BLOOD

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READER DEPT.PHYSIOLOGY

Blood is a specialized connective tissue in which there is intra cellular substance known as plasma ,and formed elements ,the red blood cell, the white blood cell ,and the platelets suspended in the plasma

Specific gravity of whole blood 1.055-1.060

Fresh blood is red ,thick ,opaque ,&slightly alkaline

FUNCTIONS OF BLOOD

1 TRANSPORT OF RESPIRATORY GASES

2 TRANSPORT OF NUTRITION

3 IT ACTS AS A VECHILE

4 DRAINAGE OF WASTE PRODUCTS

5.MAINTENANCE OF WATER BALANCE

6.MAINTENANCE OF ACID –BASE BALANCE

7.MAINTENACE OF ION BALANCE

8.REEGULATION OF BODY TEMPERATURE

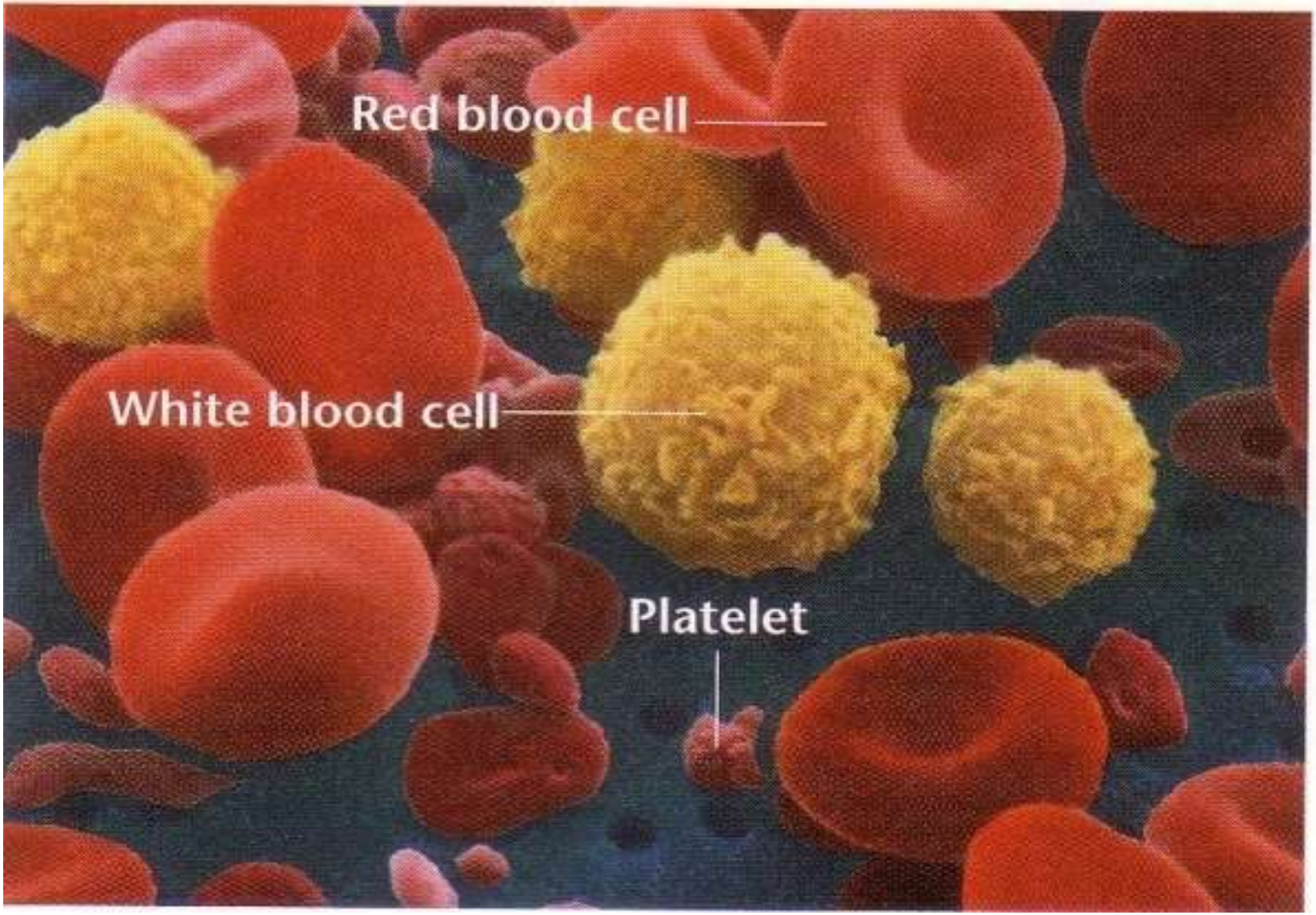
9. DEFENSIVE ACTION

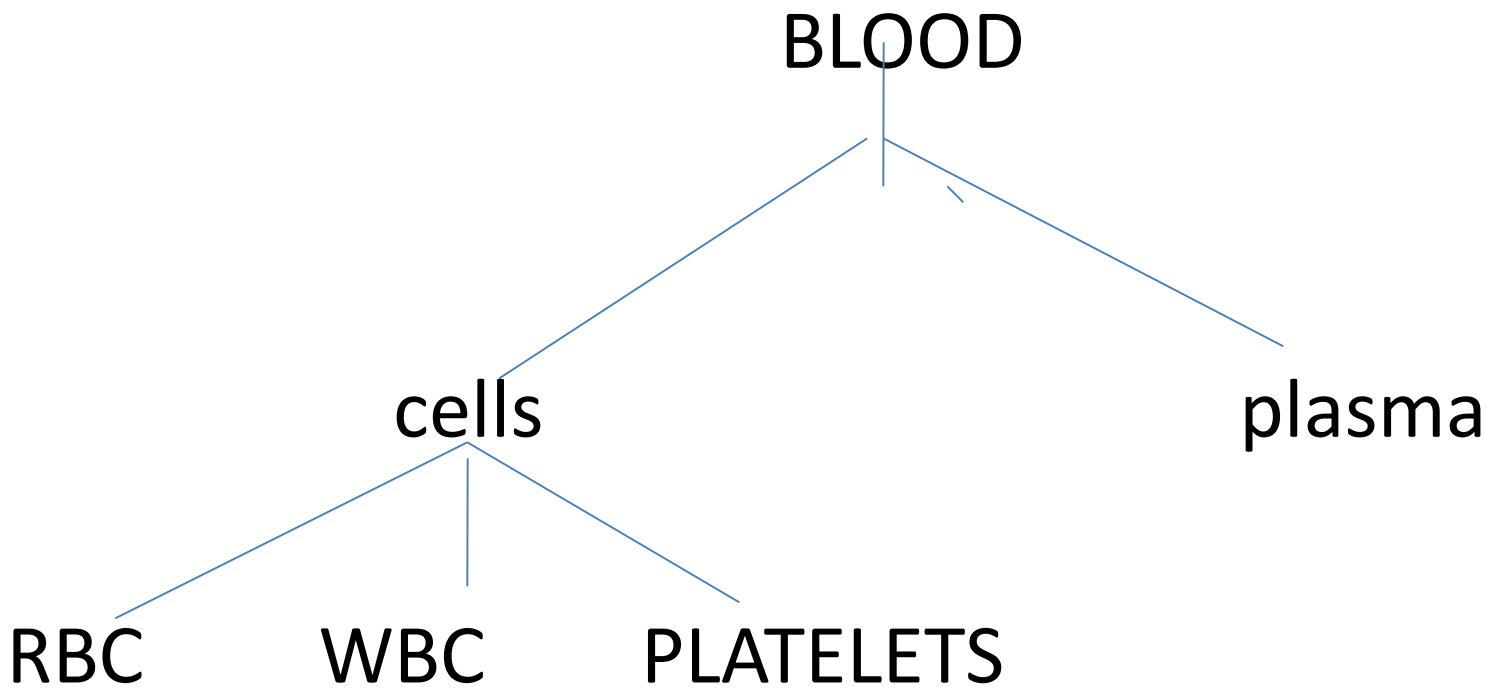
10. BY PROPERTY OF COAGULATION IT GUARDS AGAINST HAEMORRHAGE.

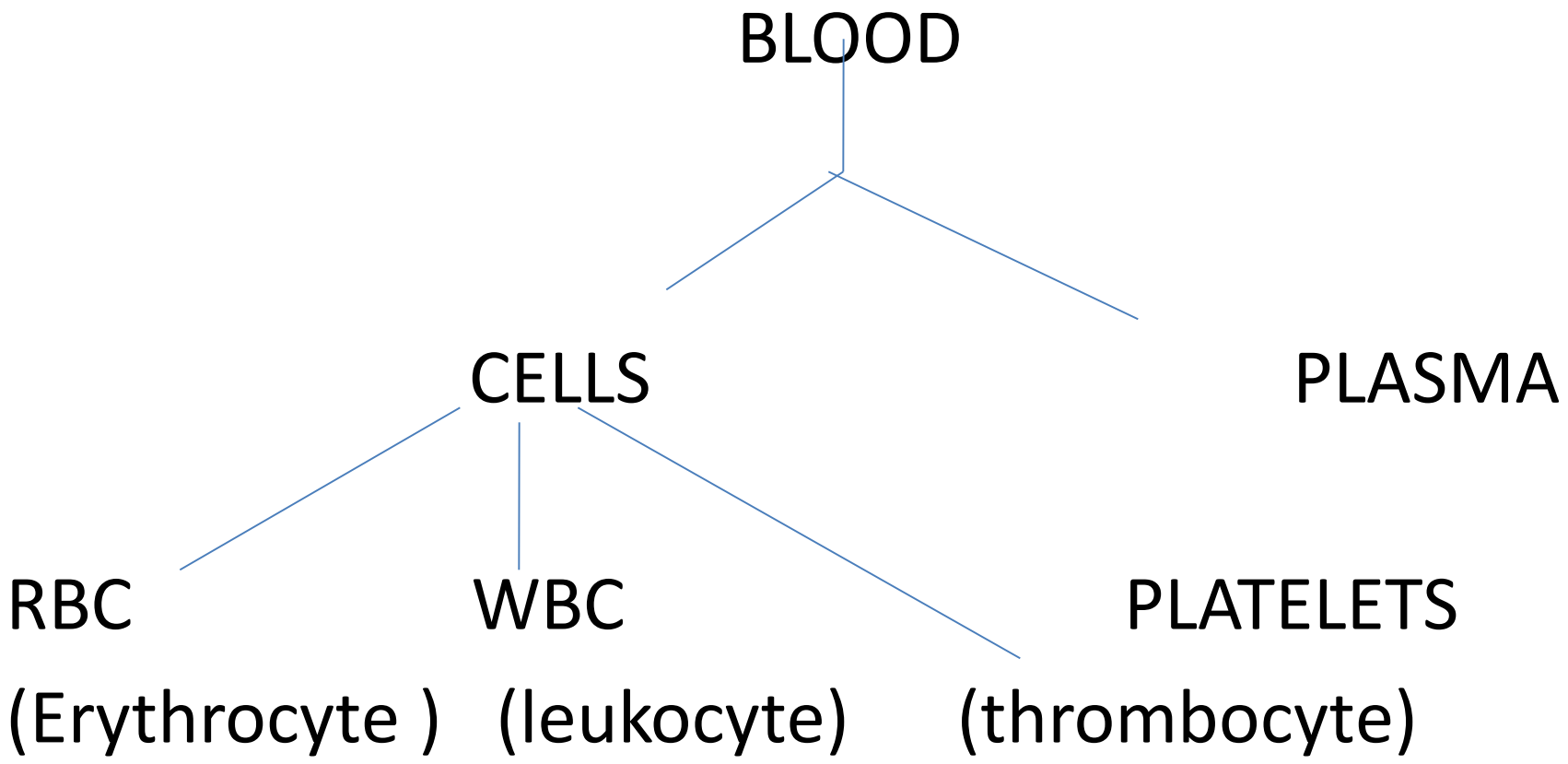
11. PLASMA PROTEINS OF BLOOD HAVE VARIOUS FUCTIONS

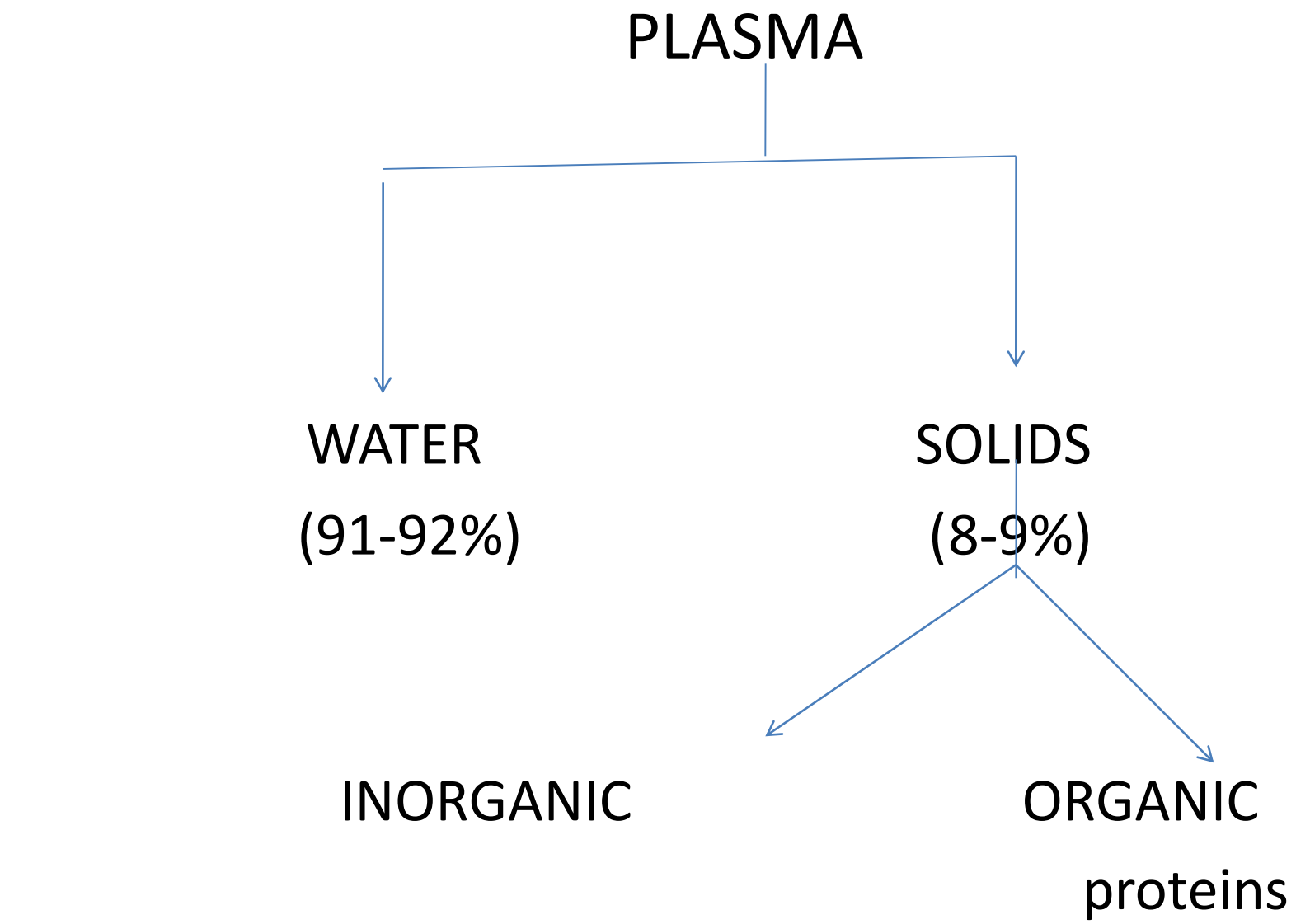
12. REGULATION OF BLOOD PRESSURE

COMPOSTION OF BLOOD




BLOOD
cells
plasma
RBC
WBC
PLATELETS


BLOOD
CELLS
PLASMA
RBC
(Erythrocyte)
WBC
(leukocyte)
PLATELETS
(thrombocyte)


PLASMA
WATER
(91-92%)
SOLIDS
(8-9%)
INORGANIC
ORGANIC
proteins
Na K, Calcium, Mg, phos iron ,copper

- **ORGANIC CONSTIUTENTS**

1)Proteins –

serum albumin ,serum globulin fibrinogen prothrombin

2)non protein nitrogenous substances

urea ,uric acid, xanthine, creatine ,creatinine ,ammonia ,amino acid

3)fats

4)CHO,

OTHER SUBSTANCES

internal secretions, antibodies ,enzymes, coloring matter like bilirubin

FORMED ELEMENTS

- RBC
- WBC
- PLATELETS

- Blood is red ,opaque,
- Having peculiar odor
- Salty
- Viscous fluid
- **Specific gravity-1.055-1.060**
- **Slightly alkaline pH-7.4**
- Osmotic pressure-25 mm of Hg

PLASMA

Plasma is fluid portion of blood

It contain 1)water (91-92%)

2)solids(7 to 8%)

SERUM??????????????????????

- SERUM IS FLUID PART OF BLLOD AFTER CLOTTING ,
- BLOOD CLOT ON STANDING , PLASMA ALLOWED TO CLOT AND AFTER SOME TIME STRAW COLOUR FLUID CAN BE SEPRETED THAT IS SERUM
- ALBUMIN GLOBULIN RATIO IS 1.5:1 THIS RATIO CHANGES IN LIVER DISEASES

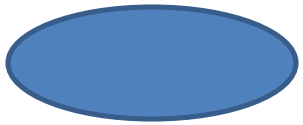
1. Total amount of plasma proteins vary from **6.5 to 7.5%**
2. Serum albumin -**4.7 to 5.7%,**
3. serum globulin -**1.3%**
4. fibrinogen -**0.2 -0.4%**

CHMISTRY OF PLASMA PROTEINS

1. **Serum albumin**

   1) Having a molecular weight 69,000

   2)Soluble in in distilled water .

   3)it is ellipsoid 

   4) small ,heat coaguable

   5)It is more compact

2.Serum globulin –

molecular weight 90,000.insoluble in water soluble in salt solutions

it is heat coaguable

having three fractions

alpha 1&alha2 β globulin gamma globulin

(combines with bilirubin) (carriage &transport of iron) (antibodies)

(Alpha 2 concern with carriage of lipids &steroids)

3.fibrinogen –

molecular weight 341000,insoluble in water ,it is distinguished from other protein due to its property of coagulation during which fibrinogen → fibrin **(clot)**

Origin of plasma proteins

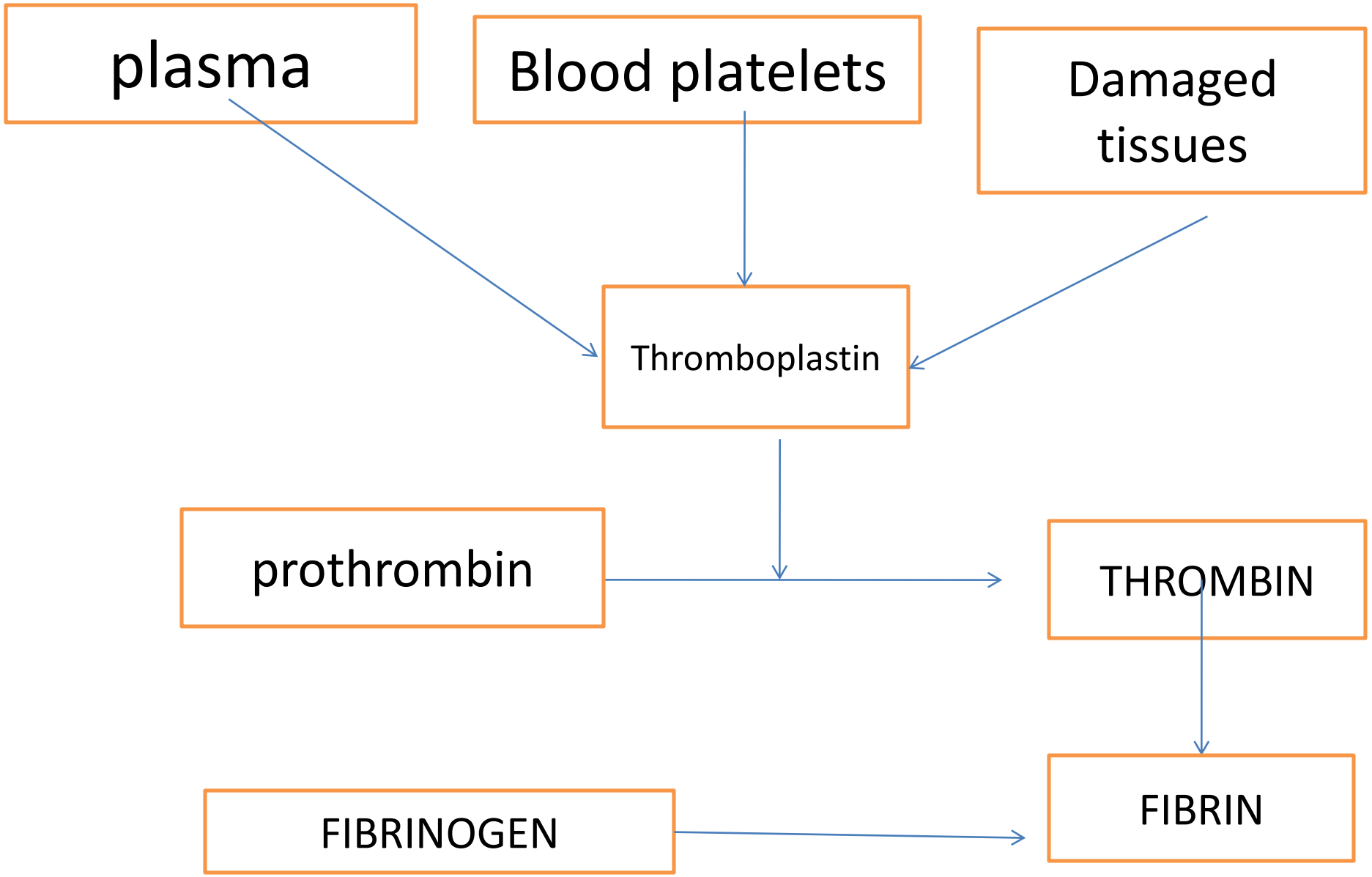
- **In embryo**-secretions of mesenchymal cell
- **In adult-** liver ,globulin form from disintegrated blood cells ,RES, lymphocyte ,from tissue cell
- **RATE OF REGENARATION**

14 DAYS

FUNCTIONS OF PLASMA PROTEINS

1.Essential for blood clotting

Fibrinogen and prothrombin are essential for coagulation of blood in following way


plasma
Blood platelets
Damaged tissues
Thromboplastin
prothrombin
THROMBIN
FIBRINOGEN
FIBRIN

2.Maintain colloidal osmotic pressure of blood

All the three proteins take part .albumin exerts the maximum osmotic pressure osmotic pressure depends upon number of molecules in solution

3.Maintain viscosity and blood pressure

Globulin is responsible for viscosity of blood and viscosity is important factor in maintaining blood pressure.

4.Concern with erythrocyte sedimentation rate

Suspension stability of blood depends upon plasma proteins esp. fibrinogen

5.Acts as buffer

To maintain acid base balance

6.acts as protein reserve

Plasma proteins serve as a store house where tissue can draw during starvation or inadequate protein diet

7.Help in co2 carriage by forming carbamino proteins

8.Form trephones

The leukocyte prepare substances from the plasma proteins ,called trephones which are necessary for nourishment and growth of damaged tissue

9.**Antibodies** .

Gama globulin concern with antibodies

- **10.Plasma proteins combine** with certain substances and help to carry in blood stream like iron, hormone, enzymes copper carried by globulin.

what is osmosis??????????????????????????

Viscosity ??????????????????????????????

Buffer?????????????????????????????????

ERTHROCYTE SEDIMENTATION RATE

Definition

while in circulation red cells remain uniformly suspended in the plasma. if anticoagulant is added to a specimen of blood and let it stand it in glass tube ,**the corpuscles** (being heavier than plasma)**are found to sediment gradually at the bottom of tube** ,while the **plasma remains as clear supernatant fluid**. this is sedimentation &rate of settling down is known as ESR.

The rate of RBC sediment in a period of one hour .it is common hematological test &nonspecific measure of inflammation

ESR is governed by balance between pro sedimentation factor –fibrinogen &those factor results sedimentation namely –ve charge of erythrocyte (zeta potential)

Sedimentation continues in three phases

1. **A short stage of aggregation with little fall**

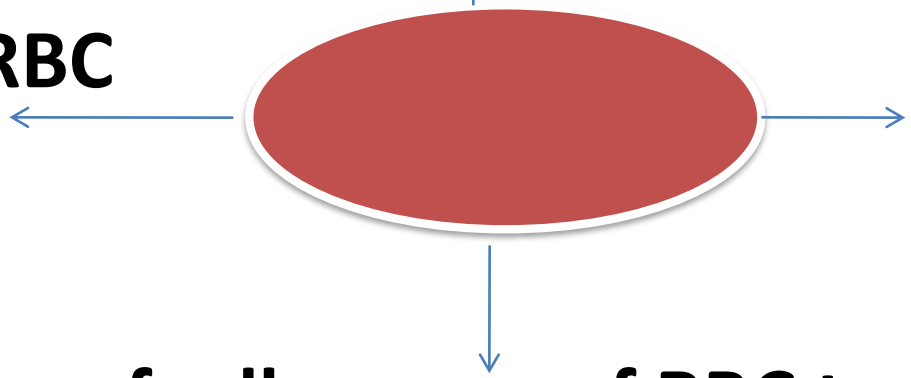
Required 10 min.

2. **True sedimentation following maximum velocity of fall required 40 min,**
3. **Finally slowing until packing is complete leaving an upper layer of clear plasma**

- **ESR depends on following factors**

density between RBC &plasma

Resistance that plasma Exert on RBC



viscosity

degree of adherence of RBC to one another

rouleaux formation

Red cell carry a negative charge ,hence any condition which increases the positive charge in plasma accelerate ESR

Two methods to measures ESR

1)WESTERGREN OR CULTER

2)WINTROBE'S TUBE METHOD

NORMAL VALUES

1.wintrobe’tube method–in male 0.0 to 6.5 mm /hr

in female 0.0 to 15mm/hr

2.Westergren methods –in male 0.0 to 15 mm /hr

in females 0.0 to 20mm/hr

ESR constituents a guide to the progress of diseases

Physiological variations –in infant lowest ,in pregnancy acceleration in beginning ,at high altitude ESR decreases

Pathological variations- in all acute infections chronic ESR increases .ESR increases in following condition

1.Tubuerculosis,collagen diseases ,anemia Rheumatoid arthritis, kidney diseases

Significance of ESR

1)It is to asses how much inflammation in body

2)It is nonspecific test does not indicate location &cause of diseases

3)monitoring response to therapy in diseases so to know progress of diseases

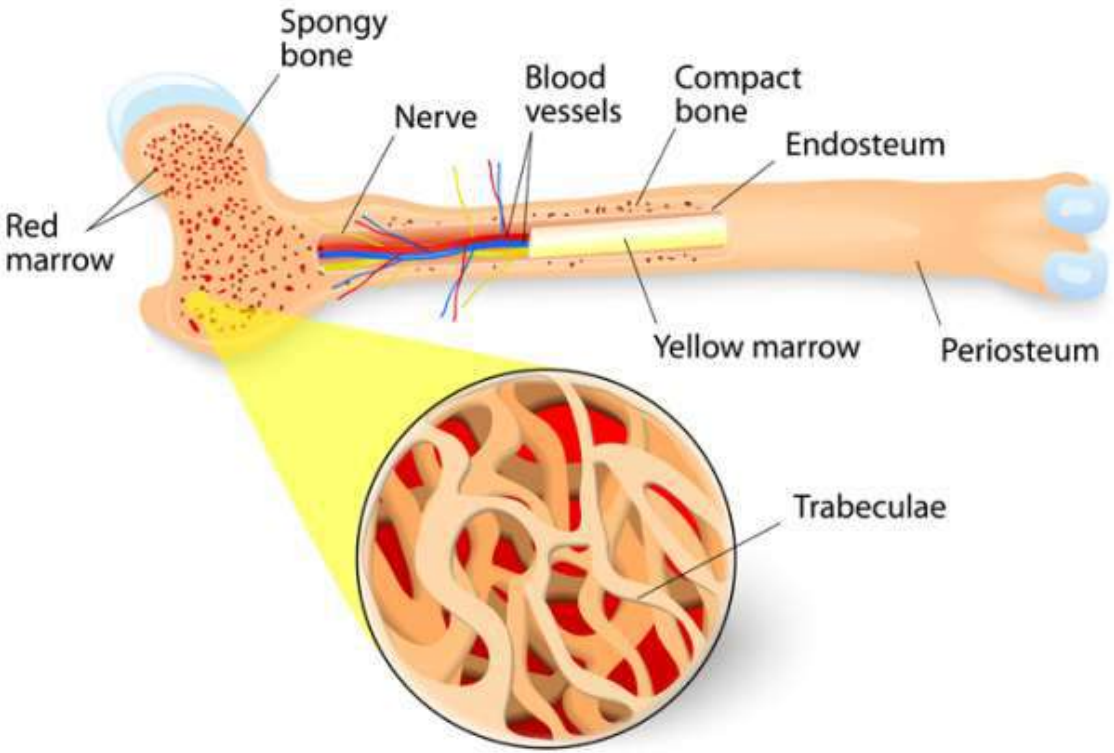
4)It help in assessing activity of destructive lesion of tissue

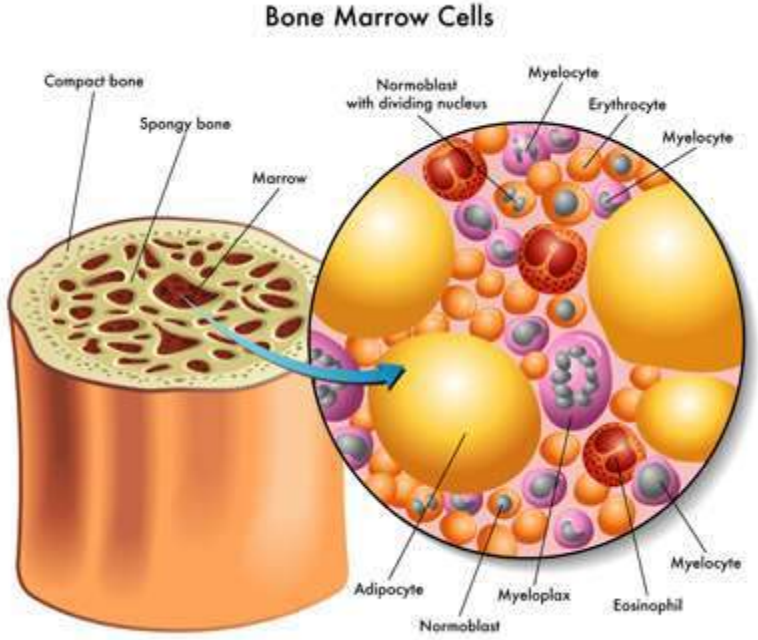
5)Severity of lesion of pyogenic infection.

ESR decreases in following conditions

Polycythemia ,sickle cell anemia ,leukemia low plasma proteins.

BONE ANATOMY




Bone Marrow Cells
Compact bone
Spongy bone
Marrow
Normoblast
with dividing nucleus
Myelocyte
Erythrocyte
Myelocyte
Myelocyte
Adipocyte
Normoblast
Myeloplax
Eosinophil

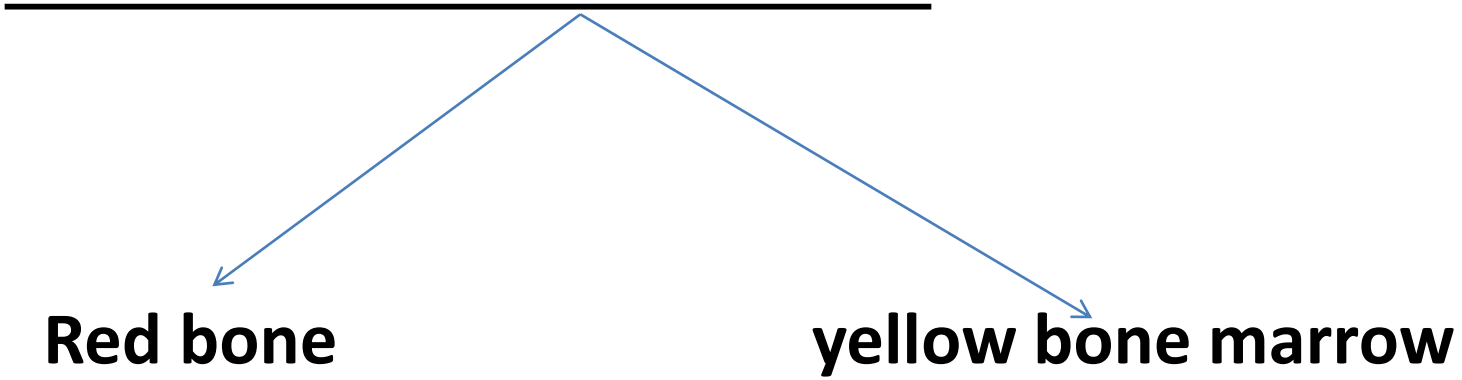
The term bone marrow and myeloid tissue are synonymous.

Myelos meaning marrow is confined in the cavities of bone

Bone marrow is spongy tissue inside some bone

Bone marrow is the cellulo vascular tissue occupying the medullary cavities of the bone

TYPES OF BONE MARROW



Red marrow	yellow marrow
1.Red cells actively Manufactured here	1.it is made up of fat reticular tissue with bld.vesse
2.In foetal stage all the Bone contain RBM In postnatal life RBM is Only located in upper end Of humerus ,femur, bones Of skull, thorax, vertebrae, Bone of pelvis	2.here red cells are not manufactured 3.in the adult life they occupy the spaces where RBM absent

1.from **birth to fourth year** all the bones contain red marrow

2. By **seven year the marrow becomes less** active &pale red on color

3.Between ten to fourteen year a patch of yellow marrow appears in the distal ends of the shaft of long bones

4. At the age of twenty entire red marrow of long bones is replaced by yellow marrow **except upper end of femur ,humerus**

6. By **the seventy years more than half of ribs and half of sternum contain yellow marrow**

Functions of bone marrow

1.Haematopoitic

Production and release of blood cells. In adult nearly 50%of the red marrow is converted into yellow marrow

All the blood cells are formed in red bone marrow.

2.Erythroclasia or destruction of RBC

Abnormal ,imperfect damaged &aged RBC are destroyed these cells are trapped &phygocytised in the macrophages of the bone marrow. **heam out of this stored as haemosiderin &ferritin** in liver ,spleen ,R.E cells &bone marrow .rest of iron or heam converted into bilirubin

3.Storage function

Bone marrow is important site for storage of iron in the form of ferritin &haemosiderin coming from food sources as transansferrin &also from destruction of RBC. through phygocytosis

4.Reticuloendothelial functions

By inactivation of toxins

5 .Immunological function

6 .Osteogenic function- cellular elements which take part in formation of bone are formed in the marrow. osteoclast, osteoblast ,osteocyte

Endosteum blood vessels are found within the marrow

7.Connective tissue function due to its connective tissue contents

BLOOD VOLUME

The blood volume means the total amount of present in circulation as well as in the blood stores

NORMAL VALUES

5 - 5.5 l in adult

In relation to body weight -**75 -80 ml/kg**

In relation to body surface-**2.5-4 l /sq meter** of body surface

Physiological variations

1) **Age –in infant the blood volume is greater in proportion to the body weight but is lesser in proportion to body surface**

2) **sex-in male blood volume is 7.5%higher than in females this is due to greater number of red cells in in males**

3)Body weight& surface area

4)pregnancy-blood volume rises due to increase of both cells &plasma

5)Muscular exercise-raises due to contraction of spleen.

6) Posture –in erect posture there is fluid passes into tissue spaces so volume decreases

7) Blood pressure- raise of blood pressure lowers blood volume by pressing out more fluid into the tissue spaces. lowered blood pressure draws in more fluid from the tissue spaces &raises blood volume

8)Altitude –at higher altitude the blood volume raises ,due to anoxia red cells increases

9)Anoxia will raise blood volume

10)Adrenaline –will raise blood volume due to splenic contraction

REGULATION OF BLOOD VOLUME

Maintenance of blood volume depends upon **balance between water intake and water loss and adjustment of fluid** interchange between **plasma and tissue spaces**

Factors involved in regulation

a)Physical factor

Blood pressure ,osmotic pressure ,diffusion, the state of permeability of the capillaries

b)The tissue space

Due to their enormous capacity ,act as a ready reservoir. any increase in blood volume will lead to passage of more fluid from the plasma to the tissue spaces .while any decrease will draw in more fluid from the tissue spaces and maintain blood volume

c)Vitamins

Vitamin c control permeability of capillary and take part in regulation

d)Endocrine or hormonal factors

the anti diuretic factor of posterior pituitary controls excretion of water through the kidney .when blood is diluted the secretion of the ADH is inhibited &thus more water lost. when blood become concentrated reverse changes occur

e)Thirst

When water contain of blood decreases ‘thirst ’is felt the person take water and thus blood volume is kept up

f)Parathyroid, by the effect on calcium metabolism, control the permeability of the blood vessels and thereby the rate of interchange between blood and tissue

g)Adrenal cortex

Decrease blood volume stimulate adrenal cortex to secrete aldesterone which promote increase absorption of Na and water to increase blood volume

h)Angiotensin also by retention of water and salt increases blood volume

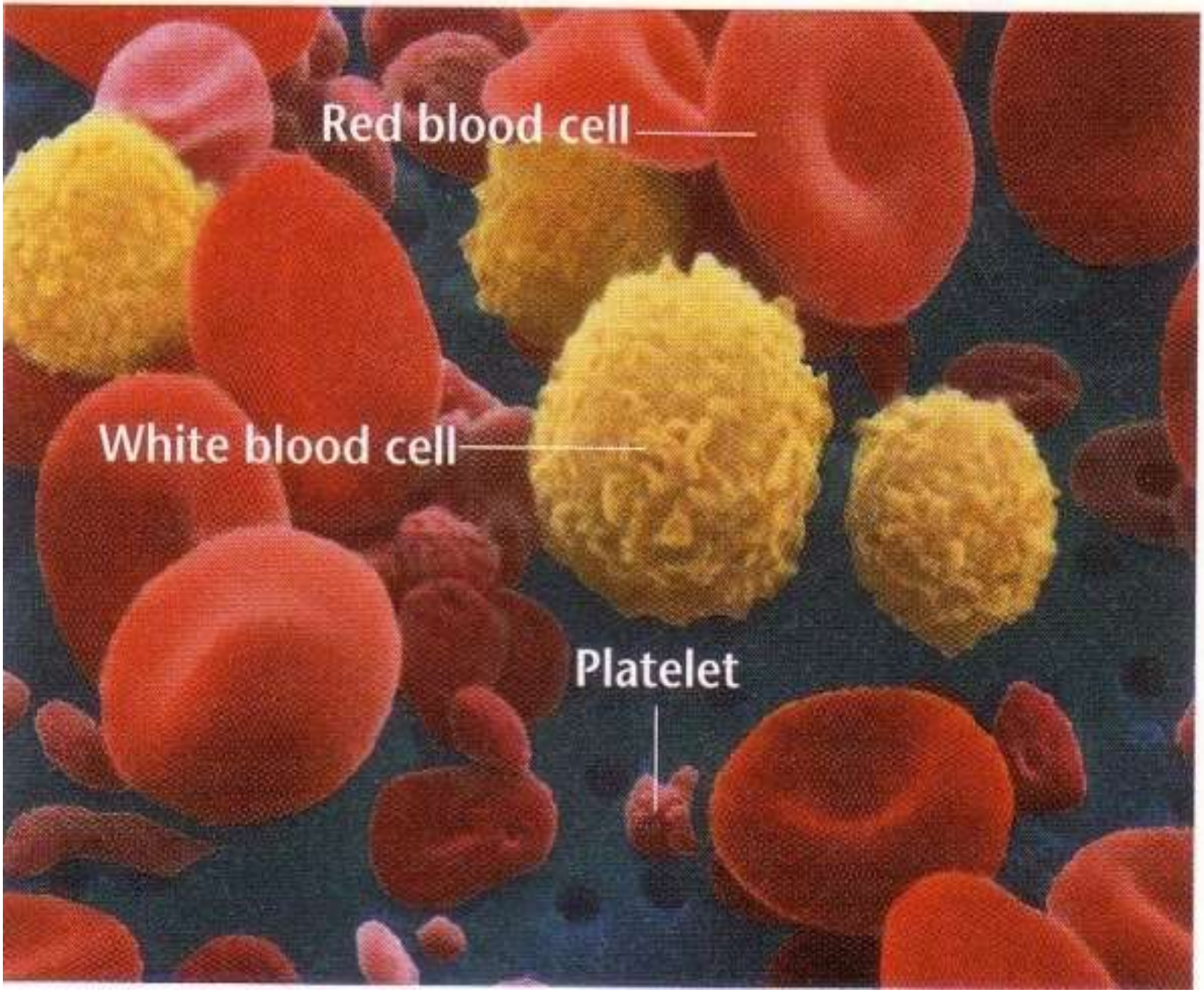
I)Atrial natriuretric factor releases when blood volume increases which stimulate Na and water excretion through kidney

Causes of increase blood volume

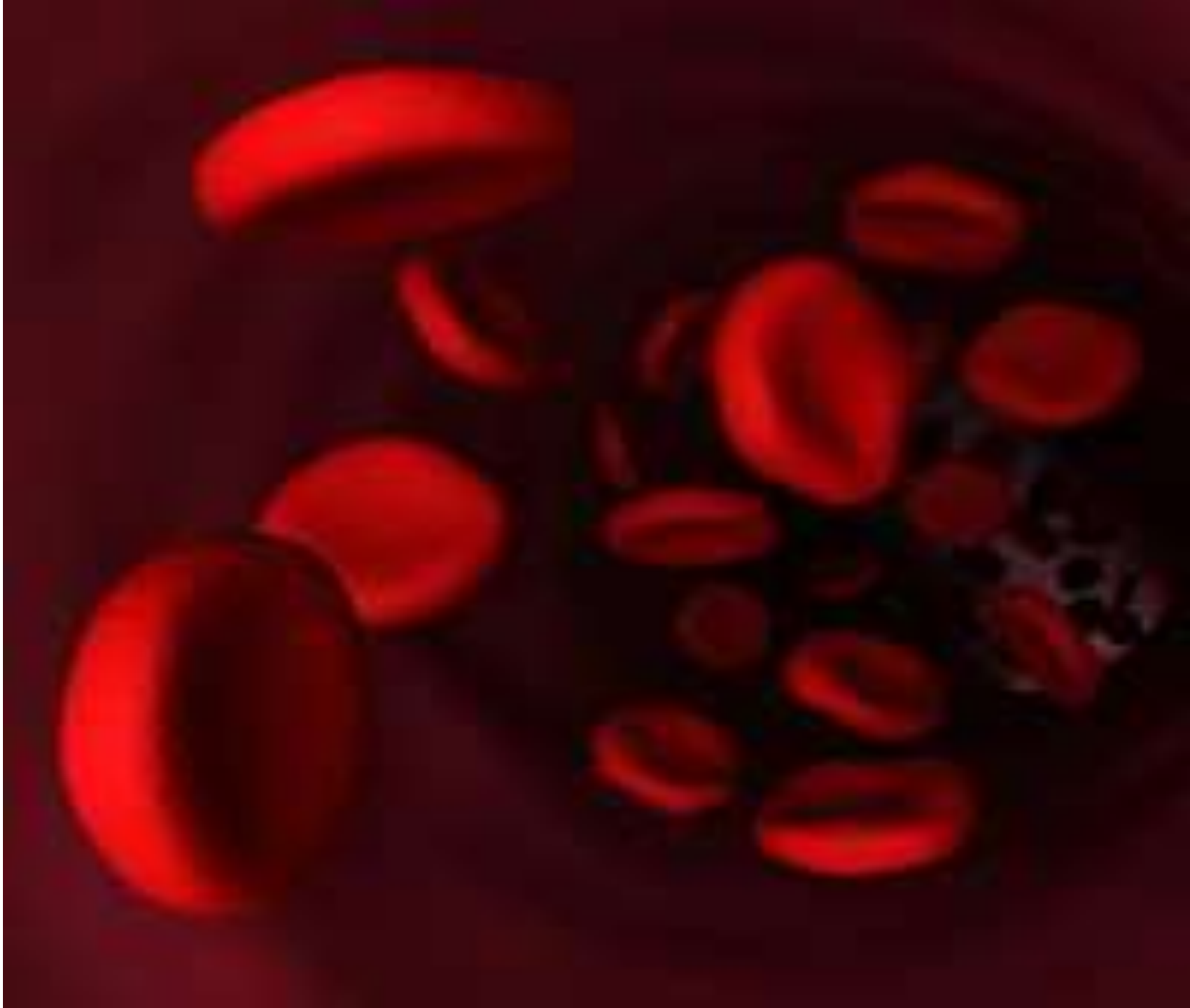
1. High temperature
2. Muscular exercise
3. Emootional excitement
4. Preganancy
5. CCF
6. Hyperthyrodisam
7. Cirrosis of liver

Causes of decrease blood volume

1. Heamorrage
2. Anaemia
3. Loss of plasma alone
4. Acute exposure to cold
5. In erect posture blood volume decrease
6. Obesity


Red blood cell
White blood cell
Platelet

RBC



FORMED ELEMENTS

RBC

Blood is red due to the presence of RBC

Also called as erythrocyte

(erythros-red)&(kytos –cell)

Red cells are red because they contain haemoglobin which is red color pigment

Human RBC are **biconcave ,non nucleated** ,

disc shaped with cytoplasm contain **red pigment haemoglobin**

7.2µ in size. **2.2 µ thickness.**

At center 1.1 µ

The cell membrane has **bimolecular lipid** structure .lipoprotein complex on membrane **contain antigen ,RBC IS soft flexible**

When viewed from side it look **dumb bell**

Advantage of biconcave shape

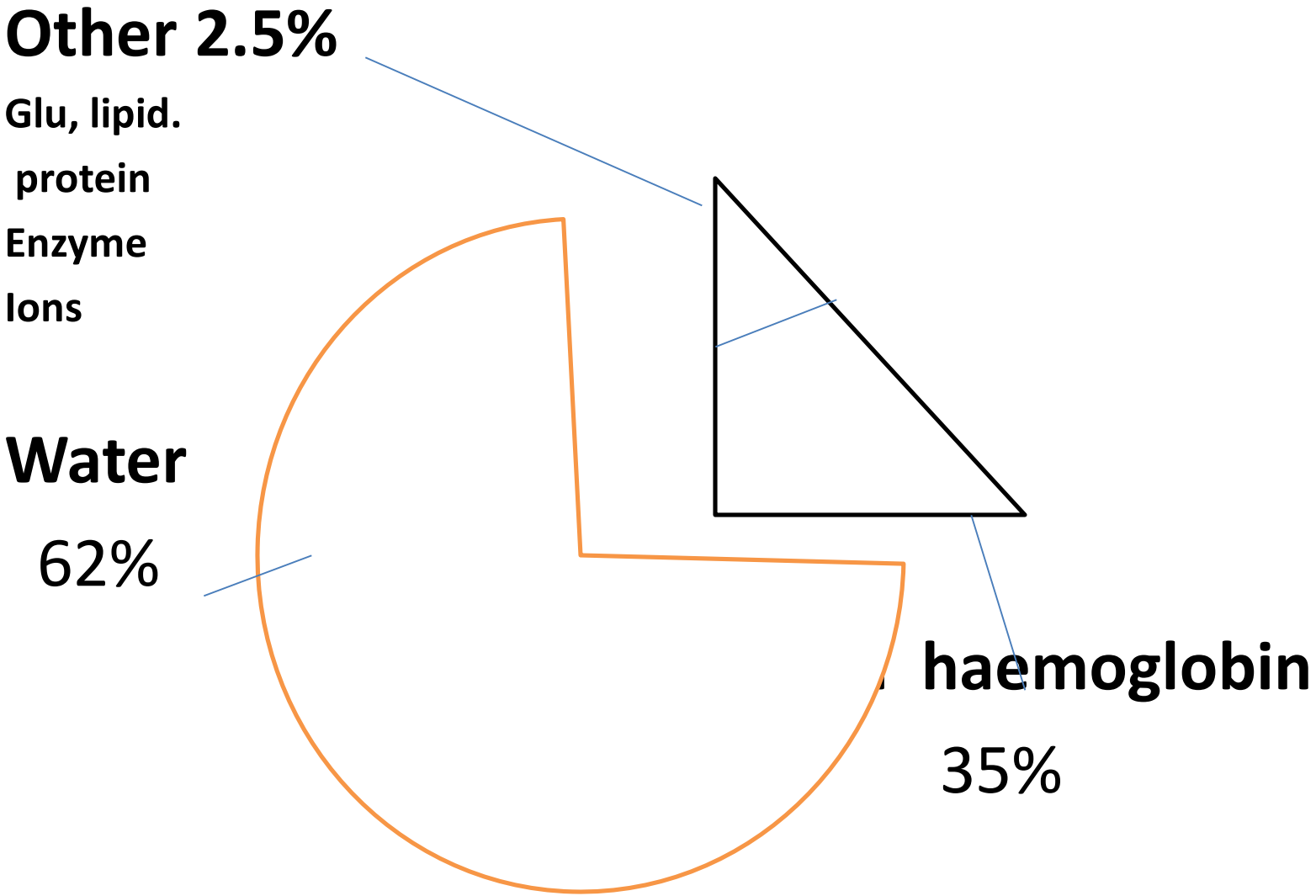
1. RBCcan easily squeeze through capillaries

2. Implies large surface of oxygen to transfer across RBC membrane

mature RBC has no nucleus ,no mitochondria ,no ribosome still it perform its functions ??????????????????????

RBC entirely depends upon glucose metabolism for its energy supply

structure of RBC



NORMAL VALUES

At birth- 6-7millions/cu mm

In adult male- 5-6 millions/cu mm

In female- 4.5-5.5 millions/cu mm

Clinically 5 millions /cu mm is taken as 100% RBC count

Life span of RBC <u>120 days</u>

Site of destruction

Tissue macrophage system

Variation in size and shape /structure

Variation in size – **anisocytosis**

Variation in shape- **poikilocytosis**

spherical shape of RBC -**spheroctosis**

During embryonic life RBC are formed in **yolk sac** .

In in early embryonic life blood cells are **produced in liver spleen**

At the 20 th Week of IUL haemopoisis begin **in bone marrow** in later life decrease in BM in increases in liver &spleen

FUNCTIONS OF RBC

1. **Respiratory** –red cells carry oxygen and carbon dioxide

2. **Acid base balance** –they help to maintain acid base balance .it is carried out by the buffering action of haemoglobin and other intracellular buffers

3. **Red cells maintain ion balance** –by the special permeability of the cell membrane the red cell help to maintain balance of positive and negative ions balance

4. **Viscosity of blood**

5. **Various pigments like bilirubin,biliverdin** are derived from haemoglobin after disintegration of red cells

ERYTHROPOIESIS

Process of formation of RBC is known as erthropoiesis

During intrauterine life 3 stages

Mesoblastic stage	**myeloid stage**	**hepatic**
Mesoderm of yolk sac	in bone marrow	in liver
Up to 3 month	middle 3 month	last 3 month

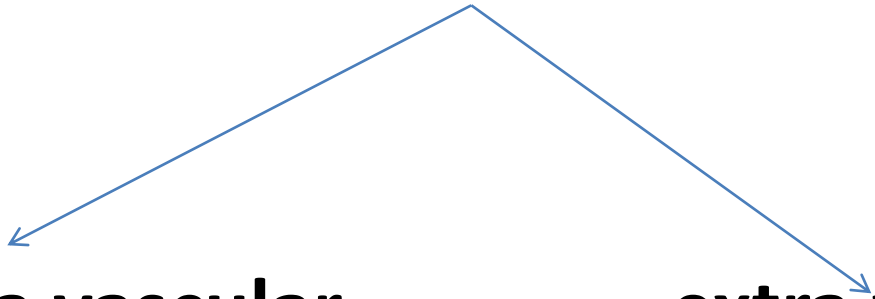
In children

- all bones of bone marrow
- in liver
- Spleen

In adult

- Red cells form in only **upper ends of long bones humerus ,femur , and vertebrae, the ribs, pelvis ,thorax.**
- In later life all the bones converted into yellow **so formation occur in liver &spleen**

Theories of erthropoiesis



Intra vascular

From capillary endothelium

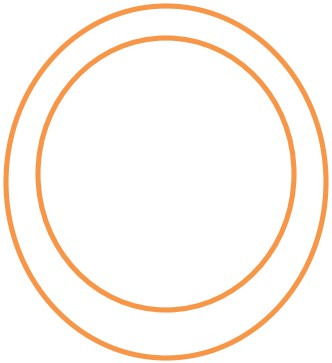
extra vascular

parent cell is extra vascular haemocytoblast by active amoeboid movements burrow onto blood sinuses multiply into mature cell

STAGES OF ERTHROPOIESIS

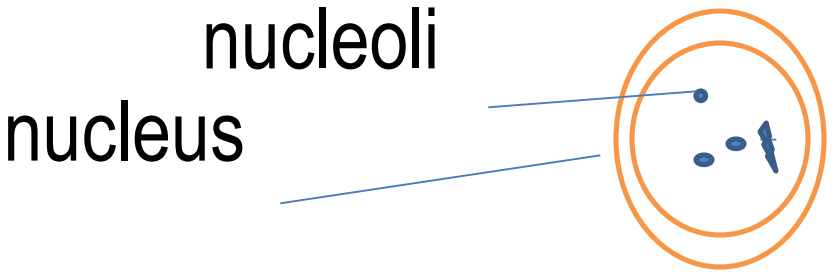
1Hemocytoblast (endothelial cell)

the big cell 18 to 23 μ with large nucleus and thin rim of deep basophilic cytoplasm



2.Prorthroblast (megaloblast)

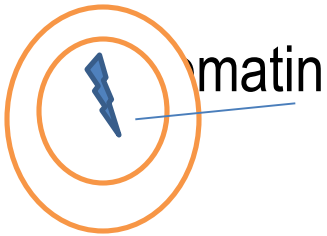
14 to 19 μ basophilic cytoplasm ,large nucleus with distinct nucleoli &reticulum of fine chromatin threads ,haemoglobin absent actively multiply into next stage



3.Early normoblast (early erythroblast)

smaller in size 11 to 17 µ

Nucleus &chromatin more dense ,nucleoli absent from this stage cell actively divide into next stage

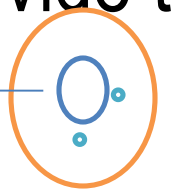


4.Intermediate normoblast (late erthroblast)

size still smaller 10 to 14 µ

Fewer mitochondria ,nucleus more condensed

No nucleoli ,haemoglobin start appearing at tis stage .cytoplasm become polychromatic from this stage cell don't divide they mature to form late normoblast



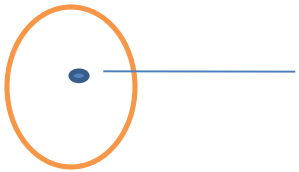
nucleus

5.Late normoblast(normoblast)

size more reduced 7 to 10 μ nucleus is

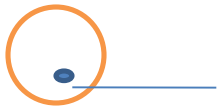
Very dense &take deep stain looking like drop of ink (ink spot nucleus)amount of haemoglobin has increases further complete loss of nucleus

Nucleus undergoes fragmenentation or at expenses of haemoglobin nucleus vanish



6.Reticulocyte

Net like structure in cytoplasm ,in normal blood there are about 1% .in new born 30 to 50% it is stage where RBC start appearing in peripheral circulation



Mature RBC non nucleated 7.2 µ

Factors affecting erthropoiesis

1)Erythropoietin

2)Anoxia

3) Dietary factors

4) Vitamins

5)Bile salts

6)castles’ factor

1. **Erthropoietin i**s glycoprotein which is secreted by kidney and liver which stimulate bone marrow to produced RBC

2. **Hypoxia /anoxia** means lack of oxygen is potent source for stimulation for production of RBC

3. Dietary factors

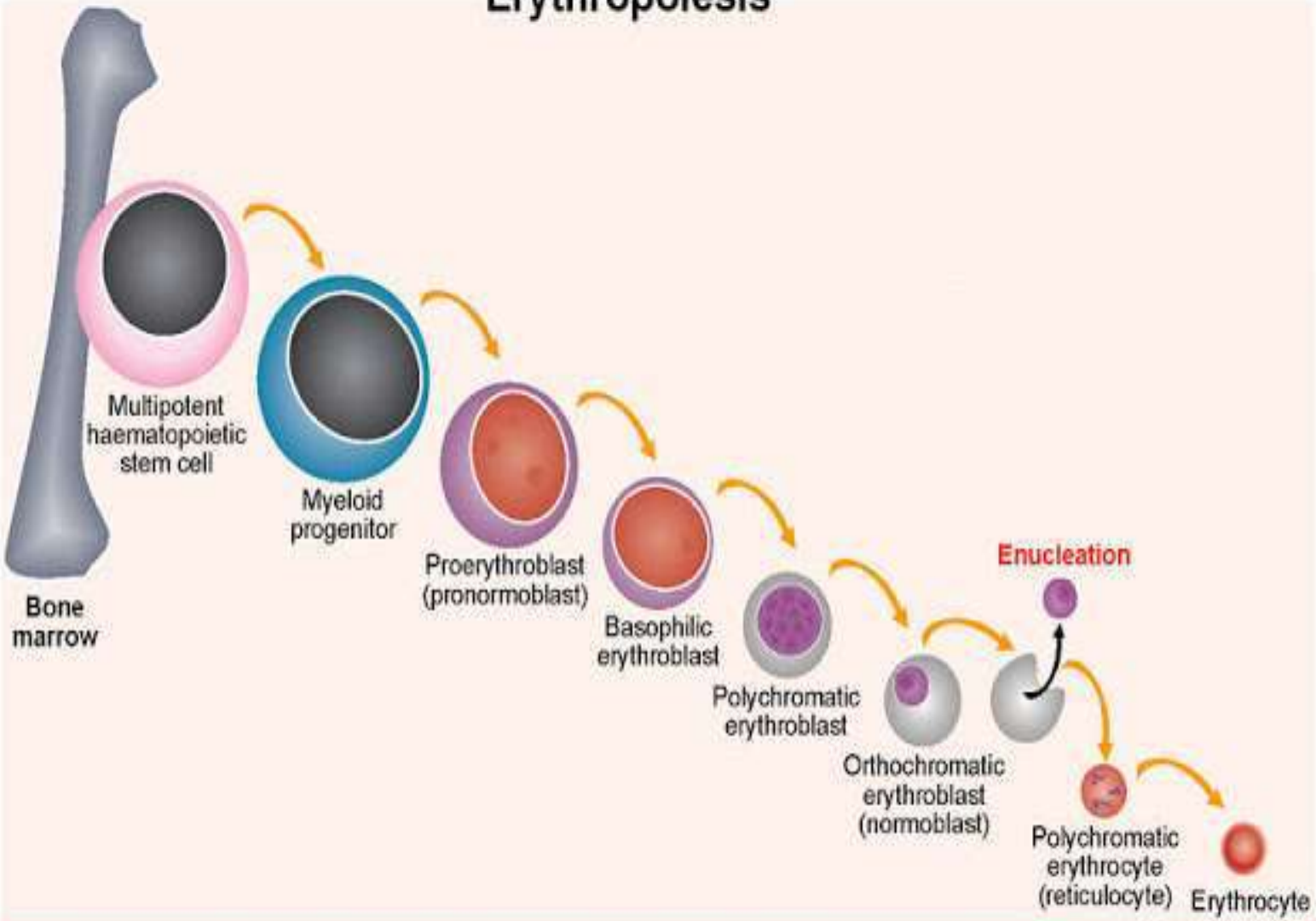
- Protein help in globin formation
- Iron mang,copper,cobalt,nickel,help in haem formation
- Calcium increases iron absorption from GIT
- **Vitamin B12 &folic acid help in synthesis of nucleic acid**

4. **Bile salts is essential** for proper absorption of metals

5. **Castles** factor or intrinsic factor

Produced by parietal cell of stomach it help in absorption of vit.B12(deficiency of this causes maturation failure will lead to megaloblastic anaemia)

Erythropoiesis



The development of erythrocytes in bone marrow is regulated by the hormone erythropoietin that stimulates the differentiation of progenitor cells into erythroid precursor cells. A number of intermediate cell stages can be identified beginning with the proerythroblast (pronormoblast). The cell nucleus is extruded at the orthochromatic erythroblast (normoblast) stage before formation of an enucleated polychromatic erythrocyte (reticulocyte). These cells are released into the circulation where they mature into functional erythrocytes.

immunopaedia.org

FATE OF RBC

1. As the cells grow senile

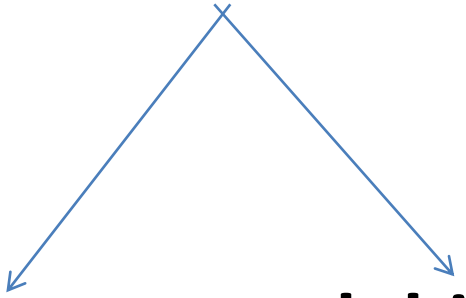
2 . Changes in their shape &size &become brittle

1. Cell throw out process like pseudopodia &become flask shaped

4.RBC disintegrated –fragmentation take place in circulation &fragments are swallowed up by R.E. cells of spleen ,liver etc. can also engulf senile red cell as a whole &break them intracellular

5.Haemoglobin released

6. Degraded choleglobin



haem **globin**

7. Heam is a iron part which help in formation of new haemoglonin ,some of the iron stored as ferritin &haemosidrin

   Globin break down into amino acids

8.Rest of haem molecule is converted

9.Yellow pigment blirubin

10.Which oxidized into green pigment biliverdin

11. Bilirubin and biliverdin combine with plasma globulin circulates through blood stream & enters in liver

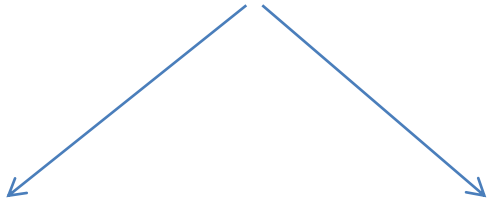
12. In liver cell bilirubin &biliverdin are separated from globulin & conjugated with uridine diphosphate glucoronate

13. Form monobilirubin &&dibilirubin glucoronide

14.Uridine diphosphate set free

15.Compound enter the duodenum through bile duct &then into intestine

16. In large intestine by bacterial flora they changed into



stercobilinogen — **urobilinogen**

Excreted in the faeces — **reabsorb &excreted in urine**

Stercobilinogen &urobilinogen responsible for brown color of stool and urine

Jaundice

is yellow discoloration of skin ,eyes &other tissue caused by the presence of excessive accumulation bilirubin in the plasma &tissue fluid

In adult normal serum bilirubin -0.2 -0.8mg%

When serum bilirubin more than 2 mg% then jaundice occurs

First site where clinically jaundice detected is sclera

HAEMOGLOBIN

Structure

Important terms

Normal values

Functions of haemoblobin

Synthesis of haemoglobin

Types of haemoglobin

1)The red oxygen carrying pigments in the RBC.

2)It is chromoprotien consisting of two parts 96%globin & 4% haem

3)Haemoglobin synthesized mainly from acetic acid & glycine ,most of synthesis occurs in mitochondria

Acetic acid converted to succinyl coA &then into two molecules of glycine

to form pyrrole compound four such pyrrole compounds combine to form a protoporphyrin known as protoporphyrin 1x

- which combines with iron to form haem . This haem combines with very long polypeptide chain called globin (synthesized by ribosome's)

Globin is forming subunit of haemoglobin called haemoglobin chain

Four such chain bind together loosely to form the whole haemoglobin molecule .

Chains may be α , β ,gamma .delta,

Molecular weight of Hb is 68000.

Properties of haemoglobin

1)Easily associated with O_2 &dissociate from O_2

2)Haemoglobin reacts with O_2 to form oxyhaemoglobin represented as HbO_2

3)The globin part of Hb directly combines with CO_2 to form carbamino compounds

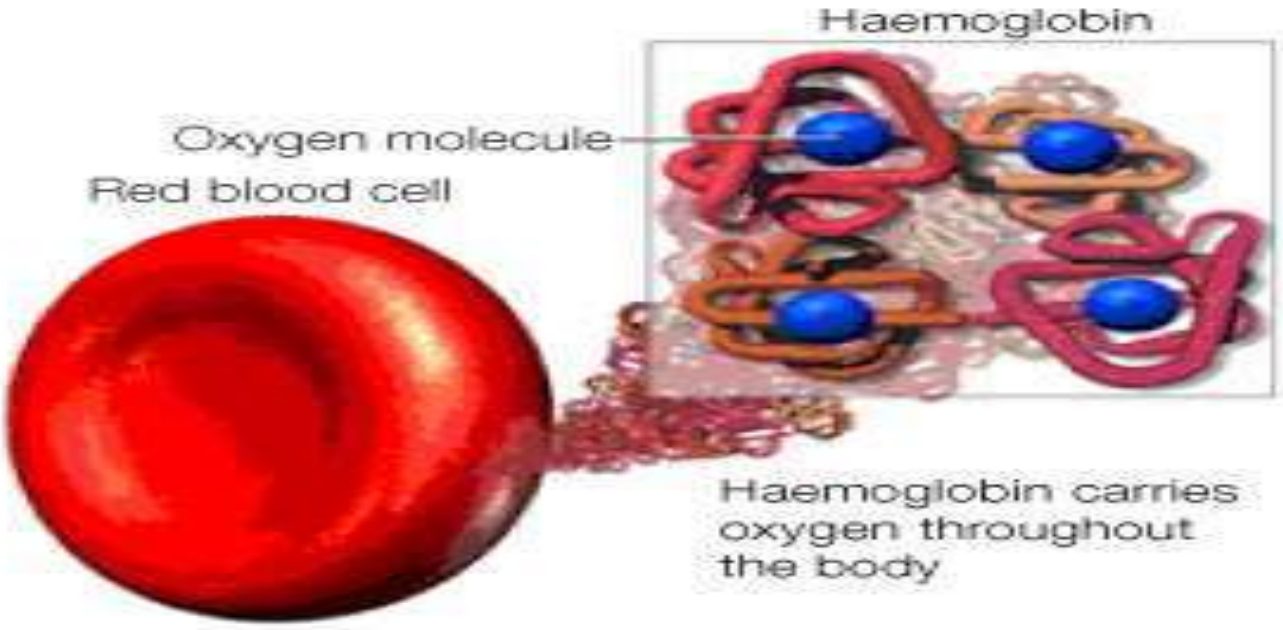
$CO_2 + HbNH_2 \longrightarrow HbNHCOOH$

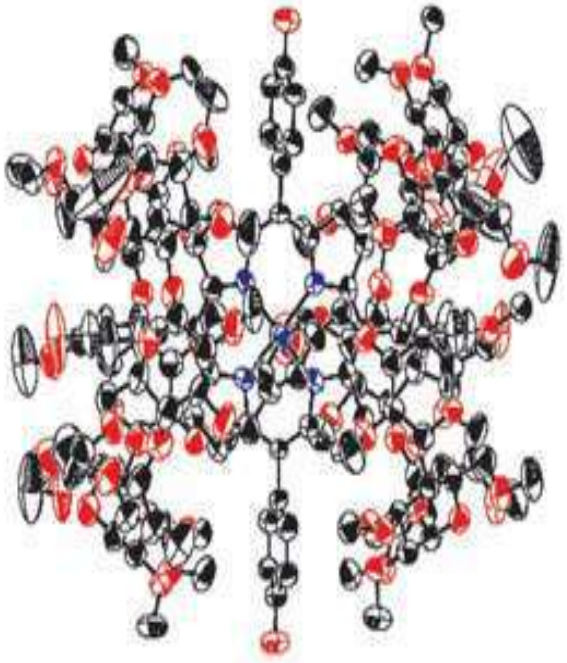
4) Hb can be easily crystallized

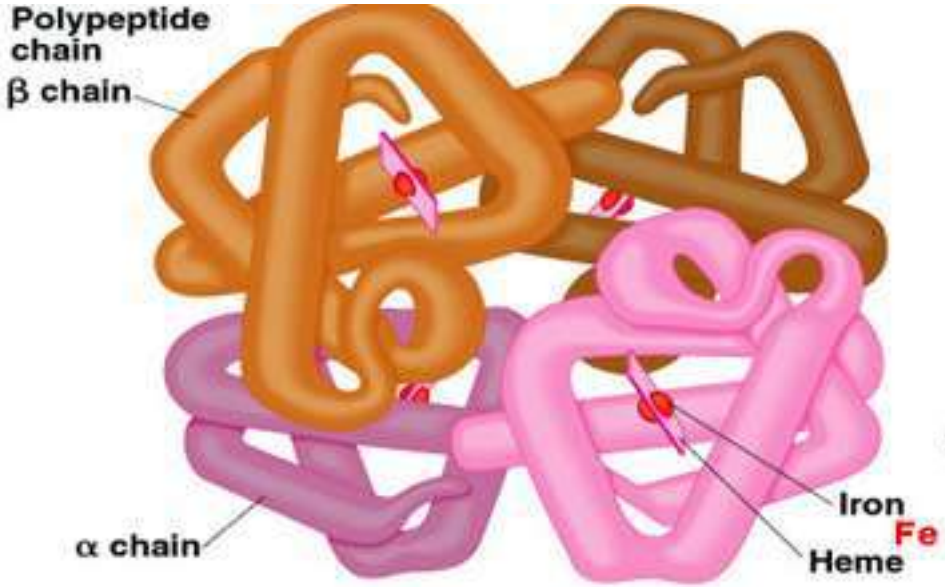
5) PH of Hb is 6.8

6) Co reacts with Hb to form carboxy-haemoglobin or carbon –monoxyhaemoglobin

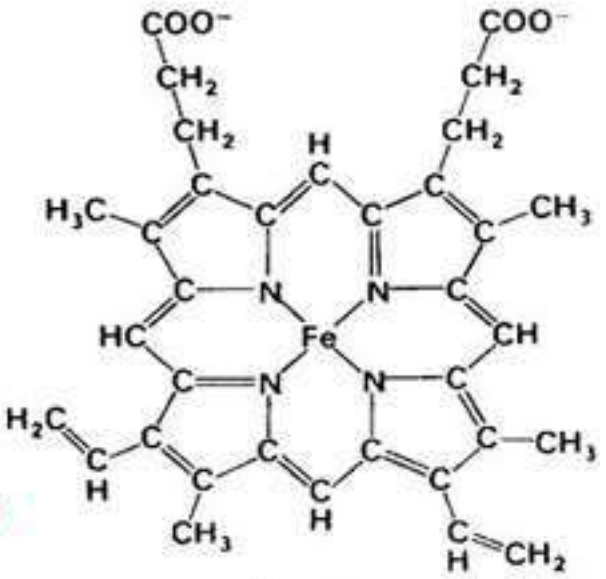
7)When reduced or oxygenated Hb is exposed to various drugs or oxidizing agents ,ferrous is oxidized to ferric form & compound is methaemoglobin (HbOH)







Hemoglobin



Heme
(Fe-protoporphyrin IX)

Catabolism -by tissue macrophage ,liver cell

<u>Normal values</u>

Adult male → 14-18 gm%

female → 12 -15.5 gm%

14.8 gm% is 100% Hb .

1 gm of Hb carries 1.34 ml of O2

Varieties of Hb

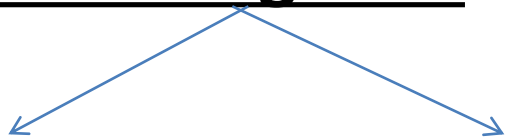
1)Adult haemoglobin

2)Foetal haemoglobin

3)Hb S

4)Miscellaneous

1Adult haemoglobin



HbA

2alpha &2 beta

HbA2

globin chain contain

2gamma &2 delta

HbA appear in foetus after 5 month of IUL

It contain 146 A.A.

2)Foetal haemoglobin

Structurally same except beta chain are replaced by gamma chain and having greater affinity towards O2

3)Hb S

Beta polypeptide chain of HbA at position of 6 one glatamic acid is replaced by valine

this is abnormal Hb so what happen??????????

It damage cell membrane ,increase fragility of RBC ,RBC become sickle shape produced anemia

4)Miscellaneous

C,E,I J,M these are also abnormal haemoglobin

<u>Haemogloninopathies</u>

Occur due **to disorder of globin synthesis**

(Like HbS)

Synthesis of polypeptide chain of globin is repressed

Due to deficient production of alpha or beta chain called thalassaemia

Thalassamia is due to impaired synthesis of one or more polypeptide chain of globin

Thaassaemia are of two types

1.Beta thalassaemia

2.Alpha thalassaemia

β thalassaemia is of two types — **major**, **minor**

In major total absence of β chain

in minor partial absence of β chain

Derivatives of Hb

HbO2.carbamino compound, carboxy haemoglobin ,sulph haemoglobin

Derived compound

Haematin. bilirubin,haem ,haemopyrrole, haematodin

Functions of haemoglobin

- essential for O_2 carriage
- It plays part in CO_2 transport
- Maintain acid base balance
- It is important buffer
- Various pigments of bile ,stool urine are formed from it

Anemia

Anaemia is clinical condition characterized by decreased in the number of RBC or haemoglobin or both

Mild anaemia – Hb 8-12 gm %

Moderate anaemia – Hb 5- 8 gm %

Severe anaemia - Hb less than 5gm%

Anaemia might be due to either **excessive blood loss or increase destruction of RBC** it might also result from either **defective formation in bone marrow** or **deficiency of maturating factor or nutritional defect**

Types of anaemia

1)Etiological anaemia

2)Morphological anaemia

Etiological anaemia

is depending upon cause

- Haemorragic anaemia
- Hemolytic anaemia
- Aplastic anaemia
- Megaloblastic or pernicious anaemia
- Folic acid deficiency anaemia

Haemorragic anaemia is(normocytic normochromic)

- Is due to blood loss as in
- Bleeding piles
- Worm infestation
- Peptic ulcer
- Menorraghagia
- Acute blood loss in accident

Hemolytic anaemia

is due to excessive destruction of RBC

- **Familial hemolytic anaemia**

Cell is small ,spherical can be easily broken down (spherocytosis)

- **Sickle cell anaemia**

HbS type ,RBC cell membrane become fragile

Mediterranean anaemia

known as thalassimia or Cooley's anaemia

A plastic anaemia

Failure of function of bone marrow

- A plastic anaemia is due to primary failure of bone marrow
- Exposure to x-ray
- Cancer in bone marrow
- Kidney diseases

Pernicious or megaloblastic anaemia

Is due to defective formation of RBC lack of intrinsic factor &extrinsic factor

Intrinsic factor is secreted from parital cell of stomach and extrinsic is vitamin B12

Folic acid deficiency anaemia

is due to deficiency of folic acid which is necessary for maturation of RBC

Morphological anaemia

is depending upon size of RBC& its Hb concentration

✓ Depending upon size of RBC

Microcytic (size of cell small)

Normocytic (size of cell normal)

Macrocytic (size of cell large)

✓ Depending upon Hb concentration

- **Hypo chromic (MCH is lesser than normal)**
- **normo chronic (MCH is normal)**
- **hyper chromic (MCH is increase)**

Signs /symptoms of anaemia

1) color of skin ,buccal mucosa ,pharynx mucous membrane ,conjunctiva ,lips tongue ,palms ,nail bed become pale

2) Increase heart rate

3) Common symptoms of GI tract nausea vomiting & headache, irritation drowsiness, faintness

Effects of anaemia

1) viscosity decrease

2) decrease resistance to blood flow in peripheral blood vessels

3) More amount of blood flow in tissue

4)Increase amount return to heart

So increase cardiac output

5) Increase pumping workload on the heart

6) In exercise pumping decrease so heart cant withstand to tissue demand .

Determination of types of anaemia

Is through blood indices

Important blood indices

1)Color index is proportion of Hb in each red cell

2)MCV is volume of packed red cell/RBC

It is volume of single RBC

MCH

Average amount of haemoglobin in a single RBC

MCHC

Amount of expressed in single RBC Hb

Increase RBC is called as polycythemia

when tissue become hypoxic ,large no. of RBC are produced this is **secondary polycythemia**

When RBC count is more than 7 to 8 million /cu mm of blood is called **polycythemia Vera**

Effects of polycythemia

increases viscosity of blood lead to decrease rate of blood flow which lead to decrease venous return

WBC/LUCOCYTE

They are nucleated living cell

No Hb

Bigger in size

They are actively amoeboid

Much lesser in number

Life span is shorter

Origin is extra vascular

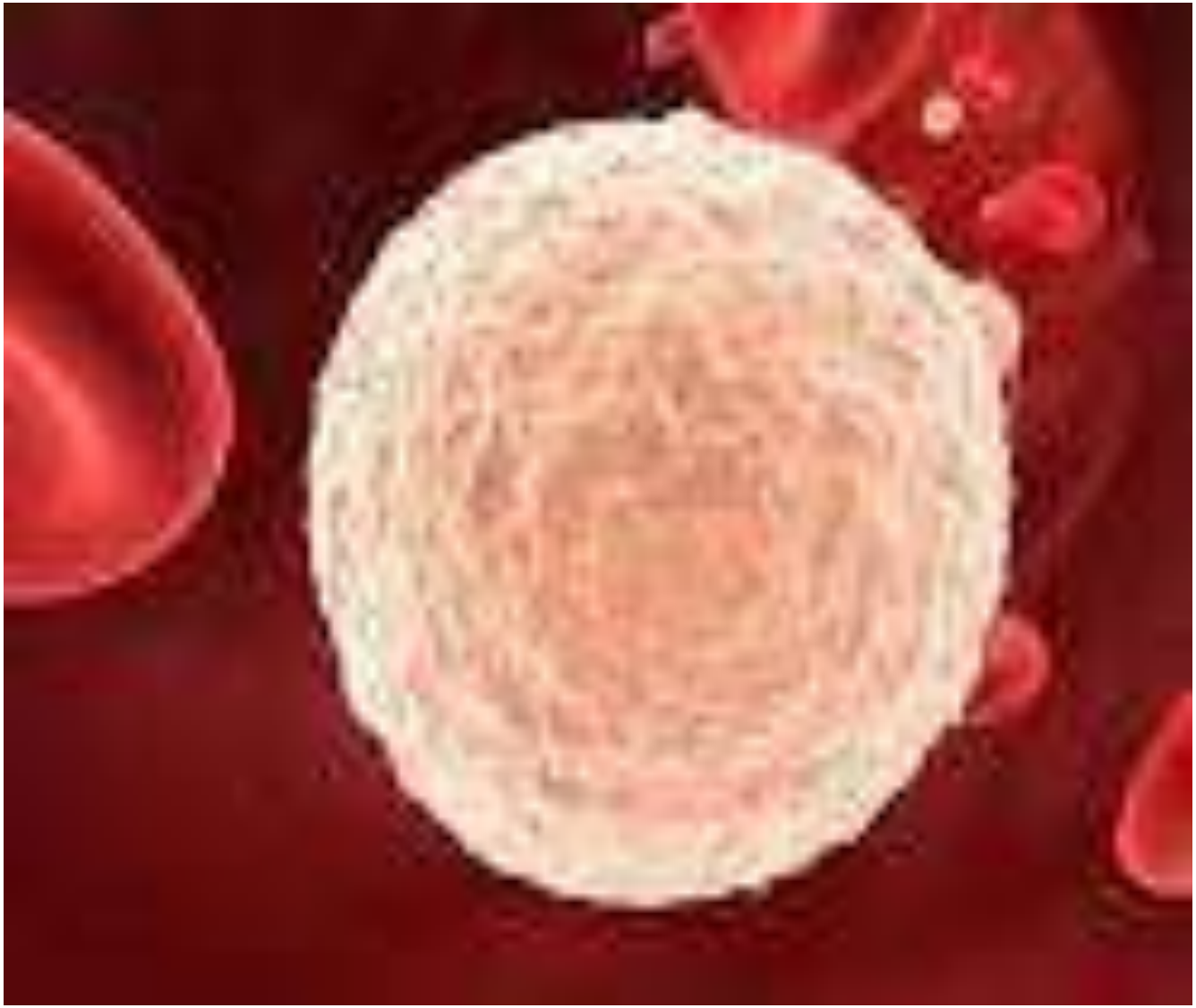
Leucocytes are rich in nucleoprotein &also contain lipids ,glycogen, cholesterol, ascorbic acid ,enzymes

Normal count of white blood cells

4000 to 11000 /cu mm of blood

RBC:WBC

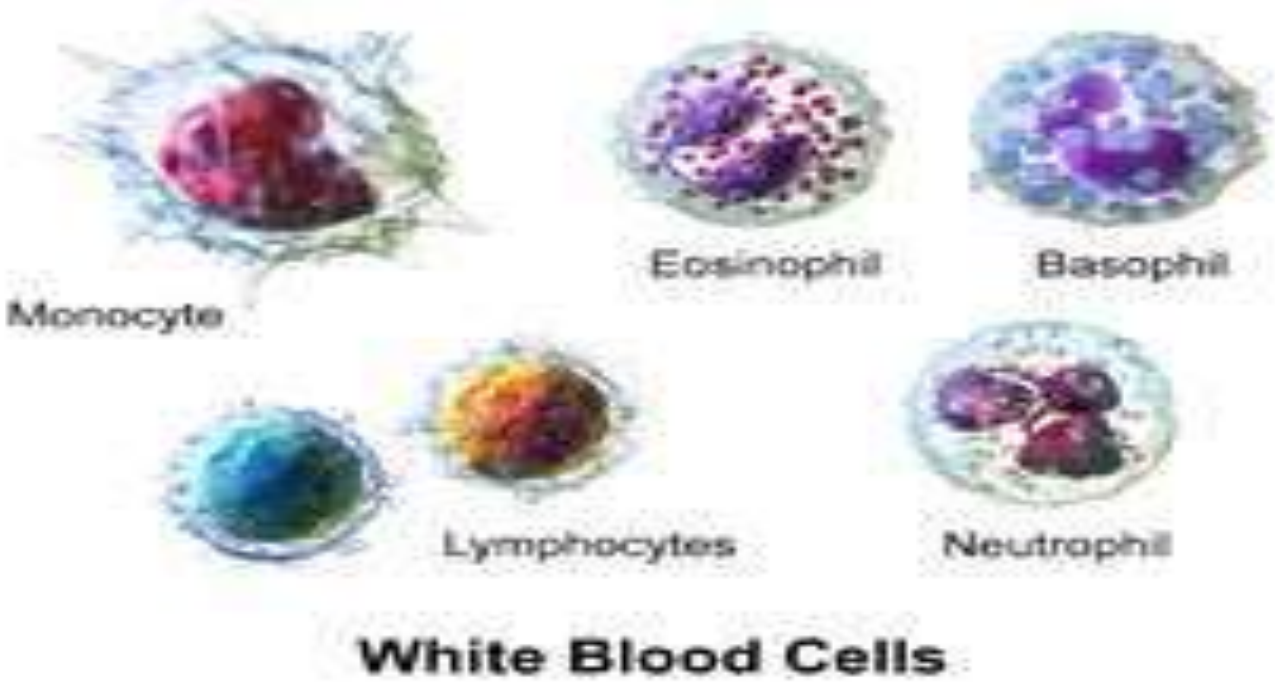
1:700



Classification of WBC

Depending upon structure ,staining property ,there are different WBC known

As differential leucocytes count



1)Granulocyte

cytoplasm contain granule

2)Agranulocyte

there is no granules in cytoplasm

Granular leukocyte are of 3 types

1)Neutrophils

2)Eosinophils

3)Basophils

1)Neutrophils

Most numerous in adult blood i.e.60 to 70%

Nucleus

- Nucleus is purple in color

- Multi lobed (2-7) so they called as polymorpho nuclear leucocytes

- Young cell have single ‘horse shoe shape nucleus’

As cell grow older nucleus become multi lobed

- Lobes are connected with one another by chromatin thread

- More the number of lobes the more mature is the Neutrophils

- Arneth count –age of Neutrophils is proportional to number of lobes in their nuclei

Cytoplasm

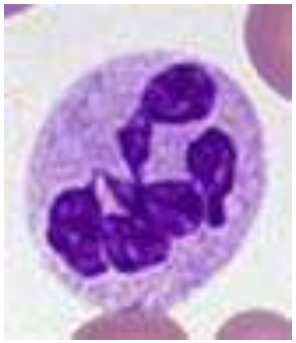
- Slight bluish in color ,granular, granules are sand like particles take acidic &basic stain so they called Neutrophils

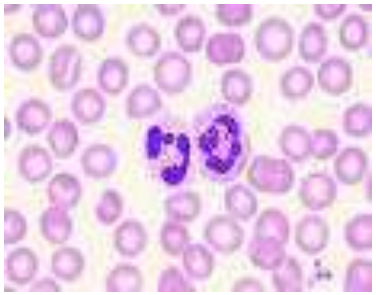
- Cytoplasm contain enzymes ,glycosides, phosphatatses, proteolytic enzymes

- They can lyse any type of substance so granules are thus regarded as lysosomes

All granulocyte liberate histamine &peroxides

Neutrophil





Functions of neutrophils

- **Phygocytosis** –whenever body get invaded by bacteria neutrophil kills the bacteria so Neutrophils are first line defense

- They contain fever producing substances endogenous Pyrogen important mediator of febrile response

Increase neutrophil count is called as **neutrophilia**

Physiological neutrophilia

- Exercise
- Epinephrine injection
- Pregnancy

Pathological neutrophilia

- Acute pyogenic infections (pus forming)

- Tissue destruction as in burns, hemorrhage, MI, after surgery

Decrease count is called as **neutropenia**

Seen in typhoid, viral fever ,bone marrow depression

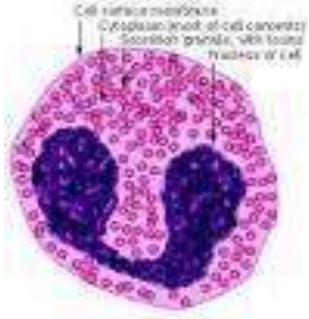
Eosinophils

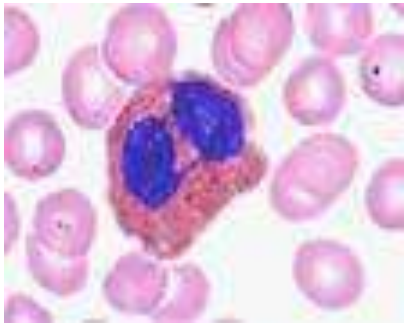
10 to 14 µm in diameter

Nucleus purple usually **bi lobed**

Cytoplasm is granular acidophilic

Coarse granules





Functions of eosinophils

- Mild phygocytic
- Collect at the sites of allergic reactions &limit their intensity by degrading effects of mediators i.e histamine
- They attack parasites that are too large to engulf
- Provide mucosal immunity mucosa of R.T. G.I. urinary tract

Increase **eosinophils is called eosinophilia** seen in following condition

1. **Allergic condition**
2. **Bronchial asthma**
3. **Parasitic infection**
4. **Skin diseases**

Decrease eosinophils is called **eosinopenia**

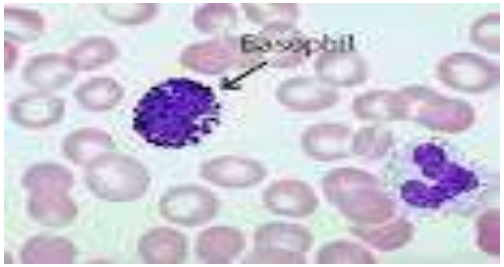
Seen after injection of ACTH

Or corticosteroids

Basophils

- 10 to 14 µm, **nucleus is kidney shape or slightly lobulated**
- cytoplasm contain large round granules which take basic stain

  granules are overlapping
- They secrete histamine ,heparin,5 HT


Basophil

Increase basophile is known as **basophilia**

Seen in chicken pox, smallpox tuberculosis ,influenza

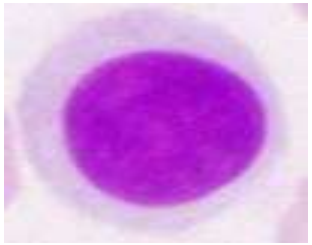
Decrease basophils is known as basopenia

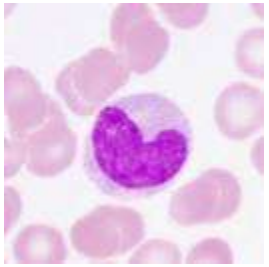
Seen after glucocrticoides

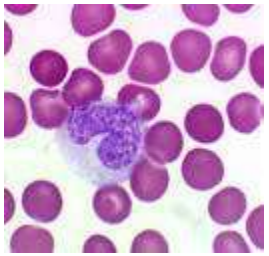
A granulocyte

cell which **don't have granules** in their cytoplasm

They are lymphocyte and mono cyte







Lymphocyte

- Are the type of white blood cells a granulocyte there three types T lymphocyte ,B lymphcyte,natural killer cell

- 7.5 μ .nucleus is large

- Basophilic cytoplasm

  No granules

T lymphocyte(thymus cell) &B lymphocyte(bone marrow or bursa derived)

are major cellular components of adaptive immune response. T cell involved in **cell mediated immune response**

B cell are primarily responsible of **humoral immunity**

- T and B cell identify invader and generate specific response that are tailored to maximum ally eliminate specific response pathogens

- B cell respond to pathogens by producing large quantities of antibodies to pathogens which neutralize foreign objects like Bactria and viruses

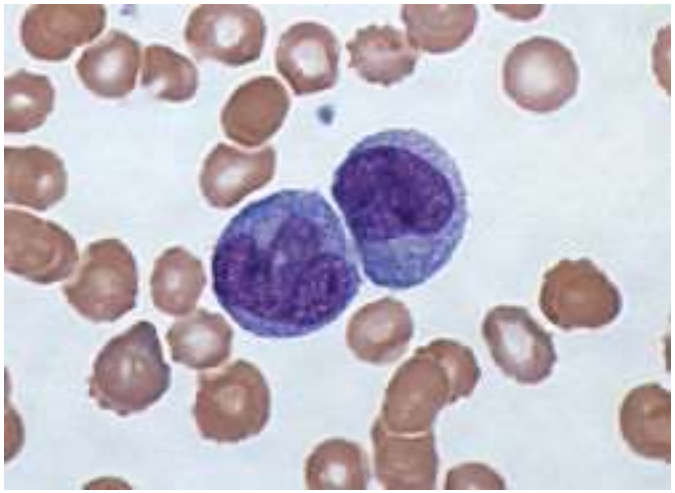
- In response to pathogens some T cell called T helper cell produce cytokines that direct the immune response
- while other T cell called cytotoxic cell produced toxic granules that contain powerful enzymes which induce the death of pathogens or infected cell

- following activation of T B cell create lasting legacy of antigens they have encountered inform of memory cell throughout life which remember each specific pathogens encountered and also mount strong and rapid response if pathogens detected again

Monocyte

- are larger WBC 10 -18 μ nucleus is round or kidney shape or horse shoe shape

- Cytoplasm clear or frosted glass like



- They are amoeboid in appearance can be differentiate into macrophages

- Produced by bone marrow from precursor called monocyte

- which migrate from blood stream to other tissue will differentiate into tissue resident macrophages .

- responsible for protecting tissues from foreign particles

- Monocyte and their macrophages have function of phagocytosis

Increase monocyte is called as monocytosis

Seen in tuberculosis ,syphilis .leukemia

- ✓ **Decrease in leukocyte is called as leucopenia** in starvation ,typhoid fever bone marrow depression

- ✓ **Increase in leucocytes is called as lucocytosis** in new born ,stress ,pyogenic infection
- ✓ **Leukemia is increase immature WBC more than 50000**

Development of WBC

Reticulum cell of bone marrow(haemocyto blast)

Primitive white blood cell

1) **Myeloblast**

2) **Myelocyte**

3) **Metamylocyte**

4) **Leukocyte**

Monocyte develop from reticulum of spleen &lymph nodes

<u>Life span of granulocyte is half day</u>

- **Neutrophils -2 to 4 days**
- **Eosinophils 8 to 12 days**
- **Basophils 12 to 15 days**
- **Lymphocyte 2 to 3 days**

Functions of WBC

1) **Phygocytosis** –Neutrophils and monocyte engulf foreign particles and Bactria digest them

when Bactria invade the body WBC pass out of blood vessel surround threatened area engulf bacteria by chemotaxisis migration of lymphocyte ,Neutrophils manufacture trypsin which digest bacteria

Dead tissue ,due to dead tissue inflammatory area becomes liquefy and so called pus is formed L &M liberate pepsin

Which convert them for removable

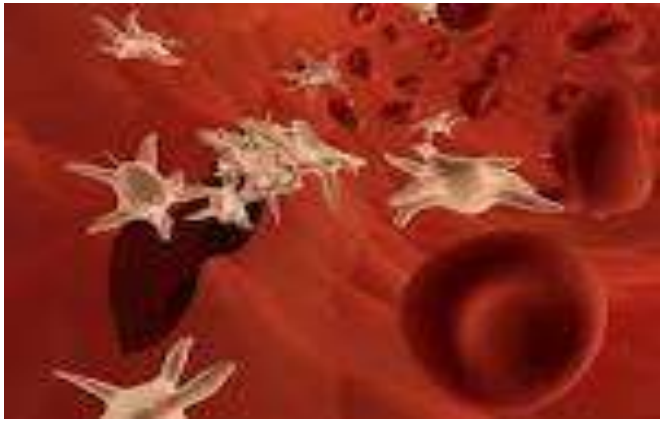
2) Antibodies formation

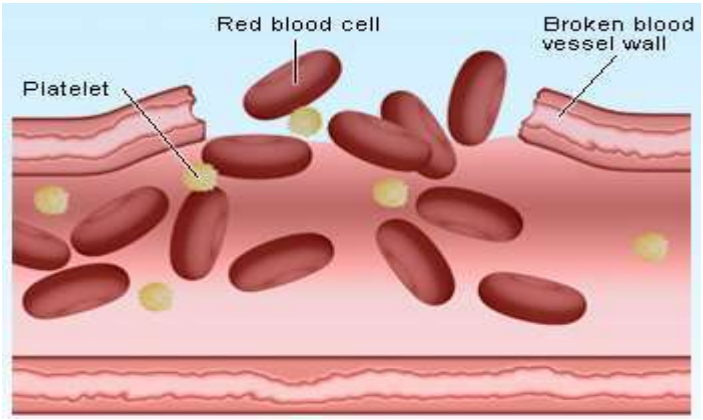
3)Fibroblast formation

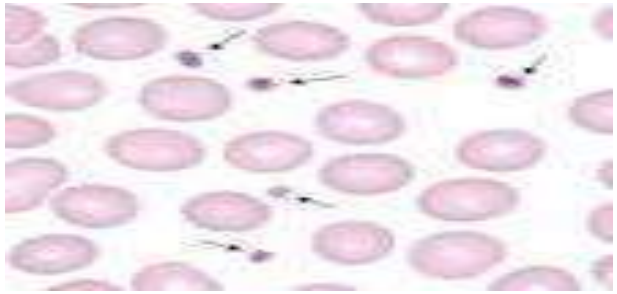
4)Formation of trephones

Intravascular coagulating factor heparin formation

5)Antihistamine formation




Red blood cell
Broken blood vessel wall
Platelet



Platelets

- Small plate like cell

  Also known as thrombocyte thrombo

  means clump cyte means cell

- Platelets are the smallest blood cell ,spherical, oval or rounded granular bodies
- 2.5µ

  Nonnucleuted

In light microscope generally two components are seen

1)Clear ground substance (hyalomere)

2)Deeply stained central portion (chromatomere)

Hylomere is seen to consist of homogeneous fine granular materials hylomere contain microtubules &microfilaments

Microfilaments contain thrombosthenin which can contract like actin &myosin in muscle so it is contractile elements responsible for change of shape of platelets

Under electron microscope chromatomere is seen to contain

1)Alpha granules

2)Mitochondria

3)Syderosomes

4)Glycogen granules

5)Ribosomes

6)Very dense granules

7)System of tubules and vesicles

Alpha granules are oval or round in shape enclosed in membrane responsible for

Platelets release reaction and aggregation

Clot resolution ,phygocytic activity

Platelets membrane 60 A=6nm

Having lipoprotein layer

Average life span 5 to 9 days

Platelets destroy in spleen &RE system

Normal value -250000-450000/cu mm

60 to 70 %in circulation remaining in spleen

Thrombocyte develop in bone marrow from

pluripotent stem cell → committed cell

megakaryoblast → premegakaryocyte

granular megakaryocytic cell

Megakyrocyte is giant cell which 35 to 60 µm

multinucleated &dense granular cytoplasm

Functions of platelets

1)Initiate blood clotting

when blood is shed the platelets disintegrate &liberate thromobopalstin which activates prothrombin into thrombin

2) **Repair capillary endothelium**

While in circulation platelets adhere to damaged endothelium lining of the capillaries and thus bring about speedy recovery

3)Contain some substance like ABO blood group antigens

4)Haemostatic mechanism

5)Hasten clot retraction

6)Platelets disintegrate 5 HT &histamine

Increase in platelets is called **thrombocytosis** seen after trauma splenectomy, splenic contraction

Platelets decrease in bone marrow depression viral infection (dengue fever)

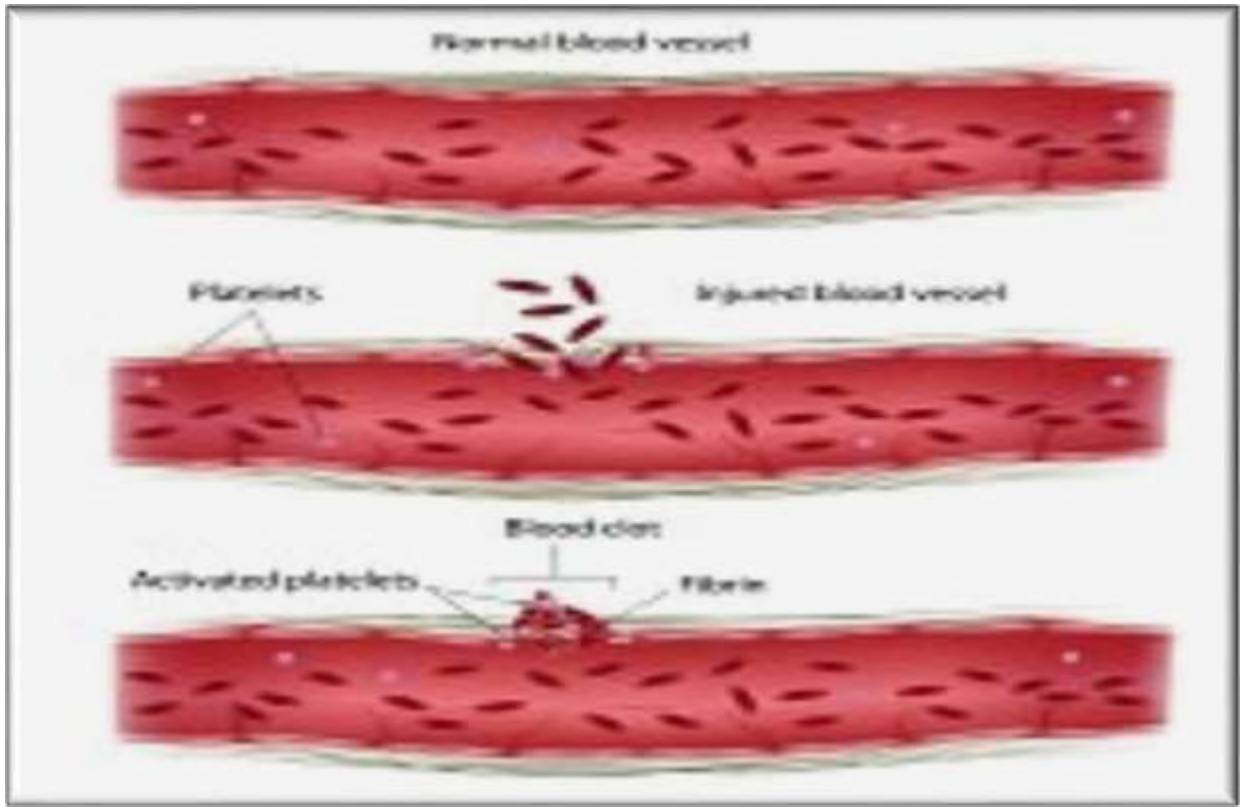
Hypersplinisam ,leukemia ,acute septic fever toxemia

Coagulation

Spontaneous arrest or prevention of bleeding by physiological process is called clotting or haemostasis

- Injury to vessel wall initiate series of events which form clot and seals of damaged blood vessels

Series of events involved in haemostasis



1) Constriction of injured blood vessels

2) Formation of temporary haemostatic plug of platelets

3) Conversion of temporary haemostatic plug into definitive haemostatic clot

4) Clot resolution

1)_when blood vessels is cut ,smooth muscle when contracted immediately which arrest blood loss temporary

2)After vasospasm platelets plug formation occur ,platelets aggregate due to secretion of thromboxane A2 which will activate platelets aggregation and this will initiate thromboplastin

3)Then activate prothrombin into thrombin

Thrombin into fibrinogen

Fibrinogen into fibrin

And this will sealed of injury

4)Dissolution of clot by fibroblast

How platelet plug formation occur????????

When platelets come in contact with a damaged vascular surface such as collagen fibers in a vascular wall or endothelial cell

They change their characteristic

They begin to swell and assume irregular forms with large number of pseudopodia protruding from surface

Contractile protein contract forcefully and cause release of granules

They become sticky ,stick to collagen fibers of vessel

They secrete ADP& thromboxane A2 they act on nearby platelets and activate other platelet thus platelet plug form

Clot formation

it is a complex series or cascade of reactions here inactive enzymes become active and activated enzymes in turn activate inactive enzymes

Fundamental reactions include

1)Formation of prothrombin activation

2)Formation of thrombin

3)Formation of fibrin

- **Those enzymes or clotting factors**

I. **Fibrinogen**
II. **Prothrombin**
III. **Thromboplastin**
IV. **Calcium**
V. **Labile factor/pro acclerine**
VI. **Accelerine**
VII. **Reconverting /stable factor**
VIII. **Antihaemophilic A factor**
IX. **Antihaemophilic B**
X. **Christmas /plasma thromboplastin**
XI. **Stuart**
XII. **Antihaemophilic C**
XIII. **Contact factor**
XIV. **Fibrin stabilizing factor**

Fundamental reactions include

1)Formation of prothrombin activation

2)Formation of thrombin

3)Formation of fibrin

1)Prothrombin activation

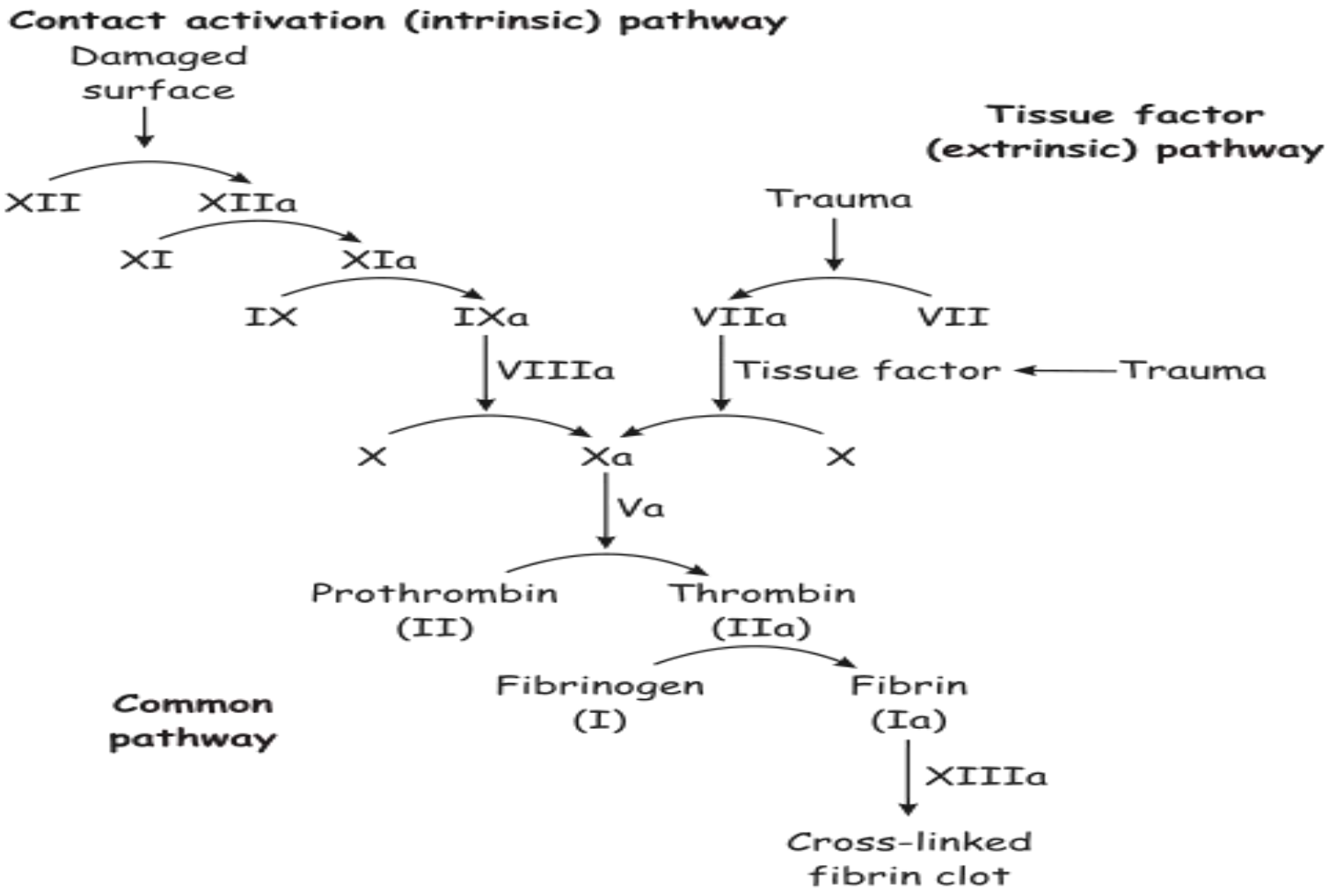
Occur in two ways

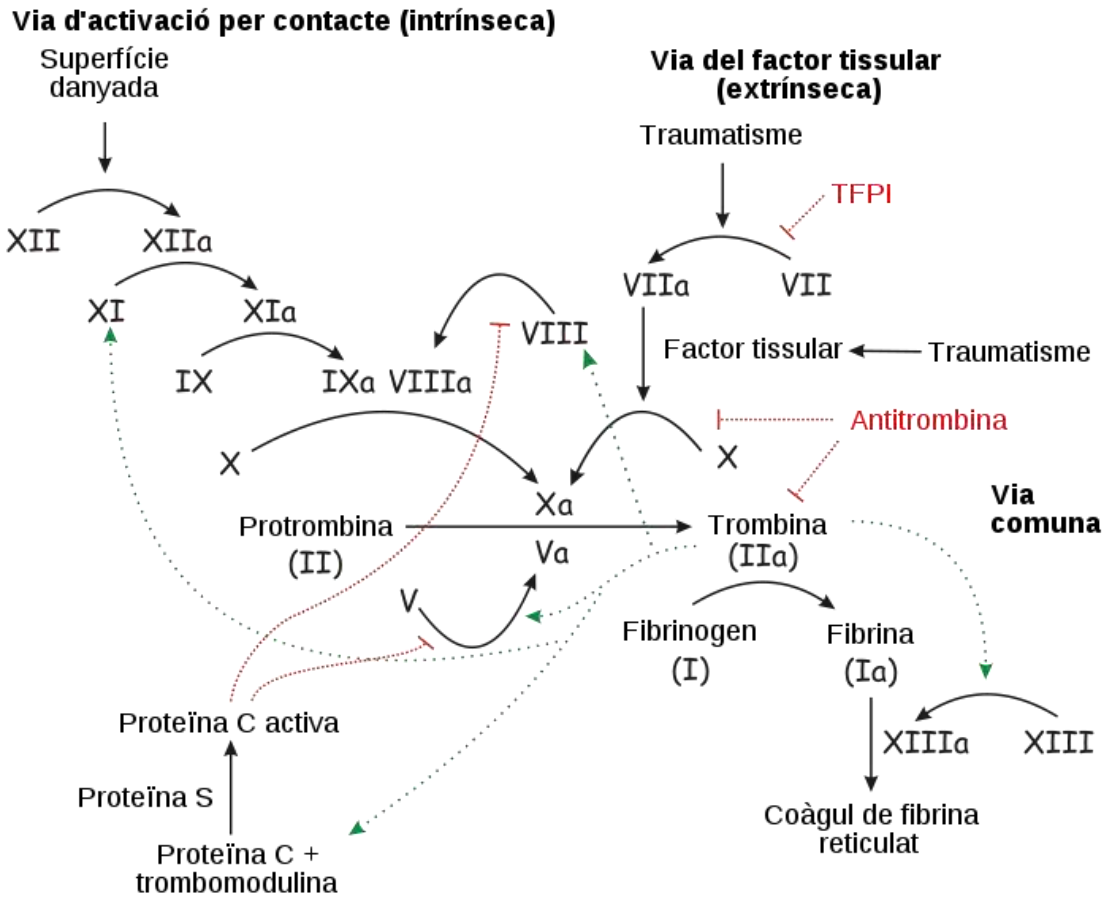
1)Extrinsic system

Is triggered by injury to vessel wall or other body tissue resulting in formation of extrinsic pathways

2)Intrinsic system

Is triggered when blood is exposed to the collagen fibers or change in blood constitutes


Contact activation (intrinsic) pathway
Damaged surface
XII
XIIa
XI
XIa
IX
IXa
VIIIa
Tissue factor (extrinsic) pathway
Trauma
VIIa
VII
Tissue factor
Trauma
X
Xa
X
Va
Prothrombin (II)
Thrombin (IIa)
Fibrinogen (I)
Fibrin (Ia)
XIIIa
Cross-linked fibrin clot
Common pathway


Via d'activació per contacte (intrínseca)
Superfície danyada
XII
XIIa
XI
XIa
IX
IXa
VIII
VIIIa
X
Xa
Va
Protrombina (II)
Trombina (IIa)
V
Proteïna C activa
Proteïna S
Proteïna C + trombomodulina
Via del factor tissular (extrínseca)
Traumatisme
TFPI
VIIa
VII
Factor tissular
Traumatisme
Antitrombina
X
Via comuna
Fibrinogen (I)
Fibrina (Ia)
XIIIa
XIII
Coàgul de fibrina reticulat

Clot retraction

Within 5 to 30 mint. Clot retract with libration of yellowish fluid called serum

Clot lysis

Liquefaction of clot plasma protein globulin contain plasminogen which activate to plasmin causes cleavage of fibrin thread breaking fibrin into smaller fragments called fibrin degradation products

Bleeding time

Is a time interval between escape of blood and stoppage of bleeding

It is 1 to 3 minutes

Clotting time

Is time interval between escape of blood and formation of clot

It is 4 to 8 minutes

Prothrombin time is 12 seconds

Bleeding disorder

Hemophilia is sex linked inherited diseases

Affecting males and females are carrier

hemophilia is due to lack of hemophilic clotting factor due to lack of prothrombin activator clotting time is prolong and bleeding time normal

Hemophilia is rare bleeding disorder in which blood doesn't clot normally or there is impair body's ability to form clot

Patient may bleed for longer time than other after injury ,may also bleed inside(internally) esp. in knees ,ankles, elbows

In general symptoms are internal or external bleeding episodes which are called “ bleed”

There are two types of hemophilia

1)Hemophilia A

2) Hemophilia B

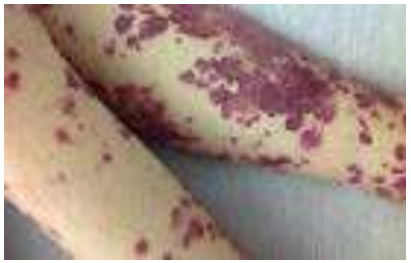
3)Hemophilia C

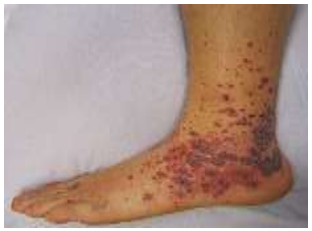
It is also known as royal disease because queen Victoria passes the mutation for hemophilia B to her son and daughter then to various royals family from Spain ,Germany ,Russia

It can be controlled by regular infusion of deficient clotting factor. life expectancy decreases

Purpura is red purple discolored spot on skin that doesn't blanch on applying pressure

That spot is caused by bleeding underneath the skin is due to deficiency of platelets





1) thrombocytopenic purpura due to deficiency of platelets
2) Thrombostenic purpura is due to abnormal platelets in circulation
3) Idiopathic thrombocytopenic purpura is due to unknown cause

Von will brand disease

bleeding disorder excessive bleeding even with mild injury.

Deficiency of vw factor

It is a protein librated by platelets and endothelium of damaged tissue

Thrombus

Is a clot formed inside blood vessel

Thrombus may form due to slowing of circulation and damaged of vascular endothelium

Athermanous patches occur in blood vessel and vascular endothelium damage in some abnormal condition masses of platelets are deposited on the damaged endothelium


THROMBUS
shutterstock

Sometimes intravascular thrombus occur in

Coronary and cerebral vessels which are called coronary thrombosis and cerebral thrombosis

DIC

Widespread clotting mechanism

Embolus

process in which thrombus or part of it is detached and carried in blood stream to arrest the blood flow in any part


AB⁻
O⁻
A⁺
O⁺
B⁻
B⁺
A⁻
AB⁺

Blood groups

there are different blood group

According to **Landsteiner** (1901)different people have different antigenic and immune properties according to which there are different blood group

ABO blood group system

Normally RBC

membrane contains antigen called **antigen**

Or **agglutinogen** which respond to corresponding **antibodies** present in plasma known as **agglutinin**

According to ABO blood group system there are two such antigen i.e. A&B

1)So person whose RBC membrane contain A antigen such person is belongs to blood group A

2)Person whose RBC membrane contain B antigen is of blood group B

3)Person whose RBC membrane contain both antigen belongs to blood group AB

Person whose RBC membrane don't contain any antigen belongs to **blood group O**

Against each antigen antibodies present in plasma like against A antigen antibodies B present

Blood group	agglutinogen	agglutinin
A	A	B
B	B	A
AB	A &B	NIL
O	NIL	antibody A&B

Once we know individual

blood group its antigen &antibodies blood transfusion done safely

During transfusion **plasma agglutinin of donor** mixed up **with recipient plasma** become so much diluted so it looses its effectiveness &**usually ignored**

But **donors antigens** meet with **recipients undiluted antibodies** in recipients body &

if it is mismatched then certain hazards occur so to avoid it . One should know compatibility

Donors group	RECIEPIENTS group			
	A	B	AB	O
A	Yes	No	Yes	No
B	No	Yes	Yes	No
AB	No	No	Yes	No
O	Yes	Yes	Yes	Yes

- **Universal red cell donors**: People with O negative blood don’t have any A, B or Rh antigens on their red blood cells, which means they can donate red blood cells to anyone

their blood cells won’t trigger the recipient’s immune system to “fight” the blood). For this reason, people with O negative blood are referred to as ‘universal donors’.

- **Universal recipients**: People with AB blood group have both A and B antigens on their red blood cells and don’t have antibodies against A or B antigens, which means they can receive red blood cells of any type

their immune system won’t fight them For this reason, they are referred to as ‘universal recipients.’

Cross matching

Blood is collected from donors and recipients

Plasma and RBC separated in each then donors cell are mixed with recipients plasma and recipients cell mixed with donors plasma

If there is **agglutination** recipients blood can be safely receive donors blood

Inheritance pattern	
Parental blood groups	**Child's blood group**
• O and O	O
• O and A	A
• O and B	O or B
• O and AB	A or B
• A and A	A or O
• A and B	O or A or B or AB
• A and AB	Aor B orAB
• B and B	O or B
• B and AB	B or A or AB
• AB and AB	A or B OR AB

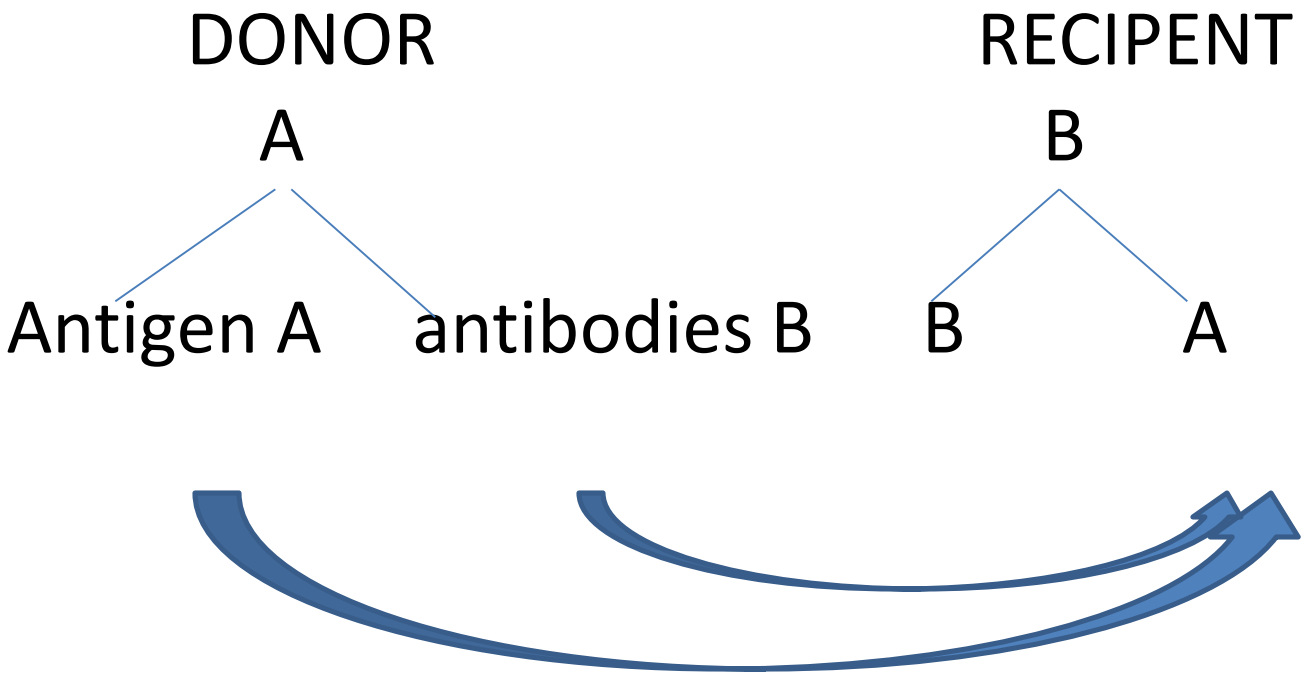
Rh system

Landsteiner and wiener in 1940 discover Rh system

First found in Rhesus monkey .according to this system Cc, Dd, Ee agglutinogens present where D is commonest antigen which is present on RBC membrane

So if person RBC membrane have **D antigen is said to be Rh positive and person whose RBC membrane don’t have D antigen is said to be Rh negative**

Transfusion reaction in ABO system



SO in above transfusion Donors antigen bind &will not dilute in recipients body where as Donors antibodies bind with recipients antibodies and get diluted

1. So mismatched blood transfusion reaction occur lead to **hemolysis of donors RBC in recipients circulation**

2. Breakdown of h**aemoglobin**

3. Increase bilirubin lead to **jaundice**

4 .Haemolysed RBC may form clumps occlude fine vessels of vital organs and cause **infarction**

5 .Due to excess breakdown of haemoglobin there may be **haemoglobinaemia**

6. Free haemoglobin excreted in renal tubule form acid haematin and block renal tubule lead to **anuria** and **renal failure**

clinical importance of Rh blood group

Rh system

D — Rh positive — D antigen

R — Rh negative — no antigen

Antigen enter recipients body

In mean while sensitization occur

And recipients blood produce antibodies

During II nd transfusion if again donor is Rh positive

D

Rh positive

R

Rh negative

Enter antigen in recipients body

Antigen while react with antibodies which are already present during first transfusion will lead to hamolysis

This is more dangerous in **pregnant women who is Rh negative**

if mother is Rh negative and foetus is Rh positive.

normally anatomical arrangement is in such way that maternal blood will not mixed with foetal blood when such ad mixer occur called as **Erythroblasto foetalis**

During pregnancy foetus may be Rh positive

then Rh agglutinogen from the foetus passes into maternal blood and stimulate the formation of Anti Rh factor (through placental barrier)

First baby may born normal

During II pregnancy if again **foetus is Rh positive** then antibodies which already mother is having enter the foetal blood and destroys the red cells of foetus

Foetus may die in uterus (causing miscarriage)

Or born alive ,suffer from **severe anemia** .blastic form in circulation lead to **hydrops foetalis**

May die if at all survive, due haemolysis of RBC increase bilirubin lead to **jaundice**

Bilirubin may cross blood brain barrier and deposited on basal ganglia cause **kerniecterus**

Treatment – anti D Immunoglobulin injection within 24 hr. of first delivery