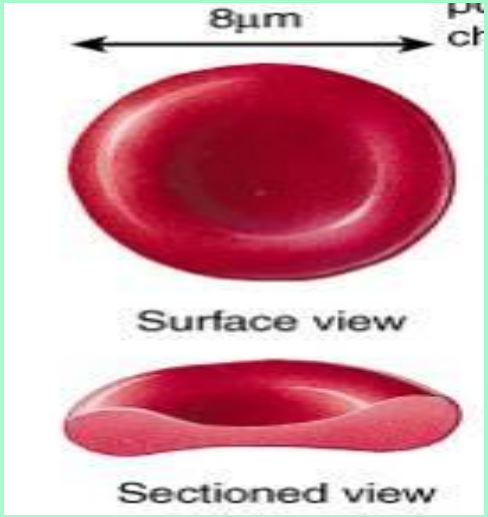
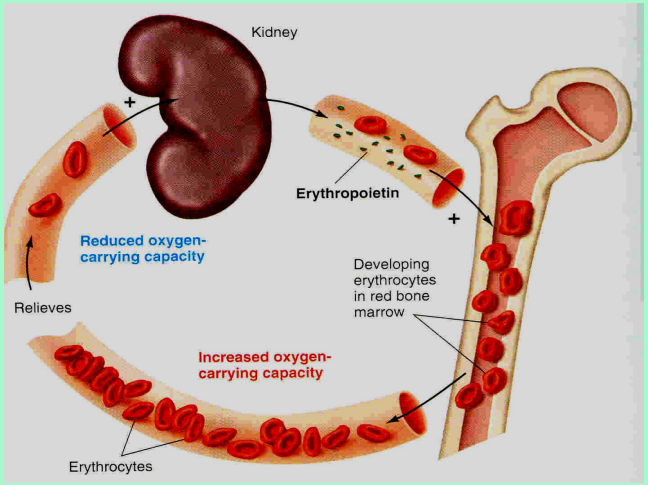
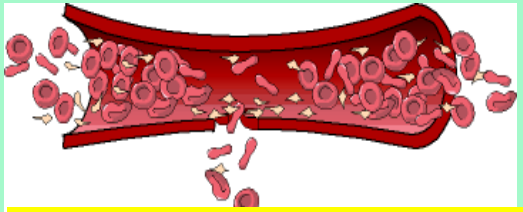
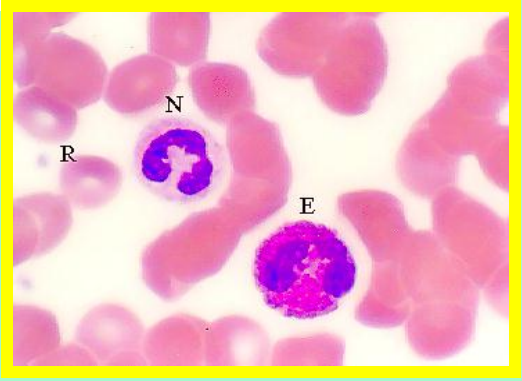
Haematology

Prof. Dr. Osama Mohamed Ahmed









Blood

- Study of blood and its components is known as haematology.
- Blood is a homogenous fluid connective tissue which circulates within cardiovascular system.
- The total blood volume is about 5600ml in a 70 kg man (8% of body weight).
- It is composed of two main parts

  -plasma 55%

  -cellular elements 45%..RBC's, WBC's and platelets

Blood

55% Plasma

- Water (90%)
- Inorganic substances
  Na, Cl
- Organic substances
  plasma proteins
  plasma lipids
  glucose & amino acids

45 % blood elements

Erythrocytes
Leucocytes
Platelets

Haematocrit or packed cell volume (PCV) is the percentage volume of blood that is contributed by red cells alone. In severe vomiting, diarrhea and severe burns, there is haemoconcentration and increase in PCV while in severe anemias, there is haemodilution and decrease in PCV.

Functions of the blood

- Transport function (transport of O_2 and CO_2 between lungs and tissues, transport of excretory products to the kidneys to be excreted, transport of absorbed nutritive substances from the alimentary canal to almost all parts of the body and transport of hormones)

- Defensive or protective function (With the help of leukocytes and antibodies present in the plasma, blood helps the body to sustain resistance against infection)

- Hemostatic function
- Homeostatic function

what's homeostasis?

Regulation of body temperature leading to thermal balance of the body

Homeostasis

maintenance of constant conditions in the internal environment

Plasma

It is a straw yellow clear fluid composed of

1. Water 90%
2. Inorganic substances – 0.9% Na^+ , Cl^- , HCO_3^-
3. Organic substances 9.1%

   -plasma proteins

   -lipids…triglycerides, cholesterol & fatty acids

   -other organic substances glucose, amino acids, vitamins, hormones, enzymes, waste products

4 Blood gases O_2 , CO_2 .

Plasma Proteins

[albumin (4-5 g%), globulins (2.3g%), prothrombin (15-40mg%) and fibrinogen (0.3g%)]

-Concentration…… 7 gm/dl

-Site of formation…..?

liver

lymphocytes (plasma cells)

-albumin/globulin ratio (normal 2:1).

-Separation of plasma proteins can be done by electrophoresis.

Functions of plasma proteins

(albumin, globulins (α, β & γ) , prothrombin and fibrinogen)

- Maintenance of colloidal osmotic pressure …albumin
- Defensive function……. γ globulins
- Blood clotting…..prothrombin and fibrinogen
- Maintenance of viscosity of the blood: viscosity is one of the factors which tries to maintain the normal blood pressure……. fibrinogen
- Buffer function (prevents drastic variations of the pH of the blood.
- transport function…(hormones, metals, drugs…..)

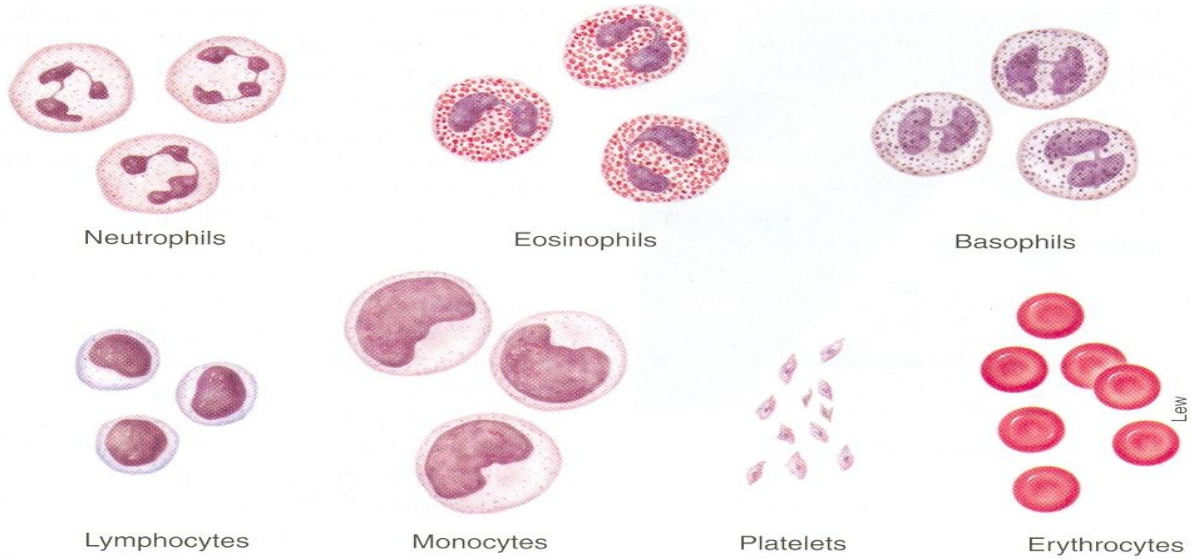
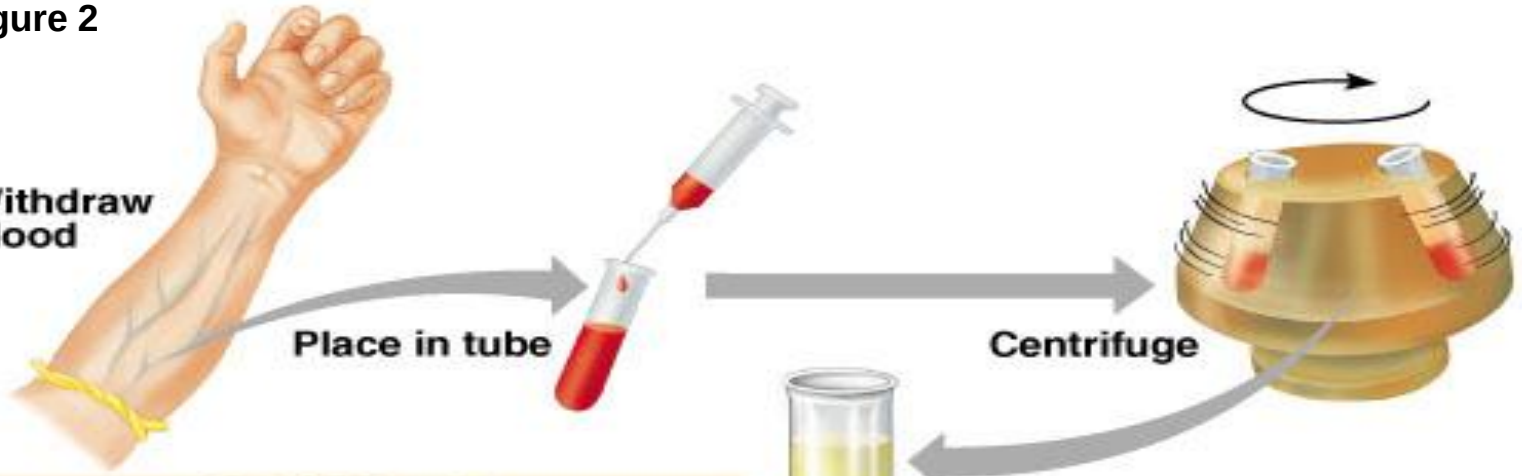


Figure 1 **The blood cells and platelets.** The white blood cells depicted above are granular leukocytes; the lymphocytes and monocytes are nongranular leukocytes.

Table 1 Formed Elements of the Blood

Component	Description	Number Present	Function
Erythrocyte (red blood cell)	Biconcave disc without nucleus; contains hemoglobin; survives 100 to 120 days	4,000,000 to 6,000,000 / mm^3	Transports oxygen and carbon dioxide
Leukocytes (white blood cells)		5,000 to 10,000 / mm^3	Aid in defense against infections by microorganisms
Granulocytes	About twice the size of red blood cells; cytoplasmic granules present; survive 12 hours to 3 days		
1. Neutrophil	Nucleus with 2 to 5 lobes; cytoplasmic granules stain slightly pink	54% to 62% of white cells present	Phagocytic
2. Eosinophil	Nucleus bilobed; cytoplasmic granules stain red in eosin stain	1% to 3% of white cells present	Helps to detoxify foreign substances; secretes enzymes that dissolve clots; fights parasitic infections
3. Basophil	Nucleus lobed; cytoplasmic granules stain blue in hematoxylin stain	Less than 1% of white cells present	Releases anticoagulant heparin
Agranulocytes	Cytoplasmic granules not visible; survive 100 to 300 days (some much longer)		
1. Monocyte	2 to 3 times larger than red blood cell; nuclear shape varies from round to lobed	3% to 9% of white cells present	Phagocytic
2. Lymphocyte	Only slightly larger than red blood cell; nucleus nearly fits cell	25% to 33% of white cells present	Provides specific immune response (including antibodies)
Platelet (thrombocyte)	Cytoplasmic fragment; survives 5 to 9 days	130,000 to 400,000 / mm^3	Enables clotting; releases serotonin, which causes vasoconstriction

Figure 2



PLASMA 55%

Constituent	Major functions
Water	Solvent for carrying other substances
Salts (electrolytes) Sodium Potassium Calcium Magnesium Chloride Bicarbonate	Osmotic balance, pH buffering, and regulation of membrane permeability
Plasma proteins Albumin Fibrinogen Globulins	Osmotic balance, pH buffering Clotting of blood. Defense (antibodies), and lipid transport
Substances transported by blood Nutrients (e.g., glucose, fatty acids, vitamins, amino acids) Waste products of metabolism (urea, uric acid) Respiratory gases (O_2 and CO_2) Hormones	

Formed Elements (cells) 45%

Cell type	Number (per mm^3 of blood)	Functions
Erythrocytes (red blood cells)	4–6 million	Transport oxygen and help transport carbon dioxide
Leukocytes (white blood cells)	4000–11,000	Defense and immunity
Platelets	250,000–500,000	Blood clotting

Table 2 Characteristics of Formed Elements of the Blood

Cell type	Occurrence in blood (per mm^3)	Cell anatomy*	Function
Erythrocytes (red blood cells, or RBCs) 	4–6 million	Salmon-colored biconcave disks; anucleate; literally, sacs of hemoglobin; most organelles have been ejected	Transport oxygen bound to hemoglobin molecules; also transport small amount of carbon dioxide
Leukocytes (white blood cells, or WBCs)	4000–11,000		
Granulocytes			
• Neutrophils 	3000–7000 (40–70% of WBCs)	Cytoplasm stains pale pink and contains fine granules, which are difficult to see; deep purple nucleus consists of three to seven lobes connected by thin strands of nucleoplasm	Active phagocytes; number increases rapidly during short-term or acute infections
• Eosinophils 	100–400 (1–4% of WBCs)	Red coarse cytoplasmic granules; figure-8 or bilobed nucleus stains blue-red	Kill parasitic worms; increase during allergy attacks; might phagocytize antigen-antibody complexes and inactivate some inflammatory chemicals

*Appearance when stained with Wright'

Cell type	Occurrence in blood (per mm^3)	Cell anatomy*	Function
• Basophils 	20–50 (0–1% of WBCs)	Cytoplasm has a few large blue-purple granules; U- or S-shaped nucleus with constrictions, stains dark blue	Granules contain histamine (vasodilator chemical), which is discharged at sites of inflammation
Agranulocytes			
• Lymphocytes 	1500–3000 (20–45% of WBCs)	Cytoplasm pale blue and appears as thin rim around nucleus; spherical (or slightly indented) dark purple-blue nucleus	Part of immune system; one group (B lymphocytes) produces antibodies; other group (T lymphocytes) involved in graft rejection, fighting tumors and viruses, and activating B lymphocytes
• Monocytes 	100–700 (4–8% of WBCs)	Abundant gray-blue cytoplasm; dark blue-purple nucleus often kidney-shaped	Active phagocytes that become macrophages in the tissues; long-term "clean-up team"; increase in number during chronic infections such as tuberculosis
Platelets	250,000–500,000	Essentially irregularly shaped cell fragments; stain deep purple	Needed for normal blood clotting; initiate clotting cascade by clinging to broken area; help to control blood loss from broken blood vessels

*Appearance when stained with Wright's

Erythrocytes

Biconcave discs

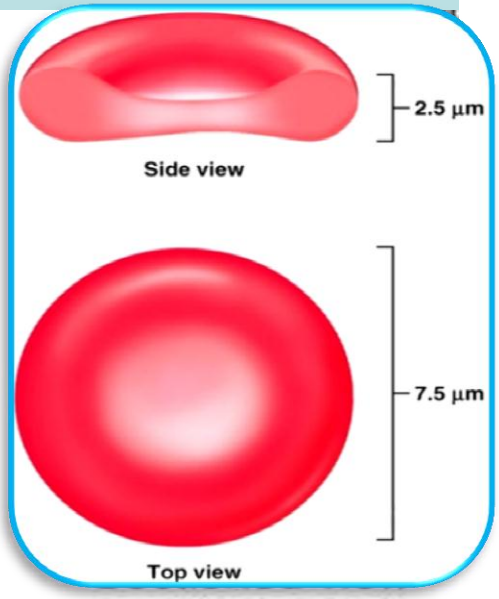
count ? /mm^3

structure

-semipermeable membrane

-hemoglobin (content and function)

-no nucleus



Erythropoiesis…….??? Define

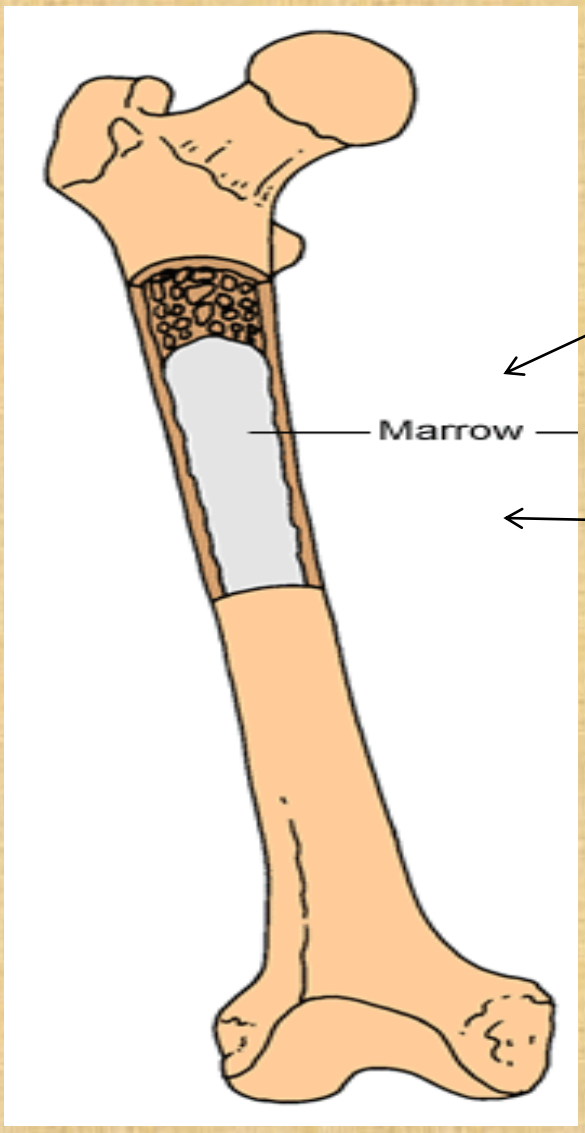
Site of hematopoiesis…..in fetus & in adult

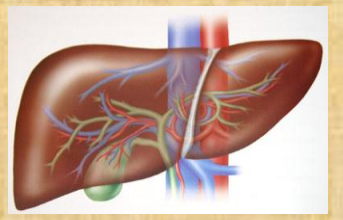
Erythropoiesis…….???

formation of new red blood cells

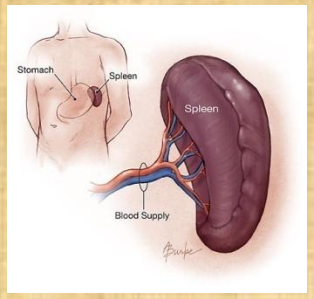
Site of hematopoiesis…..

- mesoderm of yolk sac in the 1st three months of fetal life
- liver and spleen during 3-6 months of fetal life
- red bone marrow in the rest the period of fetal life and in post- natal period





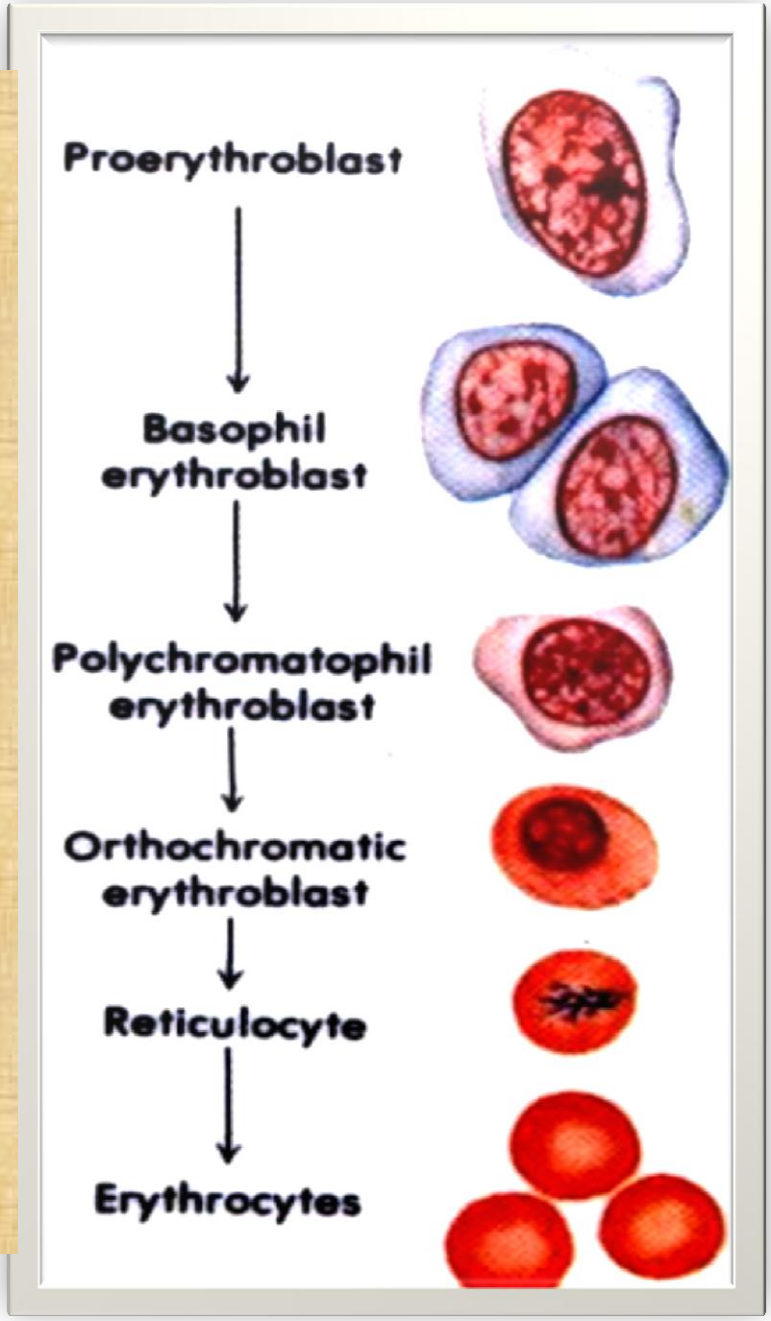
Erythropoietin



• RBCs production occurs in red bone marrow. The primitive cells, the pro-erythroblasts develop through normoblasts of various types and reticulocytes, until mature erytherocytes are formed.

• During the normoblast stage, the nucleus is lost. In the healthy adult only mature erytherocytes and few (1%) reticulocytes are found in the peripheral blood.

• Appearance of nucleated red cells indicates abnormal blood formation or irritation of the bone marrow.



Hemoglobin

Hem…..iron containing porphyrin derivatives

Globin…protein part formed of 4 polypeptide chains

Hb A …..2 α & 2 β (96- 98% of Hb in adult)

Hb A2 ….2 α & 2 δ (2.5 % of adult Hb)

Hb F ….2 α & 2 γ (Hb of fetus-more affinity to O_2)

Function of Hb

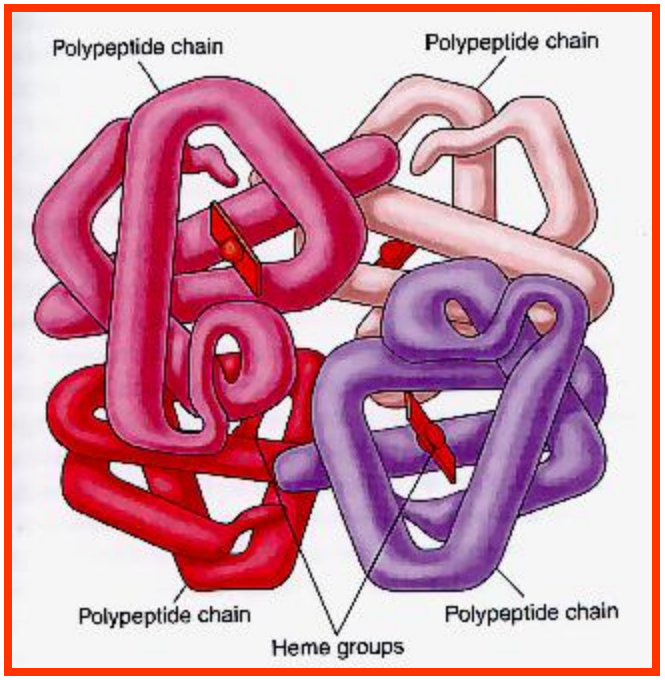
transport oxygen from lung to tissues and carbon dioxide from tissues to the lungs

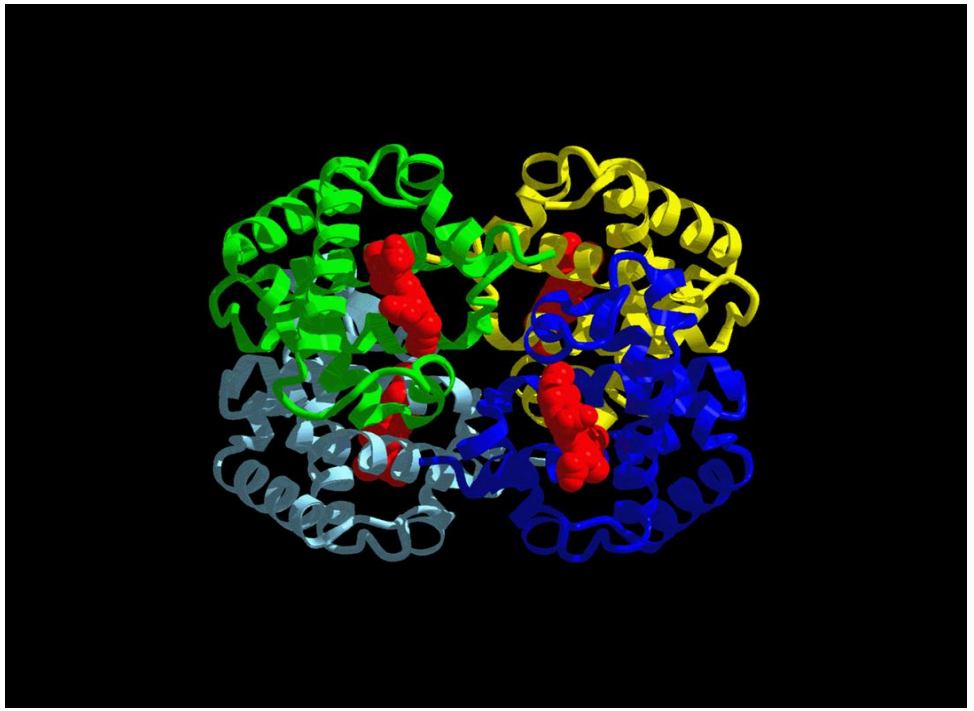
Haemoglobin abnormalities

1- Synthesis of an abnormal haemoglobin

2- Reduced rate of synthesis of normal α & β chains (the α- & β-thalassaemiais).

Hemoglobin


Polypeptide chain
Polypeptide chain
Polypeptide chain
Polypeptide chain
Heme groups



Factors affecting erythropoiesis

1. Oxygen supply to the tissues

decreased oxygen →increased erythropoietin → increased RBC number

(erythropoietin hormone ?)

2. Healthy bone marrow

3- healthy liver (why ?)

storage of Fe, Vit B12, erythropoesis in fetus

4. Diet……iron, vitamin B_{12} and folic acid as well as proteins

- iron → hemoglobin formation
- Vit B_{12} & folic acid → DNA synthesis & cell division
- proteins → globin formation

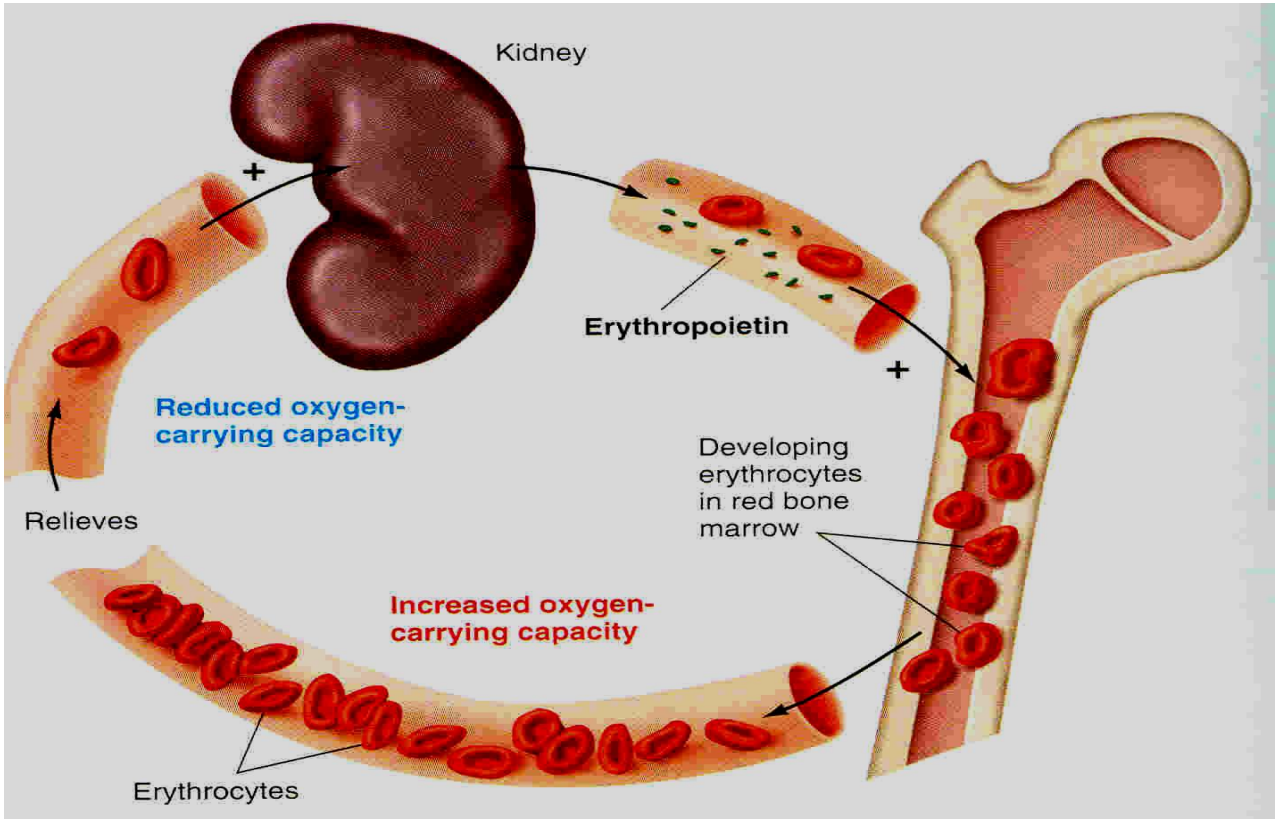
5. Hormones

androgen, thyroid & glucocorticoid hormones stimulates erythropoiesis

Erythropoietin

- Glycoprotein hormone
- Hypoxia is the main stimulus for its secretion
- In adult, 85% is formed by the kidney and 15% is formed by the liver
- It stimulates all steps of erythropoiesis and increases the production of RBCs

(anemia ?? Polycythemia ??)



Hypoxia, cobalt salts, androgens (testosterone), catecholamines, corticosteroids, growth hormone, and thyroxine.

Erythropoietin

1. production of proerythroblast from the stem cells.
2. Increasing the speed of conversion of one step to the other in the erythroblastic stages.
3. It accelerates the synthesis of Hb.

Iron

- Gastric HCl & vitamin C reduce iron from ferric state to ferrous state
- Iron is reabsorbed in upper small intestine

Folic acid

Essential for DNA synthesis & cell division

Vitamin B_{12}

- Essential for DNA synthesis, cell division & metabolism of myelin sheath
- It unites with intrinsic factor from the stomach then reabsorbed from terminal ileum
- Deficiency-----macrocytic anemia & neurological symptoms
- Treatment by injection of vit B_{12}

Anemia

It is a decrease in number of RBCs, hemoglobin content or both.

normal RBCs count…….4.5 - 5.5 million/ mm^3

normal Hb content……...13.5 15.5 gm/ dl

Types

1- ***normocytic normochromic anemia***

hemorrhage, hemolytic anemia & bone marrow depression (aplastic anemia)

2-***microcytic hypochromic anemia***

iron deficiency (Causes: decreased iron intake & absorption –chronic blood loss)

3- ***macrocytic hyperchromic anemia***

Vit. B_{12} deficiency $\longrightarrow$ absent intrinsic factor, disease of lower ileum, decreased storage in liver disease

folic acid deficiency $\longrightarrow$ decreased intake, disease of small intestine, cytotoxic drugs

Hemostasis

It is a prevention of blood loss after injury

Mechanism

- Constriction of the blood vessel
- Formation of platelet plug
- Conversion of platelet plug to a definitive clot by fibrin threads (blood clot)

Blood clotting (coagulation) is the conversion of fluid blood into semisolid jelly like mass to prevent blood loss.

Platelet plug formation

Platelet reactions

1- Platelet **adhesion** (to subendothelial collagen)

2- Platelet **activation** (swell & change the shape)

3- Platelet **release** reaction (Ca^{2+}, coagualtion factors, serotonin, thromboxane A_2.....

4- Platelet **aggregation** (platelet plug)

5- Platelet **procoagulant activity** (activation of coagulation factors)

6- Platelet **fusion** (fusion of aggregated platelets)

There are 4 basic steps in the coagulation of blood

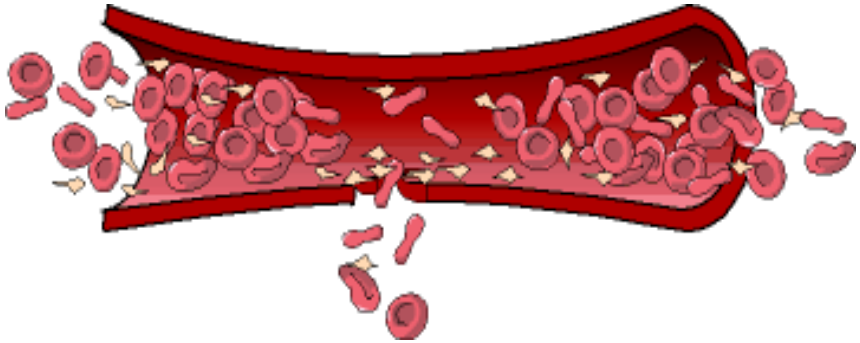
1- Platelet plug formation

2- Formation of prothrombin activator

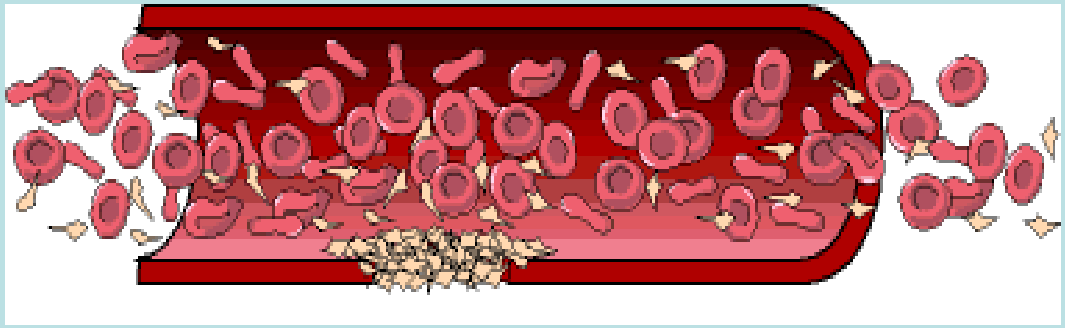
3- Conversion of prothrombin into thrombin

4- Conversion of fibrinogen to fibrin

1. Vessel damage, blood loss
2. Vascular spasm.



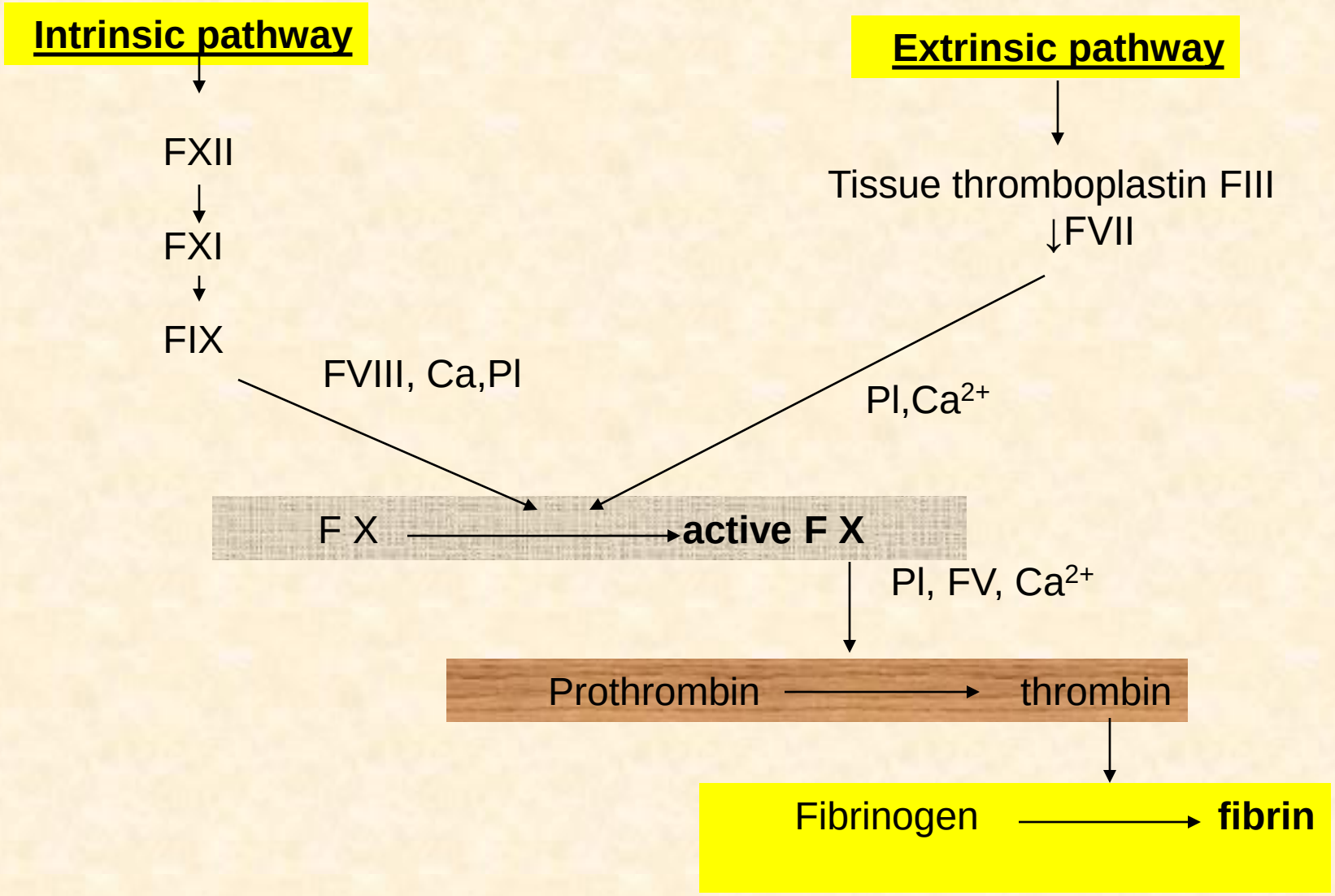
3. Platelet plug forms



4. Coagulation

Formation of blood clot

(Mechanism of blood coagulation)



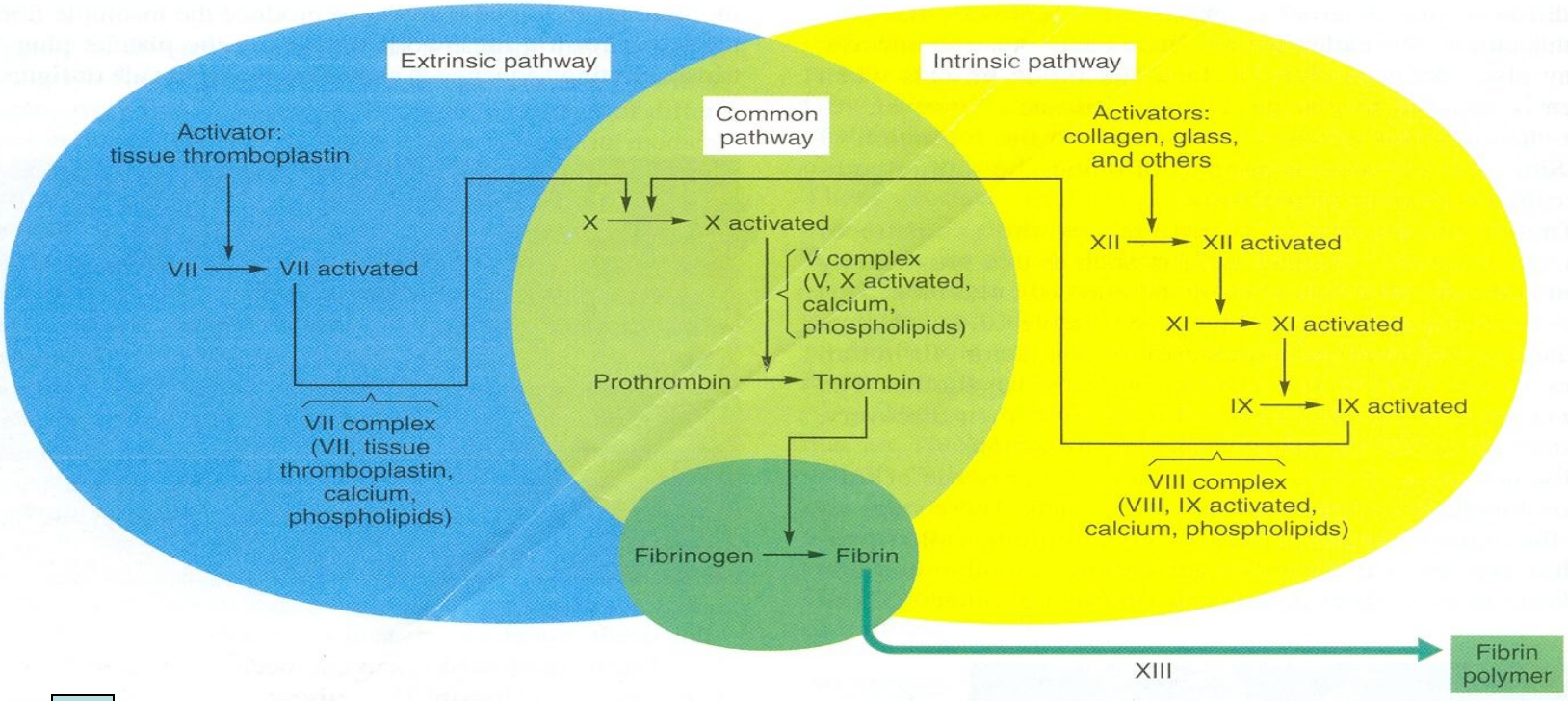


Figure **The extrinsic and intrinsic clotting pathways.** Both pathways lead to the formation of insoluble threads of fibrin polymers.

Table Some Acquired and Inherited Clotting Disorders and a Listing of Anticoagulant Drugs

Category	Cause of Disorder	Comments
Acquired clotting disorders	Vitamin K deficiency	Inadequate formation of prothrombin and other clotting factors in the liver
Inherited clotting disorders	Hemophilia A (defective factor $VIII_{AHF}$)	Recessive trait carried on X chromosome; results in delayed formation of fibrin
	von Willebrand's disease (defective factor $VIII_{VWF}$)	Dominant trait carried on autosomal chromosome; impaired ability of platelets to adhere to collagen in subendothelial connective tissue
	Hemophilia B (defective factor IX); also called Christmas disease	Recessive trait carried on X chromosome; results in delayed formation of fibrin
Anticoagulants		
Aspirin	Inhibits prostaglandin production, resulting in a defective platelet release reaction	
Coumarin	Inhibits activation of vitamin K	
Heparin	Inhibits activity of thrombin	
Citrate	Combines with Ca^{2+}, and thus inhibits the activity of many clotting factors	

Anticlotting mechanisms

General limiting reactions…smooth endothelium, rapid blood flow, heparin, liver

Specific limiting reaction

- Prostacyclin # thromboxane A_2
- Antithrombin III …… inhibits F IX, X, XI, XII
- Protein C & protein S ….inhibit F V & VIII
- Fibrinolytic system (plasmin)……lyses of fibrin

Anticoagulants (heparin , dicumarol)

Anticoagulant

	heparin	**dicumarol**
origin	Mast cells & basophils	Plant
Mode of action	Faciitates antithrombin III	Inhibit vitamin K
Site of action	In vivo & in vitro	Only in vivo
Onset	rapid	slow
Duration	short	long
Adminstration antidote	Iv, im Protamin sulphate	Orally Vitamin K

Functions of anticoagulants

Anticoagulants are used to

1- store blood in blood bank

2- maintain fluid state of blood while doing certain tests in the laboratory

3- as therapeutic agent to prevent intravascular clotting (thrombosis)

Intravascular coagulation

Causes of thromboembolic conditions

1-roughened endothelial surface of the vessels

2- slow blood flow

Causes of desseminated intravascular coagulation

1- Traumatised or dying tissues……tissue factor…. small numerous clots

2- Septicemia (presence of pathogenic microorganisms or toxins in the blood)……..bacterial toxins…..activate clotting mechanism

Abnormalities of hemostasis

Thrombocytopenic purpura

Decreased platelet count

Subcutaneous hemorrhage

Prolonged bleeding time

Vitamin k deficiency

vit K is important in formation of factors II,VII, ,IX, X in the liver

It is a fat soluble vitamin & is formed by intestinal flora

Its absorption is decreased in obstruction of bile duct

Hemophilia

Congenital sex-linked disease transmitted by females to males

Characterized by severe bleeding after trauma

It is due to absence of factor VIII or IX or XI

Blood groups

ABO system

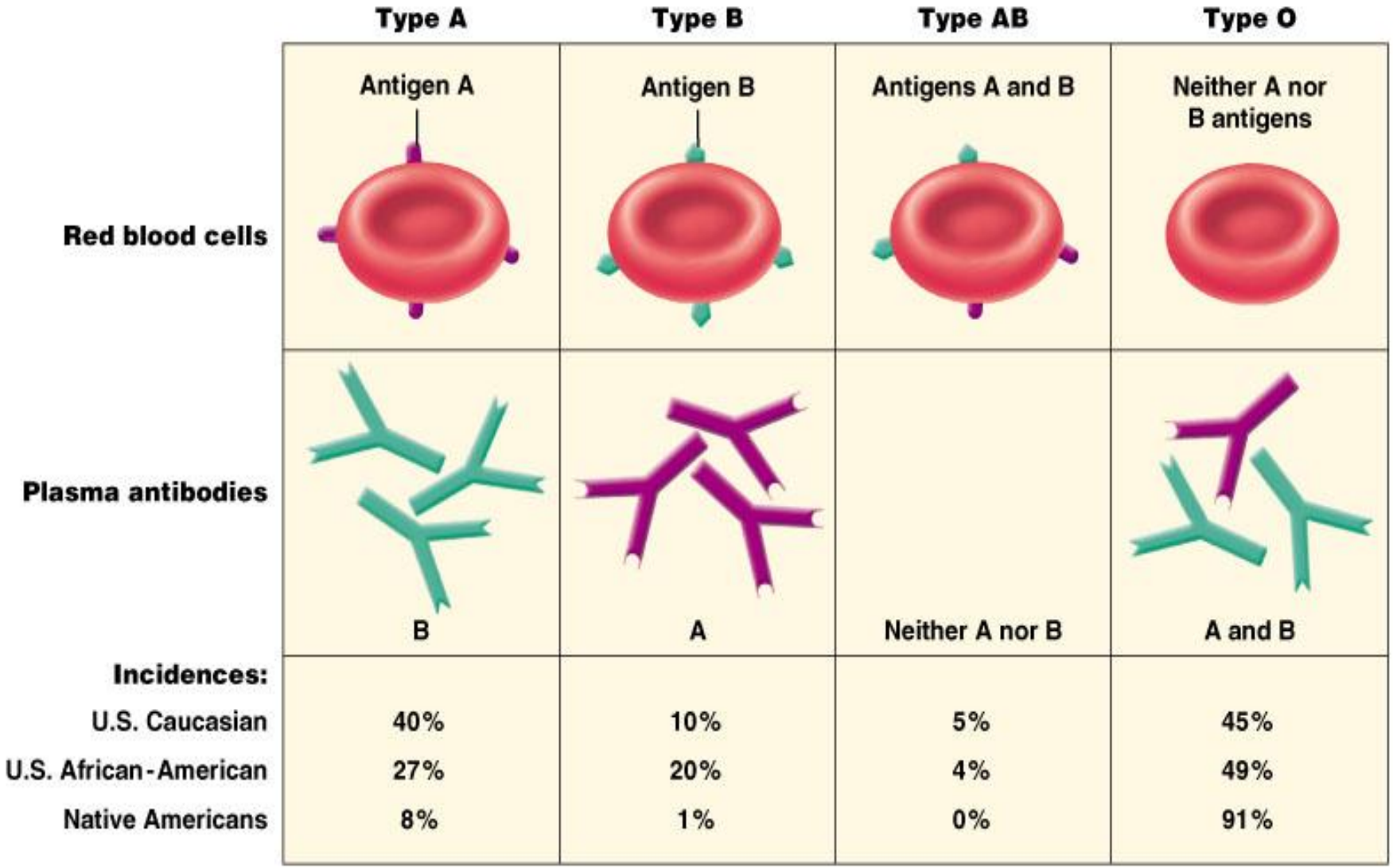
Groups A- B - AB - O

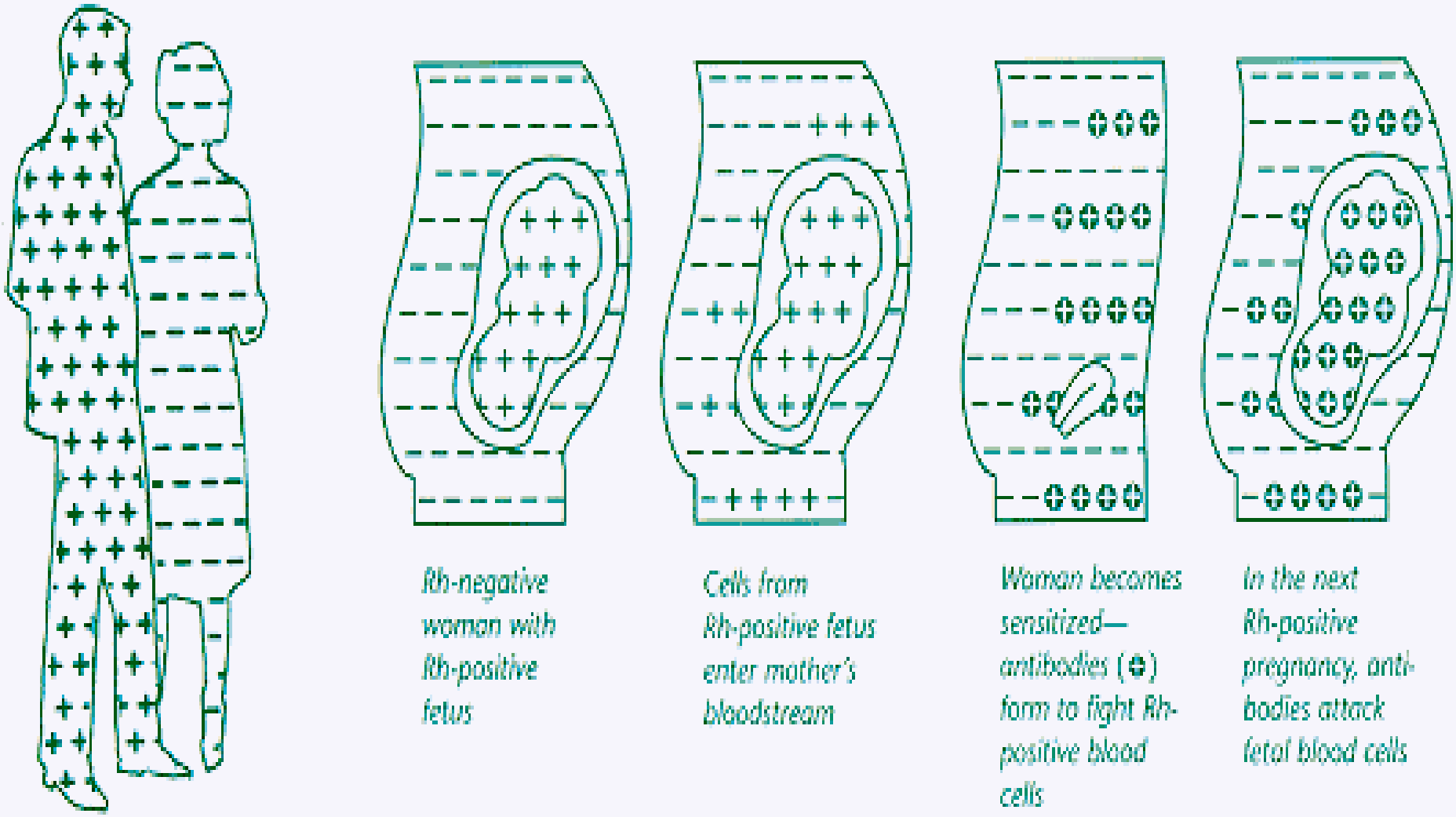
Rh blood type

Rh positive

Rh negative

Blood Types Determine Blood Compatibility





How Rh sensitization occurs.

Importance of blood group determination

- Blood transfusion
- Medico legal importance
- Erythroplastosis fetalis

White blood cells

4000-11000

Granulocytes

Neutrophils----50-70%
ingest & kill bacteria

Eosinophils 1-4 %
parasites & allergy

Basophils 0.5%
histamine & heparin

Agranulocytes

Lymphocytes 20-40%
immunity

Monocytes 2-8%
tissue macrophage

Immunity

Non specific

Doesn't' depend on antigen type
Mechanical & chemical barriers
Cells
phagocytes & macrophages
natural killer cells
Complement
interferon

Specific

Antigen specific lymphocytes

<u>Humeral</u>
Antibody-mediated
↓
Bacteria
↓
B-lymphocytes

Plasma cells (antibodies)
Memory cells(2^{ry} response)

<u>Cellular</u>
Cell-mediated
↓
Virus

Antigen presenting cells

T-lymphocytes