Blood physiology

Blood : is a tissue consist from fluid and cellular element . its apart of circulatory system , which is a closed system .

Function of blood :-

1- **it carry oxygen from the heart to the tissue through the blood vessels .**
2- **transport of materials that absorbed from GIT to the tissue .**
   e.g : vitamins , drugs …… etc .
3- **return back co2 from the tissue to the lungs and waste product of the metabolism to the kidney .**
4- **regulates body temperatures .**
5- **it acts as a buffer mechanism .**
6- **it distribute hormones and other agents which are need for cell function .**

Total volume of blood is about 5600 ml (5.6 L) regarding to the plasma 3500 ml and cellular elements 2100 ml , so the percentage is 55% plasma while the cellular elements differ from male to female , in male 47% and in female 42% .

The cells include :

Red blood cells	**(erythrocyte)**
White blood cells	**(leukocyte)**
Platelets	**(thrombocyte)**

Plasma

Its solution consist from (ions , organic , inorganic materials) one of the most important materials is plasma protein .
We have three types of plasma protein:-

1- **Albumin → 3.5 – 5 gm / 100 ml**
2- **Globulin → 2.5 - 3.5 gm / 100 ml**
3- **Fibrinogen → 0.3 gm / 100 ml**

The origin of (p.p) is liver , the globulin divided into different types
$\alpha 1$, $\alpha 2$, $\beta 1$, and δ globulin.
All of these are synthesis in liver except δ globulin from plasma cells.

Function of plasma protein

1- **Formation of plasma osmotic pressure.**
   Plasma colloid osmotic pressure consist from 75% albumin , 25% globulin , and 0% fibrinogen .
   It prevent leakage of fluid from the intravascular part to inter statial space. when osmotic pressure decrease because of hypo -proteinemia , lead to pathological condition called (edema) , it loss of fluid from the intravascular part to inter statial space.

Causes of hypo proteinemia

1- **starvation**
2- **mal absorbsion syndrome**
3- **liver disease**
4- **kidney disease (nyphrotic syndrome)**

2- **Share in buffer mechanism 15%**
3- **It carry some hormones e.g. thyroid , gonadal hormones and some certain substance like drugs , amino acid , bilirubin , to prevent their loss in urine**
4- **Share in clot mechanism through fibrinogen .**
5- **Some protein like δ globulin have defense mechanism .**

Red blood cell (erythrocyte)

Its constitute the major elements of the blood , contain the hemoglobin which gives the blood the red color.
(Rbc) range from 4.8 ± 0.2 million / ml. in female.
(Rbc) range from 5.4± 0.2 million / ml. in male.
It has a biconcave disc about 7.2 µ in diameter , lack a nucleus & cannot reproduce (average lifespan = about 120 days).

The O2 carried by the Hb , while the Co2 probably leaves the cell by diffusing through transmembrane channels. In the cell membrane the red blood cells have enzyme called (Carbonic anhydrase) so Co2 combines with water to form carbonic acid which dissociates into (H ions) and bicarbonate ions ($Hco3^-$).

$$Co2+H2o \leftrightarrow H2Co3 \leftrightarrow H+Hco3^-$$

$Hco3^-$ diffuse back out into plasma , while H ions bind to the protein portion of Hb .

Erythropoisis

In early few weeks of embryonic life (Rbc) production from the yolk sac produce primitive nucleated (Rbc) .

During the mid trimester , the production of (Rbc) from liver , spleen , and lymph nodes (extra medullary) .

In the later part of gestation until birth the production of (Rbc) mainly from bone marrow .

After birth until four years of life only bone marrow of all the bones (intra medullary) production (Rbc). From four years and up the majority of bone marrow are replaced by fat cells and it cant produce (Rbc) , it called (Yellow or inactive bone marrow).

Red bone marrow (active) still in (skull , sternum , ribs , vertebras and pelvic bones).

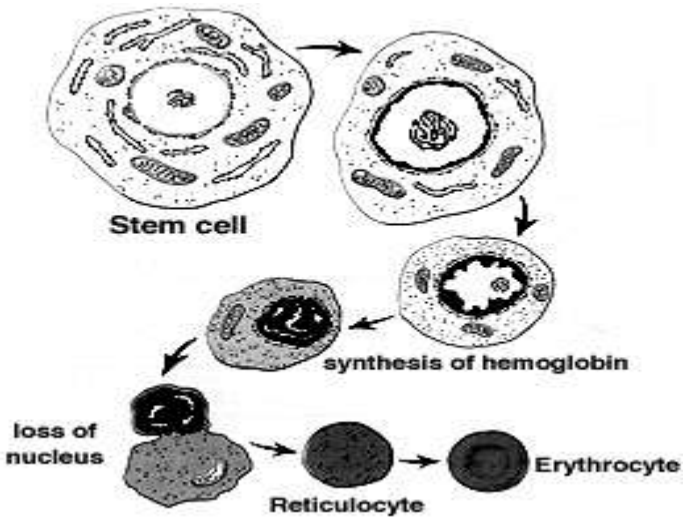
In the bone marrow , the (Rbc) production are from (Pluri potent hemipoitic stem cell) this produce (uni potent stem cells).

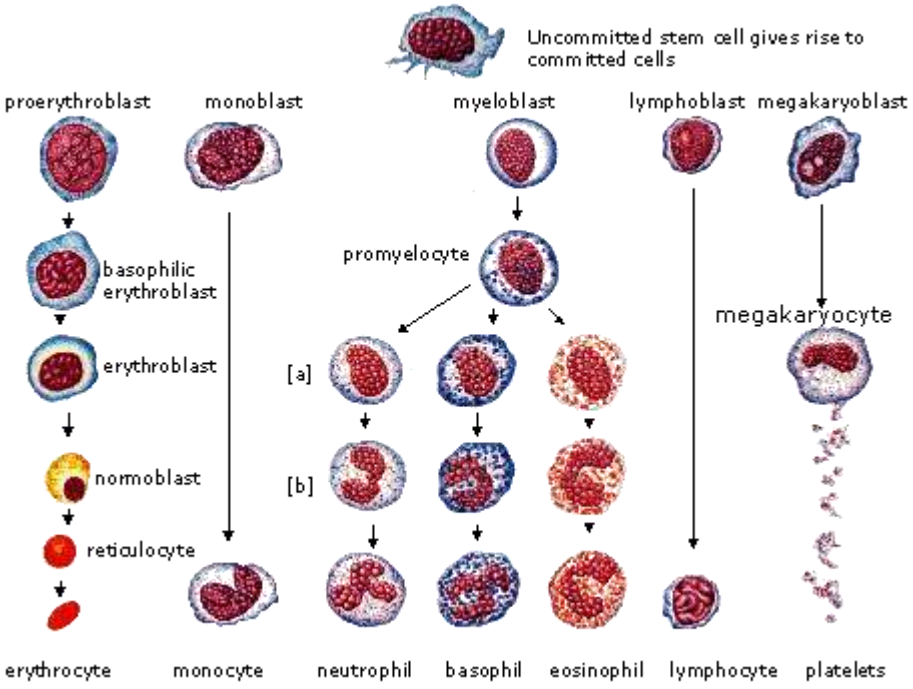
The hemolysis of (Rbc) in the spleen by reticule endothelial system so (Rbc) production = (Rbc) hemolysis.

Under the normal physiological condition the main stimulus for Erythropoisis is hypoxia (which means low O2 tension in the tissue level).When hypoxia tack place effect the kidneys lead to secretion of erythropoietin hormone , stimulus the bone marrow to produce more (Rbc).

Causes of hypoxia

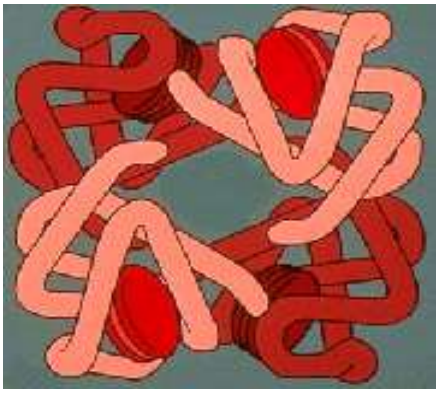
1. **anemia .**
2. **bone marrow distraction (e.g. radiation , drugs).**
3. **high altitude .**


Stem cell
synthesis of hemoglobin
loss of nucleus
Reticulocyte
Erythrocyte


Uncommitted stem cell gives rise to committed cells
proerythroblast
monoblast
myeloblast
lymphoblast
megakaryoblast
basophilic erythroblast
promyelocyte
megakaryocyte
erythroblast
[a]
normoblast
[b]
reticulocyte
erythrocyte
monocyte
neutrophil
basophil
eosinophil
lymphocyte
platelets

Hemoglobin

Is the red oxygen pigment carrying in the (Rbc) , consist from (haem+globin).
haem is the iron containg polyphyrin (pigment of Hb), this iron is in the form of ferrous state Fe^{+2} (reduced form).
Globins is polypeptide (A.A) and each one molecules of (Hb) consist from 4 sub units and each sub units consist from haem surround by globins , and each 2 globins are similar, (there are 2 pairs of globins).



Type of (Hb) according to (A.A) chain :-

1. Hb A :- constitute about (97.5%) and consist from 2α , 2 β globins the α globins consist from 141 (A.A), while the β consist from 146 (A.A).

2. Hb A2 :- constitute about (2.5%) and consist from 2α , 2 δ, globins the α globins consist from 141 (A.A), while the δ consist from 146 (A.A) but it differ from β chain in 10 (A.A).

3. Hb f :- (fetal Hb) it present in the fetus blood and immediately after birth it will change to adult (Hb) by about (6 month – 1 year)

It consist from 2α , 2 δ globins, the δ chain consist from 146 (A.A) but differ from β chain in 37 (A.A).
(Hb f) have O2 carrying capacity more than (Hb A), so if still in the blood of the person whose age more than year, then pathological condition.

Types of (Hb) according to structure attached to it :-

1. oxy hemoglobin (HbO2) :- when (Hb) combine with O2 by oxygenation process (in which Fe^{+2} in reduced from don't oxidized) . (Hb) attached loosely to the O2 . this type of (Hb) present normally in arterial blood.

2. deoxy hemoglobin :- when the blood give the O2 to the tissue , the (Hb) called deoxy (Hb) which present in capillaries .

3. dicarboxy hemoglobin : hemoglobin attached with CO2 and it normally found in veinous blood .

4. carboxy (Hb) (HbCO) :- hemoglobin attached to the carbon mono oxide(CO) this occur in case of poising with (CO) gas , the (Hb) has high affinity to (CO)more than (O2).

5. met (Hb) :- in this condition there is oxidation of (Hb) , and the iron converted from (ferrous state into ferric state).

$$Fe^{+2} \longrightarrow Fe^{+3}$$

This occur in case of exposure to certain drugs or food containing oxidizing agents (e.g. Aspirin , feva been). normally in our body we have an enzyme called (NADH) which means Dihydro Nicotine Amide , will reduce the met (Hb) into (Hb) , but in certain congenital deficiency of this enzyme the person that exposed to oxidizing agents will be formation of met (Hb) lead to cyanosis (dusky color skin) this condition called met heamoglobinemia , the iron converted from reducing state to oxidizing state which attach tightly to O2 and thus prevent the release of O2 to the tissue from the (Hb).

6. glycosylated (Hb) :- glucose attached to the terminal amino acid (valine) in each chain . this type of (Hb) increase in poorly controlled diabetes mellitus .

Anemia

It's the deficiency of (Rbc) or decrease in number of it , with or without decrease in the amount of (Hb) . OR :-
The decrease of the amount of (Hb) with or without decrease in the number of (Rbc) .

Classification of anemia

1. According to the laboratory finding (Pcv , Hb , Rbc count).

It characterized by microcytic , hypochromic anemia .

2. According to the causes :-

A. iron deficiency anemia :-

this type of anemia more common in the growing children , female , and old people . daily we have incisible loss of iron which is about (1mg / day) through feces or desquamation of skin .

causes :-

- **decrease in food intake .**
- **pregnancy , lactation .**
- **acute blood loss (hemorrhage)**
- **chronic blood loss (the person can not absorb enough iron from intestine to form (Hb) as rapid as it loss. Or in case of hemorrhoid)**

B. maturation failer anemia (megaloblastic anemia) :-

deficiency of vit B12 or folic acid and other vit B12 compound , the erythroblasts can not proliferate rapidly enough to form normal number of (Rbc) due to defect in the nuclear maturation and division (there will be defect in DNA synthesis) , the cells (Rbc) are formed mostly oversize , bizarre shape and have fragile membrane , and these cells are rupture .

deficiency of intrinsic factor from stomach mucosa lead to very slow reproduction of erythroblast in bone marrow , so they grow too large with added shapes called megaloblasts .

pernicious anemia :- its maturation failer anemia due to decrease in intrinsic factor .

C. a plastic anemia :-

Bone marrow aplasia (lethal anemia) damage of bone marrow , e.g. excessive x ray treatment , certain industrial chemicals , drugs (chloramphenicol) there will be defect in the production of (Rbc, Wbc, and platelet) .

D. hemolytic anemia :-

Its either (hereditary or acquired) make the cells very fragile , so they rupture early as they go through the capillaries especially through the sphlenic pulp easily ruptured .

<u>Type of hemolytic anemia</u> :-

1. **abnormality in shape of Rbc (hereditary spherocytosis) :-**

Rbc small in size spherical in shape rather than being biconcave discs . these cells can not be compressed , so when passing through the sphlenic pulp its easily ruptured .

2. abnormality in Hb, this include :-

a. sickle cell anemia .

b. thalasemia .

3. in computable blood transfusion .

4. G6PD enzyme deficiency .

Abnormalities of hemoglobin

The A.A sequences in the polypeptide chains of Hb are determined by globins genes . when an abnormal gene are inherited from one parent , this individual is heterozygous (i . e half of the circulation Hb is abnormal and half is normal).
when an abnormal gene are inherited from both parent , this individual is homozygous (i . e all Hb is abnormal).

a. Sickle cell anemia (HbS)

Abnormal β – chain were glutamic acid being replaced by valine in the 6th position . (HbAS) sickle cell trait , individual heterozygous rarely have sever symptoms . (HbSS) sickle cell infected , individual homozygous . this disease not present at birth , but appear from 3 – 6 months later as δ – chains (Hbf) is replaced by β – chain .

When this (Hb) is exposed to low concentration of O2 (hypoxia) crystals inside the (RBC) elongate the cell and give it the appearance of being a sickle rather than biconcave disk . this precipitated (Hb) also damage the cell membrane so the cells become highly fragile and lead to serious anemia .

b. Thalassemia or Mediterranean anemia

Decreased or absent α and β polypeptides (one of them or both of them) .

If the defect in α chain synthesis which is called (α Thalassemia) , and If the defect in β chain synthesis which is called (β Thalassemia).

If the defect in one chain synthesis (α or β) this is called Thalassemia minor

If the defect in both chain synthesis (α and β) this is called Thalassemia major .

(Hb) precipitated in form of hard crystals , RBC are small and fragile and easily ruptured upon passing through the tissues .

3. Incompatible blood transfusion (e.g. erythroblastosis fetalis)

RBC in the fetus are attacked by antibodies from Rh negative mother . the RBC become fragile and ruptured , this is lead to serious anemia .

4. Glucose - 6 – phosphate dehydrogenase deficiency (G6PD)

(G6PD) is the first enzyme in the hexose mono phosphate shunt . the function of this shunt is to service the enzyme s glutathione reductase and glutathione peroxidase which protect the RBC against damage due to oxidation , this protection is crippled in the absence of G6PD and certain drugs or food in sufficient concentration can seriously destroy the RBC (e.g. Asprine , fevabean) .

Polycythemia

1. primary polycythemia (Erythremia) , (polycythemia vera)

Its tumors condition of the organs that produce RBC, it cause excess production of WBC and platelet .

2. secondary polycythemia

When ever the tissue become hypoxia , physiological polycythemia , people live in high altitude .

Pathological polycythemia , failuer of delivery of O2 to the tissues (e.g cardiac failer , lung disease) .

Destruction of RBC

when the RBC have lived out their life span (120 days) and become too fragile to exist longer in the circulation system . the cell membrane rupture and the released Hb is phagocytes by tissue macrophage (reticule endothelial system) , (spleen , liver , bone marrow) .

the Hb is first split into globin + heme . globin be used by body its regarded as building unit . heme ring is opened to give : -

a. **free iron that is transported in the blood by transferrin.**
b. **Straight chain of 4 nuclei from which the bile pigment are formed .**

The free iron either go to the bone marrow to be used for synthesis for new Hb , or will be stored in the liver in the form of ferritine .

The first pigment formed is the biliverdin , but this is rapidly reduce to (free bilirubin) which is gradually released into the plasma .
The free bilirubin immediately combine very strongly with plasma albumin and transported in this combination through out the blood and interstitial fluid .
Within hours , the free bilirubin is absorbed through the hepatic cell membrane , in this process being released from plasma albumin .
Inside the hepatic cell that bilirubin conjugated with other substances :-

1. **80% conjugated with glucuronic acid to form bilirubin glucuronide .**
2. **10% conjugated with sulfate to form bilirubin sulfate .**
3. **10% conjugated with other substance .**

these forms is excreted by an active transport process into the (bile canaliculi) .
small portion of conjugated bilirubin returns to the plasma , either directly into liver sinusoids or indirectly by absorption into blood from bile duct and lymphatic

in the intestine , about one half of bilirubin is converted by (bacteria action) into urobilinogen , some of its reabsorbed through the intestinal mucosa into blood .

most of this is re – excreted by the liver back into the gut . 5% is excreted by the kidney into the urine .

after exposure to air in the urine , the urobiniogen become oxidized to urobilin or in the feces its become stercobilin .

Jaundice

Yellowness of the skin and also deep tissues usual cause of jaundice is large quantities of bilirubin either free or conjugated .
The normal plasma concentration of bilirubin average 0.5 mg / dl . the skin usually begins to appear jaundice when the concentration rise 3 times normal .

Causes :-

1. **increase destruction of RBC (hemolytic) .**
2. **obstruction of the bile ducts .**
3. **damage to liver cells (obstruction jaundice) .**

hemolytic jaundice

1. **excretory function of liver normal .**
2. **RBC are hemolysed rapidly and the hepatic cells cannot excrete the bilirubin as rapidly as its formed .**
3. **plasma concentration of both (free + conjugated) bile rise to above normal .**
4. **urobilinogen in intestine increase and most of this absorbed into blood and excreted in urine .**

obstruction jaundice

1. **rate of bile formation are normal .**
2. **the bile cannot pass from liver to intestine (clay color stool) the conjugated bile return to blood by rupture at congested of bile into the lymph .**
3. **decrease up tack of bilirubin into hepatic cells .**

Leukocytes (WBC)

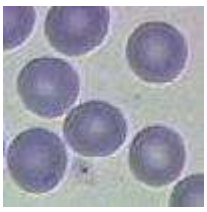
Normally from 4000 – 11000 / cmm^3 , less than 4000 leukopenia , more than 11000 leukocytosis .
Five different types of WBC are normally found in blood :-

1. **polymorphonucler neutrophiles .**
2. **polymorphonucler eosinophiles .**
3. **polymorphonucler basophiles .**

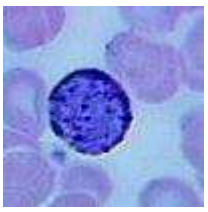
these types have granular appearance and they are called granulocytes .

4. **lymphocytes .**
5. **monocytes .**

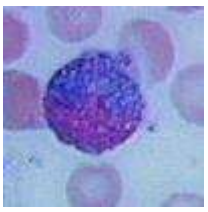
these 2 types have a granular appearance and they are called a granulocytes .



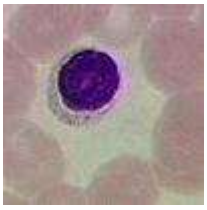
Erythrocyte
transports oxygen



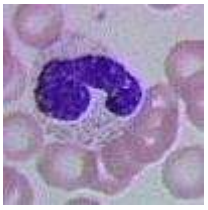
Basophil
0.5-1% WBCs; inflammatory & allergic rxns



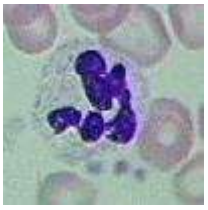
Eosinophil
2-4% WBCs; anti-helminth and phagocytic actions



Lymphocyte
20-25% WBCs;
specific immune rxns,
B & T cells



Monocyte
3-8% WBCs;
becomes macrophage -
phagocytic activity



Neutrophil
60-70% WBCs;
major phagocyte
antibacterial defenses

megakaryocytes :- are also formed in the bone marrow , they are fragment in the bone marrow , the small fragment known as platelets passing then into the blood .
the polymorphonucler cells and monocytes are normally formed only in the bone marrow .
lymphocytes and plasma cells are produced in the various lymphogenous organs including the lymph glands , spleen , thymus , tonsils , and various lymphoid rests in the bone marrow gut .

Neutrophil :- it has lobulated nuclei about 2-5 lobes , 50-70 % , life span about 4-8 hours , the main function is phagocytosis of foreign bodies so it will be regarded as the first define line because they are mature cells in the blood .

Neutrophilia :- increase number of neutrophiles either pathological or physiological
Pathological neutrophiles including :-
Burns , hemorrhage , surgery , trauma , infections ……..,
Physiological neutrophiles including :-
Drugs (epinephrine , nor epinephrine) , exercise and this can be explained as :-
When blood flow is sluggish through the tissues , large number of WBC especially neutrophiles adhere to the walls of the capillaries (margination) so the rapid flow of the blood can mobilize the leukocytes .

Eosinophil :- it has weak phagocytes , and they exhibit chemotaxis they are produced in a large number in present with parasitic infection . they attach to the parasites and release substance that kill them (e.g. schistosomia) .
It collect in tissues in which allergic reactions have occurred , because the mast cell and basophiles participate in allergic reaction and release eosinophiles chemotactic factors .

Then causes eosinophil migrate toward the inflamed allergic tissue and secrete substance that deactivate both heparin and histamine and detoxity some of the inflammation area (e.g. asthmatic persons , allergic skin reaction)

Basophiles :- basophile + mast cell release substance (heparin) into blood that can prevent blood clotting and also can speed the removed of fat substance from blood after fatty meal .
The antibodies (IgE) has special property to attach it self to mast cell and basophile then react with antigen and rupture of these cell and release large quantities of histamine , bradykinin , serotonin , heparin , lead to local vascular and tissue reaction that cause the allergic manifestation .

A granulocyte :- which included :-
Monocytes :- they are actively phagocyte and contain peroxidase and lysosomal enzyme they enter the circulation from the bone marrow , but after about 24 h they enter the tissue . when its in the blood they are immature , so it cant perform phagocytosis . when they reach to the tissue they become larger and mature to become tissue macrophage . in the tissue they can perform phagocytosis and stay several months or years , so they regarded as second define line .
Macrophage in certain tissue can mobile to other tissues so they called mobile macrophage . these cells can migrate in response to chemotactic stimuli and engulf and killed bacteria by process generally similar to those occurring in neutrophiles .
There are different types of tissue macrophage :-

1. **in the liver called kupffer cells .**
2. **in the lung called alveolar cells .**
3. **in the skin called histocytes .**
4. **in the brain called microglial cells .**

Inflammation :-
when any tissue is embedded by invading bacteria , viruses , and other injurious agent the body will response in a process called inflammation .

1. **there will be increase in blood flow (hotness) .**
2. **vasodilatation (redness) .**
3. **increase in permeability of the blood vessels (swelling) .**
4. **the response of neutrophiles and macrophage will be .**

mechanism of working :-

1. **diapedesis :- the neutrophile and macrophage can squeeze through the pores of blood vessels , even through a pores is much smaller than the size of the cells .**

2. **amoeboid motion :- both neutrophile and macrophage move through the tissue by amoeboid motion .**
3. **chemotaxis :- when tissue become inflamed , a number of different products can cause chemotaxis of both neutrophiles and macrophage causing them to move toward the inflamed area :-**
    - **some of the bacterial toxin .**
    - **degenerative products of the inflamed tissues .**
    - **several product of reaction of the complement system .**
    - **several reaction products cause by plasma clotting in the inflamed area .**
    - **still other substance .**

Phagocytosis

The phagocytes must be selective to the material (foreign bodies , bacteria , viruses , and other injuries agent) . on other wise some of the normal cells of the body would be ingested , so phagocutosis depended on :-

1. **surface of the particle is rough .**
2. **the most natural substance of the body have protective protein coats that repel phagocytosis .**
3. **the body has a specific means for recognize certain foreign materials , this is the function of the immune system that develop (Abs) against infection agent like bacteria , these (Abs) adhere to the bacterial membrane and make them susceptible for phagocytosis .**

(Abs) molecule also binding with the complement . the complement is an additional part of immune system , some product of complement that cover the bacteria and make them very susceptible to the phagocytosis , this is called opsonization . complement can also attach to some bacteria even in the absence of (Abs) and this also called opsonization . the neutrophile and macrophage first attach to the receptors on the

particles , then send pseudopodia in all direction and meet together on the opposite side and fuse . this creates an enclosed chamber containing the particle , this is known as phagocytic vesicle (phagosome) . when foreign particle phagocytized , lysosomes come to contact with phagocytic vesicle and membrane fuse with the membrane of the vesicle and dumping many digestive enzymes of the lysosome into the vesicle , so it become digestive vesicle .

A neutrophiles can usually phagocytized 5-20 bacteria while macrophage are much more power , they have ability to engulf up to 100 bacteria also can engulf the dead bacteria and neutrophiles .

The neutrophiles and macrophages also contains bactericidal agents that kills most of bacteria . also they contain oxidizing agents formed by the enzymes in the membrane of the phgosome or special organelles called peroxisome . these oxidizing agent is :-

1. **superoxide (O2-)**
2. **hydrogen peroxide (H2O2)**
3. **hydroxyl ions (OH-)**

and anther lysosomal substance in the phagosome is lysozyme , a chemical that can cause dissolution of the lipid membrane of the bacteria .

Immunity :-

the ability to resist almost all type of invading substances (defense against infection disease). there are two main branches of immunity :-

1. **non specific or natural or passive defense mechanism .**
2. **specific or active mechanism or acquired immunity.**

Non specific which include :-

A . physical defense (skin , mucus , and tight junction between epithelial cells of the mucus membrane) .

B . chemical defense (stomach acid (Hcl) , lysozyme in saliva and tears , complement , and phagocytosis) .

Specific which include :-

A . humeral immunity (Abs from B - lymphocyte) .

B . cell mediated immunity (cells from T- lymphocyte) .

Antigen :-

Its substance protein or large polysaccharide and should have large molecular weight . (Ag) stimulation of inactivated lymphocyte results in development of humeral or cell mediated immune response .
Humeral response involve (Abs) from B- lymphocyte activated to (Ag) .
Cellular immunity involve special group of (WBC) called T- lymphocyte , these produced in the bone marrow but mature in the thymus . these cells come indirect contact with the foreign invader , there are several types of T- cells :-

1. **killer T- cells :- which move from the lymph nodes where they are normally found to the tissue where the pathogen is located and destroy it .**
2. **helper T- cells :- get involved by stimulation the B- lymphocytes , that can greatly enhance the immune response by making Abs .**
3. **suppressor T- cells :- help to stop down the immune response by shutting down B- cells .**
4. **memory T- cells :- in this type if the same foreign invader infect a person in second time , the immune system can respond much more rapidly .**

Antibodies from B- cells :-

1. **IgG :- it has high Ag affinity and can cross the placenta barrier and protect the new born for a several months .**
2. **IgM :- its responsible the primary immune response and this type can not cross the placenta barrier .**
3. **IgA :- this type are present in equal a mounts in secretion such as saliva , gastric juice , pancreatic and intestinal juice . it protect mucosal surface in the guts respiratory and urinary tracts .**
4. **IgE :- it mainly bound to basophiles and mast cells and involved in the pathogenesis of allergic disease .**

Vaccination

is iatrogenous immunity and give two type of immunity :-

1. **active immunity :- its produced by injected dead or attenuated organism that cant produced disease but can sensitize the immune system to produced Abs or activated cells .**

2. **passive immunity :- by injected Abs or activated cells , this type of immunity last for several days or weeks .**

Production of W.B.C

The W.B.C produced from bone marrow , the production affected by hormones or glycoprotein called colony stimulating factors that stimulate bone marrow during infection to produce more W.B.C these include :-

1. **Granulocytes colony stimulating factors .**
2. **Granulocytes macrophage colony stimulating factors .**
3. **Multi potential colony stimulating factors .**
4. **Macrophages colony stimulating factors .**

Blood groups :-

The difference in human blood are due to the presence or absence of certain proteins molecules called antigens and the antibodies .
The (Ags) are located on the surface of the (R.B.C) and the (Abs) are in the blood plasma
We have two main system :-

1. ABO system :-
The membrane of human red cells contain a variety of (Ags) called (agglutinogens) the most important and best known of these are A and B .
The individual are divided into major blood groups A , B , AB and O on the basis of the agglutinogen .
There are A and B (Ags) in many tissue other than blood , they have been found in salivary glands , pancreas , kidney , liver , lungs , testes , semen and amniotic fluid .
(Abs) to agglutinogen are called (agglutinins) they may occur naturally by exposure to the red blood cells from anther individuals (e.g. blood transfusion , labour)
Individuals with type A , those who have agglutinogen A on their red cells , always have titer of an antibodies against agglutinogen B called Anti -B- agglutinin or B- agglutinin .

Phenotype **genotype**

41%	**A**	**AA , AO**
10%	**B**	**BB , BO**
45%	**O**	**OO**
4%	**AB**	**AB**

If individual inherited the same (Ag) from each parent , called homozygous . If individual inherited different (Ag) from each parent , called heterozygous .

2. Rh system :-

The system composed of many antigens , D is the most antigenic and Rh positive $(Rh)^+$ means that the individual has agglutinogen D .

Neither $(Rh)^+$ nor $(Rh)^-$ have anti D antibody , but $(Rh)^-$ can produce anti D antibody when injected with D positive cells .

So according to these 2 systems we have 8 blood groups :-

A- , A+ , AB- , AB+ , B- , B+ , O - , O + .

There are other antigen called sub groups , and these are important in blood transfusion.

Transfusion reaction :-

Dangerous hemolytic transfusion reaction occurs when blood is transfused into individual with un incompatible blood type .

An individual who has agglutinins against the red cells in the transfusion , when recipient plasma has agglutinins against donor s red cells . antibody of the donor will diluted with plasma of the recipient , so it have very little effect .

So before blood transfusion we must do :-

1. **blood grouping of the donor and recipient .**
2. **cross matching test . (RBC from the donor with plasma of the recipient .**

Erythro plastosis fetalis

when Rh negative mother carriers an Rh positive fetus . small amount of fetal blood leak into the mother at the time of delivery or in abortion . this lead to develop significant titers .

during the next pregnancy the mother agglutinins cross the placenta to the fetus and they cause hemolysis . if hemolysis in the fetus is sever , the fetus may die in the uterus or may develop anemia , sever jaundice and edema .
treatment in this case by administering a single dose of anti Rh antibody (anti D antibody) during post partum period (72 h) to cause a passive immunity to the mother .

Platelets

They are small , granulated bodies , 2-4 micrometer in diameter . there are about 150000 – 350000 / micro liter .
In the blood the half life of about 4 days , the megakaryocytic in the bone marrow form the platelet . they contain actin , myosin , glycogen , lysosoms , and two type of granules :-

1. **dense granules :- which contain non protein substances that are secreted in response to platelet activation including , serotonin , ADP , and other adenine nucleotides .**
2. **α granules :- contain secreted protein , clotting factors and platelet derived growth factor (PDGF).**

The platelet have no nucleus and they play a role in stopping the bleeding (hemostasis)
Hemostasis includes series of events :-

1. **local vaso constriction :- there will be spasm to injured blood vessels to stop the bleeding . we have two refluxes , nerve reflux , pain muscular reflux construction of the smooth muscle in the wall of the blood vessels**

2. **platelet plug :- when a blood vessels is damaged , the endothelium is disrupted and under lying layer of collagen is exposed . collagen attracts platelets which adhere to it and liberate serotonin and ADP and thromboxine A that rapidly attracts other platelets . also the von willebrand factors lead to more aggregation and a lose plug of aggregated platelets is formed . this mechanism occurs in small injury.**

3. **clot formation :- this occurs in case of severe bleeding . in the body there are two types of substances , one is pro coagulants (lead to clot formation) second is anti coagulants (prevent the clot formation). Normally the anti coagulants more than pro coagulants , when vessels is ruptured the activity of the pro coagulants in the area of damage become much greater than that of the anti coagulants and then a clot does develop . clotting takes place in three steps :-**

A. **sub. or complex of sub. called (prothrombin activator) is formed in response to rupture of the vessels or damage to the blood itself .**
B. **the prothrombin activators catalyze the conversion of prothrombin into thrombin .**
C. **the thrombin acts as an enzyme to convert fibrinogen into fibrin threats that enmesh platelets , blood cells , and plasma to form clot itself . prothrombin activator which will convert prothrombin into thrombin and this is also by the effect of Ca ions , then the thrombin will act to convert fibrinogen into fibrin (fibrin monomer) this will convert to fibrin threats under the effect of fibrin stabilizing factor + Ca ions , this fibrin threats will form clot . so the mesh work of fibrin threats which run in all direction and contain (RBC , WBC , platelets and plasma).**

4. **clot reaction :- mean that the clot will lose the fluid part or the water , the fluid that lost from this mesh is called serum and this is important to make the clot stronger .**

prothrombin :- is type of plasma protein which is also called α globulins , the prothrombin is formed in liver , so when liver diseased lead to decrease in prothrombin formation and this lead to bleeding tendency .

Vitamin K :- is important in the synthesis of prothrombin , so in case of deficiency of it this lead to decrease of production of prothrombin formation and this lead to bleeding tendency .

Fibrinogen :- is also type of plasma protein , this also synthesis in liver . so if liver disease leading to bleeding tendency .

Role of Ca ions :-

It has an important for all steps of intrinsic and extrinsic mechanism , so absence of Ca ions effect clot formation .
In vivo decrease level of Ca ions inside the body lead to tetany (continuous muscles contraction or spasm) and then death . so we can not use substance to reduce level of Ca ions inside the body .
In vitro by using deionizing sub. like citrate ions or precipitating sub. like oxalate can be used as anticoagulants because they lead to decrease Ca ions level .

Lysis of clot (fibrinolytic system) :-

This process started by production of substance called (Thrombodulin) that secreted by the endothelial cells . its function to convert thrombin to anti coagulant sub.
Thrombin is a pro coagulant sub. but with thrombodulin it become anti coagulant because it lead to formation of complex lead to convert protein C to active protein C and this with co factor protein S will inactivate factor (v , viii) .
At the same time protein C will activate anther factor which is plasminogen to plasmin .
The plasmin (fibrinolysin) lysis of clot and will be absorbed normally by the blood .

Factors prevent clot formation :-

1. **endothelial surface factors : the smoothness of the endothelial surface of blood vessels .**
2. **protein layer presented above the endothelial layer reject the platelets aggregation and clotting factors .**
3. **the anti thrombin action of fibrin (increase amount of fibrin lead to the inhibition of thrombin formation , i.e. fibrin has negative feed back mech. effect on thrombin) .**
4. **anti thrombin III (α globulin)**
5. **heparin , its weak anti coagulants but with anti thrombin III its effect will increase the heparin + anti thrombin III inhibit activated factor IX , X , XI , XII .**

Causes of bleeding tendency :-

1. **vitamin K deficiency .**
2. **liver disease .**
3. **thrombocytopenia , thrombosthenia .**
4. **hemophilia A and B . deficiency of factor VIII and IX .**

Anti coagulants :-

1. **heparin in vivo and in vitro .**
2. **Ca deionizing agent , sodium citrate , oxalate (in vitro only) .**
3. **warfarin (dicumerol) act in vivo only by inhibiting the clotting factor VII , IX , X , by competitive inhibition with vit . K to the active site of enzyme that is responsible for synthesis this clot factors .**
4. **putting the blood in special smooth tubes (siliconized tube) .**