WELCOME

TO

PATHOPHYSIOLOGY

UNIT 3

TOPIC :

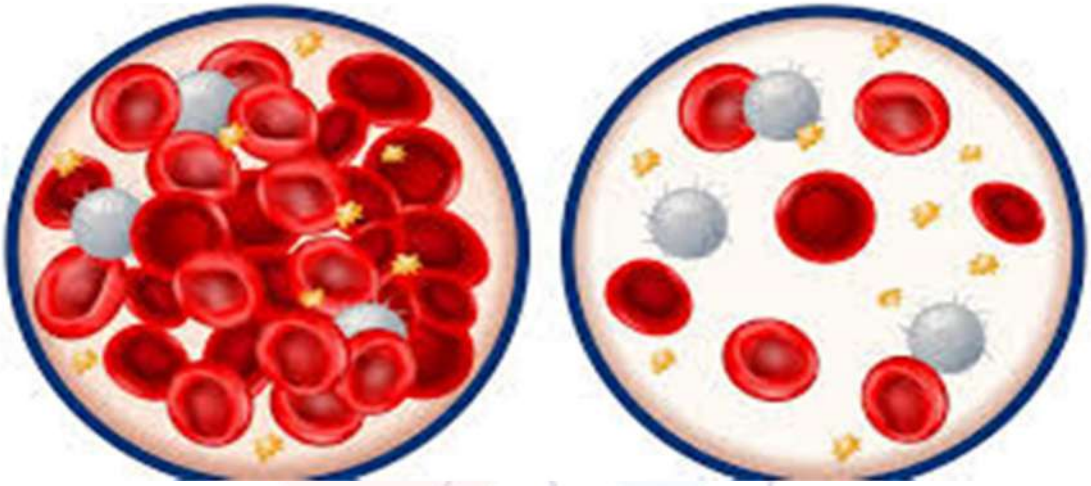
- **Haematological Diseases:**

  Iron deficiency, megaloblastic anemia (Vit B12 and folic acid), sickle cell anemia, thalasemia, hereditary acquired anemia, hemophilia

Haematological Diseases

Iron Deficiency Anaemia (Microcytic Anaemia) M.A

→ A condition in which blood doesn't have enough healthy RBCs is called Anaemia , and if it is due to lack of iron it is called Iron deficiency Anaemia or M.A



Etiology

- Lack of Iron
- lack of iron in diet
- Inability to absorb iron
- Pregnancy (in this condition iron demand increased)
- Genetics
- Heavy blood loss due to any reason

Pathogenesis

lack of Iron in body (due to any reason)

↓

Affected haemoglobine production

↓

Unhealthy RBCs

↓

Iron deficiency Anaemia

Clinical Manifestations

- Weakness
- Extreme Fatigue
- Pale Skin
- Chest pain
- Shortness of Breath
- Increased heart rate
- Headache
- Dizziness
- Brittle nails
- Inflammation in tongue

Non Pharmacological Management

❖ Increase in diet :

- Vitamin C
- Red meat
- Dark Green leafy vegetables
- Nuts
- Dry Fruits
- Iron fortified Cereals.

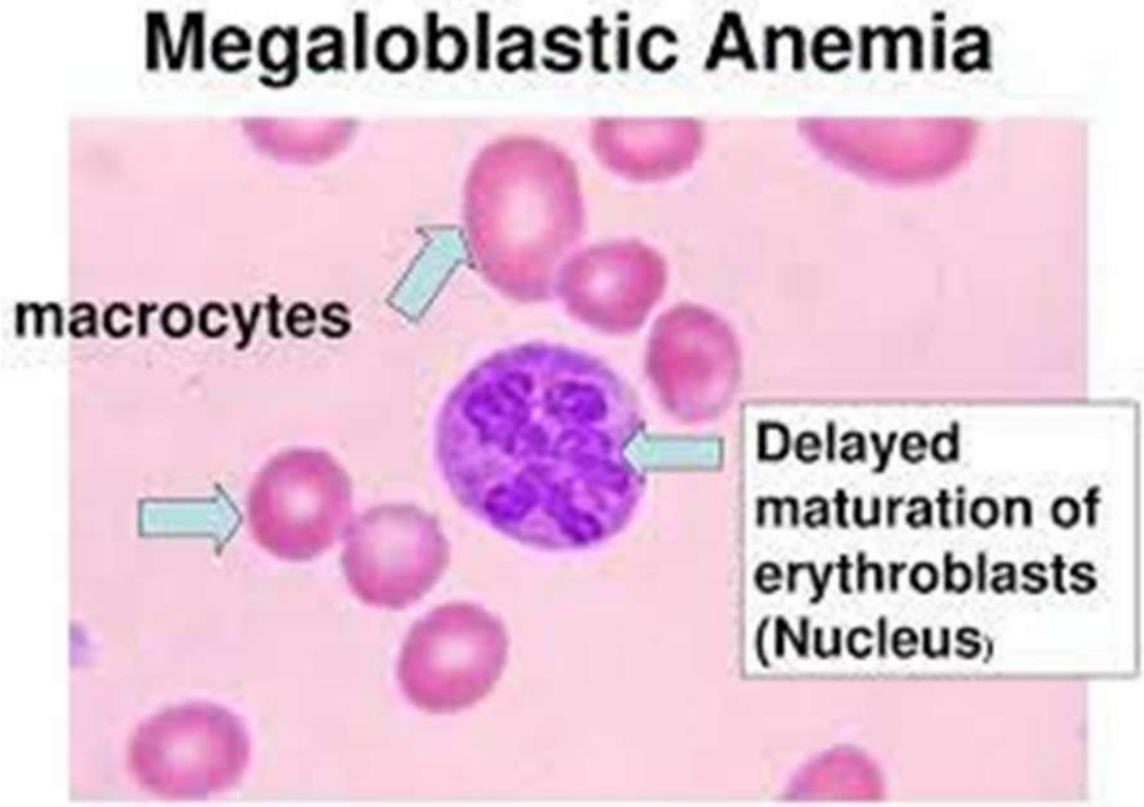
Pharmacological Managements

◈ **Oral iron :** Ferrous sulphate, ferrous aminoate, ferrous gluconate, ferrous succinate, carbonyl iron, iron calcium complex.

◈ **Parenteral iron :** Iron sucrose, iron dextran, iron isomaltoside, ferric carboxy maltose, ferric pyrophosphate citrate.

Megaloblastic Anaemia

→ Megaloblastic Anaemia is a condition in which Bone marrow makes large structurally abnormal and immature RBCs , Due to lack of Vitamin B 1 2 and B9.



Etiology

- Lake of Folic Acid
- Lack of Cobalamin

Pathogenesis

Blood Formation
↓
lack of Vitamin B12 and B9
↓
Abnormal Formation of RBCs
↓
Magaloblastic Anaemia

Clinical Manifestations

- Weakness
- Extreme Fatigue
- Pale Skin
- Chest pain
- Shortness of Breath
- Increased heart rate
- headache
- Dizziness
- Diarrhoea
- Loss of appetite

Non Pharmacological Management

- For Vitamin B12 Eggs , red meat , bran , Milk , liver . for Vitamin B 9 liver , kidney , eggs , Dark green Veg.

Pharmacological Management

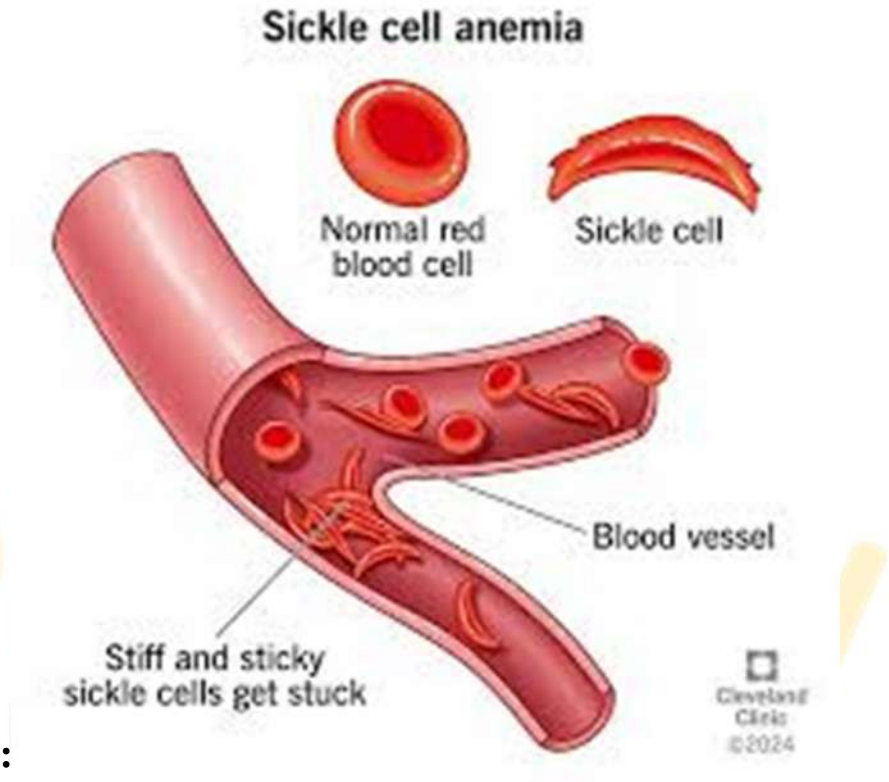
- **Oral iron :** Ferrous sulphate, ferrous aminoate, ferrous gluconate, ferrous succinate, carbonyl iron, iron calcium complex.
- **Parenteral iron :** Iron sucrose, iron dextran, iron isomaltoside, ferric carboxy maltose, ferric pyrophosphate citrate.
- **Maturation factors :** Hydroxocobalamin, methyl cobalamin, cyanocobalamin, folinic acid/leucovorin.

Sickle Cell Anemia

→ Sickle Cell Anemia is a genetic blood disorder caused by a mutation in the gene that encodes the β-globin chain of hemoglobin (HbA).

→ This leads to the production of abnormal hemoglobin (HbS), which causes RBCs to become sickle- or crescent-shaped, especially under low oxygen conditions.

→ These abnormally shaped RBCs are rigid, sticky, and tend to block blood flow, leading to pain, organ damage, and anemia.



Etiology (Cause):

- **Genetic mutation** in the **HBB gene** (on chromosome 11) → substitution of **valine for glutamic acid** at position 6 of β-globin chain.
- **Autosomal recessive inheritance**:
  - **Homozygous (SS)** → Sickle Cell Disease
  - **Heterozygous (AS)** → Sickle Cell Trait (usually asymptomatic)

Pathogenesis:

- ❖ Mutation in HBB gene
- ❖ Production of HbS (sickle hemoglobin)
- ❖ Under low oxygen, HbS polymerizes → RBCs become sickle-shaped
- ❖ Sickle cells are rigid and sticky
- ❖ Blockage of small blood vessels → tissue ischemia, pain, organ damage
- ❖ Shortened RBC lifespan (~20 days vs 120 days) → Hemolytic anemia

Clinical Manifestations:

- ⅄ Chronic anemia (fatigue, pallor)
- ⅄ Pain crises (due to blocked vessels; also called vaso-occlusive crises)
- ⅄ Swelling in hands and feet
- ⅄ Jaundice (due to hemolysis)
- ⅄ Delayed growth and puberty in children
- ⅄ Frequent infections (due to splenic dysfunction)
- ⅄ Shortness of breath
- ⅄ Vision problems
- ⅄ Stroke or organ damage in severe cases

Non-Pharmacological Management:

- Avoid high altitudes and extreme temperatures
- Hydration: Drink plenty of fluids
- Balanced diet rich in iron and folic acid
- Prevent infections through vaccination and hygiene
- Genetic counseling for affected families

Pharmacological Management:

Supportive Treatment:

- **Folic acid**: Helps with RBC production
- **Analgesics**: For pain crises (paracetamol, NSAIDs, opioids)

- **Antibiotics**: For infections (especially in children with spleen damage)
- **Vaccinations**: Pneumococcal, Haemophilus influenzae, meningococcal

Specific Therapies:

- **Hydroxyurea**: Increases fetal hemoglobin (HbF) production, reduces sickling
- **Blood transfusions**: For severe anemia or stroke prevention
- **Iron chelators** (e.g., deferoxamine): If repeated transfusions cause iron overload

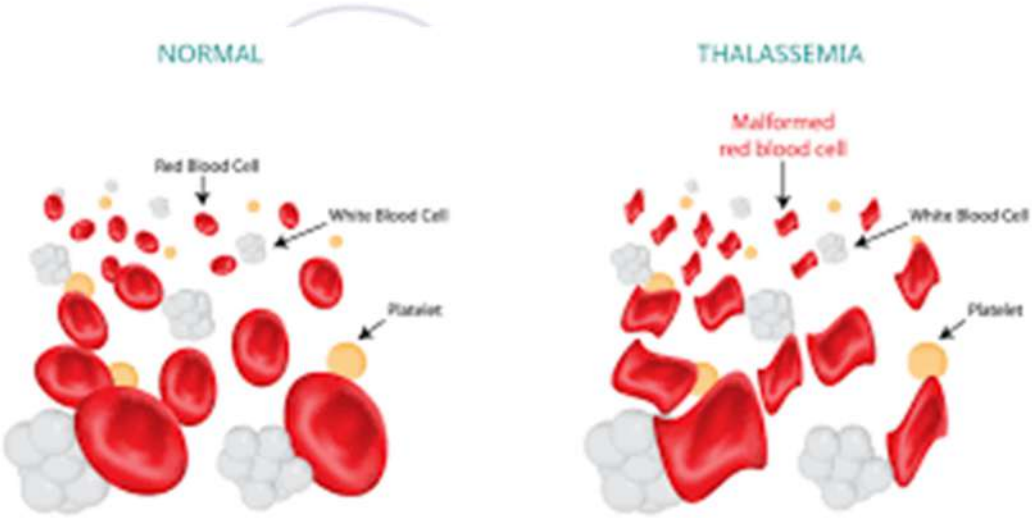
Curative Treatment:

- **Bone marrow / stem cell transplant** (only curative option, used in selected cases)

Thalassemia

→ Thalassemia is a hereditary blood disorder caused by defective or reduced synthesis of one or more globin chains of hemoglobin.

→ This leads to defective hemoglobin formation, resulting in microcytic hypochromic anemia and destruction of red blood cells (hemolysis). It is common in populations from the Mediterranean, Middle East, Africa, and South Asia.



Types of Thalassemia:

1. **Alpha Thalassemia:**
   - Caused by deletion or mutation in α-globin genes on chromosome 16.
   - Severity depends on how many of the 4 α-genes are affected:
     - 1 gene → Silent carrier
     - 2 genes → Mild anemia (Alpha Thalassemia trait)
     - 3 genes → Hemoglobin H disease (moderate to severe)
     - 4 genes → Hydrops fetalis (fatal in utero)
2. **Beta Thalassemia:**
   - Caused by mutation in β-globin gene on chromosome 11.
   - **Types:**
     - **β^+** = partial reduction

        - β^0 = total absence
    - **Clinical forms:**
        - **Beta Thalassemia Minor** (trait): Mild, usually asymptomatic
        - **Beta Thalassemia Major** (Cooley's anemia): Severe anemia in early childhood
        - **Beta Thalassemia Intermedia**: Milder than major but more than trait

Etiology (Cause):

- Genetic mutation inherited in an autosomal recessive pattern
- Both parents must be carriers for the child to develop major form
- Common in regions with high malaria prevalence (carriers may have survival advantage)

Pathogenesis:

- Mutation → Deficient synthesis of globin chains
- Imbalance in α and β chain production
- Unpaired globin chains accumulate and damage RBC precursors
- Ineffective erythropoiesis and hemolysis
- Anemia → Increased erythropoietin → Bone marrow expansion
- Extramedullary hematopoiesis and iron overload due to transfusions

Clinical Manifestations:

Thalassemia Major:

- Severe anemia (from early infancy)
- Pale skin, fatigue, weakness
- Growth retardation, delayed puberty
- Bone deformities (chipmunk facies, frontal bossing)
- Splenomegaly and hepatomegaly
- Iron overload (due to frequent transfusions)
- Heart failure, jaundice

Thalassemia Minor:

- Usually asymptomatic
- Mild microcytic anemia
- Detected during routine blood test

Non-Pharmacological Management:

- Genetic counseling for carriers
- Prenatal diagnosis via chorionic villus sampling (CVS)
- Iron-rich diet not advised (risk of overload)
- Avoid infections and maintain good hygiene

Pharmacological Management:

Supportive Treatment:

- **Folic acid supplements** for RBC production
- **Blood transfusions** (every 2–4 weeks for major form)

Iron Overload Management:

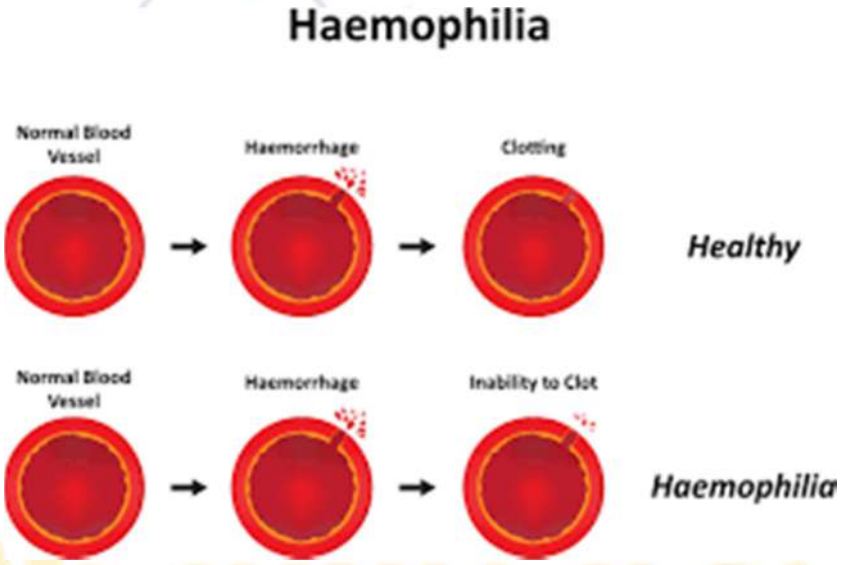
- **Iron chelating agents**:
  - Deferoxamine (IV/SC)
  - Deferiprone (oral)
  - Deferasirox (oral)

Curative Therapy:

- **Bone marrow / stem cell transplant** (especially in children)
- **Gene therapy** (emerging option)

Hemophilia

- Hemophilia is a genetic bleeding disorder where the blood does not clot properly due to the deficiency or absence of specific clotting factors.
- It leads to prolonged bleeding, even from minor injuries, and spontaneous internal bleeding in severe cases.
- It is usually inherited in an X-linked recessive pattern, affecting mostly males, while females are carriers.



Types of Hemophilia:

Type	Deficient Factor	Frequency
Hemophilia A	Factor VIII	Most common (~80%)
Hemophilia B	Factor IX (Christmas disease)	~15–20%
Hemophilia C	Factor XI	Rare, mild, affects both genders

Etiology (Cause):

- Genetic mutation on the X chromosome
- X-linked recessive inheritance:
  - Males (XY): One defective X → Disease
  - Females (XX): One defective X → Carrier (usually asymptomatic)
- Rarely may be acquired due to autoimmune destruction of clotting factors

Pathogenesis:

1. Mutation in gene coding for clotting factor →
2. Deficiency of Factor VIII or IX →
3. Inadequate formation of fibrin clot →
4. Delayed or absent blood clotting →
5. Prolonged bleeding following trauma or spontaneously in severe cases

Clinical Manifestations:

- ❖ Prolonged bleeding after cuts, surgery, or dental procedures
- ❖ Spontaneous bleeding into joints (hemarthrosis) → joint swelling, pain, and deformity
- ❖ Bruising and hematomas
- ❖ Nosebleeds (epistaxis)
- ❖ Blood in urine (hematuria) or stool
- ❖ Intracranial bleeding (in severe cases, life-threatening)
- ❖ Excessive bleeding after circumcision (in infants)

Non-Pharmacological Management:

- ▪ Avoid trauma or injury
- ▪ Use soft toothbrush and avoid contact sports
- ▪ Genetic counseling for families with known history
- ▪ Educate caregivers and school staff

- Avoid IM injections, aspirin, NSAIDs (increase bleeding risk)

Pharmacological Management:

Replacement Therapy:

- Factor VIII concentrate (for Hemophilia A)
- Factor IX concentrate (for Hemophilia B)
- Given IV during bleeding episodes or prophylactically

Other Therapies:

- **Desmopressin (DDAVP)**:
  - Used in mild Hemophilia A
  - Increases release of stored Factor VIII
- **Antifibrinolytics**:
  - Tranexamic acid, epsilon aminocaproic acid to prevent breakdown of clots
- Gene therapy (emerging and promising in clinical trials)