Blood

Definition: Classified as a connective tissue and complex with liquid intercellular material (plasma) in which the blood cells are suspended.

Functions of the blood:
1- Transport functions: it carries O\textsubscript{2} and nutrients to tissues and waste products of metabolism, e.g. CO\textsubscript{2} and urea to lungs and kidney.
2- Homeostatic functions: it distributes heat around the body from warmer organs, e.g. liver and gut to peripheral organs in order to maintain the body temperature constant.
3- Buffer functions: it keeps H\textsuperscript{+} concentration of extracellular fluid constant at pH of 7.4 by buffers like Hb, plasma proteins and bicarbonate.
4- Protective functions: against infection by leucocytes and antibodies in the plasma.
5- Clotting functions: stops further loss of blood during injury.

Composition of the blood: it consists of:
1- Formed elements (blood cells), of which there are three types:
   a. Red cells – erythrocytes
   b. White cells – leucocytes
   c. Platelets – thrombocytes
2- Plasma

Formation of blood (haemopoiesis)

Definitions:
Erythropoiesis: formation of erythrocytes
Leucopoiesis: formation of leucocytes
Thrombopoiesis: formation of thrombocytes (platelet)

Sites of blood formation:
1- In the foetus
   a. Yolk sac in the first 3 months of life
   b. Haemopoiesis starts in liver and spleen in the 4\textsuperscript{th} month until the 7\textsuperscript{th} month of intrauterine life
   c. Bone marrow: in the 4\textsuperscript{th} month of intrauterine life and from the 7\textsuperscript{th} month of intrauterine life until birth, it becomes the only haemopoietic organ

2- After delivery and throughout life, gradually red marrow is replaced by fatty yellow marrow at the ends of long bones and flat bones, e.g. skull, iliac bones, 25% of the cells in red marrow are erythrocyte precursors while 75% are leucocyte precursors.
Red blood cells (erythrocytes):

Development:
Primitive stem cell $\rightarrow$ proerythroblast $\rightarrow$ early, intermediate and late normoblast $\rightarrow$ reticulocyte $\rightarrow$ erythrocyte or mature red cell.

Structure:
Non-nucleated cell shaped like a flat biconcave disc.

Life span: 120 days

Red blood cell count in peripheral blood:
- Males – 4.8-5.8 million cells/mm$^3$
- Females – 4.2-5.2 million cells/mm$^3$

Old RBC are destroyed in the spleen (reticulo-endothelial system). Old RBC are deficient in enzymes. Degraded cells release iron which is reused for Hb synthesis, globulin which is degraded with a.a pools and haem (pigment) converted to bilirubin which is excreted in bile.

Functions of RBC:
- Transport of O$_2$ from lungs to tissues and CO$_2$ from tissues to lungs for excretion helped by
  - Their biconcave shape adapted the RBC for the gas transport function
  - Their cell membrane is elastic and distortable, facilitate their movements through terminal capillaries where O$_2$ is delivered and CO$_2$ is removed

Nutritional requirements for red cell production:
1- Amino acids. a.a are needed for the synthesis of globulin protein deficiency causes hypoplastic anaemia (reduce cellularity of the bone marrow) in Kwashiorkor.
2- Iron. Iron deficiency causes microcytic hypochromic anaemia (small red cell with reduced Hb content).
3- Vitamins. There are several vitamins essential for normal haemopoiesis:
  a. Vitamin B12 and folic acid, important for the synthesis of nucleoprotein, deficiency of either leads to the production of nucleated red cell precursors $\rightarrow$ megaloblastic (macrocytic) anaemia (pernicious anaemia). Intrinsic factors from the stomach is required for absorption of vitamin B12 from terminal ileum.
  b. Vitamin C, as a reducing agent. It facilitate the absorption of iron from the gut. It is involved in the normal metabolism of vitamin B12 and folic acid, deficiency of both is common (vitamin C and folic acid) result in normocytic, macrocytic or microcytic anaemia with normochromic or hypochromic red cells.
  c. Pyridoxine (B6), important for haem and nucleoprotein production. Its deficiency causes hypochromic microcytic anaemia.
  d. Vitamin E, essential for the synthesis of erythrocyte membrane, deficiency causes haemolytic anaemia in infants.
4. Trace elements, copper, cobalt (stimulates formation of erythropoietin), zinc, manganese or nickel.
Control of erythropoiesis:
Erythropoietin (hormone) – hypoxia or blood loss triggers erythropoietin synthesis from the kidney or liver which acts on the bone marrow to stimulate erythropoiesis.

Action:
1. It stimulates the early stem cell (erythropoietin sensitive stem cell) to differentiate into a proerythroblast.
2. It stimulates self-replication and proliferation of erythropoietin sensitive stem cells. It doesn’t affect the maturation stage of erythrocyte production.

Androgens, thyroid hormones, cortisol and growth hormone are important for normal erythropoiesis. Deficiency result in normochromic normocytic anaemia.

Mechanism of production of erythropoietin

Hypoxia, blood loss
↓
Blood O₂ levels
↓
Tissue (kidney or liver) hypoxia
↓
Production of erythropoietin
↓
Plasma erythropoietin
↓
Stimulation of erythrocyte production
↓
Erythrocytosis

Iron metabolism:
Total amount of iron in the body of healthy adult is 3-5 gms.

Distribution of iron in the body
1- Haemoglobin 65-75%
2- Storage (available) iron 20% presents as protein-iron compound ferritin in the liver, spleen and bone marrow
3- Cellular or tissue (non-available) iron presents in cells or enzymes
4- Transport or plasma iron
Absorption of iron, transport and storage:

- Iron in food present in the oxidized ferric state $\text{Fe}^{3+}$ and better absorbed in the reduced ferrous state $\text{Fe}^{2+}$
- Gastric acidity and the reducing agents in diet as vitamin C facilitate this reduction
- Maximal absorption of iron in the duodenum by active transport to the mucosal cell
- Inside the cell iron becomes attached to non-ferritin protein carrier and it is either:
  - Transferred across the serosal border and picked up by transferrin to be distributed to different parts of the body
  - Stored inside the cell by combining with an intracellular apoferritin to form ferritin
- In the plasma iron converted to ferric $\text{Fe}^{3+}$
- It combines with transferrin to form ferric-protein complex
- Transferrin distributed iron to various body cells for storage or utilization
- Iron stored in the reticuloendothelial system (liver, spleen and bone marrow)
- Iron stored in 2 forms: ferritin (65%) and haemosiderin (35%)
- Diet provides 10-20 mg/day, only 10-15% of ingested iron is absorbed 1-2 mg/day

Factors decreased iron absorption:

- Presence of phosphate, oxalates, phytates in diet
- Surgical removal of the stomach (gastricomy) or achlorhydria (lack HCl) $\rightarrow$ $\downarrow$ $\text{Fe}^{3+}$ reduction
- Malabsorption syndrome
Absorption of iron depends on 2 factors:
1) The size of iron stores, it depends on the saturation
2) The rate of erythropoiesis, if it is high $\rightarrow \uparrow$ absorption

Excretion of iron:
0.5-1 mg/day lost through several routes:
1- Faeces, unabsorbed ingested iron in addition to iron desquamated from intestinal epithelial cells, also small amount in bile and saliva
2- Skin from desquamated cells, lost hair, nails and sweat
3- Urine

Haemoglobin Hb:
- Hb $\uparrow$ the ability of the blood to carry $O_2$ to 60 folds
- Hb carries $O_2$ to the tissues and transport $CO_2$ from the tissues to the lungs.
  Plasma carries 0.3 ml $O_2$/100ml but whole blood carries 20ml $O_2$/100ml
- Conjugated protein formed of haem and globin
- Composed of 4 subunits $2\alpha$ and $2\beta$ chains
- Each unit contains a red iron-porphyrin or haem group bound to a polypeptide chain called globin

Types of Hb:
1- Adult haemoglobin (HbA), consists of $2\alpha$ and $2\beta$ chains, it constitutes 98% of Hb in adults
2- Haemoglobin A2 (HbA2), it forms $\sim$ 2% of Hb
3- Haemoglobin F (HbF), it forms the major Hb during intrauterine life and it drops to 1% during puberty

Functions of Hb:
1) Carriage of $O_2$. Each subunit of Hb carries 2 $O_2$ atoms
2) Carriage of $CO_2$ from the tissues to the lungs
3) Buffer. Hb is a protein so it acts as a buffer in the blood

Breakdown of Hb:
- It breaks down into its components, globin and haem
- Globin degraded to a.as $\rightarrow$ for a.a. pools in the body
- Iron reused in Hb synthesis
- Haem group converted to biliverdin which is reduced to bilirubin (both are bile pigments) $\rightarrow$ excreted in bile
- Bilirubin released from the reticuloendothelial system, it bounds to albumin which increases its solubility
- Bound bilirubin pass to the liver and conjugated to glucoronic acid and it becomes water soluble and is excreted in bile into the small intestine
- In the small intestine is converted by bacterial action to urobilinogen
- Some of the urobilinogen remain in the small intestine and excreted in stool and the rest absorbed into the blood and excreted by the kidneys in urine
**Jaundice**
Yellowish colouration of skin, sclera and other tissues due to accumulation of excess bilirubin in the plasma and tissue fluids.

Total plasma bilirubin = 0.5-1 mg/100ml
Jaundice = exceeds 2 mg/100ml

**Anaemia**

*Definition:*
Decrease in the concentration of Hb in the blood below the normal level for the same age and sex.
Male = 14-16 gm/dl; Female = 12-14 gm/dl

*Symptoms of anaemia:* tiredness and easy fatigability due to ↓ in the O$_2$ supply to the tissues.

*Causes and classification:*
1- Blood loss
   a) Acute as in car accident
   b) Chronic due to chronic bleeding from GIT, e.g. piles, peptic ulcer, worms in the small intestine
2- Diminished red cell production by the bone marrow
   a) Deficiency of the nutritional substances required for erythropoiesis
      • Iron deficiency causes microcytic (small size cell) hypochromic (light red colour due to ↓ Hb). It is the commonest type of anaemia in developing countries due to ↓ iron intake in diet.
      • Vitamin B12 and folic acid deficiency causes megaloblastic anaemia (large nucleated red cell precursor)
   b) Diminished red cell production due to invasion of the bone marrow by cancer cells, radiation or drugs (aplastic anaemia)
3- Excessive destruction of red cells (haemolytic anaemia)
   a) Presence of abnormal Hb as Hbs (sickle cell anaemia)
   b) Blood group incompatibility (the cause from outside the red cell)
Leucocytes

Are heterogenous population of nucleated cells lacking Hb.

Total WBC count is 4000-10000 cells/mm$^3$

**Function:**
Defense function against invading organisms.

**Classification**

Granulocytes (Cytoplasmic granules):

1. Neutrophil (or polymorphonuclear PMN) 60-70% (40-60%), lobulated nucleaus (2-5 lobes), the cytoplasm contains fine granules which stain purplish, formed at bone marrow and stay in the blood for 7-10 hours and then migrate to tissue.

   Function of neutrophils:
   Defence against infections. Some mature neutrophils join the circulation and called circulating granulocytes, others deposit along the walls of small vessels (marginal granulocyte).

Acute infections:

Chemotaxis:
1) Movement of neutrophils towards the site of infection. Attracted by chemotactic substances, e.g. bacterial products, damaged leucocyte or other tissue components.
2) Margination: they lie along the walls of the closest capillaries
3) Diapedesis: neutrophils squeeze themselves between endothelial cells to move out of the capillaries towards bacteria

Phagocytosis:

- The process by which the neutrophil ingest the foreign organism
- Certain substances as $\gamma$-globulins (IgG) complement C4 which coat the bacteria $\rightarrow$ opsonization
- Opsonin: are agents in the plasma which coat bacteria or foreign particles for phagocytosis
- Opsonization: the process of coating bacteria and foreign substances for phagocytosis

Phagocytosis occurs in steps:
1) Recognition and opsonization
2) Close adhesion between the outer membrane of the neutrophil and bacteria
3) Invasion of the neutrophil membrane and encirclement of the bacterium by pseudopods
4) Fusion of the pseudopodia to enclose the bacterium in a phagocytic vacule
Microbial killing:
1. Fusion of neutrophil granules with phagocytic vacuole
2. Discharge of antimicrobial agents from the granules, e.g. lysozymes, myeloperoxidase, lactoferrin
3. Killing and digestion of the bacteria

2. Eosinophils: 2-4% (0.5-1%)  
The nucleus is formed of 2 lobes. There is large coarse granules staining red.  
Formation: in the bone marrow  
Life span: 4-8 hours  
Function:  
In chronic inflammation:  
• Chemotaxis: chemotactic substances includes histamine, Ag-Ab complex, 5-HT (5 hydroxytryptamine), bradykinin, specific eosinophil chemotactic factor  
• Phagocytosis: the same as neutrophils  
• Microbial killing: less than that of neutrophils

Eosinophilia:  
• Chronic inflammation  
• Allergic diseases of skin and lungs  
• Parasitic infection, e.g. worm infection

3. Basophil: 0-2% (0.5-1%)  
The nucleus is rarely segmented with its margin obscured by the cytoplasm. The cytoplasm contains large, coarse, rounded or dark granules.  
Formation: bone marrow  
Life span: 4-8 hours  
Function:  
• Not known with certainty, but contains heparin, histamine, 5-HT and RNA (ribonucleic acid)  
• It is rich in histamine and heparin, so it resembles tissue mast cells

Agranulocytes (without cytoplasmic granules)

1. Monocytes: 2-8% (6-10%) – the nucleus is kidney shaped. The cytoplasm is grey blue with fine reddish granule  
Formation: bone marrow  
Life span: few hours to 6 days then it moves to tissue transform to tissue macrophage (histocyte) which is more effective
Function:  
• Direct function: phagocytosis and killing of invading bacteria  
• Indirectly by interacting and cooperating with lymphoid cells of the immune response

2. Lymphocytes: 20-30% (20-40%) – types, small, intermediate and large  
Formation: bone marrow, thymus, lymph nodes, other lymphoid tissues  
Life span: T cells, 100-300 days (long-lived lymphocytes); B cells, 2-7 days (short-lived lymphocytes)
Function (lymphocytes are the central cells in immunity):

- T cells (Thymus dependent cells) principal mediators of cellular immune response
  - Play a minor role in the synthesis of Igs (Abs)
- B cells (Thymus independent cells)
  - Once they are stimulated by Ag, they develop into large plasma cells, which produce Abs
  - They are the principal mediator of humoral immune response (Igs) Abs

**Leukaemia**: Neoplastic growth of the stem cells in the bone marrow or lymphoid tissue leads to myeloid or lymphocytic leukaemia

**Leucocytosis**: increased in the total number of leucocyte count above the normal level

Physiological leucocytosis:
1) Diurnal variation lower count in the morning and maximum in the afternoon
2) After protein meal
3) Following exercise
4) Stress and adrenaline injection

Pathological leucocytosis:
1- Following bacterial infections, e.g. (pyogenic infections as tonsillitis, appendicitis, wounds infection.
2- Acute bacterial infection $\Rightarrow$ ↑ neutrophil
3- Chronic and viral infection $\Rightarrow$ ↑ lymphocytes

**Leucopenia**: ↓ in total number of leucocyte count below the normal level, in malnutrition, typhoid fever, some drugs, vitamin B12 and folic acid deficiency

Plasma proteins (3 types):
- Albumin – 4-8 g/100mL
- Globulins – 2-3 g/100mL
- Fibrinogen – 0.3 g/100mL
- Total – 7 g/100mL

Functions of plasma proteins:
1- Transport functions of lipoproteins, hormones, lipids and bilirubin (α and β globulin)
2- Definitive function (Igs)
3- Reserve body proteins
4- Osmotic function (albumin) which controls the exchange of fluid between blood and tissues
5- Viscosity of plasma (fibrinogen and globulins)
6- Important in blood clotting (fibrinogen)
The blood groups:
- Depends on the presence or absence of glycoproteins (Ags) on the surface of RBC
- There are many types, but the most important are 2 groups ABO and rhesus (Rh) systems

The ABO system:
- It depends on whether the red cells of the individual contains one, both or neither of the two blood group antigen A and B
- There are 4 main ABO groups: A, B, AB and O

<table>
<thead>
<tr>
<th>Blood group</th>
<th>Agglutinogen (Ag on the RBC)</th>
<th>Agglutinin (Abs in plasma)</th>
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<tbody>
<tr>
<td>A</td>
<td>A</td>
<td>Anti-B</td>
</tr>
<tr>
<td>B</td>
<td>B</td>
<td>Anti-A</td>
</tr>
<tr>
<td>AB</td>
<td>A &amp; B</td>
<td>--</td>
</tr>
<tr>
<td>O</td>
<td>None</td>
<td>Anti-A &amp; Anti-B</td>
</tr>
</tbody>
</table>

- The blood Ags are called agglutinogens in the RBC. Antibodies in the plasma are called agglutinins
- Agglutinins are not present at birth and they start to appear between the 2nd and 8th month of life

The Rhesus (Rh) blood group system:
- It depends on the presence or absence of the rhesus antigen (D) on the surface of red blood cells. If present, the person is D-positive or Rh-positive. If absent, the person is D-negative or Rh-negative
- There are at least 3 sets of alternative Ags with Rh system D or d, C or c, E or e, but D antigen is the strongest and most important clinically

Rhesus antibodies:
Are not naturally occurring Ab, it occurs as a result of immunization from
1- Transfusion of Rh –ve individual with Rh +ve blood
2- The presence of Rh +ve foetus in Rh –ve mother (entry of some of Rh Ag of the foetus into the mother blood which will provoke the production of Abs)

Importance of blood group:
Important in blood transfusion between individuals, so for safe blood transfusion, should follow the following steps:
1. Blood grouping for both ABO and Rh systems should be done for both the donor and recipient
2. Cross matching should be done (donor cell are mixed with recipient’s serum to find if the recipient’s plasma contains Abs to the donor cells). Also cross matching is done between the recipient’s cells and the donor’s plasma.
AB group individuals are called universal recipients because their plasma contains neither anti-A nor anti-B antibodies, so they can receive blood from all ABO group.

O group individuals are called universal donors because their blood lack both A and B antigens, so they can donate safely to all ABO groups.

**Complications of blood transfusion:**
Complications of the blood transfusion results from Ag-Ab reaction between donor and recipient (due to incompatible blood transfusion) which can lead to:

1. Haemolysis of red cells, allergic or febrile reaction
2. Transmission of disease from the donor to the recipient, e.g. malaria, syphilis, viral hepatitis and AIDS

**Rhesus incompatibility between mother and foetus (haemolytic disease of the newborn):**
When Rh~ve mother gets pregnant with Rh~ve foetus. The 1st baby escape this effect, but if the 2nd baby is Rh~ve, Abs from the mother (due to incompatible pregnancy or incompatible blood transfusion) will react with the foetus blood → haemolysis of the foetal blood. Anti D Abs are given to the mother as a prophylactic after delivery (which will react and get rid of the foetal Rh~ve cells to prevent immunization of the mother).
Haemostasis:

Definition: haemostatic mechanisms prevent blood loss from intact vessels and stop excessive bleeding from injured vessels.

Components for normal haemostasis:
  a) Local vascular factors
  b) Platelets
  c) Coagulation (fibrin formation)
  d) Fibrinolysis

A) Local vascular factors:
  Immediate localized vasoconstriction of the injured vessel wall and lasts for less than 1 minute.
  • Humoral factors:
    o Localized release of vasoconstrictor serotonin (5-hydroxy tryptamine) from platelets
    o Systemic release of catecholamine from the adrenal medulla
  • Neural factors:
    N.B. Acute hypoxia and metabolic acidosis diminish this important response

B) Platelets
  Produced and released from the bone marrow, pass through the spleen before reaching the blood stream, where they survive 3-5 days.
  Normal platelet count 100,000 – 400,000 platelets/mm³ (~ 250,000/mm³)

Functions:
  • Platelets adhere to the injured site of the blood vessel few seconds after injury. Exposed collagen in the vessel wall attracts platelets to adhere to it and trigger the release of endogenous platelet adenosine diphosphate (ADP) which increases the stickiness of platelets.
  • Platelet aggregation in the presence of ADP with one another to form fragile and reversible primary haemostatic plug.
  • After aggregation, platelets start release the following substances:
    o 5-HT, a potent vasoconstrictor
    o platelet phospholipid or platelet factor 3 (PF3), which is essential for the process of blood coagulation
    o proteins, e.g. platelet β-thromboglobulin (βTG) and platelet factor 4 (PF4, heparin neutralizing factor)
    o thromboxane A2 (TXA2), a prostaglandin formed from arachidonic acid. It is a potent vasoconstrictr and aggregation agent. Aspirin ingestion inhibits TXA2 formation (Aspirin used in coronary heart disease). For stronger clot formation, other clotting factors are needed, e.g. thrombin.
C) Blood Coagulation
- A series of biochemical reaction which leads to activation of the thrombin enzyme
- Thrombin will change soluble plasma protein (fibrinogen) to insoluble protein (fibrin)
- Prothrombin (inactive thrombin) is activated by intrinsic and extrinsic pathways
- Activation is a cascade reaction involve 12 clotting factors, circulating in precursor forms

**Intrinsic pathway:**
- The trigger is the activation of factor XII by contact with foreign surface, collagen of injured blood vessels and glass
- Activated factor XIIa will activate factor XI, activated factor XIa will activate factor IX, activated factor IXa will act in the presence of factor VIII, Ca^{2+} and phospholipid to activate factor X
- Following this step, the pathway is common for both

**Extrinsic pathway:**
- Triggered by material from damaged tissues (tissue thromboplastin) in the presence of factor VII, Ca^{2+} will activate factor X

**Common pathway:** Activated factor X with factor V, PF3 and Ca^{2+} forms thrombokinase complex and convert prothrombin to thrombin (proteolytic enzyme). Thrombin splits two short peptide chains (fibrinopeptide A & B) from fibrinogen to form fragile aggregate of fibrin. This fragile fibrin form a network with factor XIII and Ca^{2+} to form strong fibrin.

D) Fibrinolysis
Enzymatic breakdown of fibrin by naturally occurring enzyme (plasmin) which prevent intravascular blocking.
- Balance between clotting and fibrinolysis
- Excess fibrinolysis leads to tendency for bleeding
- Excess clotting leads to blocking of blood vessels
- Plasminogen conversion to plasmin by activators in blood, tissues and urine
- Plasmin digest intra- and extravascular deposit of fibrin to fibrin degeneration product (FDP)
- Unwanted effect is digestion of clotting factors including fibrinogen, factor V and factor VIII

Plasmin is controlled by:
1- Inhibition of plasminogen activators (antiactivators)
2- Inhibition by inhibitors of plasmin (anti-plasmins) which are produced by the liver
   - Thrombocytopenic purpura (↑ bleeding time than normal) (normal: 2-5 mins) due to ↓ number of platelets.
   - Haemophilia (prolonged clotting time than normal) (normal: 5-8 mins) due to factor VIII deficiency.
Activation of Coagulation Mechanism

**Intrinsic pathway**

Contact activation with
1. Foreign surface
2. Collagen of injured blood vessels
3. Glass

\[ \text{XII} \rightarrow \text{XIIa} \]
\[ \text{XI} \rightarrow \text{XIa} \]
\[ \text{IX} \rightarrow \text{IXa} \]

\[ \text{VIII} \rightarrow \text{Ca}^{2+} \rightarrow \text{P} \]

**Extrinsic pathway**

Tissue factor – material from damaged tissue (tissue thromboplastin)

\[ \text{II} \rightarrow \text{IIa} \]

\[ \text{V} \rightarrow \text{Ca}^{2+} \rightarrow \text{P} \]

\[ \text{I} \rightarrow \text{fibrinogen} \rightarrow \text{Ia} \rightarrow \text{fibrin-soluble} \]

\[ \text{XIII} \rightarrow \text{Ca}^{2+} \rightarrow \text{Insoluble fibrin} \]

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**The Fibrinolytic Enzyme System**

Plasminogen activator
(in blood, tissues & urine)

\[ \text{Plasminogen} \rightarrow \text{X} \rightarrow \text{Plasmin} \]

Anti-activators

\[ \text{Coagulation} \rightarrow \text{Fibrin} \rightarrow \text{FDP} \]

Anti-plasmins
**Anticoagulants:**

Substances which inhibit the process of blood coagulation.

*Common used anticoagulant:*

1- Substances which removed Ca\(^{2+}\) ions from the blood
   a. Citrate (used in blood bank)
   b. Oxalate, ethylene diamine tetra-acetate (EDTA) used in clinical laboratories

2- Heparin
   mucopolysaccharide found in many tissues, e.g. liver, lungs, granules of mast cells and basophil.
   **Action:**
   - Act as a direct antithrombin
   - Prevent the conversion of prothrombin to thrombin
   **Uses:**
   - During open heart surgery to prevent venous thrombosis
   - In post-operative period to prevent venous thrombosis
   - In laboratories for blood collection

3- Warfarin and phenindione
   suppresses the synthesis of vitamin K dependent factors (II, VII, IX and X) by the liver.
   - widely used in clinical practice
   - advantage over heparin:
     o can be given orally (heparin by injection)
     o has longer half life (last for 48 hrs) while heparin (6-8 hrs)

*Naturally occurring anticoagulants:*

- Present in small concentration in the plasma in order to control the clotting mechanism.
- Antithrombin III protein (which inactivate clotting factors VIII and V)
**Haemorrhagic (bleeding disorders):**
Disease conditions characterized by excessive bleeding tendency due to defect in the haemostatic system, caused by:
- a- Vascular defects: either congenital or acquired
- b- Platelet defects either decrease their number (thrombocytopenia) or defect in their function (thrombocytopathy)
- c- Coagulation defects: either congenital or acquired.

**Congenital coagulation defects:**
- The commonest disorder is haemophilia A, due to factor VIII deficiency and haemophilia B or Christmas disease due to deficiency of factor IX.
- Characterized by excessive bleeding from skin, mucous membranes, joints after minor trauma or surgery, e.g. tooth extraction
- Patient treated by replacing the clotting factor (fresh blood transfusion, fresh frozen plasma or clotting factor concentrate)

**Acquired coagulation defects:**
Due to diminished production of clotting factor in liver disease and vitamin K deficiency or consumption of platelet and clotting factor as in DIC (due to extensive activation of clotting mechanism in vivo).