welcome

ERYTHROPOISIS

Presented by

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I MD Repertory

FUNCTIONS OF BLOOD

1. Respiratory
2. Excretory
3. Nutritional
4. In various homeostatic processes

a) Body temperature and blood

b) Ph and blood

5. In various defence mechanisms-WBC, Lymphocytes, Plasma
6. Transport of other substances-drugs , hormones etc.

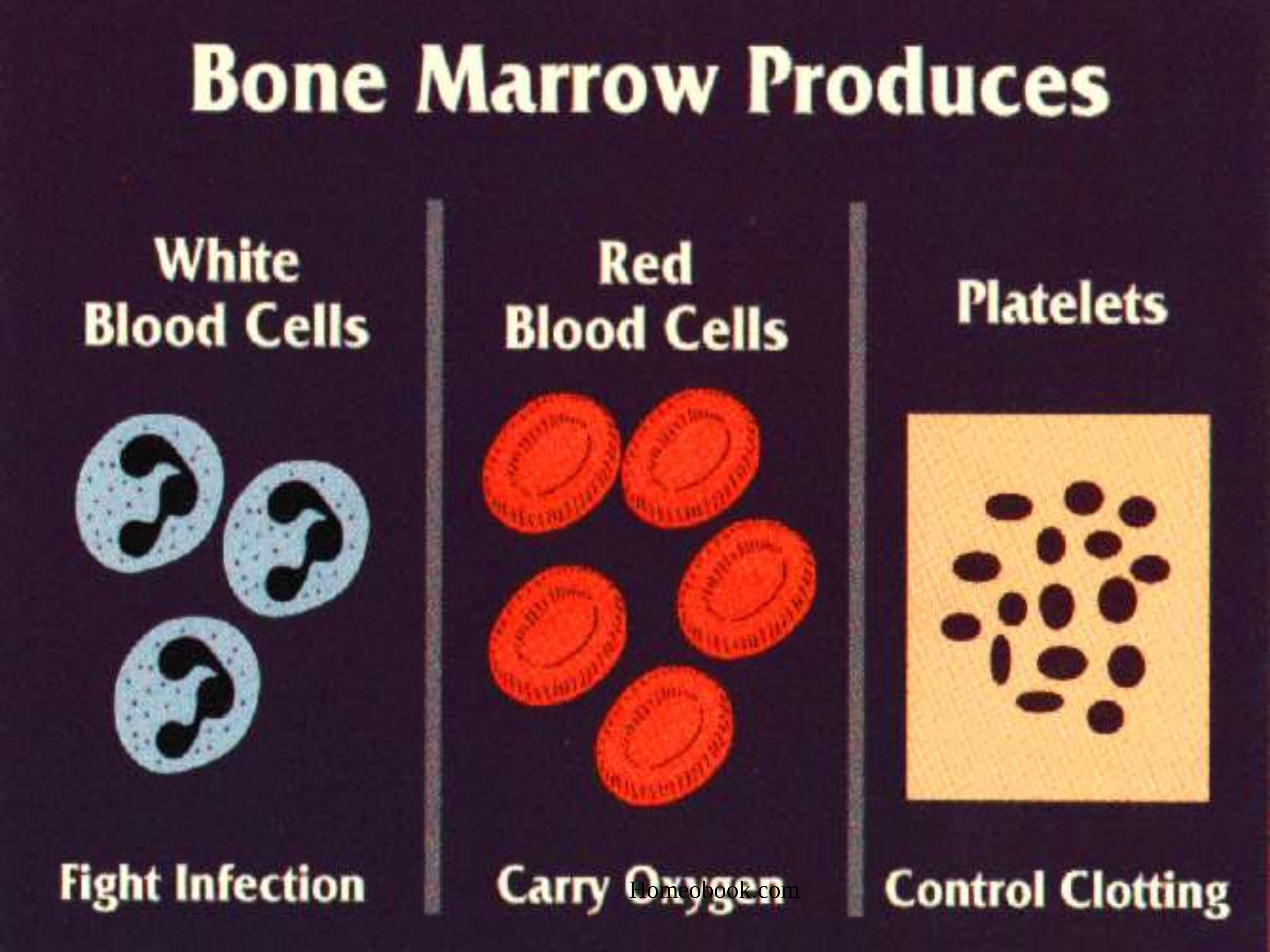
RED BLOOD CELL

- Blood contains plasma & 3 cells

1. Red blood cell,
2. White blood cells &
3. Platelets.

MAJOR FUNCTIONS OF THE FORMED ELEMENTS

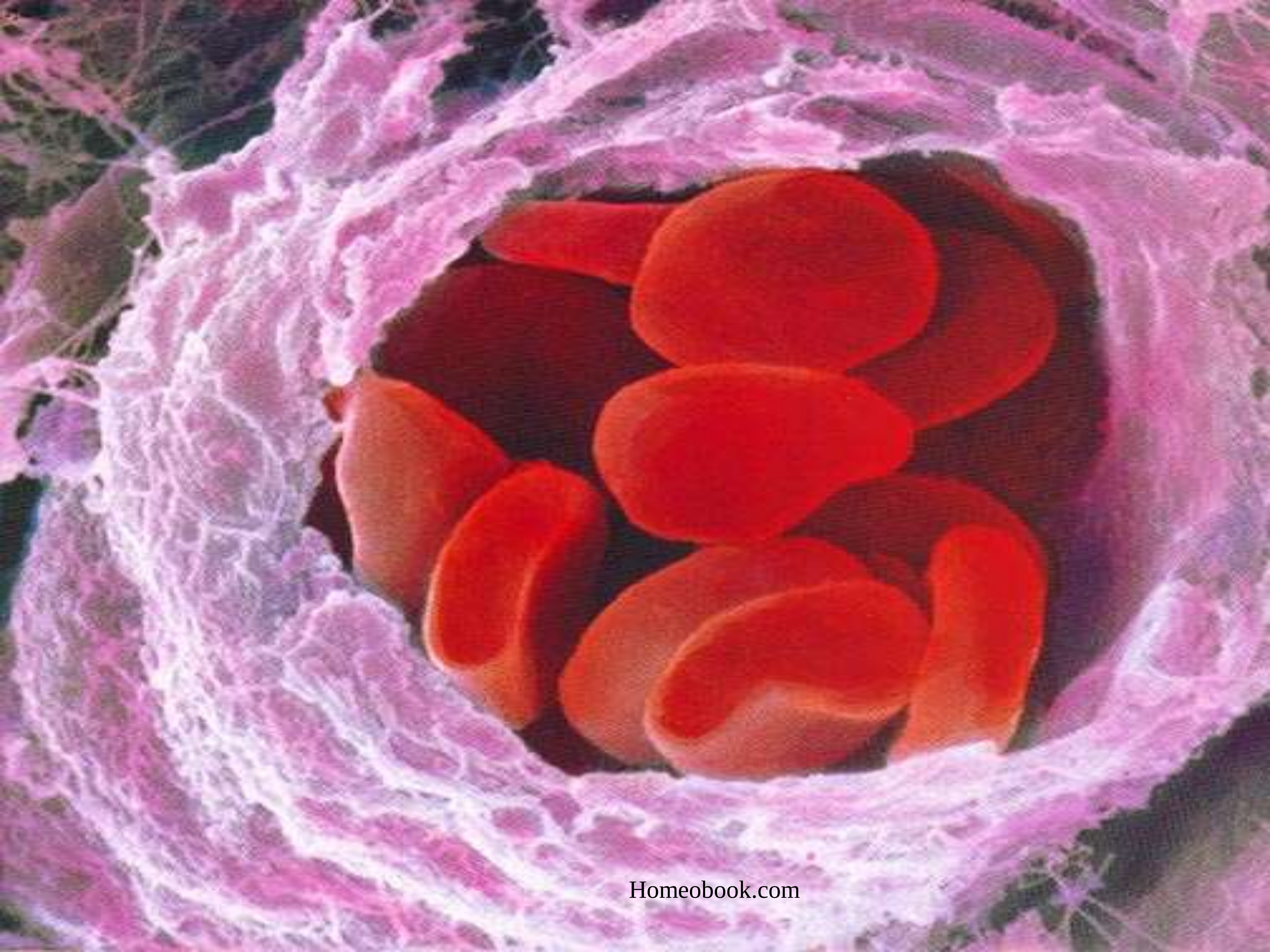
- **ERYTHROCYTES**- carriage of **O**2 from lung to peripheral tissues and carriage of **co**2
- **LEUCOCYTES**- defence of the host against bacterial/viral/foreign body invasion. Defence against cancer
- **PLATELETS**- Hemostasis(arrest of bleeding)


Bone Marrow Produces
White Blood Cells
Red Blood Cells
Platelets
Fight Infection
Carry Oxygen
Control Clotting

Red Blood Cells (Erythrocytes)

The first person to describe red blood cells was the Dutch biologist Jan Swammerdam, who had used an early microscope in 1658 to study the blood of a frog

Red blood cells(**erythrocytes**) are major formed elements of the blood, contain pigmented Hb molecule.



- A schistocyte is a red blood cell undergoing cell fragmentation, or a fragmented part of a red blood cell .
- The color of erythrocytes is due to the heme group of hemoglobin.

Morphology of red blood cells

1. Circular biconcave discs
2. mean diameter of about 7.8 micrometers thickness of 2.5 micrometers at the thickest point and 1 micrometer or less in the center.
3. The average volume of the red blood cell is 90 to 95 cubic micrometers.

- The shape of red blood cells can change remarkably as the cells squeeze through capillaries.
- Actually, the red blood cell is a “bag” that can be deformed into almost any shape, because the normal cell has a great excess of cell membrane for the quantity of material inside, deformation does not stretch the membrane greatly and, consequently, does not rupture the cell.


b

- Advantages of biconcavity of RBC

1. ***Increases the surface area*** ,so that O2 gets a bigger area for diffusion.
2. ***Can squeeze*** itself through a capillary more easily

No nucleus,

no ribosome,

no mitochondria,

no endoplasmic reticulum and centriole.

- The cell membrane contains the usual materials the lipids and proteins some protein materials eg. The glycophorin, contain the blood group antigens.
- Inner side of cell membrane contain **spectrin(contractile) and actin.**

Concentration of Red Blood Cells in the Blood.

- In men, the average numberof red blood cells is 4.5-6.5$\times 10^{6}$ cells / per cubic millimeter
- In women, it is3.8-5.8 $\times 10^{6}$ cells / per cubic millimeter
- Persons living at high altitudes have greater numbers of red blood cells.

Quantity of Hemoglobin in the Cells.

- Red blood cells have the ability to concentrate hemoglobin in the cell fluid up to about 34 grams in each 100 milliliters of cells .
- The concentration does not rise above this value, because this is the metabolic limit of the cell’s hemoglobin- forming mechanism.

when haemoglobin formation is deficient, the percentage of haemoglobin in the cells fall and the volume of the red cell may also decrease

ERYTHROPOIESIS

- **Introduction**
- Normally loss of huge quantity of RBC occurs daily
- In order to compensate Erythropoiesis occurs
- starts in 3rd week of intra uterine life and continues as long as the person remains alive.

- Blood forming tissues , that is , tissues which produce the RBC's , WBC's ,and platelets are divided into

1. Myeloid tissue and
2. Lymphoid tissue

- Myeloid tissue means the **red bone marrow**.
- It produces the RBC's, the granulocytes(neutrophils, eosinophils and basophils), monocytess and platelets.
- In the fetal life it also produces the precursors of the lymphocytes

- Lymphoid tissue include the **lymph nodes, the thymus and the spleen**.
- They produce the lymphocytes.

Site of erythropoiesis.

- In the intra uterine life

Mesoblastic stage

1. starts in 3rd week of intra uterine life.
2. 3rd week – 3rd month of intra uterine life, primitive, nucleated red blood cells are produced in the mesoderm of *yolk sac* (intra vascular erythropoiesis)

- 3rd month - 5th month, the *liver* is the main organ for production of red blood cells, also produced in the *spleen* and *lymph nodes*.this phase is called the *hepatic phase*.

- 5th month onwards and after birth,red blood cells are produced exclusively in the *red bone marrow.* This phase is thus called the **myeloid phase.**
- By the time when baby is born , all erythropoiesis occurs in red bone marrow.

–Post natal erythropoiesis

- As stated early , this occurs normally in the red bone marrow

DISTRIBUTION OF THE RED BONE MARROW

- Two types 1)red and 2)yellow.
- Blood formation including erythropoiesis occurs in red bone marrow only.
- At birth all marrows are RBM’s
- In an adult, over age of 20 yrs , RBM can be found only in the 1) flat bones(cranial bones, ribs, sternum , vertebra, pelvic bones) and 2) in the upper end of the long bones(humerus and femur)

Extramedullary hemopoiesis

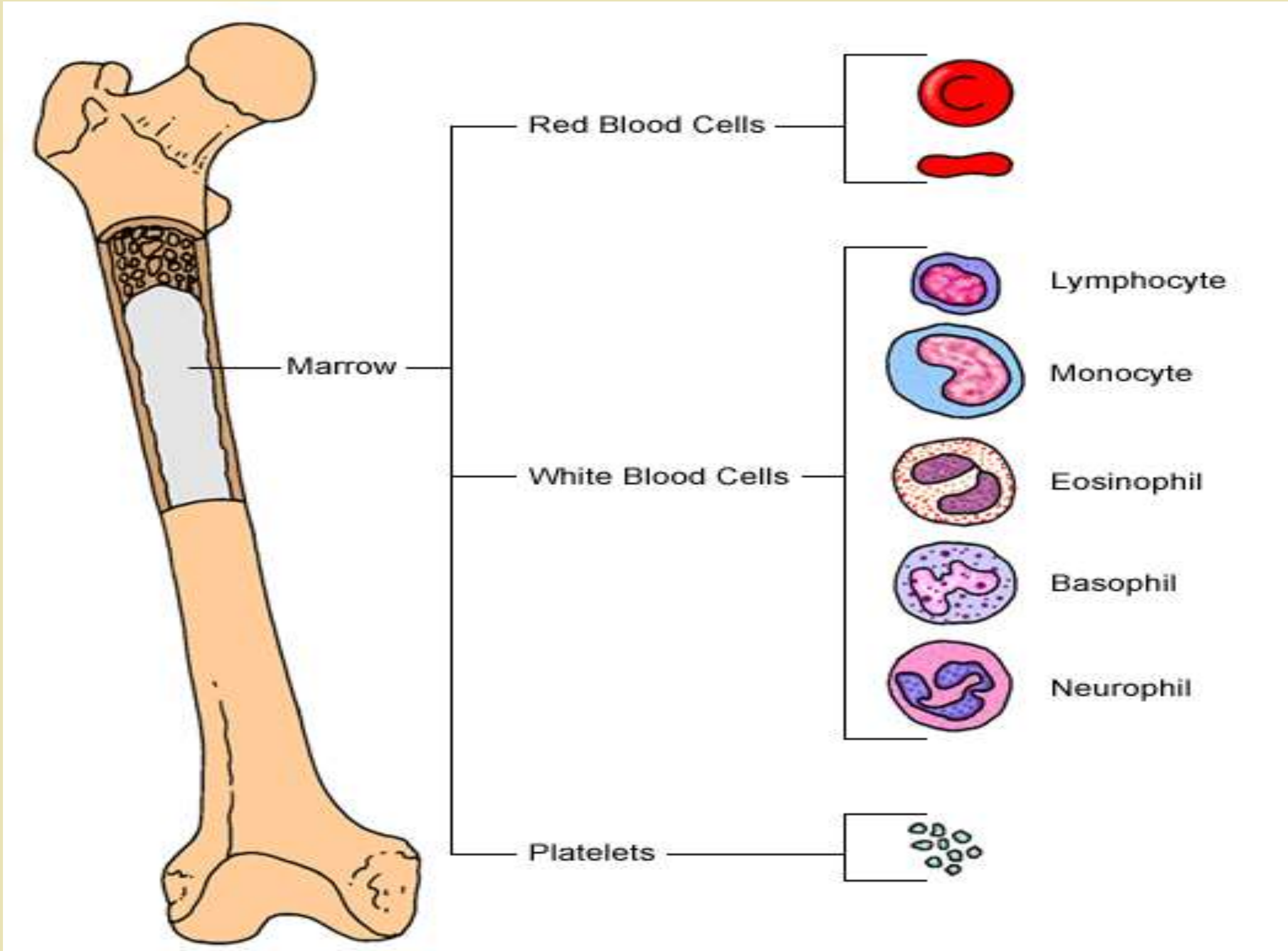
- when there is necessity of increased erythropoiesis, the YBM is converted into RBM. If necessity is still more intense , even the liver and spleen starts erythropoiesis in the adult(the thymus never forms blood cells, whatever may be the intensity of demand) . these are instances of ***extramedullary hemopoiesis*** (medulla= bone marrow) and may be seen in some diseases.

HISTOLOGY OF THE RBM

- The RBM consists of

1. Large no of sinusoids
2. Adventitious cells outside the sinusoids and
3. Blood forming cells between the adventitious cells

- Sinusoids are capillaries with larger diameters. Their walls contain big pores which big molecules and blood cells can pass. The sinusoids criss cross with one another forming a network.
- The adventitious cells eventually become fat cells.
- The blood cells are the precursors of the erythrocytes, leukocytes and platelets.


Red Blood Cells
Marrow
White Blood Cells
Platelets
Lymphocyte
Monocyte
Eosinophil
Basophil
Neurophil

THE NORMAL RED BONE MARROW BLOOD CELL PICTURE

1. Granulocytes and their precursors 60%
2. Erythrocyte and their precursors 20%
3. Lymphocytes,monocytes &their precursors10%
4. Others(non identifiable&degenerated cells)10%

- For bone marrow examination ,In case of anemia,, in adult, the sternum is punctured and the RBM aspirated.
- In children as sternum puncture is risky tibia or pelvic bone is usually punctured.

STAGES OF DEVELOPMENT

- **The most primitive cell is called the "pluripotent stem cell".**
- **This cell divides and differentiates and can give rise to erythrocyte, granulocyte, monocyte,lymphocyte & platelets.**

- The pluripotent stem cells give rise to the "**commited stem cells**" .
- one type of commited stem cells give rise to myeloid series(RBC, granulocytes,monocytes & platelets). Other type of commited stem cells give rise to lymphocytes.

Cells commited to produce the myeloid series now divide and differentiate further to produce the daughter cells called

“the progenitor cells”

. one type of progenitor cells give rise to cells of erythroid series, another granulocyte-monocyte and so on.

- Progenitor cells are also called **“the colony forming unit”** ,ex: CFU-E, CFU-GM etc.

- For RBC there are two progenitor cells
- 1) BFU-E(burst forming unit erythrocyte) &
- 2)CFU-E

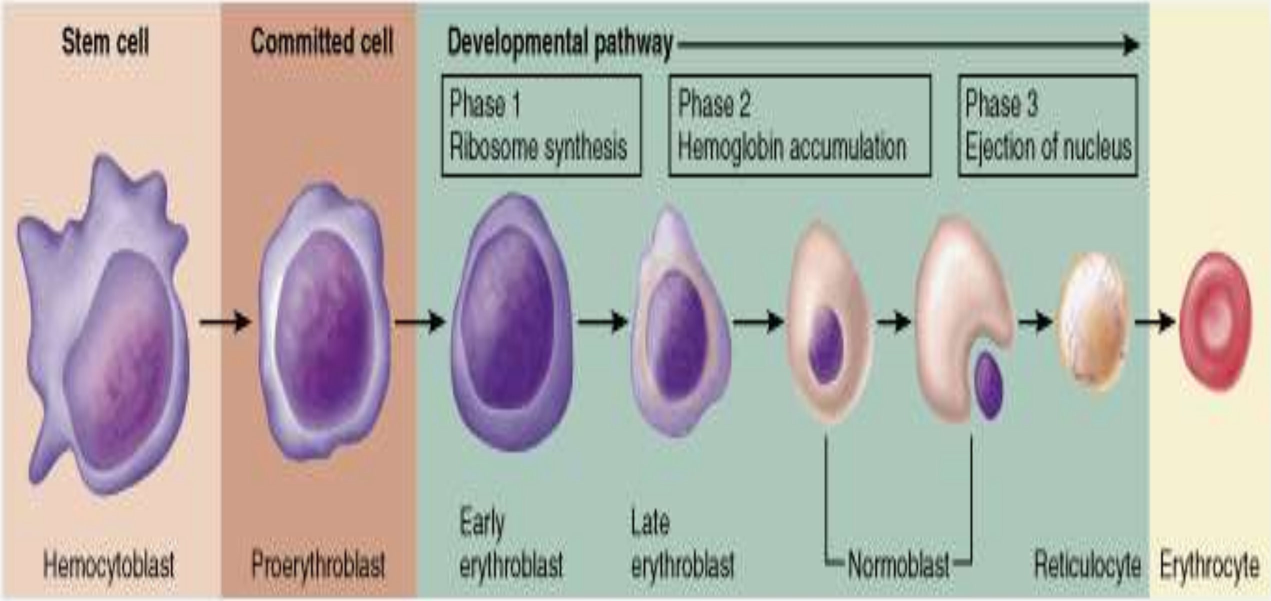
- **From the progenitor CFU-E, the *pronormoblast cell* (which is the first in the series of the morphologically recognisable cell in the erythroid series) develops.**
- It has a large nucleus with free ribosomes in the cytoplasm giving the cytoplasm a basophilic appearance.

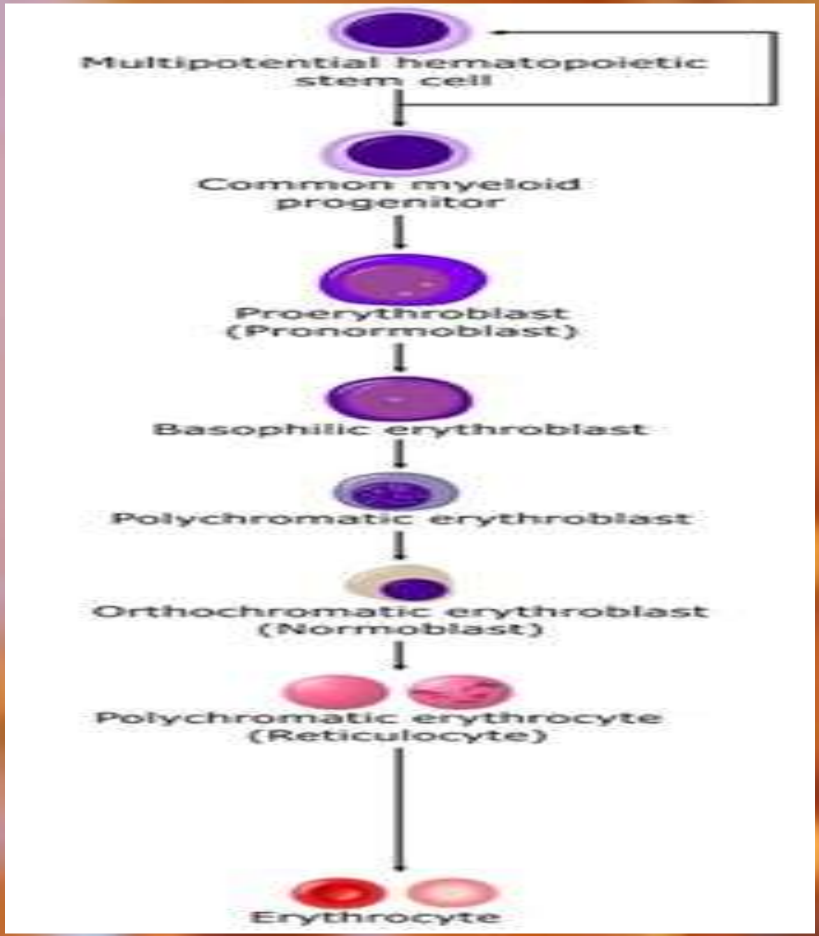
- **From the pronormoblast, *early normoblast*(large basophilic normoblast) develops.**
- Smaller than the proerythroblast with a smaller nucleus but a more basophilic cytoplasm due to increased numbers of ribosomes in the cytoplasm.
-

- **Early normoblast inturn , gives rise to *intermediate normoblast* (polychromatophilic normoblast).**
- This is the last precursor cell capable of mitosis and is smaller than the basophilic erythroblast. Its cytoplasm appears greyer due to the increased acidophilic staining caused by the presence of ***haemoglobin***.

- **From intermediate normoblast develops the *late normoblast* (orthochromatic normoblast).**
- slightly larger than a mature erythrocyte but it does contain a small dense nucleus, deeply stained (***pyknotic nucleus)*** . Hb present in fair amount.

- **From late normoblast develops the reticulocyte.**
- Nucleus absent
- **The reticulocyte inturn gives rise to the matured RBC.**
- **Normally , the reticulocyte matures for one or two days in the bone marrow and then enters the peripheral blood. When the cell enters the peripheral blood it is still not a matured RBC, but a reticulocyte in advanced stage of maturation.**


Stem cell
Committed cell
Developmental pathway
Phase 1
Ribosome synthesis
Phase 2
Hemoglobin accumulation
Phase 3
Ejection of nucleus
Hemocytoblast
Proerythroblast
Early
erythroblast
Late
erythroblast
Normoblast
Reticulocyte
Erythrocyte


Multipotential hematopoietic stem cell
Common myeloid progenitor
Proerythroblast (Pronormoblast)
Basophilic erythroblast
Polychromatic erythroblast
Orthochromatic erythroblast (Normoblast)
Polychromatic erythrocyte (Reticulocyte)
Erythrocyte

- In The RBC membrane the contractile material ***spectrin*** is so placed that , the erythrocyte become biconcave.
- Congenital spectrin deficiency leads to the disease , ***hereditary spherocytosis***, where RBCs are round and hemolyse easily.

- Time taken for pronormoblast to late normoblast development is 4days;
- from pronormoblast to reticulocyte is about 8days.

- The nucleus becomes smaller and smaller as the cell matures.
- Thus it is very big in pronormoblast stage but pyknotic in late normoblast stage and absent in reticulocyte and RBC.
- The pyknotic nucleus of late normoblast is extruded to form a reticulocyte.

- As the cell becomes more and more mature , the cytoplasm becomes more and more abundant.

- Hb appears on and from the intermediate normoblast stage . because of this the polychromatophilia is seen.
- Gradually Hb increases in amount, until as in matured RBC.

- The cell is capable of dividing (mitotic division) till it becomes intermediate normoblast.
- From this stage onwards, the division ceases and maturation continues. Therefore , in the earlier stages, both cell division and maturation dominates and after the stage of intermediate normoblast all division ceases.

- Why the cytoplasm stains with basic dyes in earlier phases of erythropoiesis whereas it stains with acid dyes like eosin in later phases?

- In the earlier phases, the cytoplasm contains enough RNA and this nucleic acid takes up the basic dyes and thus looks bluish.
- with maturation, Hb which is eosinophilic appears, so that, the cytoplasm becomes reddish.
- In an intermediate stage , some areas in the cytoplasm take basic stain, and some other areas take eosin stain, explaining the polychromatophilic.

STEM CELL

- A stem cell is a primitive cell that gives rise to blood cells like RBC/WBC/platelet. In short a stem cell is a forefather of matured blood cells.
- For normal hemopoiesis about 500 stem cells are necessary.

- A stem cell has two characteristics

1. **self renewal**
2. **differentiating**

Stem cells from one individual can be transfused to another by bone marrow transfusion .

Clone of RBCs:

- all the RBCs derived from a single stem cell belong to a single clone.
- As there are normally , many stem cells , RBCs of a normal person are *polychromatic.*

Blast cells

- normally stem cells cannot be identified by microscope. But blast cells can be identified by microscope.
- Blast cells are immature cells .
- blast cells represent a stage of development of erythroid/myeloid/lymphoid/platelet series.

- Thus in erythroid series there are **normoblasts** (early-intermediate-late);
- in the WBCs , there are **myeloblasts** (neutrophilic /eosinophilic /basophilic) and **lymphoblasts**.
- In the platelet series, there is **megakaryoblast.**

- Blast cells of any kind , should not be normally present in the peripheral blood. Their presence in the bone marrow is a sign of abnormality.

FACTORS INFLUENCING ERYTHROPOIESIS

- Hematopoietic **growth factors- erythropoietin**
- Some **vitamins** and
- **Iron and copper**

Role of Erythropoietin

- The total mass of red blood cells in the circulatory system is regulated within narrow limits, so that (1) an adequate number of red cells is always available to provide sufficient transport of oxygen from the lungs to the tissues, yet (2) the cells do not become so numerous that they impede blood flow.

- **Tissue Oxygenation Is the Most Essential Regulator of Red Blood Cell Production.**
- Any condition that causes the quantity of oxygen transported to the tissues to decrease ordinarily increases the rate of red blood cell production

1. ANEMIA

In anemia, the bone marrow immediately begins to produce large quantities of red blood cells.

- Destruction of major portions of the bone marrow by any means, especially by x-ray therapy, causes hyperplasia of the remaining bone marrow, thereby attempting to supply the demand for red blood cells in the body.

2. high altitudes

- At very *high altitudes,* where the quantity of oxygen in the air is greatly decreased, insufficient oxygen is transported to the tissues, and red cell production is greatly increased. Factor that controls red cell production is the tissue demand for oxygen.

3. cardiac failure and *lung diseases (COPD)*

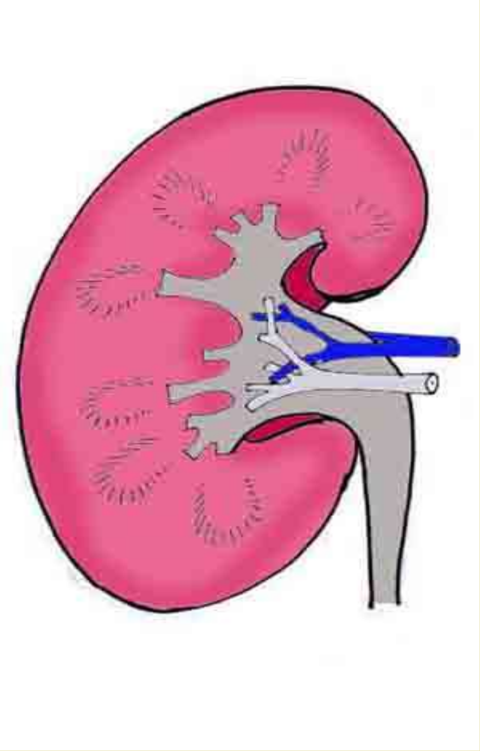
- This is especially apparent in prolonged *cardiac failure* and in many *lung diseases(COPD),* because the tissue hypoxia resulting from these conditions increases red cell production, with a resultant increase in hematocrit and usually total blood volume as well.

Erythropoietin Stimulates Red Cell Production, and Its Formation increases in Response to Hypoxia.

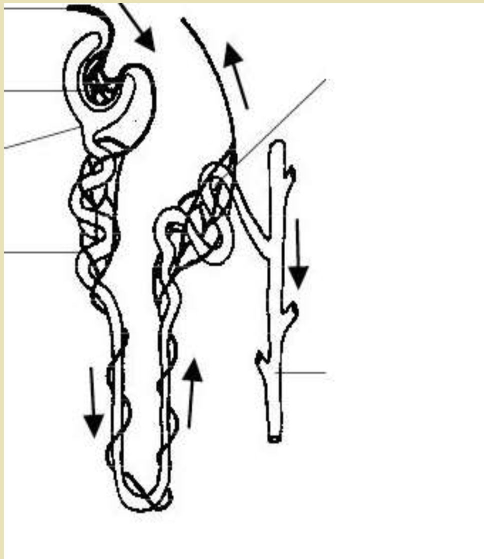
- The principal stimulus for red blood cell production in low oxygen states is a circulating hormone called *erythropoietin,* a glycoprotein with a molecular weight of about 34,000.
- In the absence of erythropoietin, hypoxia has little or no effect in stimulating red blood cell production.

Role of the Kidneys in Formation of Erythropoietin

- 90 per cent of all erythropoietin is formed in the kidneys;
- the remainder is formed mainly in the liver.
- It is not known exactly where in the kidneys the erythropoietin is formed.



- One likely possibility is that the renal tubular epithelial cells secrete the erythropoietin, because anemic blood is unable to deliver enough oxygen from the peritubular capillaries to the ***highly oxygen-consuming tubular cells***, thus stimulating erythropoietin production



- At times, hypoxia in other parts of the body, but not in the kidneys, stimulates kidney erythropoietin secretion

- In particular, both **norepinephrine** and **epinephrine** and several of the **prostaglandins** stimulate erythropoietin production

- When both kidneys are removed from a person or when the kidneys are destroyed by renal disease, the person invariably becomes very anemic
- because the 10 per cent of the normal erythropoietin formed in other tissues (mainly in the liver) is sufficient to cause only one third to one half the red blood cell formation needed by the body.

- When a person is placed in an atmosphere of low oxygen, erythropoietin begins to be formed within minutes to hours, and it reaches maximum production within 24 hours.
- no new red blood cells appear in the circulating blood until about 5 days later.

- Important effect of erythropoietin is to stimulate the production of proerythroblasts from hematopoietic stem cells in the bone marrow.
- once the proerythroblasts are formed, the erythropoietin, further speed up the production of new red blood cells.

- Erythropoietin is now commercially available (produced by recombinant DNA technique) and is administered in 1)chronic renal failure cases undergoing ***dialysis***

  2)patients receiving ***anticancer chemotherapy*** which is producing damage of RBM and anemia

  3) in patients of AIDS receiving ***AIDS chemotherapy***

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VITAMINS

- For erythropoiesis

1. 1)vit. B12.
2. 2)folic acid.
3. 3)pyridoxine and
4. 4)vit. C are needed

Vit. B12

- *Vit. B12 deficiency in human beings , due to dietary deficiency is very rare, but mainly due to* ***fault in absorption.***
- absorption of vit. B12 can be deficient leading to defective formation of RBC. Clinically the condition is called **megaloblastic anemia.**

- An adult human being stores about 5mg. Of vit.B12 in his liver.this storage is enough for 5yrs.

- **Daily requirement: *3-5* µg.**

- In vit. B12 deficiency instead of normoblasts, megaloblasts which are abnormal cells, are found.
- Normoblasts when mature become normocyte or normal RBC, but Megaloblasts when mature produce mainly larger than normal red cells called *macrocytes.*

- lack of vit. B12 causes some abnormality of DNA → 1) there is no cell division but cytoplasmic accumulation remains unhampered leading to bigger sized abnormal cells called megaloblasts

  2) many of the precursor cells die leading to anemia.

- Vit. B12 deficiency also causes some neurological disorders.
- ***Demyelination*** and death of neurons occur in spinal cord and brain leading to paralysis and /or sensory disturbances and/or insanity.

FOLIC ACID

- 5,10 Methylene THF,which is active form of Folate fot DNA synthesis.

(mitosis.)

- Peripheral blood or RBM reveals macrocytic megaloblastic anaemia—just as in Vit B12 deficiency anaemia.
- In Folic Acid defiency neurological disorder doesnot occur

- Daily requirement of Folic Acid in non – pregnant persons is 50µg but in pregnancy requirement rises.
- Total body reserve for Folic acid is 5-20mg which can last for only few months .

Pyridoxine&Vit C

- Spontaneously occurring pure Pyridoxine deficiency anaemia must be very rare in man .
- Vit C deficiency can lead to anaemia

Influence of endocrine hormones

- Androgens
- Hypothyroidism

Applied physiology

- 1.Common conditions where erythropoesis is deficient
- ***1.Bonemarrow hypofunction***(BM hypoplasia or aplasia).Here not only the erythropoesis but the entire haemopoesis suffers.
- ***2.Lack of erythropoetic factors*** like VitB12,Folate, VitC ,Iron.
- ***3.Excessive blood transfusion***

- 2.Common conditions where erythropoesis becomes excessive
- 1.***Anaemia***(provided the RBM is healthy)
- 2.Where there is ***excessive Erythropoetin*** generation.eg;COPD,high altitude

- Reticulocyte count is assessed by the number of reticulocytes per every 100 RBCs in peripheral blood.

- A high reticulocyte count (more than 3%) indicates stepped up erythropoesis
- low reticulocyte count(less than 0.5%) indicates suppression of RBM.

Metabolism of RBC

- Because of absence of mitochondria, ribosome, RER,nucleus etc. In mature RBC, many metabolic processes are absent . thus, TCA cycle of Krebs is absent in the RBC and generation of ATP is poor.

- Nevertheless, glucose is metabolised within the RBC and energy in the form of ATP are present.

- 90% glucose entering the RBC is utilised for energy synthesis in the form of ATP & reduced nucleotides (NAD & NADPH) by ***EMBDEN-MEYERHOFF PATHWAY***

- 10% glucose entering the RBC is utilised for energy synthesis in the form of reduced NADP by ***PENTOSE MONOPHOSPHATE PATHWAY***

Metabolism in the RBC is needed for the following reasons;

- 1. For maintaining the **sodium potassium pump.**

  Lack of energy in the RBCs cause them to become rigid , fragile and spheroidal in shape, all leading to their lysis as they pass through the spleen.

2. The enzyme methemoglobin reductase together with NADH prevents the iron to become ferric iron and **prevent oxydative damage** by methemoglobinemia

Erythrocyte sedimentation rate(ESR)

- anticoagulant (sodium citrate)
- rouleaux formation,
- clear supernatant plasma above, whose length in mm after the end of 1^{st} hour

- Normal values of ESR in male

  1-10 mm/1hr

- Normal values of ESR in females

  3-15mm/hr

- Rouleaux formation increases when there is increase of ***plasma fibrinogen*** and ***γglobulin***.
- Most infections , inflammations and destructive diseases cause increase of γglobulins (including fibrinogen).
- Therefore ESR increases in most acute as well as in chronic infections, collagenous disease(eg. RA), tuberculosis ,cancers etc.

- A rise in ESR indicates the presence of infective/inflammatory/destructive disease *but does not help in specific diagonosis*
- ESR values are important for prognostication as well as for assessment of progress in a person under treatment.

Life span of RBC

- Normally the life span of RBC is 120 days

fate of RBC

- As the age of RBC increases, the enzymes which protect the erythrocyte from the damaging effects of oxygen begin lose their efficiency, therefore oxidative damages begin to appear and RBC becomes rather rigid, spheroidal and fragile

fate of RBC.....

- During circulation the erythrocytes pass through the spleen where RBCs have to pass through vessels whose diameters are very narrow, and the fragile RBCs as a result are ruptured.
- Only the completely young and healthy RBCs with a sufficient degree of biconcavity (‘**discocyte**’) can survive.

fate of RBC....

- Spleen is the slaughter house for the RBCs. But when the erythrocytes are diseased , their fragility increases and they break down when passing through other structures also, particularly liver.

- **PCV**: whole blood mixed with a suitable anticoagulant is centrifuged in *wintrobe's hematocrit tube for a long time.* All the blood cells become packed at the bottom . thus PCV (hematocrit value) can be obtained.
- Normally PCV is about 45 in 100ml of blood.

RBC INDICES

- An average matured RBC has
- 1) volume
- 2) Hb content
- 3) Hb saturation
- In anemia, for diagonosis of type as well as the assessment of the intensity , response to treatment etc . these values should be estimated.

MCV

means mean corpuscular volume, ie.
Volume of an average RBC

Calculation:

$$MCV = \frac{PCV \times 10}{\text{No. Of millions of RBC}/\mu l} \text{ cub } \mu$$

- **Normal value of MCV=90 cubic micron.**

1. Value higher than 100= macrocyte seen typically in vit. B12 – folate deficiency anemia
2. Value less than 80microcyte seen typically in iron deficiency anemia
3. Values between 80-90= normal=normocytosis

MCH

- **MCH** = quantity of Hb in average RBC

- MCH= Hb in 100 ml of blood × 10
  -- pg
  No. Millions of RBC/ µl

$$MCH = \frac{\text{Hb in 100 ml of blood} \times 10}{\text{No. Millions of RBC}/\mu l}\ \text{pg}$$

- **Normal value: 28-30 pg.**

MCHC

MCHC =quantity of Hb present in 100 ml of RBC(not 100ml of blood)

$$MCHC = \frac{\text{Hb in grams /100ml} \times 100}{PCV}$$

- Normal value: 34%,
- MCHC can’t be more than 34% because in normal persons an RBC holds maximum amount of Hb which can be held.

Colour index(CI)

- **14.5 gm Hb is regarded as 100% Hb. Similary 5 million/ µl is 100% RBC. Therefore if a person has 14.5 gm Hb and 5 million/ µl RBC, his CI will be 1. Range of CI is .9-1%**

$$CI = \frac{\%\text{ of Hb}}{\%\text{ of RBC}}$$

Low CI seen in microcytic anemias and high in macrocytic anemias

Aplastic Anemia

Bone marrow aplasia means lack of functioning bone marrow. For instance, a person exposed to gamma ray radiation from a nuclear bomb blast can sustain complete destruction of bone marrow, followed in a few weeks by lethal anemia. Likewise, excessive x-ray treatment, certain industrial chemicals, and even drugs to which the person might be sensitive can cause the same effect.

Erythroblastosis fetalis

- Rh-positive red blood cells in the fetus are attacked by antibodies from an Rh-negative mother. These antibodies make the Rh-positive cells fragile, leading to rapid rupture and causing the child to be born with serious anemia.
- The extremely rapid formation of new red cells to make up for the destroyed cells in erythroblastosis fetalis causes a large number of early *blast* forms of red cells to be released from the bone marrow into the blood.

Polycythemia

- **Secondary Polycythemia.** Whenever the tissues become hypoxic because of too little oxygen in the breathed air, such as at high altitudes, or because of failure of oxygen delivery to the tissues, such as in cardiac failure, the blood-forming organs automatically produce large quantities of extra red blood cells. This condition is called *secondary polycythemia,*
- and the red cell count commonly rises to 6 to 7 million/mm3,about 30 per cent above normal.

- A common type of secondary polycythemia, called *physiologic polycythemia,* occurs in natives who live at altitudes of 14,000 to 17,000 feet, where the atmospheric oxygen is very low.The blood count is generally 6 to 7 million/mm3;
- this allows these people to perform reasonably high levels of continuous work even in a rarefied atmosphere.

Polycythemia Vera (Erythremia).

- a pathological condition
- Polycythemia vera is caused by a genetic aberration in the hemocytoblastic cells that produce the blood cells
- in which the red blood cell count may be 7 to 8 million/mm3 and the hematocrit may be 60 to 70 percent instead of the normal 40 to 45 per cent.

- The blast cells no longer stop producing red cells when too many cells are already present.
- It usually causes excess production of white blood cells and platelets as well.
- the viscosity of the blood in polycythemia vera sometimes increases from the normal of 3 times the viscosity of water to 10 times that of water

Pathological variations

- **VARIATION IN SIZE**
- microcytes – iron deficiency anaemia, prolonged forced breathing, increased osmotic pressure in blood
- macrocytes – megaloblastic anaemia, muscular exercise, decreased osmotic pressure in blood.
- anisocytosis – pernicious anaemia

VARIATION IN THE SHAPE

- Crenation – shrinkage as in hypertonic solution
- Spherocytosis – globular form as in hypotonic solution
- Sickle cell – cresentic cell as in sickle cell anaemia
- Poikilocytosis – unequal shapes due to deformed cell membrane.

- **VARIATION IN STRUCTURE**
- Punctuate basophilism : The striated appearance of RBC by the presence of dots of basophilic materials(porphyrin) is called punctuate basophilism. It occurs in conditions like lead poisoning.
- Rings : Ring or twisted strands of basophilic material appear in the periphery of the RBCs. This is called the goblet ring. This occurs in various types of anaemia.

SYNTHESIS

- **GENERALS - LABORATORY findings - erythrocytes - decreased**
- acetan. benzol. calc-ar. irid-met. lec. mang-act. nat-n. plb. trinit. zinc.

ACETANILIDUM (Antifebrinum)

- Depresses heart, respiration and blood pressure, lowers temperature.
- Cyanosis and collapse. Increased susceptibility to cold.
- *Destroys red blood corpuscles*;
- pallor.

BENZENUM-COAL NAPHTHA BENZOL $C_6 H_6$

- Influence on the circulatory system.
- causes a slowing of the pulse stream.
- In the human provers it resulted in a ***decrease of the red cells and increase of white cells.***
- It ought to be of use in Leukaemia.

CALCAREA ARSENICOSA (calc-ar.)

- FEAR OF BIRDS
- - ANXIETY: about future, health.
- - *Slightest emotion causes palpitations.*
- *CHILLY.* obesity
- Epilepsy and heart diseases;palpitation
- ***Nephritis. Kidney region sensitive to pressure***
- ***Hb and red corpuscles are low***

IRIDIUM METALLICUM (The Metal)

- Intestinal putrefaction and septicaemia.
- ***Anaemia, increases red corpuscles***.
- Exhaustion after disease.
- ***Nephritis of pregnancy.***
- Head.-Though confused. "Woodeny" feeling in right side of head.

LECITHIN (lec.)

- Acts on blood
- ***Used in anaemia*** and convalescence, neurasthenia and insomnia.
- ***Increasing the no. of red corpuscles and amount of Hb.***
- Excellent galactogoge
- Head- pulsating and ringing in ears

MANGANUM ACETICUM

- ***Causes anaemia with destruction of RBC***
- Jaundice,***nephritis and albuminurea***
- Fatty degeneration of liver
- Syphilitic and chlorotic pts with general anemia and paralytic symptoms
- Growing pains and weak ankles
- ALL TROUBLES SETTLE IN THE EARS. Pain from other organs ext. to and concentrating in ears.
- Deafness in damp weather. Whistling, tinnitis

NATRUM NITRICUM (Nitrate of Sodium)

- Haemoglobinuria
- ***Anaemia and hydraemia***. Exhaustion, must rest frequently when walking.
- Heart.- Pain in region of heart. Pulse slower and softer.

PLUMBUM METALLICUM (plb.)

- ***Rapid reduction in no. of RBC. pallor***
- Progressive muscular atrophy, rapid emaciation.
- Constrictive sensation with desire to stretch
- Acute nephritis
- Tinnitis , fainting
- Cardiac weakness,pulse small,soft,dichrotic
- Face -Skinny, earthy hue
- Blue line along margins of gums.
- Palpitations
- Constipation

TRINITROTOLUENUM (trinit.)

- ***Destructive action of T.N.T. on the red blood corpuscles is responsible for the anemia and the jaundice*** with their secondary Symptoms like breathlessness, dizziness, headache, faintness, palpitation, undue fatigue, muscle cramps and cyanosis;
- Later stages of the poisoning produce toxic jaundice and aplastic anemia

ZINCUM METALLICUM

- OVER-STIMULATION OF NERVOUS SYSTEM, leading to exhaustion of it.
- Defective vitality. Chorea from fright or suppressed eruption.
- Convulsions with pale face and no heat
- ***Marked aneamia with profound prostration***
- ***Causes dicrease in the no. and destruction of RBC***

- **GENERALS - LABORATORY findings - erythrocytes - increased**
- cortico.

- **GENERALS - ANEMIA - hypochromic**
- beryl.
- **GENERALS - ANEMIA - macrocytic**
- beryl.

- **GENERALS - ANEMIA - nutritional complaints; from**
- alet. alum. *Calc-p.* ferr. ferr-p. helon. nux-v.

ALETRIS FARINOSA (alet.)

- An anaemic, relaxed condition, especially of the female
- The patient is tired all the time, and suffers from prolapsus, leucorrhoea,
- Marked anaemia. Chlorotic girls and pregnant women.
- Fainting spells, with vertigo.
- Leucorrhoea due to weakness and anemia. Habitual tendency to abortion.

CALCAREA PHOSPHORICA

- Anaemic children who are peevish, flabby, have cold extremities and feeble digestion
- SLOW learning to talk, walk.
- Ailments from MAL-ASSIMILATION.
- Bones become soft, brittle. Fractures don't heal.
- Emaciation. Weakness.
- SLOW CLOSING OF FONTANELLES.
- GROWING PAINS.

- **GENERALS - POLYCYTHEMIA**
- cean. cob-n. cortico. lach. phos. x-ray

CEANOTHUS AMERICANUS (cean.)

- A left-sided remedy generally.
- Anaemic patients where liver and spleen are at fault.
- Marked blood pressure
- Enormous enlargement of the spleen. Splenitis
- Leukaemia

- **MURPHY:**
- Clinical-Blood,general-red blood cells-
- -decay,rapid:***kali phos***
- ***-*** dissolution of – sec
- -irregular, smaller:***apis***

- Clinical-blood, general-polycythemia,blood- carc.,ferr,phos
- Clinical-polycythemia, blood-carc.,ferr,phos
- Clinical-anemia,general- iron, deficiency, anemia- **FERR.,FERR-P,**

ARS,BELL,CALC,CALC-P,CARBN-S,COCC,FERR-AR,FERR-MET,GRAPH,LYC,MANG,NAT-M,NIT-AC,PHOS, PLAT,PULS,SENEC,SEP,SULPH

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THANK YOU …………