BLOOD

Haematology is the branch of science concerned with the study of blood, blood-forming tissues, and disorders related to them.

Blood is a **liquid connective tissue** consisting of cells surrounded by a liquid extracellular matrix called **plasma**.

Blood circulates continuously throughout the body due to the pumping action of the heart.

Functions of blood transport include:

- Oxygen from lungs
- Nutrients from the gastrointestinal tract
- Hormones
- Heat
- Antibodies and immune cells
- Clotting factors
- Waste products

Physical Characteristics of Blood

- Denser and more viscous than water
- Slightly sticky
- Temperature: **38°C (100.4°F)**
- pH: slightly alkaline, **7.35–7.45** (average 7.4)
- Color depends on oxygen content:
    - Bright red – oxygenated blood
    - Dark red – deoxygenated blood
- Blood volume:
    - Adult male: **5–6 liters**
    - Adult female: **4–5 liters**
- Specific gravity: **1.050–1.060**

Functions of Blood

Transportation

- Oxygen, carbon dioxide
- Nutrients
- Hormones
- Heat
- Waste products

Regulation

- Maintains homeostasis of body fluids
- Regulates pH using buffer systems
- Regulates body temperature through heat-absorbing and cooling properties of plasma water

Protection

- **Clotting** prevents excessive blood loss after injury
- **Defense** mechanisms include:
    - Phagocytosis by WBCs
    - Blood proteins such as antibodies, interferons, and complement system

Composition of Blood

Blood consists of **two components**:

1. Blood plasma
2. Formed elements

Blood plasma is a clear, straw-colored extracellular matrix containing dissolved substances.

- Plasma forms **55%** of blood volume
- Formed elements constitute **45%**
- These can be separated by centrifugation or by allowing blood to stand

Formed elements include:

- Blood cells
- Cell fragments

Plasma

Plasma consists mainly of:

- **Water** (acts as solvent, transport medium, and heat regulator)
- Dissolved and suspended substances (about 8%)

Plasma contains:

- Plasma proteins
- Inorganic salts (electrolytes)
- Nutrients
- Waste products
- Hormones
- Gases

Plasma Proteins

Plasma proteins are produced by the **liver** and constitute **7.5%** of plasma. They create osmotic pressure that keeps plasma fluid within circulation.

Functions of Plasma Proteins

- Maintain colloid osmotic pressure (mainly albumin, 70–80%)
- Contribute to blood viscosity (fibrinogen and globulins)
- Role in blood coagulation (fibrinogen, prothrombin)
- Defense function (γ-globulins)
- Maintain acid-base balance (buffering action)
- Transport substances such as:
    - CO_2
    - Thyroxine
    - Cortisol
    - Vitamins A, D, E, B_{12}
    - Bilirubin
    - Drugs
    - Calcium and copper
    - Free haemoglobin
- Serve as reserve proteins
- Maintain suspension stability of RBCs
- Fibrinolytic function

Inorganic Salts (Electrolytes)

Positive ions:

- Na^+
- K^+
- Ca^{2+}
- Mg^{2+}

Negative ions:

- Cl^-
- PO_4^{3-}
- SO_4^{2-}
- HCO_3^-

Functions:

- Ca^{2+} – muscle contraction
- Ca^{2+}, Na^+, K^+ – nerve impulse transmission

- PO_4^{3-} – acid-base balance

Nutrients

Nutrients are essential for:

- Cellular growth
- Development
- Metabolism

Examples include glucose, amino acids, and vitamins, transported from absorption sites to tissues.

Waste Products

Waste products transported in blood include:

- Urea
- Uric acid
- Creatinine
- Bilirubin
- Ammonia

These are formed in the liver and transported to kidneys for excretion. Carbon dioxide is transported to lungs for expiration.

Gases

Oxygen:

- Less than 2% is dissolved in plasma
- More than 98% is transported bound to haemoglobin as **oxyhaemoglobin**

Carbon dioxide:

- Mostly transported as bicarbonate ions (HCO_3^-) in RBCs

Formed Elements

Blood has **three types of formed elements**:

1. Red blood cells (RBCs / erythrocytes)
2. White blood cells (WBCs / leukocytes)
3. Platelets (thrombocytes)

RBCs transport oxygen and carbon dioxide.
WBCs provide defense mechanisms.
Platelets help in blood clotting.

Haemopoiesis

Most blood cells are formed in **red bone marrow**, a highly vascular connective tissue.

Some lymphocytes are also formed in lymphoid tissues.

All blood cells originate from **pluripotent stem cells** and undergo several stages of development.

The process of blood cell formation is called **haemopoiesis**.

- In infancy, all bone marrow is red and haemopoietic
- Over the next 20 years, much of it converts to yellow marrow
- In adults, haemopoiesis occurs in flat bones, irregular bones, and ends of long bones such as sternum, ribs, pelvis, and skull

Red bone marrow contains **hemocytoblasts**, which give rise to:

- Myeloid stem cells
- Lymphoid stem cells

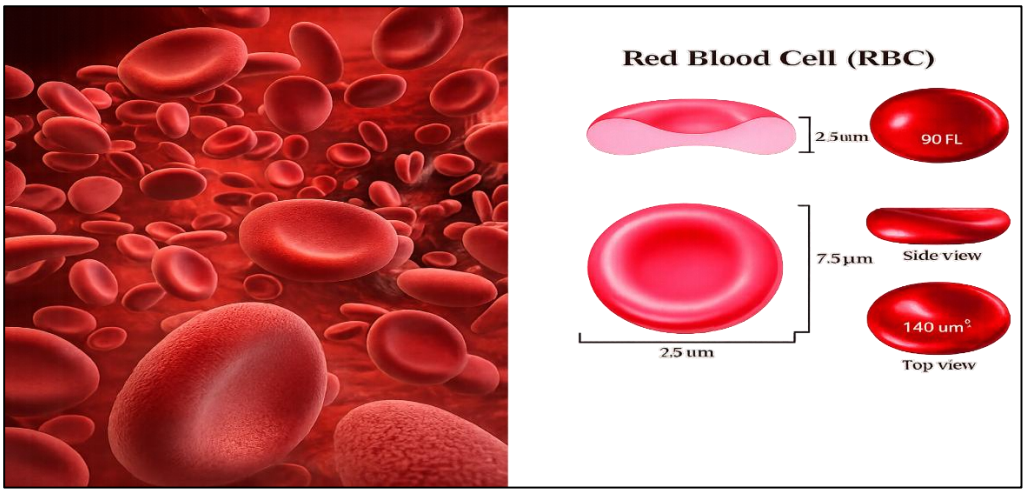
Myeloid stem cells form RBCs, platelets, monocytes, neutrophils, eosinophils, basophils, and mast cells.
Lymphoid stem cells form lymphocytes.

Regulation of Haemopoiesis

Haemopoiesis is regulated by **haemopoietic growth factors**, including:

- Erythropoietin (EPO) from kidneys – increases RBC formation
- Thrombopoietin (TPO) from liver – stimulates platelet formation
- Cytokines, colony-stimulating factors (CSFs), and interleukins – stimulate WBC production

Erythrocytes (RBCs)



- Most abundant blood cells
- Biconcave disc-shaped
- No nucleus or organelles
- Diameter: **7 µm**
- Contain haemoglobin

Normal count:

- Adult male: **5.4 million/µL**
- Adult female: **4.8 million/µL**

Life span: **120 days**

Main function: oxygen transport

Haemoglobin

Each RBC contains approximately **280 million haemoglobin molecules**.

Haemoglobin consists of:

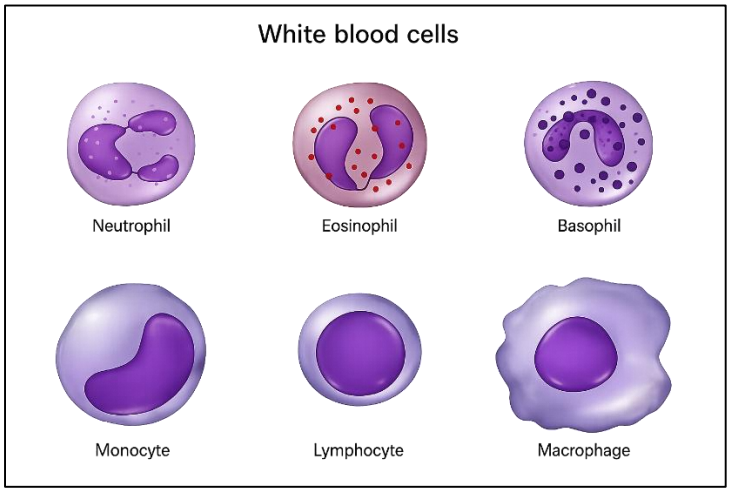
- Globin protein (2 alpha and 2 beta chains)
- Four heme groups, each containing Fe^{2+}

Each haemoglobin molecule can bind **four oxygen molecules**.

Leukocytes (WBCs)

- Largest blood cells
- Contain nucleus and organelles
- Do not contain haemoglobin

- Function in defense and immunity



Types:

- Granulocytes: neutrophils, eosinophils, basophils
- Agranulocytes: lymphocytes and monocytes

Platelets (Thrombocytes)

- Very small, irregular disc-shaped cell fragments budded off from the cytoplasm of megakaryocytes in red bone marrow
- 2-4 µm in diameter
- No nucleus, cytoplasm packed with granules containing variety of substances that promote blood clotting which causes haemostasis (Cessation of bleeding)
- Life span is 8-11 days
- Aged & dead removed by macrophages, mainly in spleen
- Normal count is 150,000 – 400,000/ µL
- 1/3rd platelets are stored in spleen – emergency store – to control excessive bleeding

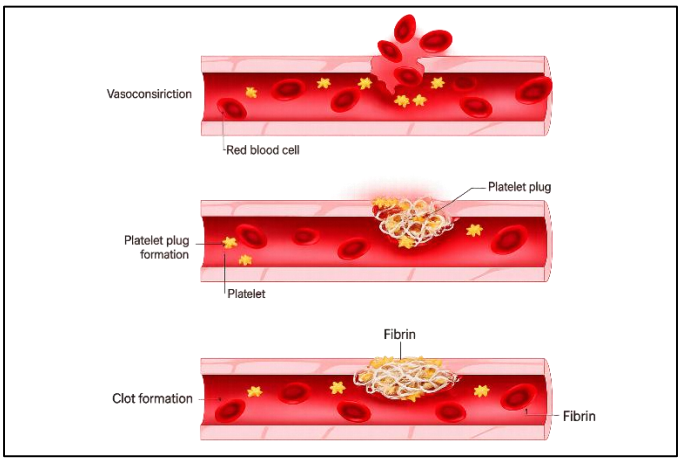
Haemostasis

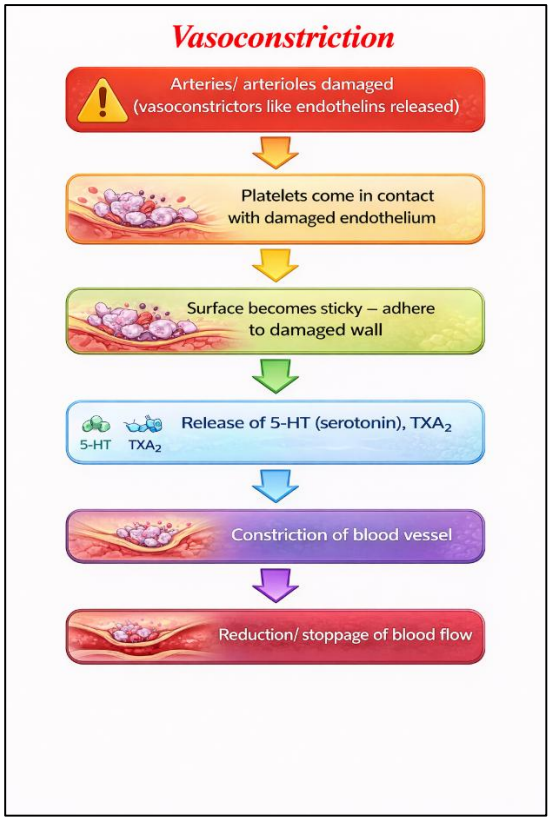
Haemostasis is the process that stops bleeding and includes:

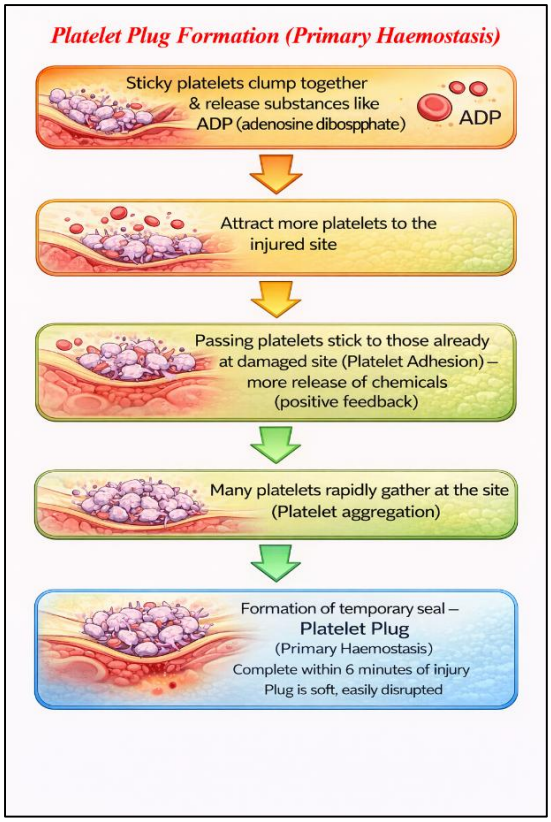
- A sequence of responses that stops bleeding is called Haemostasis
- When blood vessel is damaged/ injured – loss of blood is stopped & healing occurs in a series of overlapping processes
- Platelets play a vital role
- Successful haemostasis prevents haemorrhage (loss of large amount of blood from vessels)

- Haemostasis prevents haemorrhage from smaller vessels; medical intervention is required in larger vessels
- 3 mechanisms reduce blood loss. They are –

1. ***Vasoconstriction/ Vascular spasm***
2. ***Platelet plug formation***
3. ***Blood clotting/ Coagulation***







Coagulation/ Blood Clotting/ Secondary Haemostasis

- Clotting/ Coagulation is the process of gel formation (blood clot), which involves a series of chemical reactions that culminate in formation of fibrin threads
- Involves a positive feedback mechanism
- Clotting factors play a major role
- Clotting factors are synthesized by hepatocytes & released into blood stream
- They are as follows –
- I. Fibrinogen
- II. Prothrombin
- III. Thromboplastin (tissue facator)
- IV. Calcium ions
- V. Labile factor, Proaccelerin, accelerator globulin
- VII. Stable factor, proconvertin (serum prothrombin conversion accelerator)
- VIII. Antihaemophilic globulin (AHG), antihaemophilic factor A
- IX. Christmas factor, plasma thromboplastin component (PTC), antihaemophilic fcator B
- X. Stuart factor, prower factor, thrombokinase
- XI. Plasma thromboplastin antecedent (PTA), antihaemophilic factor C
- XII. Hageman factor/ contact factor/ antihaemophilic factor D
- XIII. Fibrin stabilising factor

- Clotting is a complex cascade of enzymatic reactions in which each clotting factor activates many molecules of next one in fixed sequence
- Finally, a large quantity of insoluble protein fibrin is formed
- This process involves 3 stages

1. 2 pathways – extrinsic & intrinsic pathways leads to formation of prothrombinase. Next two steps have common pathway
2. Prothrombinase converts prothrombin into thrombin
3. Thrombin converts soluble fibrinogen into insoluble fibrin, which forms threads of clot

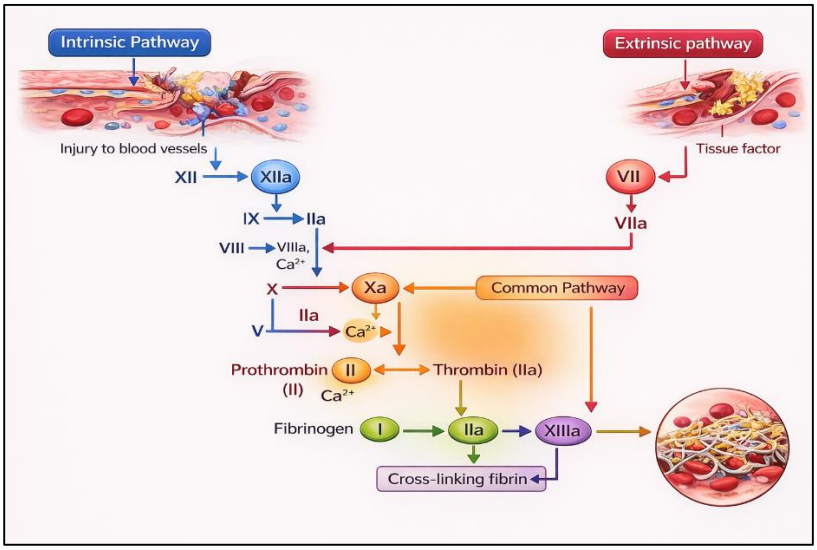
Extrinsic Pathway

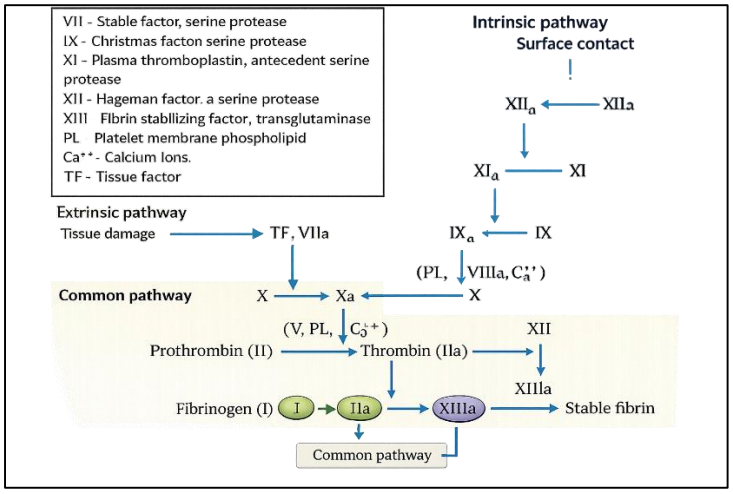
- Occurs rapidly within seconds
- A tissue protein called tissue factor/ thromboplastin leaks into blood from cells outside blood vessels *i.e.* damaged tissue – initiates formation of Prothrombinase
- In the presence of Ca2+, tissue factor begins a sequence of reactions ultimately activates clotting factor X
- Activated CF X combines with factor V in the presence of Ca2+ to form active enzyme prothrombinase

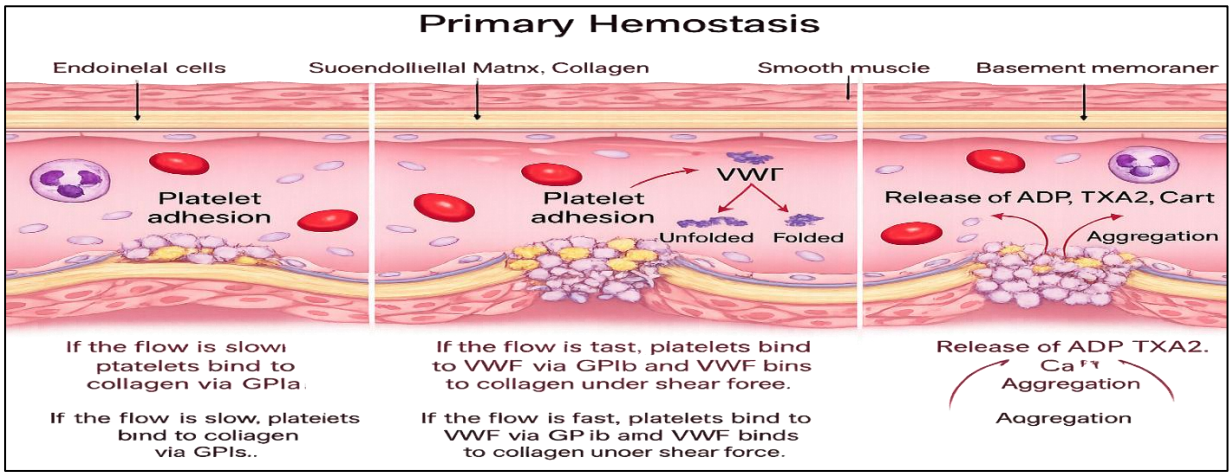
Intrinsic Pathway

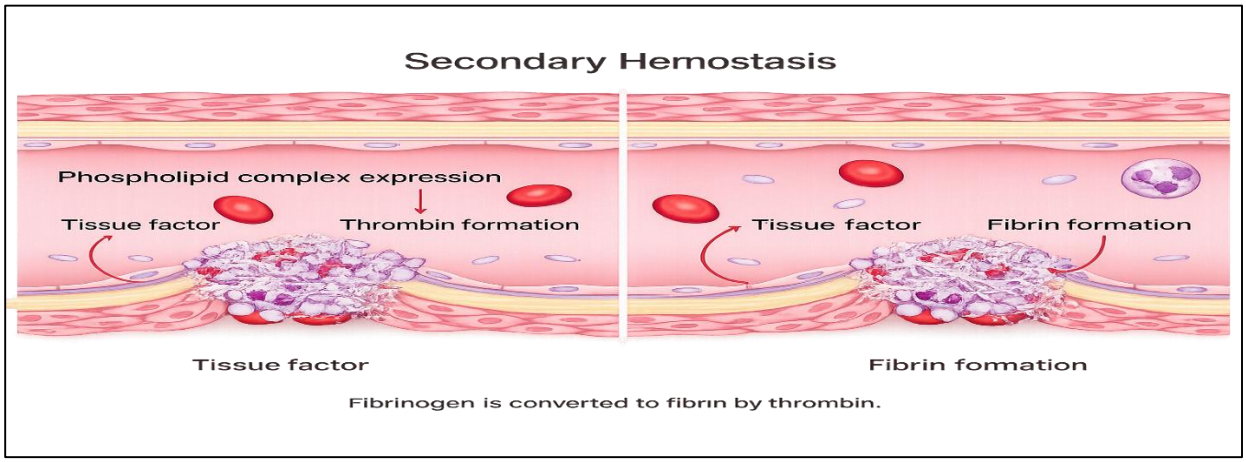
- More complex mechanism, occurs more slowly – takes several minutes
- Activators are either in direct contact with blood or contained within the blood
- Triggered when blood comes into contact with damaged blood vessel lining (endothelium)

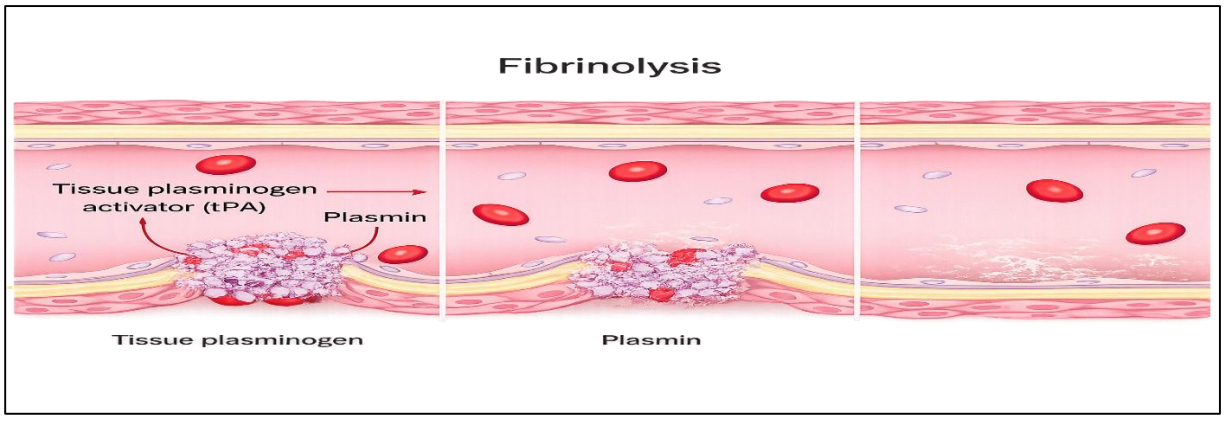
- Contact with exposed collagen fibers activate CF XII – begins a sequence of reactions that eventually activates CF X
- Platelet phospholipids & Ca2+ also activate factor X
- Activated factor X combines with factor V to form active enzyme prothrombinase





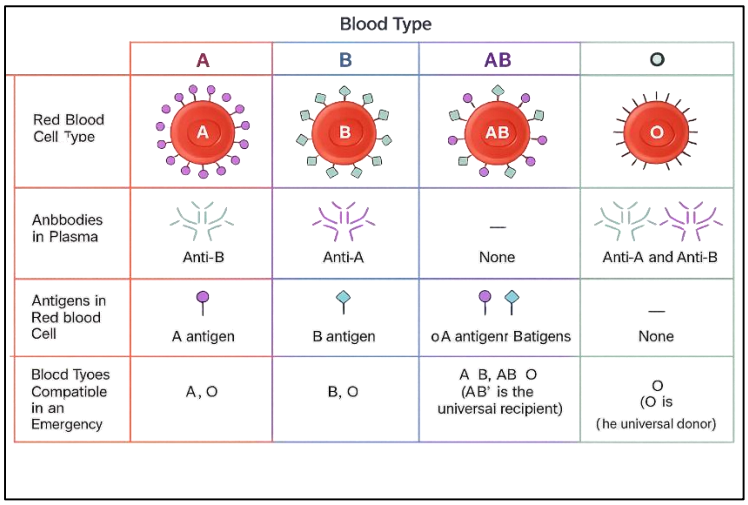






Blood Groups

Blood groups are determined by antigens on RBC surfaces.



- Surface of RBC carries a range of different proteins called antigens – stimulate an immune response if transferred from one individual (donor) into bloodstream of an incompatible individual
- Antigens composed of glycoproteins & glycolipids – determine individual's blood group
- Antigens also called agglutinogens
- Based on the presence or absence of various antigens – blood is categorised into different blood groups
- There are at least 24 blood groups & more than 100 antigens that can be detected on surface of RBCs

Two major blood group systems:

- **ABO system**
- **Rh system**

Agglutination occurs when incompatible blood is transfused, leading to haemolysis.

ABO Blood Group/ ABO System

Antigens

- Based on two glycolipid antigens called A & B
- People whose RBCs display only antigen A – type A blood group
- People whose RBCs display only antigen B – type B blood group
- People having both A & B antigens – type AB
- People that have neither antigen A nor antigen B – type O

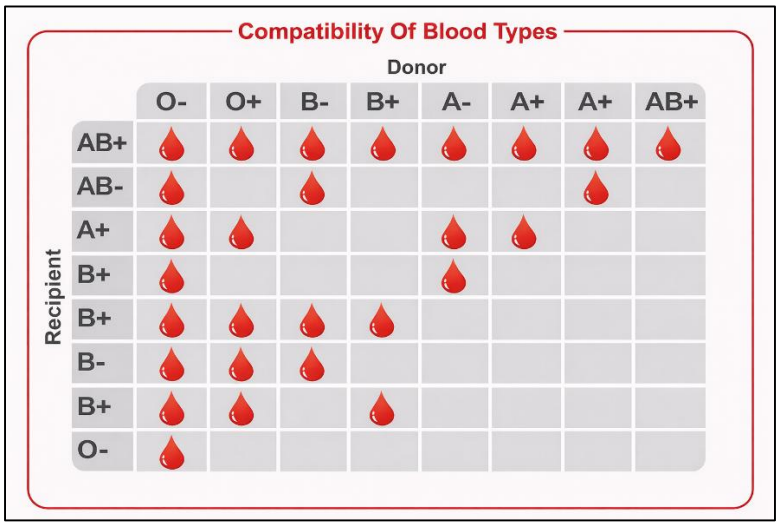
Antibodies

- Plasma usually contains antibodies called agglutinins – reacts with A or B antigens if two are mixed

- Anti-A antibody – reacts with antigen A
- Anti-B antibody – reacts with antigen B
- Antibodies are not present for the antigens of self RBCs
- Antibodies are large IgM-type antibodies – do not cross placenta

Rh Blood Group/ The Rhesus System

- Rh blood group so named because the Rh antigen/ Rh factor was first found in the blood of Rhesus monkey
- People whose RBCs have Rh antigens – called Rh+
- People whose RBCs lack Rh antigens – called Rh-
- Normally blood plasma does not contain anti-Rh antibodies
- If Rh- person receives Rh+ blood transfusion – anti-Rh antibodies start to produce & remain in blood
- During 2nd time transfusion of Rh+ blood – cause agglutination & haemolysis of RBCs in donated blood (Haemolytic disease on new born)



Blood Transfusion

Transfusion is a process of transfer of whole blood or blood components (RBCs only or plasma only) into the blood stream or directly into redbone marrow. If individuals are transfused with blood of the same group i.e. possessing same cell surface antigens – immune system will not recognise them as foreign & will not reject them

- If given blood from an individual of different blood type i.e. with different antigen – immune system generates antibodies – causes agglutination/ clumping of RBcs

- Agglutination is antigen-antibody response in which RBCs become cross-linked to one another

- Cross-linking causes activation of plasma proteins of complement family, leading to haemolysis of RBCs – release haemoglobin into blood plasma
- ***Ex:*** **Recepient (Group A)** **Donor (Group B)**

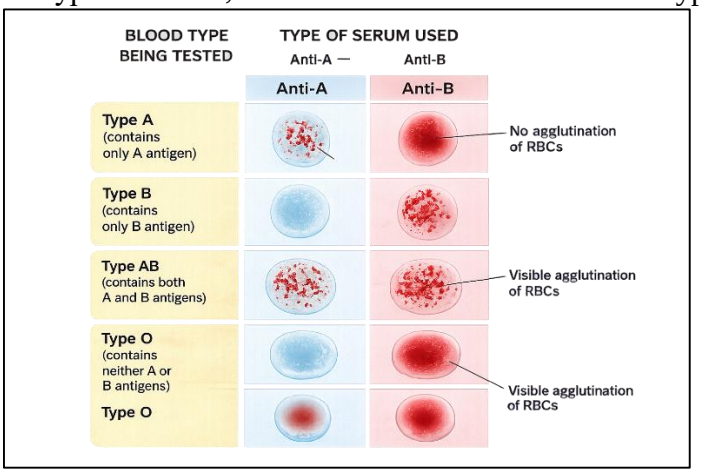
  - Antigen A *- Antigen B*

  - Anti B antibody *- Anti A antibody*

- Anti B antibody bind to antigens B – cause agglutination & haemolysis
- Anti A antibodies bind to antigens A – so diluted that no significant agglutination occurs
- Blood type can be identified by sample of saliva as well
- To avoid blood-type mismatches, patient's blood is cross-matched to potential donor blood or screened it for presence of antibodies

Ex: Anti A serum, Anti b serum

- Once patient's blood type is known, donor blood of same ABO & Rh type is selected



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Blood transfusion is the transfer of blood or its components into circulation to:

- Treat anaemia
- Increase blood volume
- Improve immunity

Blood must be properly matched to prevent agglutination and haemolysis.

BLOOD DISORDERS

ERYTHROCYTE DISORDERS

ANAEMIAS

Anaemia:
Inability of blood to carry enough oxygen to meet body needs.

Due to:

- Low Hb levels
- Production of faulty Hb

Classification based on cause:

- Anaemia due to production of insufficient or defective erythrocytes
    - Causes: iron deficiency, vitamin B12 / folic acid deficiency, bone marrow failure
- Anaemia due to blood loss or excessive erythrocyte breakdown (haemolysis)
- Anaemia can cause abnormal changes in red cell size or colour

A. PATHOPHYSIOLOGIC

I. Anaemia due to increased blood loss

II. Anaemia due to impaired red cell production / insufficient or defective erythrocytes

a. Cytoplasmic maturation defects

1. Deficient haem synthesis – iron deficiency anaemia
2. Deficient globin synthesis – thalassaemic syndromes

b. Nuclear maturation defects

- Vitamin B12 and/or folic acid deficiency
- (Megaloblastic anaemia)

c. Defect in stem cell proliferation and differentiation

III. Anaemias due to increased red cell destruction

- Haemolytic anaemia

B. MORPHOLOGIC

Based on red cell size or colour, Hb content, red cell indices:

1. **Microcytic, hypochromic** – iron deficiency, thalassaemia
2. **Normocytic, normochromic** – haemolytic
3. **Macrocytic** – megaloblastic

Symptoms

- Asymptomatic
- Symptoms relate to inability to supply enough oxygen
- Pallor
- Fatigue
- Breathlessness on exertion

Compensatory mechanisms:

- Tachycardia
- Palpitations

IRON DEFICIENCY ANAEMIA

- Most common form of anaemia
- Diet sources: red meat, fortified cereals, highly coloured vegetables
- Stored in the liver
- RBC count normal but microcytic and hypochromic
- Contains less Hb

Normal Hb:

- Men: 13.2–16.6 g/dl
- Women: 11.6–15 g/dl

Severe anaemia:

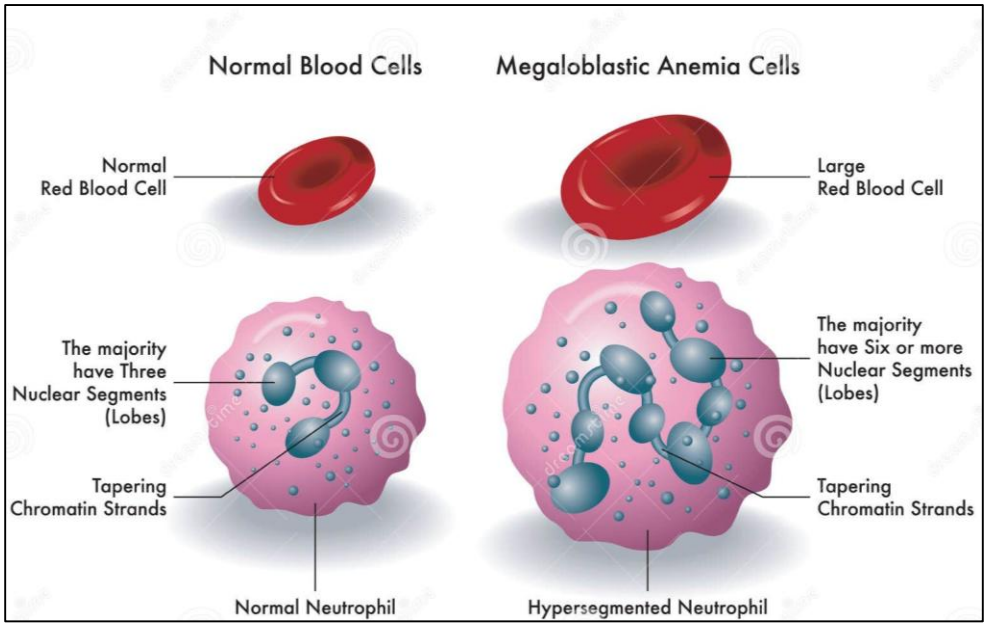
- < 9 g / 100 ml blood

Causes:

- Deficient intake
- Unusually high requirements
- Malabsorption / poor absorption

VITAMIN B12 / FOLIC ACID DEFICIENCY ANAEMIA

- Also called megaloblastic anaemia
- Deficiency impairs maturation of erythrocytes
- Rate of DNA & RNA synthesis reduced
- Delay in cell division
- Abnormally large erythrocytes (megaloblasts)
- Immature Hb of each cell normal or increased
- Cells fragile, lifespan reduced to 40–50 days
- Depressed production and early lysis cause anaemia



APLASTIC / HYPOPLASTIC ANAEMIA

- Occurs due to failure of bone marrow
- Decreased number of erythrocytes
- Leukopenia and thrombocytopenia likely
- Pancytopenia present

Features:

- Anaemia
- Diminished immunity
- Tendency to bleed

Causes:

- Cytotoxic drugs

- Ionising radiation
- Chemicals like benzene and derivatives
- Viral hepatitis

Symptoms:

- Infections
- Anaemia
- Bleeding
- Bruising

HAEMOLYTIC ANAEMIAS

- Increased erythrocyte breakdown
- RBC lifespan shortened
- Jaundice or splenomegaly may occur

Types:

- Congenital
- Acquired

CONGENITAL ANAEMIA

- Genetic abnormality leads to abnormal haemoglobin
- Increased red cell membrane fragility
- Reduced oxygen-carrying capacity and lifespan

SICKLE CELL ANAEMIA

- Abnormal haemoglobin molecules
- Misshapen during deoxygenation
- RBCs become sickle-shaped
- Obstruction of blood flow
- Intravascular clotting
- Tissue ischaemia and infarction
- Rapid haemolysis leads to anaemia

Symptoms:

Acute:

- Pain in hands and feet due to vessel blockage

Long-term:

- Cardiac disease
- Kidney failure
- Retinopathy
- Poor tissue healing
- Slow growth in children
- Risk of stroke and seizures
- Pregnancy complications
- Respiratory complications
- Delayed sexual maturity

THALASSAEMIAS

- Inherited disorder
- Abnormal haemoglobin production
- Reduced erythropoiesis
- Increased haemolysis

Symptoms:

- Mild asymptomatic to life-threatening anaemia

Moderate to severe:

- Bone marrow expansion
- Splenomegaly

Most severe:

- Regular blood transfusions
- Iron overload

HAEMOLYTIC DISEASE OF NEWBORN

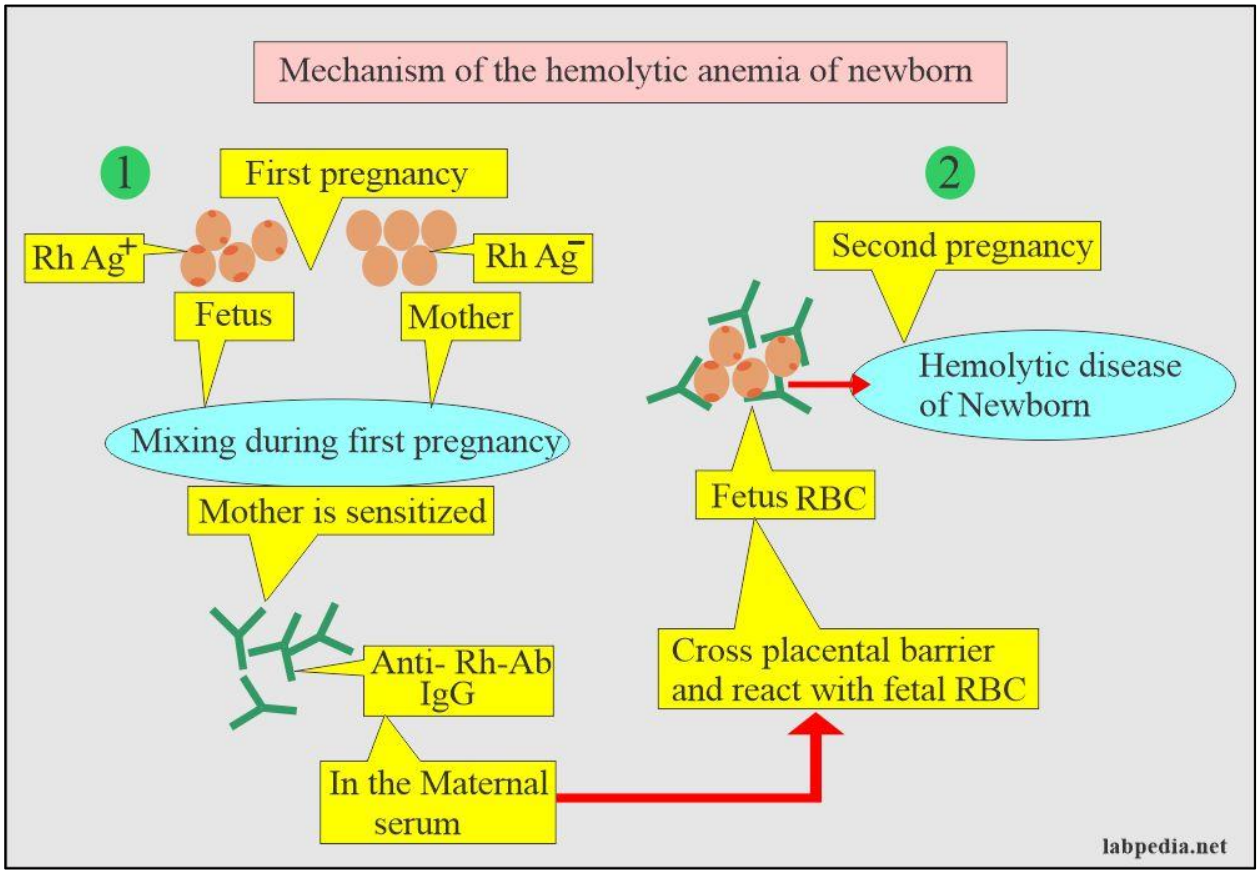
- Mother forms antibodies against baby's RBCs
- Fetal erythrocytes destroyed

Severe cases:

- Death in womb due to profound anaemia

Less severe:

- Anaemia corrected by transfusion
- Now less common
- Rh- mother given anti-Rh injection within 72 hours of delivery of Rh+ baby



ACQUIRED HAEMOLYTIC ANAEMIA

- No familial or racial factors

Causes:

- Chemical agents (sulphonamides, lead, arsenic)
- Microbial toxins
- Autoimmunity
- Blood transfusion reactions

POLYCYTHAEMIA

- Abnormally high RBC count
- Increased blood viscosity
- Slowed blood flow
- Increased risk of clotting, ischaemia and infarction

Causes:

- Reduction in plasma volume (burns)

Primary polycythaemia

- Genetic mutation affecting erythropoietin control

Symptoms:

- Itching
- Tiredness
- Headache

Secondary polycythaemia

- Compensatory response to hypoxia
- Living at altitude
- Heart failure
- Heavy smoking
- High EPO levels

LEUKOCYTE DISORDERS

LEUKOPENIA

- Reduction in white blood cells
- Total count < 4000 / cubic mm

Granulocytopenia (Neutropenia)

- Low granulocytes
- Neutrophils mainly affected

Agranulocytosis

- Extreme shortage or absence of granulocytes

Causes:

- Cytotoxic drugs
- Bone marrow irradiation
- Bone marrow disorders
- Severe infections

LEUKOCYTOSIS

- Increased leukocytes
- WBC > 11,000 / cubic mm
- Protective response in disease

LEUKAEMIA

- Malignant proliferation of WBC precursors
- Cancer of blood
- Immature blast cells accumulate

Effects:

- Anaemia
- Thrombocytopenia
- Leukopenia
- Reduced immunity

Causes:

- Environmental factors
- Viral infections
- Genetic factors
- Chemicals

TYPES OF LEUKAEMIA

Acute Leukaemias

- Sudden onset
- Involve immature blast cells
- Bone marrow failure
- Anaemia, haemorrhage, infections
- Mouth and upper GIT commonly affected

Types:

- **AML:** Myeloblast proliferation; age 25–60; often cured
- **ALL:** Mainly children; 70% cure rate; primitive B-lymphocytes involved

Chronic Leukaemias

- Less aggressive
- Cells in "cyte" stage
- Leucocytosis present

CML:

- Chromosome 9 & 22 abnormality (Philadelphia chromosome)
- Progresses to AML
- Fatal within 5 years

CLL:

- Proliferation of B-lymphocytes
- Seen in elderly
- Survival up to 25 years

HAEMORRHAGIC DISEASES

THROMBOCYTOPENIA

- Platelet count < 150,000 / cubic mm
- < 30,000 → spontaneous bleeding

Causes:

- Reduced platelet production

- Increased destruction

Autoimmune Thrombocytopenic Purpura

- Children and young adults
- Triggered by viral infections
- Antiplatelet antibodies destroy platelets
- Presence of purpura

VITAMIN K DEFICIENCY

- Required for clotting factor synthesis
- Deficiency causes abnormal clotting

Haemorrhagic disease of newborn

- Low vitamin K stores
- Bleeding in early life
- Risk of brain haemorrhage

Adults:

- Liver disease
- Biliary obstruction
- Fat malabsorption
- Antibiotic therapy

DISSEMINATED INTRAVASCULAR COAGULATION (DIC)

- Inappropriate activation of coagulation
- Intravascular clot formation
- Fibrin deposition
- Tendency to haemorrhage

Occurs in:

- Severe infections
- Trauma
- Placental abruption
- Acute pancreatitis
- Advanced cancer

- Massive blood transfusion

CONGENITAL DISORDERS – HAEMOPHILIA

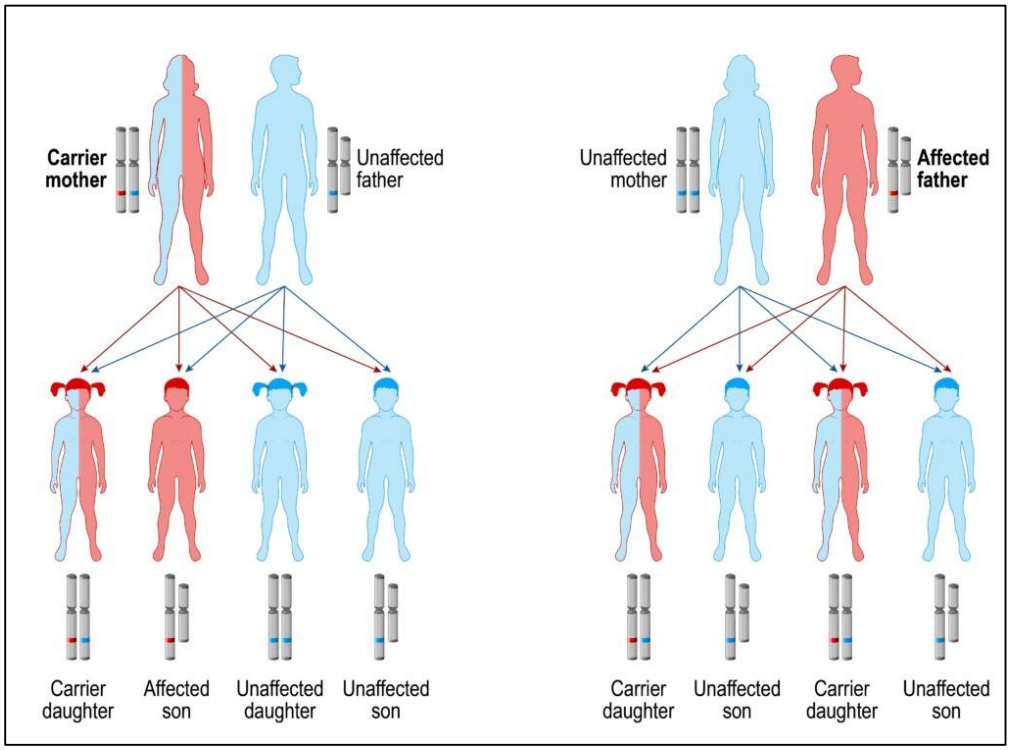
- Inherited clotting disorders
- Genes on X chromosome
- Abnormal clotting factors VIII or IX
- Affected males develop haemophilia
- Females are carriers

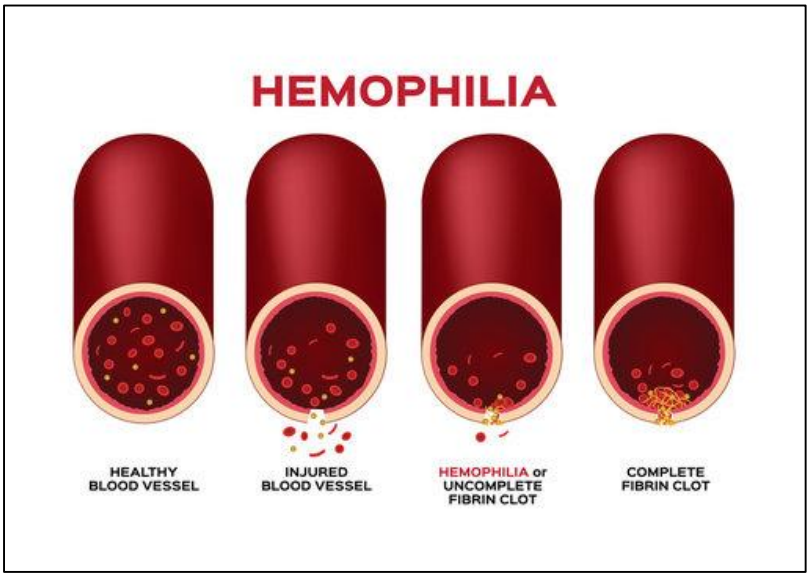
Features:

- Severe prolonged bleeding
- Bleeding without injury
- Recurrent joint bleeding
- Permanent joint damage

Types

- **Haemophilia A:** Factor VIII deficiency
- **Haemophilia B:** Factor IX deficiency





VON WILLEBRAND DISEASE

- Deficiency of von Willebrand factor
- Low factor VIII levels
- Most common inherited bleeding disorder
- Affects males and females equally