Blood system common characteristics. Blood as transport medium and the internal environment of organism.

Prof. Zaporozhets T.Viber +380972420098

WHAT IS BLOOD?

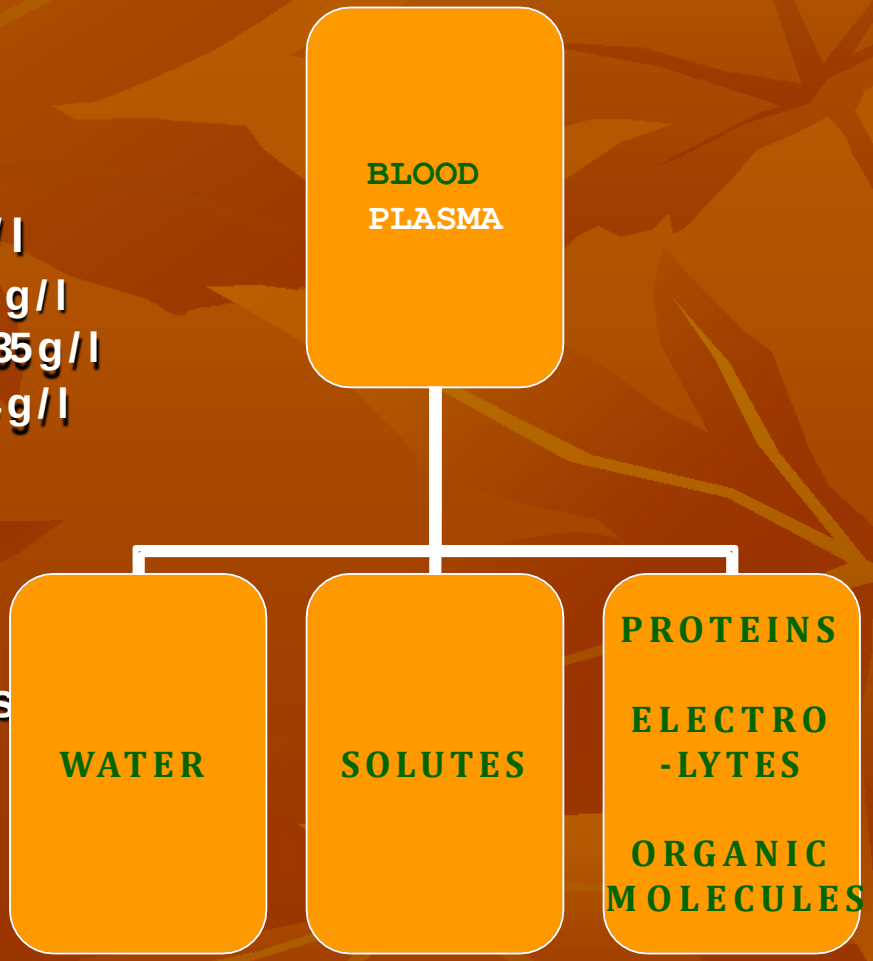
- IT IS A LIQUID CONNECTIVE TISSUE
- IN AN AVERAGE 70 Kg MAN:
  - 100 Trillion cells.
  - Of which 25 trillions are Red Blood Cells!
  - The average blood volume is 5 - 6 lts.
  - It is roughly 7% of the total body weight.

Blood amount

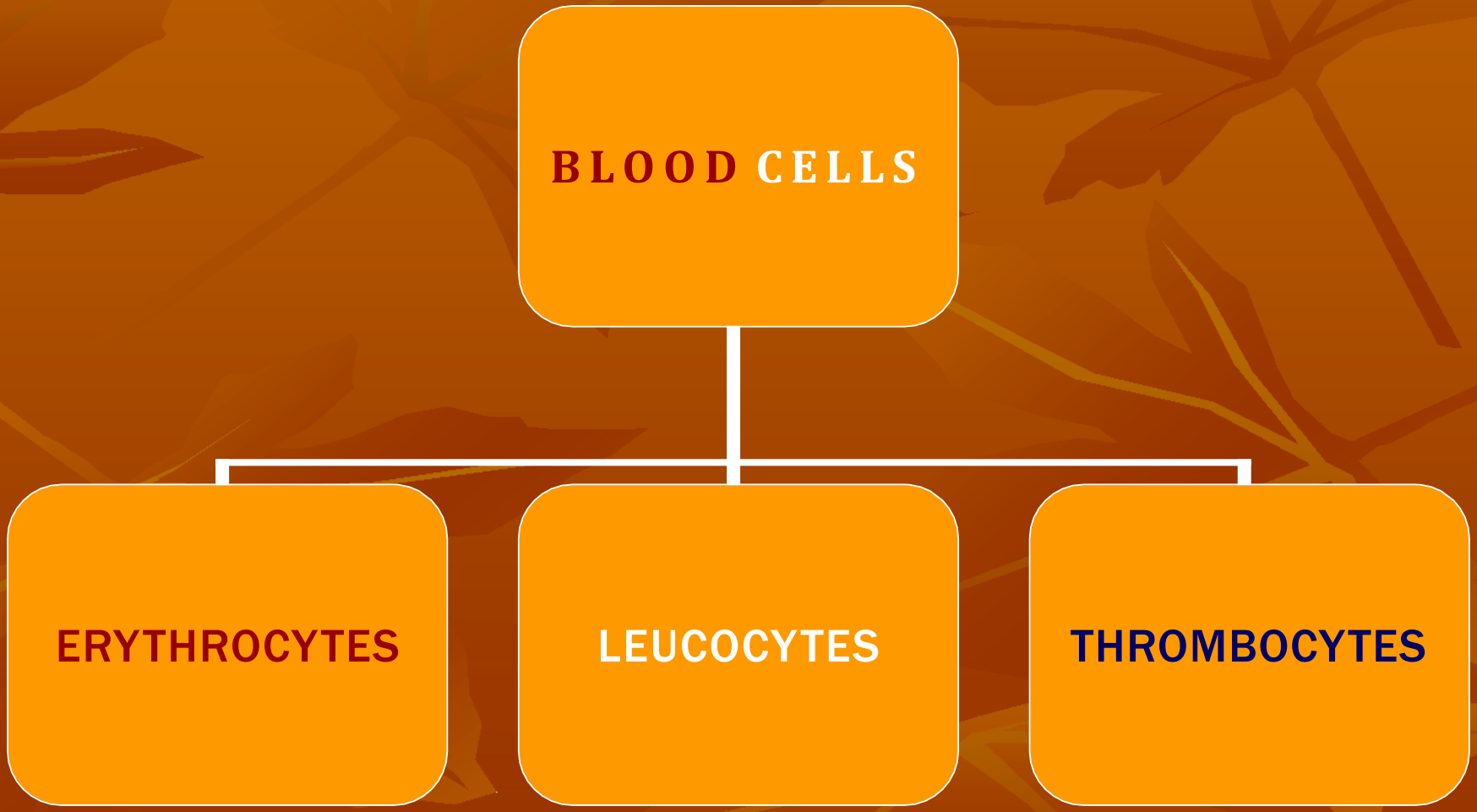
- In newborn – 15% from body
- In 1 year – 10%.
- Normovolemia – normal blood volume;
- Hypovolemia - blood volume decreasing:
- hemorrhage, hard physical activity, hyperthermia.
- Hypervolemia – blood volume increasing.

THE COMPOSITION OF BLOOD PLASMA

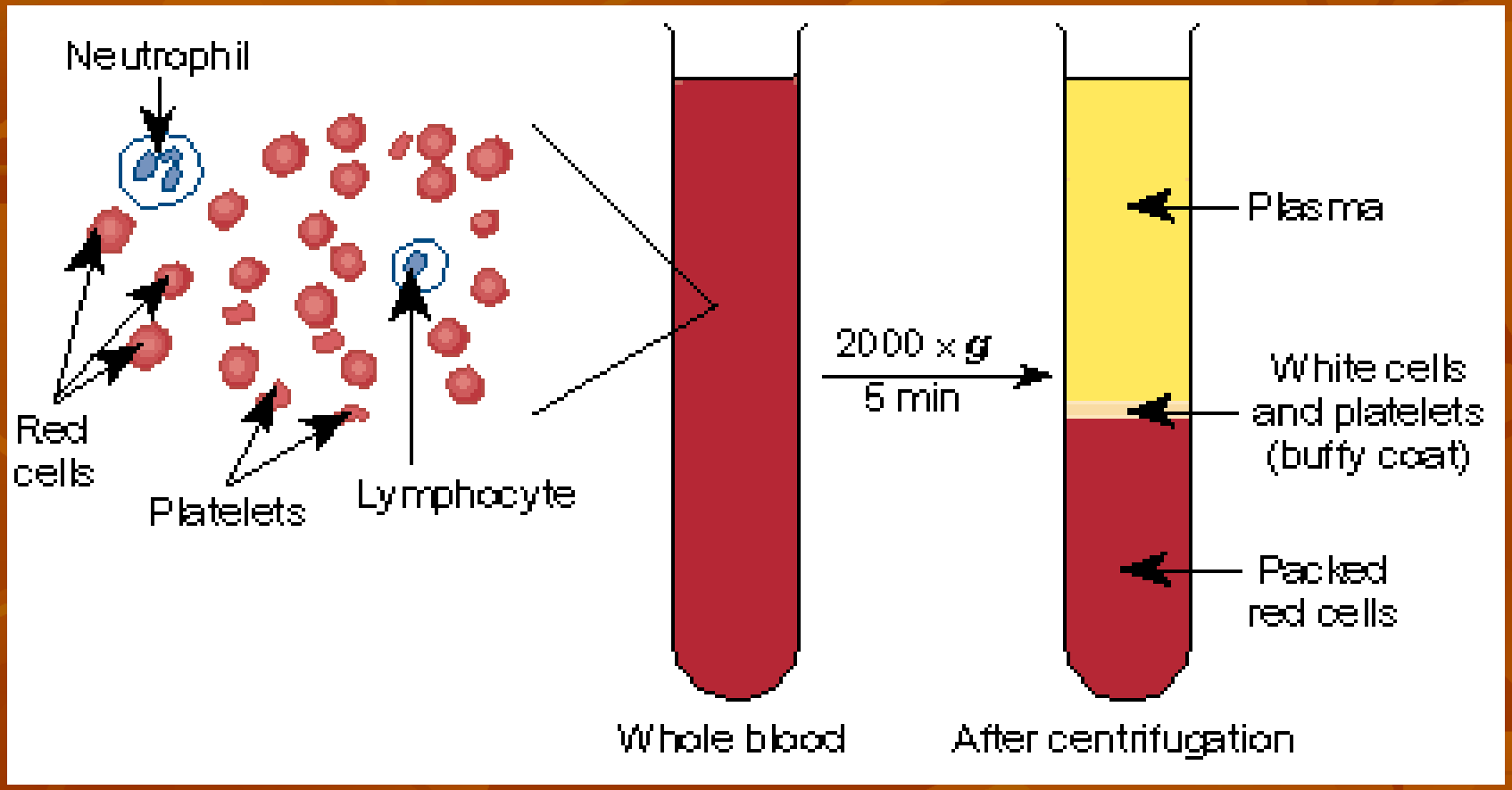
- The Liquid: Plasma:
  - Water, the solvent
  - The solute:
    - Proteins: 65-85 g / l
      - Albumin 35-50 g / l
      - Globulins: 30-35 g / l
        Fibrinogen 2-4 g / l
    - Electrolytes:
      - Na+
      - K+
      - Ca++
    - Organic molecules
      - Urea
      - Glucose
      - Lipids



THE FORMED ELEMENT: CELLS



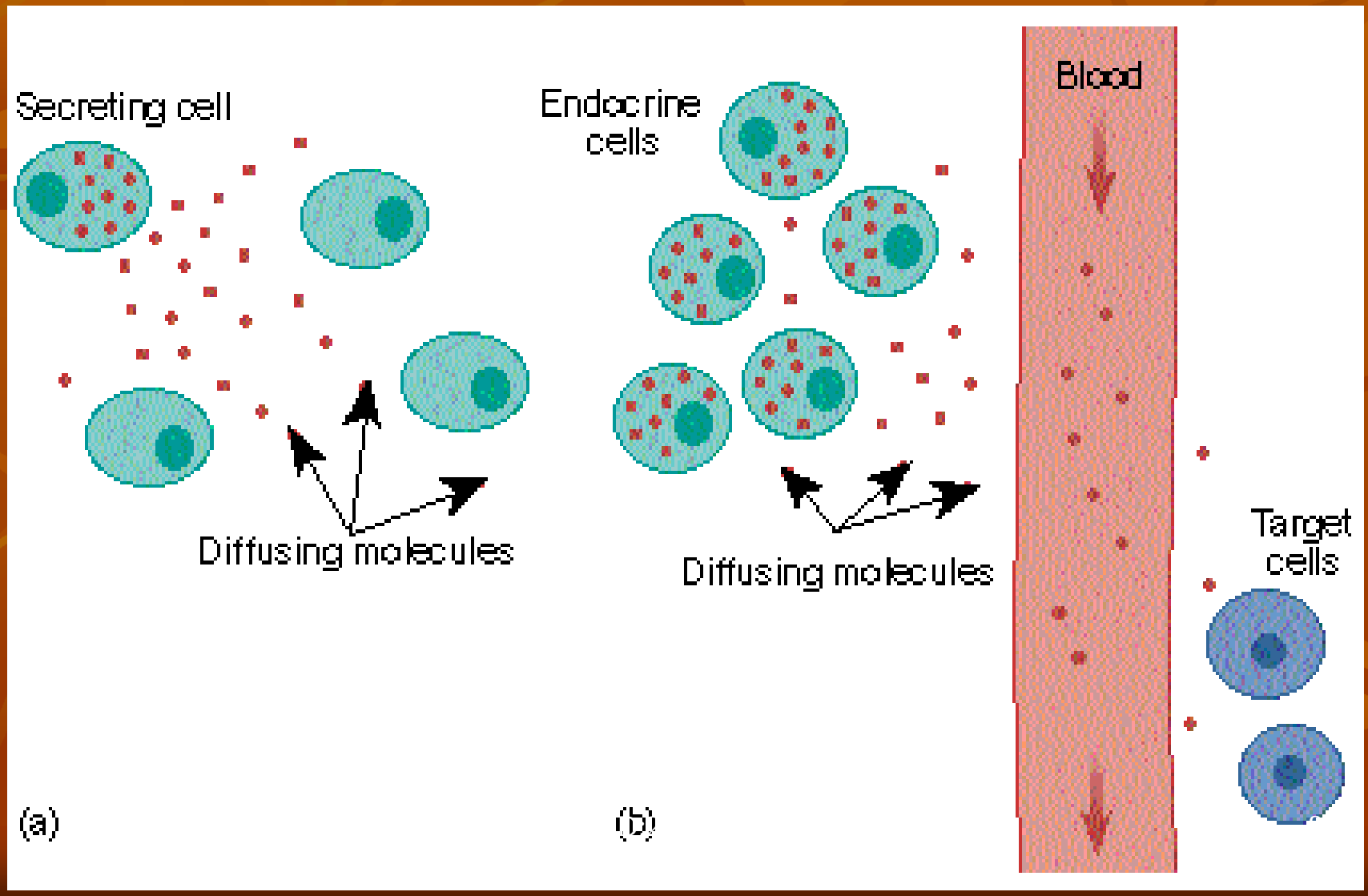
BLOOD: COMPOSITION



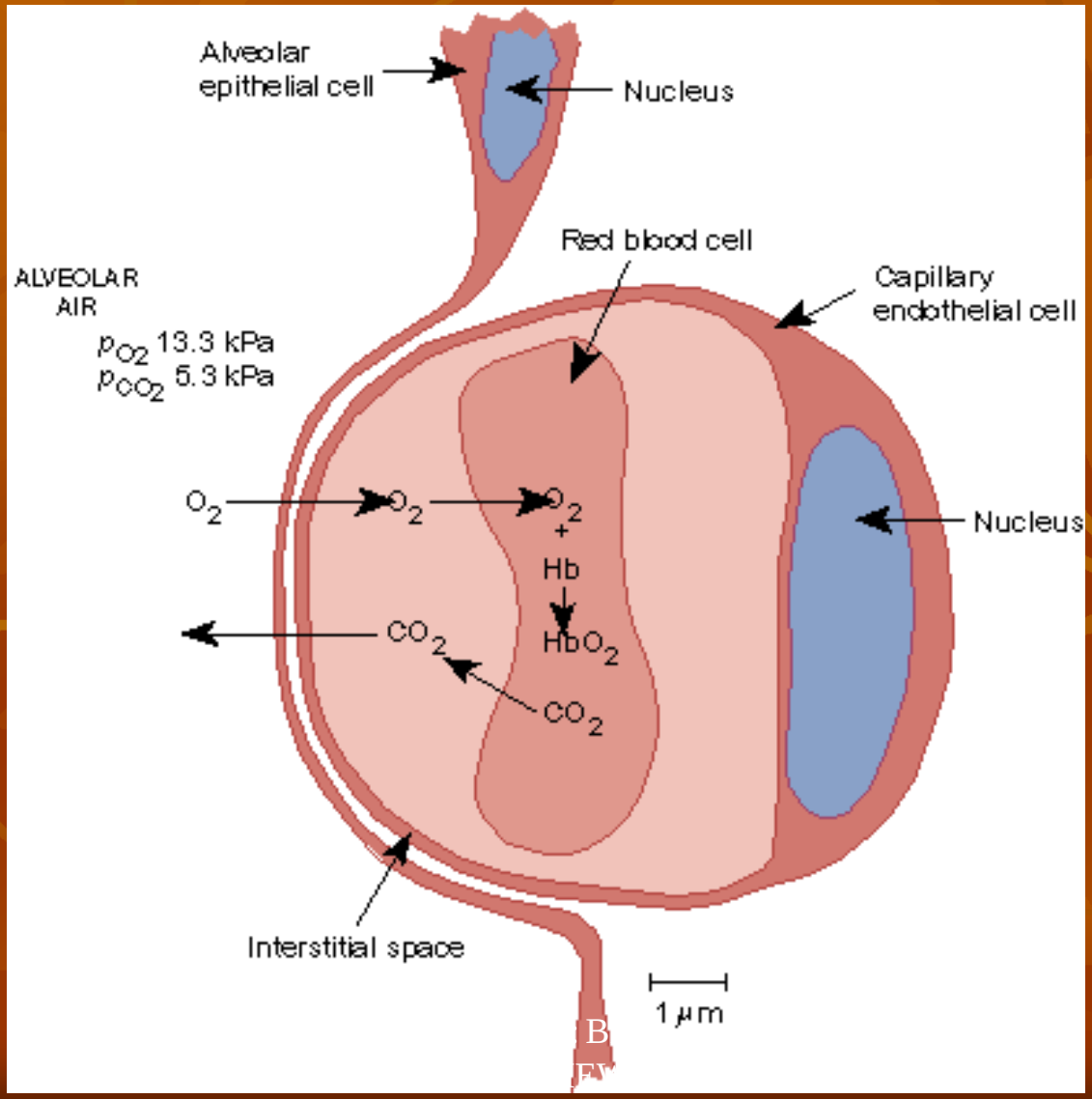
FUNCTIONS OF BLOOD

- NUTRITIVE
- RESPIRATORY
- EXCRETORY
- BODY DEFENCE: immynity,phagocytosis,hemostasis,fibrinolysis
- TRANSPORT:
  - HORMONES
  - VITAMINS
  - DRUGS

BLOOD:TRANSPORTING HORMONE MOLECULES HORMON



OXYGEN & CO_2 TRANSPORT



FUNCTIONS OF BLOOD

- HOMEOSTATIC FUNCTION:
  - ACID BASE BALANCE.
  - ELECTROLYTE BALANCE.
  - HEMOSTASIS.
  - THERMOREGULATION.

Organic Substances of the Plasma

- **Proteins:** The proteins present in the plasma are albumin, globulin and fibrinogen. These are specifically known as plasma proteins.
- **Carbohydrates:** The carbohydrate is present in plasma mainly in the form of glucose.
- **Fats:** The lipid substances present in plasma are the neutral fats, phospholipids and cholesterol.
- **Amino acids:** Plasma contains both essential and nonessential amino acids.
- **Nonprotein nitrogenous substances**: The plasma also contains some nonprotein nitrogenous substances like ammonia, creatine, creatinine, xanthine, hypoxanthine, urea and uric acid.

Organic Substances of the Plasma

- **Internal secretions:** The plasma contains many hormones.
- **Enzymes:** The enzymes like amylase, carbonic anhydrase, alkaline phosphatase, acid phosphatase, lipase, esterase, protease and transaminase are present in plasma.
- **Antibodies:** The plasma contains many antibodies, which are called immunoglobulins.

Inorganic Substances of the Plasma

- Sodium
- Calcium
- Potassium
- Magnesium
- Chloride
- Iodide
- Iron
- Phosphates
  Copper.

FUNCTIONS OF PLASMA PROTEINS

- **1. ROLE IN COAGULATION OF BLOOD**

  Fibrinogen is essential for the coagulation of blood.

  2. ROLE IN DEFENSE MECHANISM OF BODY

  The gamma globulins play an important role in the defense mechanism of the body by acting as antibodies (immune substances). These protein are also called immunoglobulins.

- **3. ROLE IN TRANSPORT MECHANISM**

  Plasma proteins are essential for the transport of various substances in the blood. Albumin, alpha globulin and beta globulin are responsible for the transport of the hormones, enzymes and respiratory gases, particularly carbon dioxide.

- **4. ROLE IN MAINTENANCE OF ONCOTIC PRESSURE IN BLOOD**

  Because of their large size, the plasma proteins cannot pass through the capillary membrane easily and remain in the blood. In the blood these proteins exert the colloidal oncotic pressure. The oncotic pressure exerted by the plasma proteins is about 25 mm Hg.

- **5. ROLE IN REGULATION OF ACID BASE BALANCE**
- Plasma proteins, particularly the albumin, play an important role in regulating the acid base balance in the blood.
- **6. ROLE IN VISCOSITY OF BLOOD**
- The plasma proteins provide viscosity to the blood, which is important to maintain the blood pressure. Albumin provides maximum viscosity than the other plasma
- proteins.
- **7. ROLE IN ERYTHROCYTE**
- **SEDIMENTATION RATE (ESR)**
- Globulin and fibrinogen of the plasma accelerate the tendency of rouleaux formation by the red blood cells. Rouleaux formation is responsible for ESR, which is an important diagnostic and prognostic tool for the clinic
- ians

DECREASE IN ALL FRACTIONS OF PROTEINS—HYPOPROTEINEMIA

- Hypoproteinemia occurs in the following conditions:
- Hemorrhage
- Extensive burns
- Pregnancy
- Malnutrition
- Prolonged starvation
- Cirrhosis of liver and
- Chronic infections like chronic hepatitis or chronic nephritis.

INCREASE IN ALL FRACTIONS—HYPERPROTEINEMIA

- Dehydration and
- Acute infections like acute hepatitis or acute nephritis

EXPRESSION OF BLOOD VOLUME

- Usually Blood Volume is expressed in **liters**.
- It can also be expressed in **relation to body weight**.
  - It is 7% Body Weight
- Another way to express it is in terms of **Body Surface Area**.
  - Whole Blood : 2.8 Lts/M^2
  - Plasma : 1.5 Lts/M^2

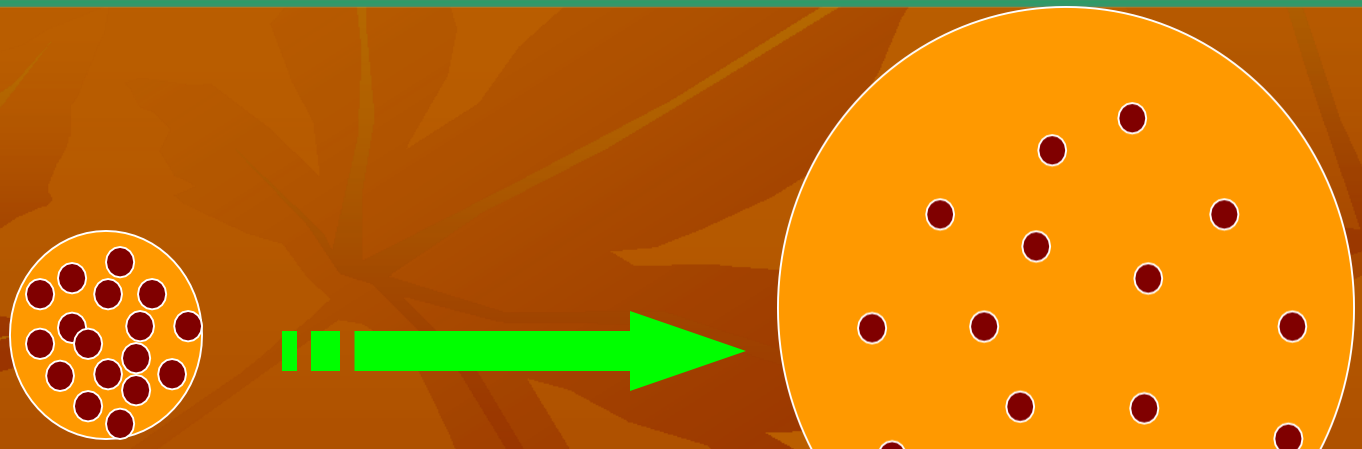
METHODS OF MEASURING BLOOD VOLUME

- IN HUMANS: ONLY INDIRECT METHODS
- DYE DILUTION TECHNIUE:
- PRINCIPLE:
  - Injection of a known volume of non toxic substance into the circulation.
  - Measuring the dilution of this injected dye after some time.
  - This gives us the Plasma volume.

WHAT IS BLOOD VOLUME?

- The total amount of blood in circulation plus the amount of blood in the reservoirs constitutes the "Blood Volume"
- The average adult 70 kg man has a blood volume of 5 to 6 litres.

DYE DILUTION TECHNIQUE



V_1 = VOLUME
C_1 = CONCENTRATION OF DYE

V_2 = VOLUME
C_2 = CONC. OF DYE

$V_1 \times C_1 = V_2 \times C_2$

OR

$$V_2 = \frac{V_1 \times C_1}{C_2} = \frac{\text{Amount of Dye injected}}{\text{Conc. Of the dye in the Plasma}}$$

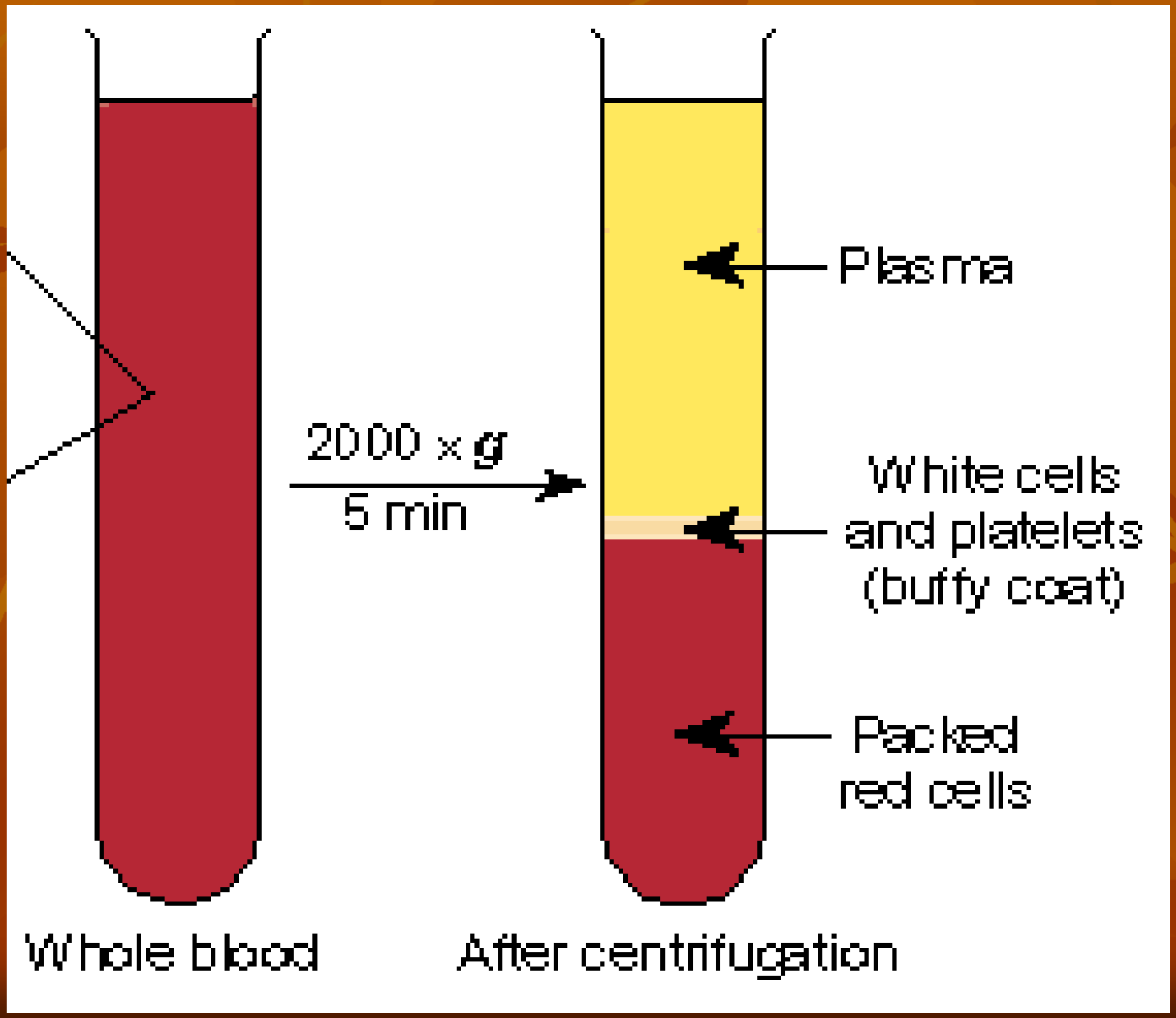
HEMATOCRIT (PCV)

- The volume of erythrocytes in the whole blood expressed in percentage is the **Hematocrit**.
- This is also called as Packed Cell Volume or **PCV**.
- This is determined by the **Wintrobe**'s tube, using a Centrifuge.

HEMATOCRIT

- A mixture of blood and double oxalate ($K - NH_4$) is taken up to 100 mark in the Wintrobe's tube.
- The tube is placed in the centrifuge.
- It is rotated at 3,000 rpm for 30 minutes.
- The Hematocrit is then read off the tube.
- Blood Volume = $\frac{\text{Plasma Volume X 100}}{\text{100 - PCV}}$

HEMATOCRIT


2000 x g
5 min
Plasma
White cells
and platelets
(buffy coat)
Packed
red cells
Whole blood
After centrifugation

BLOOD VOLUME: PHYSIOLOGICAL VARIATIONS

- AGE
- SEX
- TEMPERATURE
- BODY WEIGHT
- BODY SURFACE AREA

- PREGNANCY
- EXERCISE
- POSTURE
- HYPOXIA
- EMOTIONS

BLOOD VOLUME & AGE

AGE	BLOOD VOLUME in Liters
AT BIRTH	0.3
6 Months	0.5
1 year	0.7
2yrs 6 months	1.0
4 years	1.3
7 years	1.7
10 years	2.5(Girls); 3.2 (Boys)
ADULTS	5 (Men) 4.5 (Women)

BLOOD VOLUME: PHYSIOLOGICAL VARIATIONS

1. **SEX:**
   - Males have more blood volume than females.
2. **TEMPERATURE:**
   - Acute exposure to cold causes reduction in blood volume due to Plasma water loss to tissues.

BLOOD VOLUME: PHYSIOLOGICAL VARIATIONS

3. BODY WEIGHT:

- **It is usually 7% of the Body Weight.**

4. BODY SURFACE AREA:

- **2.8 Lts/Square Meters of BSA**

BLOOD VOLUME: PHYSIOLOGICAL VARIATIONS

5. PREGNANCY:

- Increases by 20 – 30% due to mass of fetus.

6. EXERCISE:

- Vigorous exercise causes an increase.

7. POSTURE:

- Changing from lying down to erect.

BLOOD VOLUME: PHYSIOLOGICAL VARIATIONS

8. HYPOXIA:

- Seen in High altitudes.
- ↑Erythrocytes
- So ↑Blood volume.

9. EMOTIONS:

- Excitement causes an increase in the Blood volume.

BLOOD VOLUME: PATHOLOGICAL VARIATIONS

- DECREASE IN BLOOD VOLUME IS HYPOVOLEMIA. CAUSES:

1. BLOOD LOSS:
2. SHOCK:
   - Crushing Injury
   - Cardiogenic
   - Neurogenic
   - Psychogenic.

HYPOVOLEMIA: CAUSES (CONTD)

3. HEMOLYSIS:

- Mismatched transfusion
- Snake bite
- Black water fever
- Hemorrhagic Plagues/Dengue
- Measles

HYPOVOLEMIA: CAUSES (CONTD)

4. DEHYDRATION:

- Diarrhea
- Cholera
- Gastroenteritis
- Burns
- Hyperemesis.

HYPOVOLEMIA: CAUSES (CONTD)

5. ANEMIA:

- Decreased RBC volume
- Plasma may increase.

6. OBESITY:

- Blood volume per body weight decreases though Blood volume per BSA may be normal.

7. HYPOTHYROIDISM (MYXEDEMA):

- Decrease in Blood volume.

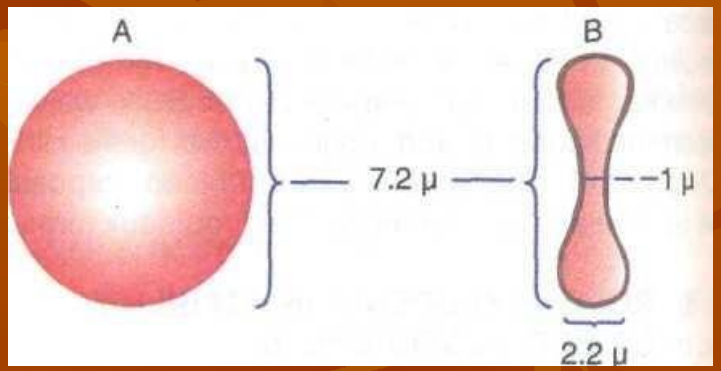
8. ACUTE COLD: Decreases blood volume.

TREATMENT FOR BLOOD LOSS

- TRANSFUSION OF WHOLE BLOOD OF THE SAME BLOOD GROUP & TYPE.
- INFUSION OF PLASMA
- INFUSION OF DEXTRAN OR NORMAL SALINE.

Red Blood Cells

- Normally, the red blood cells are disc shaped and biconcave (dumb-bell shaped).
- Diameter: 7,2(6.9-7.5).



10 μm

Val His Leu Thr Pro Glu Glu ···

1 2 3 4 5 6 7

(a) Normal red blood cells and the primary structure of normal hemoglobin

10 μm

Val His Leu Thr Pro Val Glu ···

1 2 3 4 5 6 7

(b) Sickled red blood cells and the primary structure of sickle-cell hemoglobin

VARIATIONS IN NUMBER OF RED BLOOD CELLS

- At **birth**, the red blood cell count is 8 -10 millions/cu mm of blood ($7,0 \times 10^{12/L}$). The count decreases within 10 days after birth due to destruction of cells causing physiological jaundice in some infants. However, in infants and growing children, the cell count is at a level higher than the value in adults.
- In adult males: $4,0\text{-}5,1 \times 10^{12/L}$

- Before puberty and after menopause in females the red blood cell count is similar to that in males. During reproductive period of females, the count is less than in males (4.5 millions/cu mm).(3,7-4,7 x $10^{12/L}$).
- The abnormal increase in the red blood cell count is called polycythemia.

VARIATIONS IN SIZE OF RED BLOOD CELLS

Microcytes

- Microcytes are the red blood cells of small size and are present in the following conditions:
- Iron deficiency anemia
- Prolonged forced breathing and
- Increased osmotic pressure in blood
-

Macrocytes

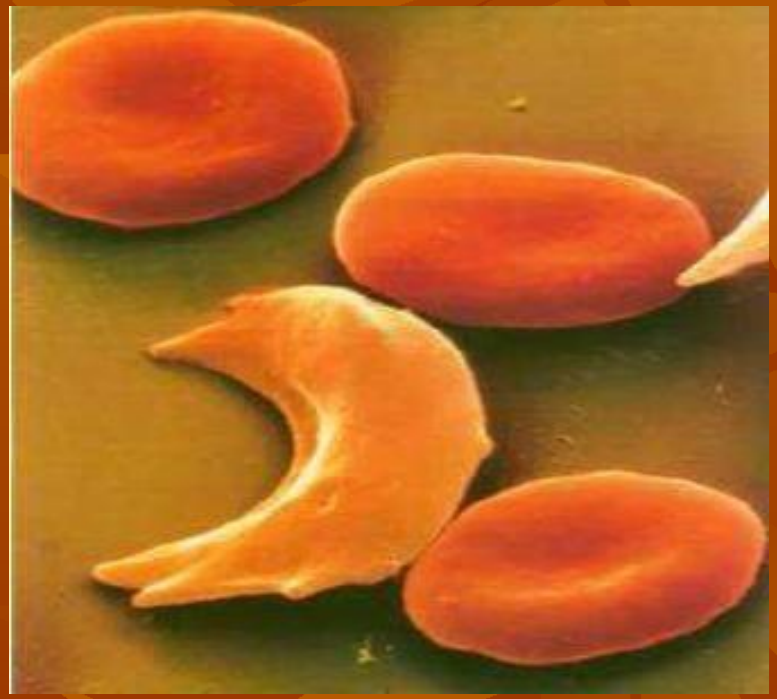
- Macrocytes are the red blood cells with larger size. The macrocytes are present in the following conditions:
- Megaloblastic anemia
- Muscular exercise and
- Decreased osmotic pressure in blood

Anisocytes

- The red blood cells with unequal size are called the anisocytes. This happens in pernicious anemia.

VARIATIONS IN SHAPE OF RED BLOOD CELLS

- 1. Crenation :Shrinkage as in hypertonic solution
- 2. Spherocytosis :Globular form as in hypotonic solution
- 3. Elliptocytosis :Elliptical shape as in certain types of anemia
- 4. Sickle cell :Crescentic shape as in sickle cell anemia
- 5. Poikilocytosis :Unequal shapes due to deformed cell membrane. The shape will be of flask, hammer or any other unusual shape.

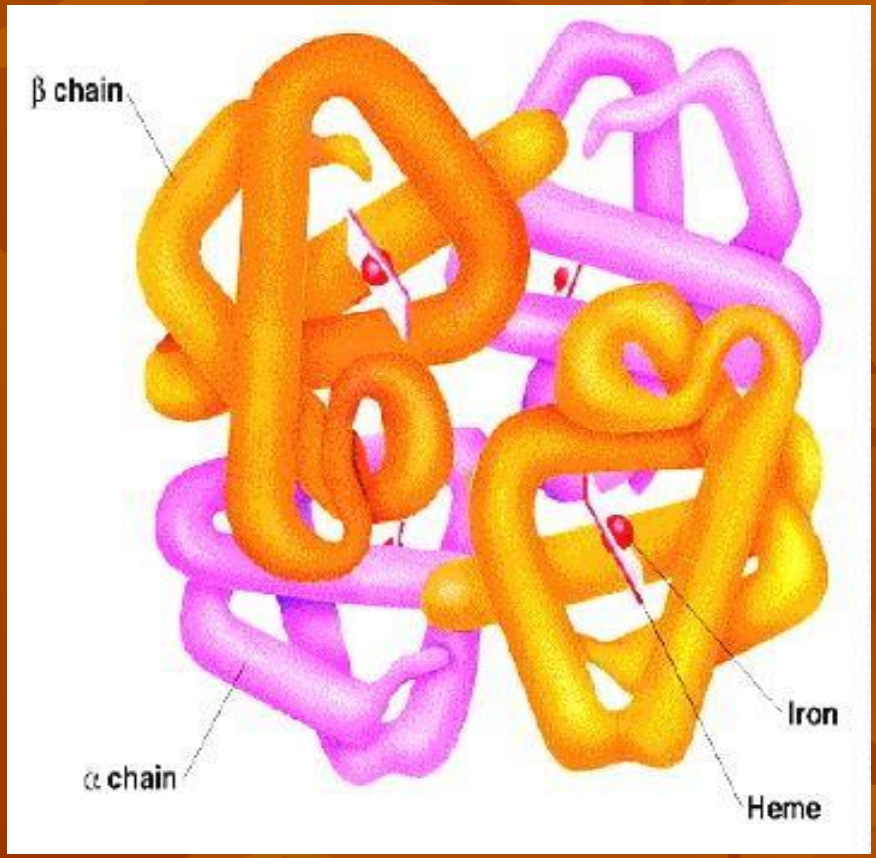


FUNCTIONS OF RED BLOOD CELLS

- Erythrocytes transport oxygen from the lungs to the tissues. The hemoglobin in red blood cell combines with oxygen and 97% of oxygen is transported as oxyhemoglobin.
- Red blood cells transport carbon dioxide from the tissues to the lungs. The hemoglobin in red blood cell combines with carbon dioxide and form carbhemo-globin. About 30% of carbon dioxide is transported in this form.
- Hemoglobin in red blood cell also functions as a good buffer.
- Red blood cells carry the blood group antigens like A agglutinogen, B agglutinogen and Rh factor. This helps in determination of blood group and blood transfusion

Hemoglobin

- • Multi-subunit protein (tetramer)
- – 2 a and 2 b subunits
- • Heme
- – One per subunit
- – Has an iron atom
- – Carries O2
- • In red blood cells



TYPES OF HEMOGLOBIN

Hemoglobin is of two types namely:

- Adult hemoglobin-HbA
- Fetal hemoglobin-HbF

NORMAL VALUES

- Average hemoglobin (Hb) content in blood is 14 to 16 gm%. In adult males, it is 15 gm% and in adult females, it is 14.5 gm%.
- The hemoglobin content at different age is:

At birth	:	25 gm%	210 g/l
After 3rd month	:	20 gm%	132 g/l
After 1 year	:	17gm%	127 g/l
In adult males	:	15gm%	132-160 g/l
In adult females	:	14.5 gm%	115-145 g/l

ABNORMAL HEMOGLOBIN

- **Hemoglobin S:** This is found in sickle cell anemia.lr,
  this, the alpha chains are normal and beta chainsai abnormal.
- **Hemoglobin C**: This occurs in hemoglobin C diseasi
  Here, the beta chains are abnormal.
- **Hemoglobin E:** This occurs in hemoglobin E disease
  Here also the beta chains are abnormal.

Compound Hemoglobin

- • **Oxyhemoglobin:**
- – Normal heme contains iron in the reduced form (Fe2+).
- – Fe2+ shares electrons and bonds with oxygen.
- • **Deoxyhemoglobin:**
- – When oxyhemoglobin dissociates to release oxygen, the
- heme iron is still in the reduced form.
- – Hemoglobin does not lose an electron when it combines with O_2

- Methemyoglobin:

– Has iron in the oxidized form (Fe3+).

– Blood normally contains a small amount.

- • Carboxyhemoglobin:

–The reduced heme is combined with carbon monoxide.

–The bond with carbon monoxide is **210** times stronger than the bond with oxygen.

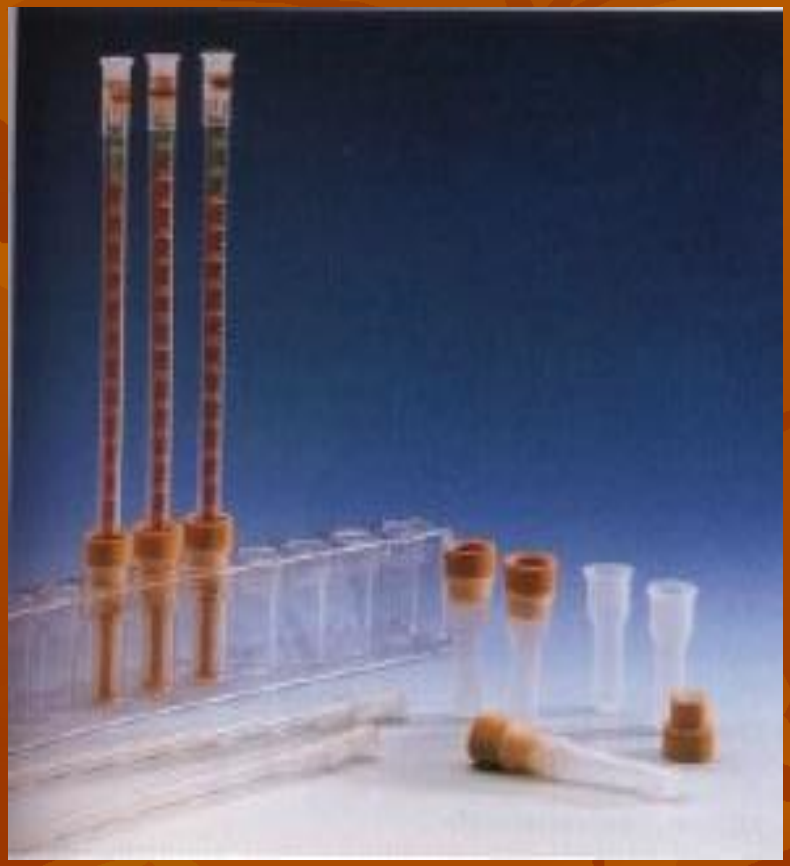
Erythrocyte Sedimentation Rate

NORMAL VALUES OF ESR

- *By Westergren's Method*

. I

- In males 3 to 7 mm in one hour
- In females 5 to 9 mm in one hour



Factors Affecting the ESR

- **Physical:**
- Temperature
- Vibration
- Tilting of tube
- Bore of tube
- Dilution

- **Patient Related:**
- PCV
- Ability of cells to form rouleaux

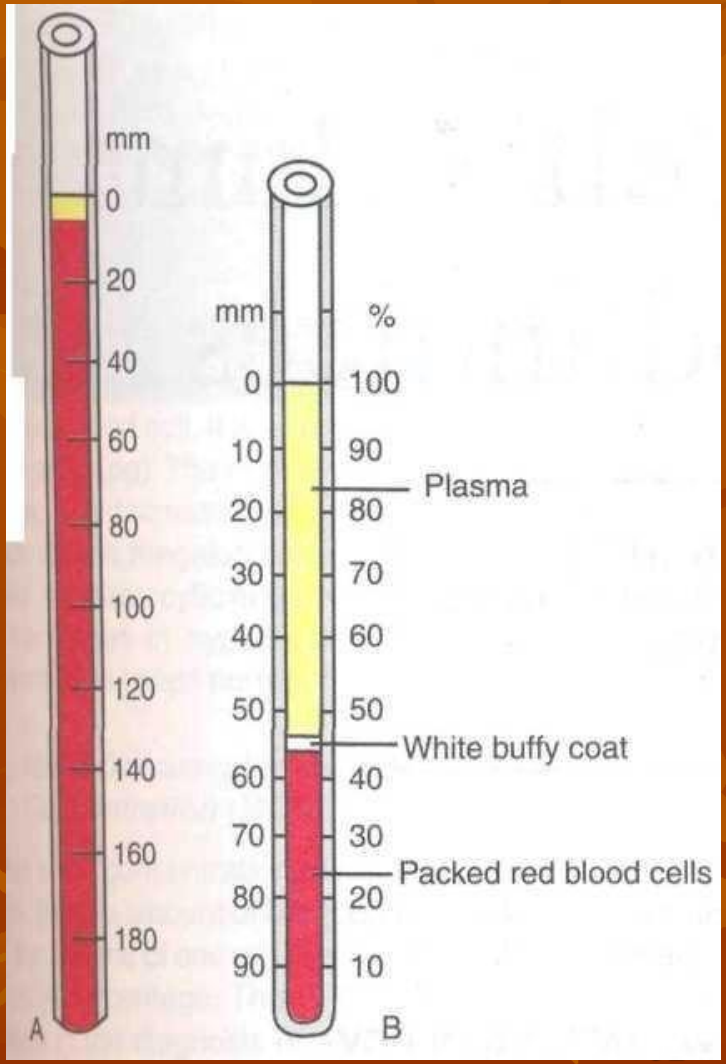
ESR Reference Ranges

- Westergren's method:
- Males < 50 years 0 - 7 mm in one hour

  > 50 years 0 - 10 mm in one hour

- Females < 50 years 0 - 9 mm in one hour

  > 50 years 0 - 15 mm in one hour



Factors Affecting the ESR

- **High MW proteins:**
- Fibrinogen
- Acute phase proteins
- Immunoglobulins

- **Rouleaux formation**:
- Increase sedimentation

ESR: Significance

- Non - specific test

Useful as a screening test for inflammatory disease

- **Increased ESR**:

Acute/chronic infection or inflammation

Neoplasia or degenerative disease

Trauma

Immunological injury

- **Decreased ESR:**

Polycythaemia

Hypofibrinogenaemia (severe liver disease)

Abnormalities of Rbc membranes

Blood Indices

DIFFERENT BLOOD INDICES

- Following are the various blood indices:
- Mean Corpuscular Volume (MCV)
- Mean Corpuscular Hemoglobin (MCH)
- Mean Corpuscular Hemoglobin Concentrati (MCHC)
- Colour Index (CI).

Colour Index

- This is calculated by dividing the hemoglobin percentage by the red blood cell count percentage.

- Thus, the Colour Index =
- RBC % / Hemoglobin % = 53.3%

HEMOPOIESIS & ERYTHROPOIESIS

HEMOPOIESIS: INTRO

- Hemo: Referring to blood cells
- Poiesis: "The development or production of"
- The word Hemopoiesis refers to the production & development of all the blood cells:
  - Erythrocytes: Erythropoiesis
  - Leucocytes: Leucopoiesis
  - Thrombocytes: Thrombopoiesis.
- Begins in the 20th week of life in the fetus & continues in the red bone marrow till death.

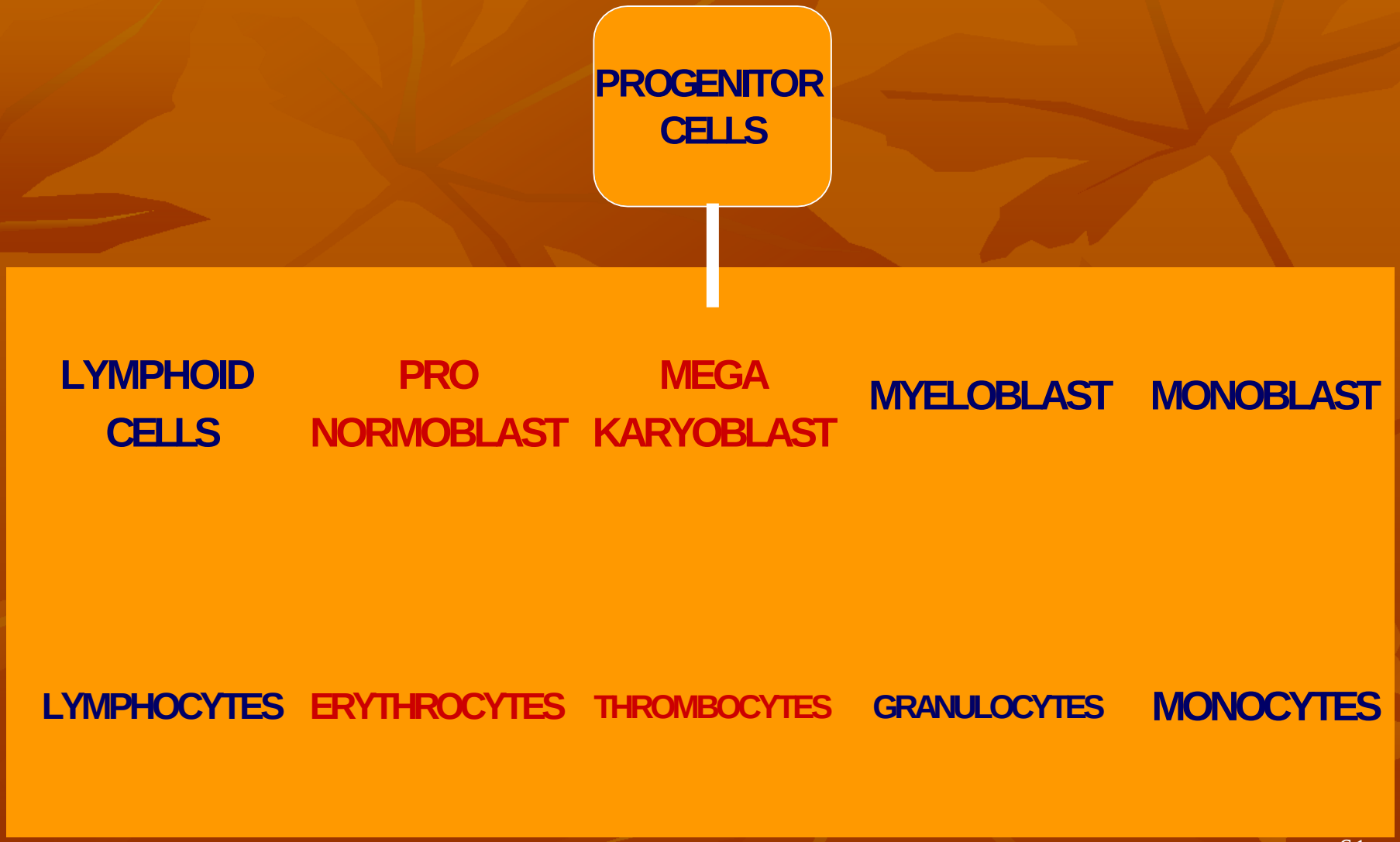
STEM CELL THEORY

- All blood cells are produced by the **bone marrow**.
- They come from a single class of primitive mother cells called as:
- **PLURIPOTENT STEM CELLS**.
- These cells give rise to blood cells of:
  - **Myeloid** series: Cells arising mainly from the bone marrow.
  - **Lymphoid** series: cells arising from lymphoid tissues.

PROGENITOR CELLS

- Committed stem cells lose their capacity for self-renewal.
- They become irreversibly committed.
- These cells are termed as "Progenitor cells"
- They are regulated by certain hormones or substances so that they can:
  - Proliferate
  - Undergo Maturation.

BLOOD CELLS: DEVELOPMENT



ERYTHROPOIESIS: SITES/PHASES

- **INTRAUTERINE LIFE:**
  - **INTRAVASCULAR PHASE: Upto 3rd month of Intra Uterine Life.**
    - **Endothelial cells = = = RBCs**
  - **HEPATIC PHASE: 3rd to 5th month IUL**
    - **Liver & Spleen**
    - **nRBCs from Mesenchymal cells.**
  - **MYELOID PHASE: From 5th month of IUL onwards.**

ERYTHROPOIESIS: SITES/PHASES CONTD.

- POST NATAL LIFE:
  - CHILDREN:
    - Predominantly Red Bone Marrow of skeleton:
      - Axial &
      - Appendicular.
  - ADULTS:
    - Red Bone Marrow of Axial Skeleton.

ERYTHROPOIESIS

- PROERYTHROBLAST
- BASOPHILIC ERYTHROBLAST
- POLYCHROMATOPHILIC ERYTHROBLAST
- ORTHOCHROMATIC ERYTHROBLAST
- RETICULOCYTE
- MATURE ERYTHROCYTES

FACTORS REGULATING ERYTHROPOIESIS

- SINGLE MOST IMPORTANT REGULATOR: "TISSUE OXYGENATION"
- BURST PROMOTING ACTIVITY
- ERYTHROPOIETIN
- IRON
- VITAMINS:
  - Vitamin B_{12}
  - Folic Acid
- MISCELLANEOUS

ERYTHROPOIETIN

- A hormone produced by the Kidney.
- Nowadays available as Synthetic Epoieti
- Increases the number of:
  - Nucleated precursors in the marrow.
  - Reticulocytes & Mature Erythrocytes in the blood.

VITAMINS

- **B_{12}: Cyanocobalamine & Folic Acid:**
  - Is also called Extrinsic Factor of Castle.
  - Needs the Intrinsic Factor from the Gastric juice for absorption from Small Intestine.
  - Deficiency causes Pernicious (When IF is missing) or Megaloblastic Anemia.
  - Stimulates Erythropoiesis
  - Is found in meat & diary products.

IRON

- Essential for the synthesis of Hemoglobin.
- Deficiency causes Microcytic, Hypochromic Anemia.
- Deficiency causes the commonest type of Anemia.






It's finished!