formed when iron molecule of hemoglobin is oxidized from normal ferrous state to ferric state.
- Methemoglobin is also called **ferrihemoglobin.** Normal methemoglobin level is 0.6% to 2.5% of total hemoglobin.

SULFHEMOGLOBIN

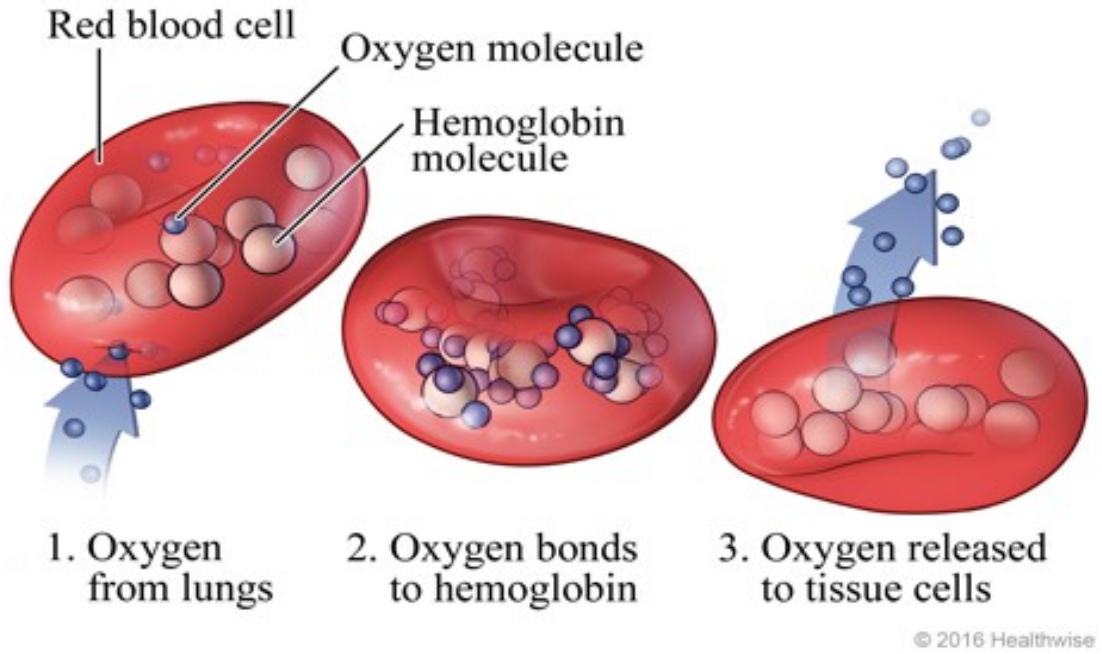
- Sulfhemoglobin is the abnormal hemoglobin derivative, formed by the combination of hemoglobin with hydrogen sulfide.
- It is caused by drugs such as phenacetin or sulfonamides.
- Normal sulfhemoglobin level is less than 1% of total hemoglobin.
- Sulfhemoglobin cannot be converted back into hemoglobin.
- Only way to get rid of this from the body is to wait until the affected RBCs with sulfhemoglobin are destroyed after their lifespan.

FUNCTIONS OF HEMOGLOBIN

TRANSPORT OF RESPIRATORY GASES

- Main function of hemoglobin is the transport of respiratory gases:

1. **Oxygen from the lungs to tissues.**
2. **Carbon dioxide from tissues to lungs.**



TRANSPORT OF OXYGEN

- When oxygen binds with hemoglobin, a physical process called **oxygenation** occurs, resulting in the formation of oxyhemoglobin.
- Oxyhemoglobin is an unstable compound and the combination is reversible, i.e. when more oxygen
- is available, it combines with hemoglobin and whenever oxygen is required, hemoglobin can release oxygen readily.

TRANSPORT OF CARBON DIOXIDE

- When carbon dioxide binds with hemoglobin, carbhemoglobin is formed.
- It is also an unstable compound and the combination is reversible, i.e. the carbon dioxide can be released from this compound.
- The affinity of hemoglobin for carbon dioxide is 20 times more than that for oxygen.

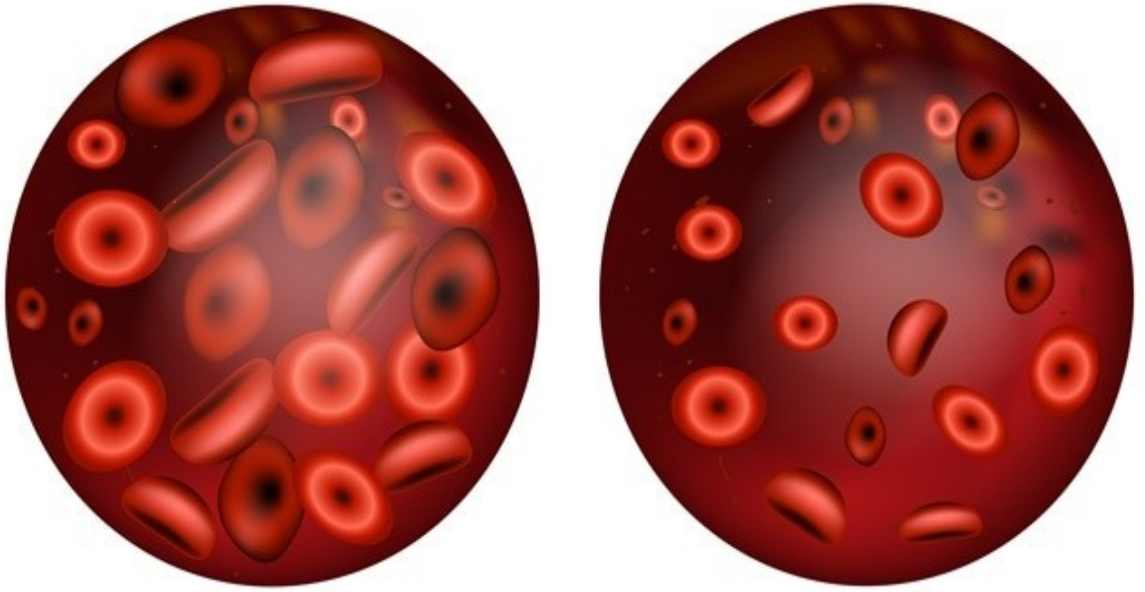
BUFFER ACTION

- Hemoglobin acts as a buffer and plays an important role in acidbase balance.

ANEMIA

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

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



- 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:

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.

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

ETIOLOGICAL CLASSIFICATION

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

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

1. HEMORRHAGIC ANEMIA

- Hemorrhage refers to excessive loss of blood.
- Anemia due to hemorrhage is known as hemorrhagic anemia.

- It occurs both in acute and chronic hemorrhagic conditions.

A. 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.
- 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.

B. 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.

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 hemolized 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:

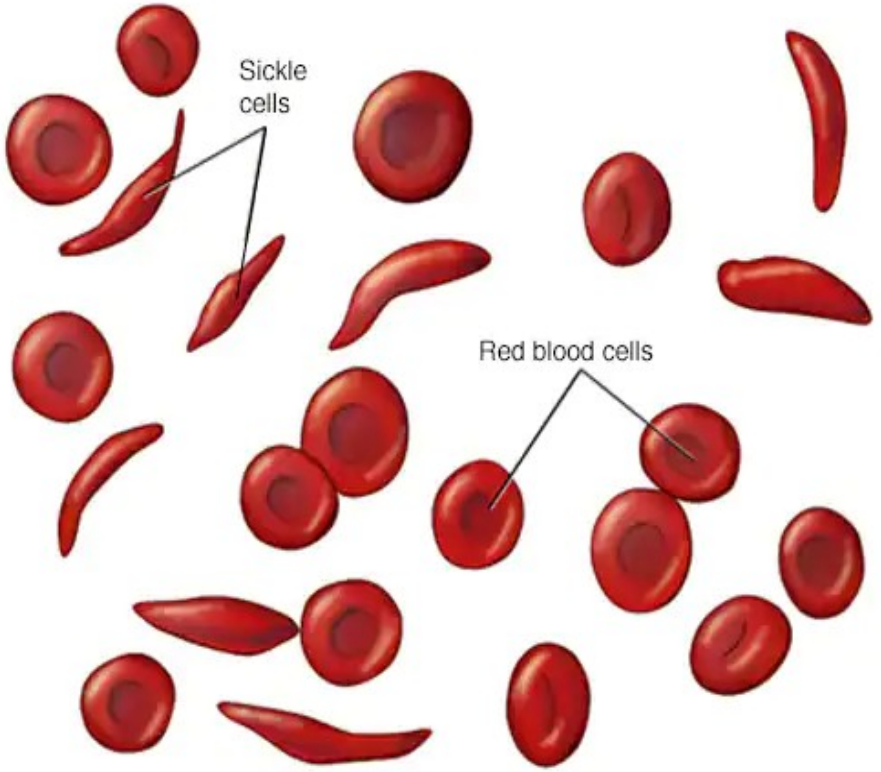
  i. Liver failure
  ii. Renal disorder
  iii. Infections like hepatitis, malaria and septicemia
  iv. Drugs such as penicillin, antimalarial drugs and sulfa drugs
  v. Poisoning by chemical substances like lead, coal and tar
  vi. Autoimmune diseases such as rheumatoid arthritis and ulcerative colitis.

B. INTRINSIC HEMOLYTIC ANEMIA:

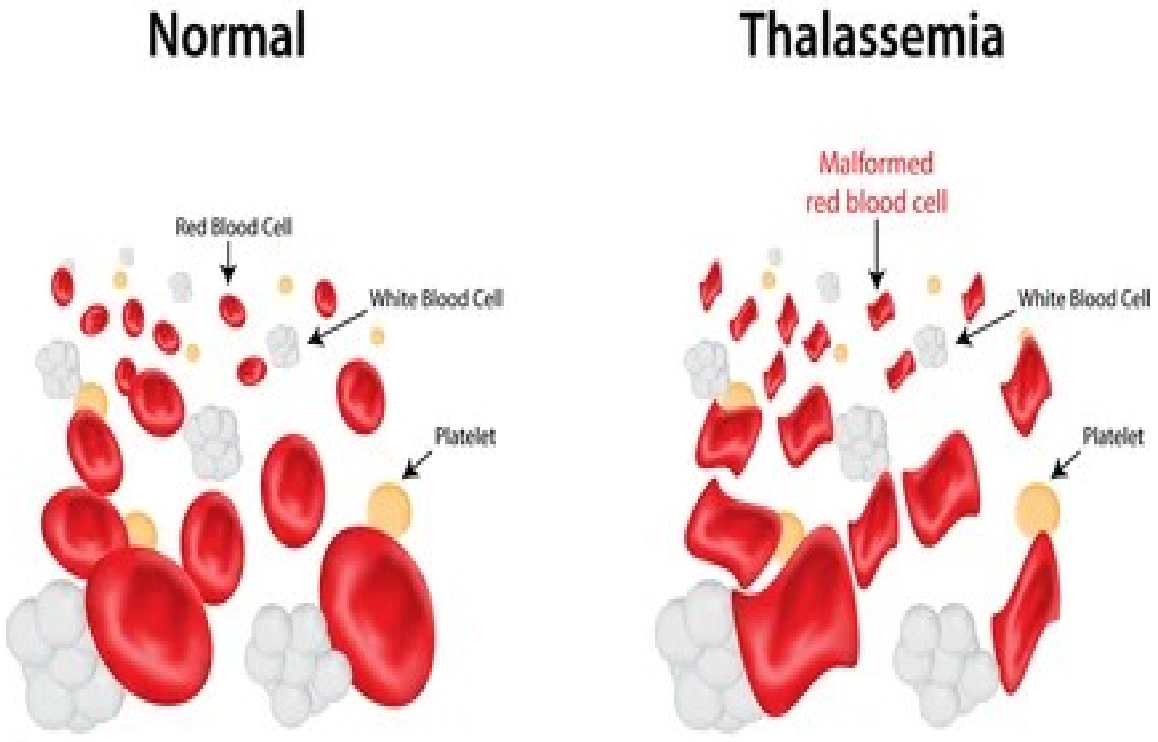
- It is the type of anemia caused by destruction of RBCs because of the defective RBCs.
- There is production of unhealthy RBCs, which are short lived and are destroyed soon.
- Intrinsic hemolytic anemia is often inherited and it includes sickle cell anemia and thalassemia.
- Because of the abnormal shape in sickle cell anemia and thalassemia, the RBCs become more fragile and susceptible for hemolysis.

I. SICKLE CELL ANEMIA

- Sickle cell anemia is an inherited blood disorder, characterized by sickle shaped red blood cells.
- It is due to the abnormal hemoglobin called hemoglobin S.
- In this, α chains are normal and β chains are abnormal.



B. THALASSEMIA



- Thalassemia is an inherited disorder, characterized by abnormal hemoglobin.
- It is also known as **Cooley's anemia** or **Mediterranean anemia.**
- Thalassemia is of two types:
  - **i. α thalassemia**
  - **ii. β thalassemia.**
- The β thalassemia is very common among these two.
- 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.

C. 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:

I. IRON DEFICIENCY ANEMIA

- Iron deficiency anemia is the most common type of anemia.
- It develops due to inadequate availability of iron for hemoglobin synthesis.
- Causes of iron deficiency anemia are loss of blood, decreased intake of iron, poor absorption of iron from intestine and Increased demand for iron in pregnancy.

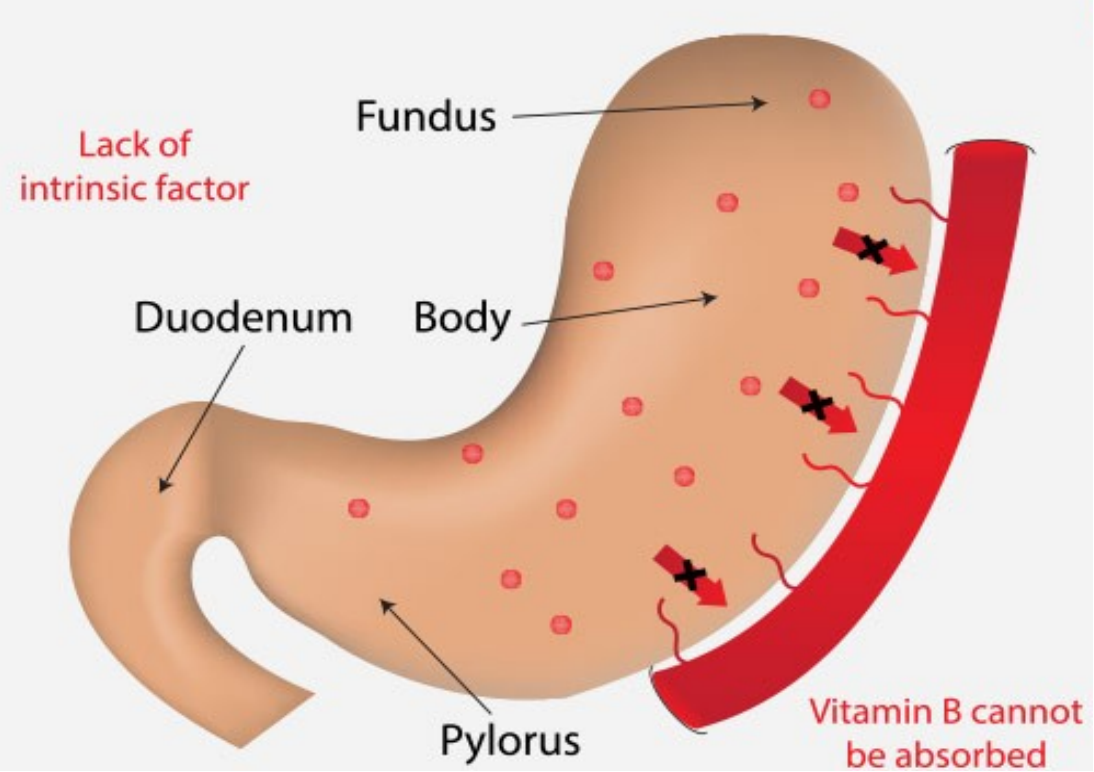
- Features of iron deficiency anemia are brittle nails, spoon shaped nails **(koilonychias),** brittle hair, atrophy of papilla in tongue and **dysphagia** (difficulty in swallowing).

II. PROTEIN DEFICIENCY ANEMIA

- Due to deficiency of proteins, the synthesis of hemoglobin is reduced.

III. 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.



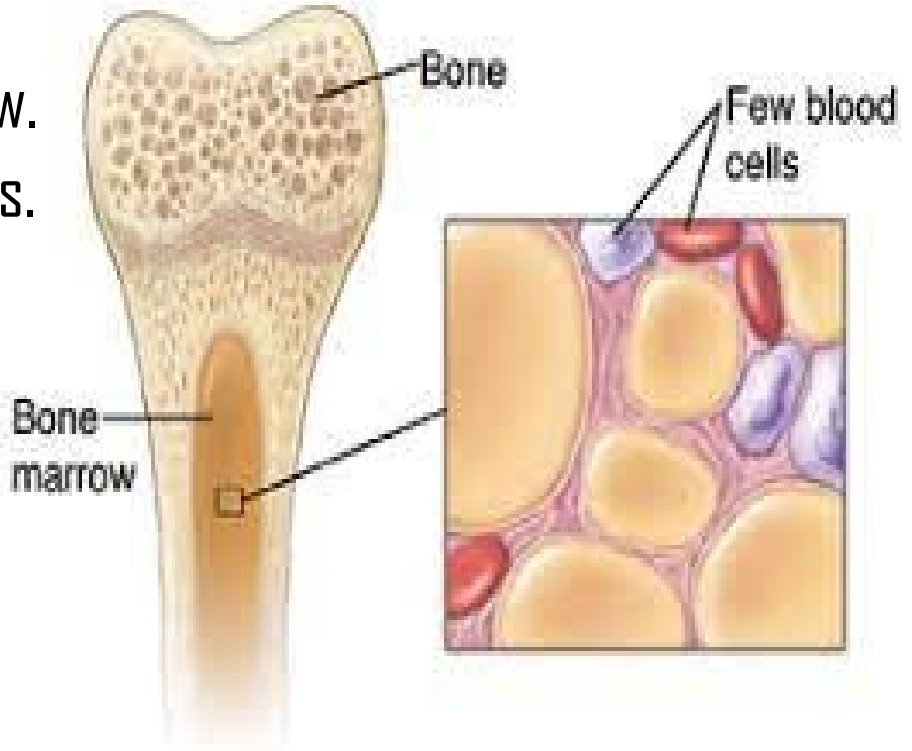
- The gastric atrophy results in decreased production of intrinsic factor and poor absorption of vitamin B12, which is the maturation factor for RBC.
- RBCs are larger and immature with almost normal or slightly low hemoglobin level.
- Before knowing the cause of this anemia, it was very difficult to 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.

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

D. 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 Xray or gamma ray radiation.
  ii. Presence of bacterial toxins, quinine, gold salts etc.
  iii. Tuberculosis.
  iv. Viral infections like hepatitis and HIV infections.



E. 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.

- Common causes anemia of chronic diseases:
  i. Noninfectious 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.
  iv. Neoplastic disorders (abnormal and disorganized growth in tissue or organ) such as cancer of lung and breast.

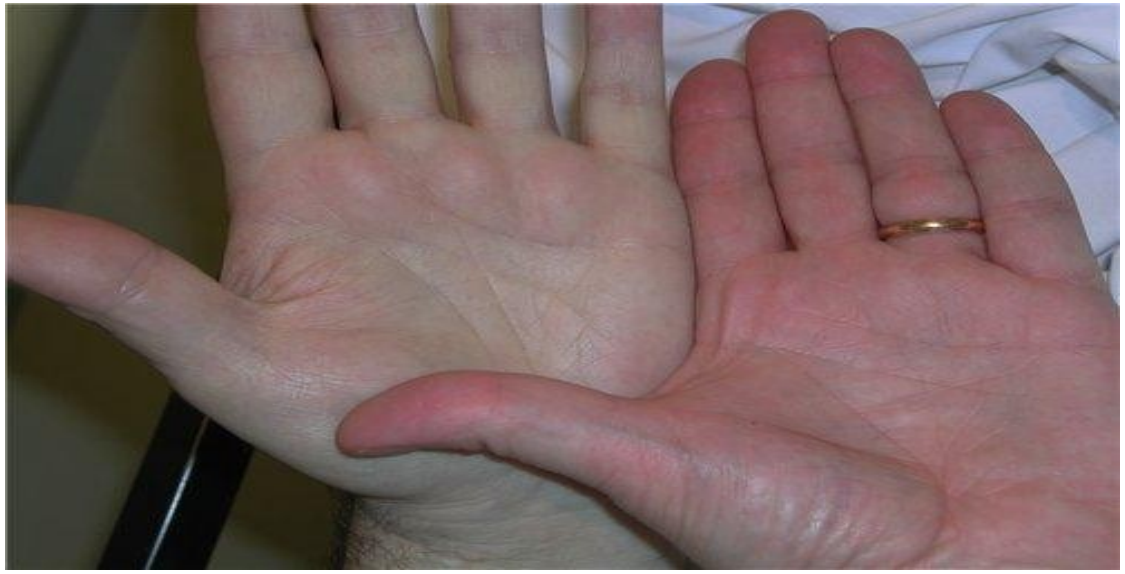
ETIOLOGICAL CLASSIFICATION OF ANEMIA

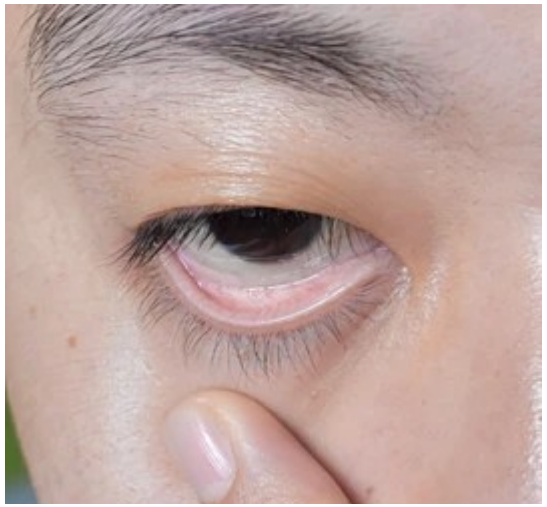
Type of anemia	Causes	Morphology of RBC
Hemorrhagic anemia	Acute loss of blood	Normocytic, normochromic
	Chronic loss of blood	Microcytic, hypochromic
Hemolytic anemia	Extrinsic hemolytic anemia: i. Liver failure ii. Renal disorder iii. Hypersplenism iv. Burns v. Infections – hepatitis, malaria and septicemia vi. Drugs – Penicillin, antimalarial drugs and sulfa drugs vii. Poisoning by lead, coal and tar viii. Presence of isoagglutinins like anti Rh xi. Autoimmune diseases – rheumatoid arthritis and ulcerative colitis	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	i. Non-infectious inflammatory diseases – rheumatoid arthritis ii. Chronic infections – tuberculosis iii. Chronic renal failure iv. Neoplastic disorders – Hodgkin's disease	Normocytic, normochromic

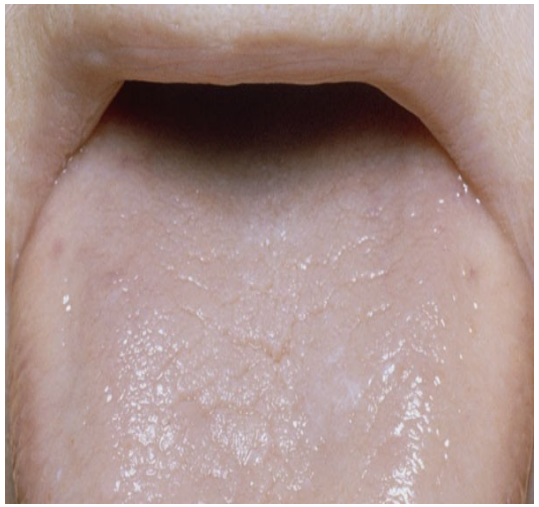
SIGNS AND SYMPTOMS OF ANEMIA

I. 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 looses the elasticity and becomes thin and dry.
- The nails become brittle and easily breakable.







II. 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.

III. RESPIRATION

- There is an increase in rate and force of respiration.
- Sometimes, it leads to breathlessness and dyspnea (difficulty in breathing).

IV. 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.

V. METABOLISM

- Basal metabolic rate increases in severe anemia.

VI. KIDNEY

- Renal function is disturbed. Albuminuria is common.

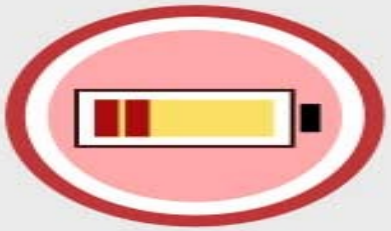
VII. REPRODUCTIVE SYSTEM

- In females, the menstrual cycle is disturbed.
- There may be menorrhagia, oligomenorrhea or amenorrhea

VIII. 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.

ANEMIA SYMPTOMS



FATIGUE

HEADACHE

YELLOWISH SKIN

IRREGULAR HEARTBEATS

CHEST PAIN

COLD HANDS

DIZZINESS

LEG CRAMPS

INSOMNIA

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