HUMAN PHYSIOLOGY (normal)

LECTURE 11. Physiology of the Blood System

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Properties of the Blood

- Blood is a **connective tissue** in **fluid** form
- Color: Blood is **red** in color
- Volume: Average **volume** of blood in a normal adult is **5 L** (4.5 L in females), about **8%** of the body weight or **80–85 ml/kg** body weight
- Blood contains the **blood cells** which are called **formed elements** and the liquid portion known as **plasma**

Functions of Blood

Transport function

- **Nutritive** function (transport of glucose, amino acids, lipids and vitamins)
- **Respiratory** function (transport of respiratory gases – oxygen and carbon dioxide)
- **Excretory** function (transport of waste products)
- **Thermoregulation** (transport of heat)

Regulatory function (transport of hormones and enzymes)

Homeostasis maintaining (regulation of water balance, acid-base balance, body temperature)

Defensive Function (defense against toxins and pathogens and blood clotting)

The Composition of Whole Blood

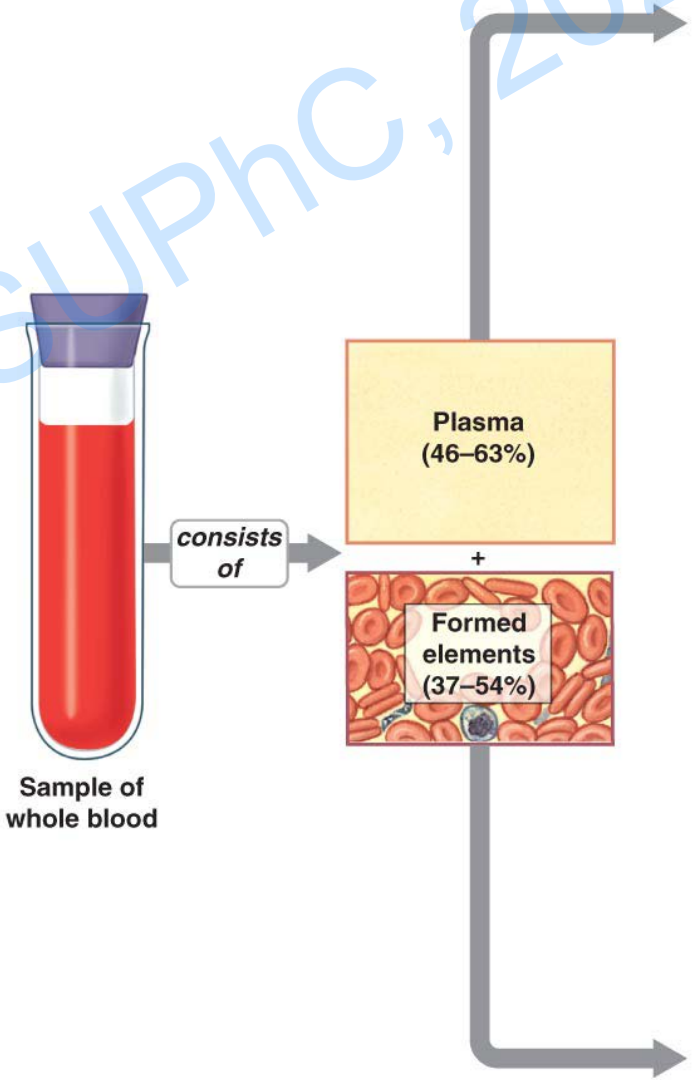
Plasma (about the 55%) fluid consisting of:

- water (more than 90%)
- dissolved substances – organic, inorganic, gases

Formed elements (less than 45%)

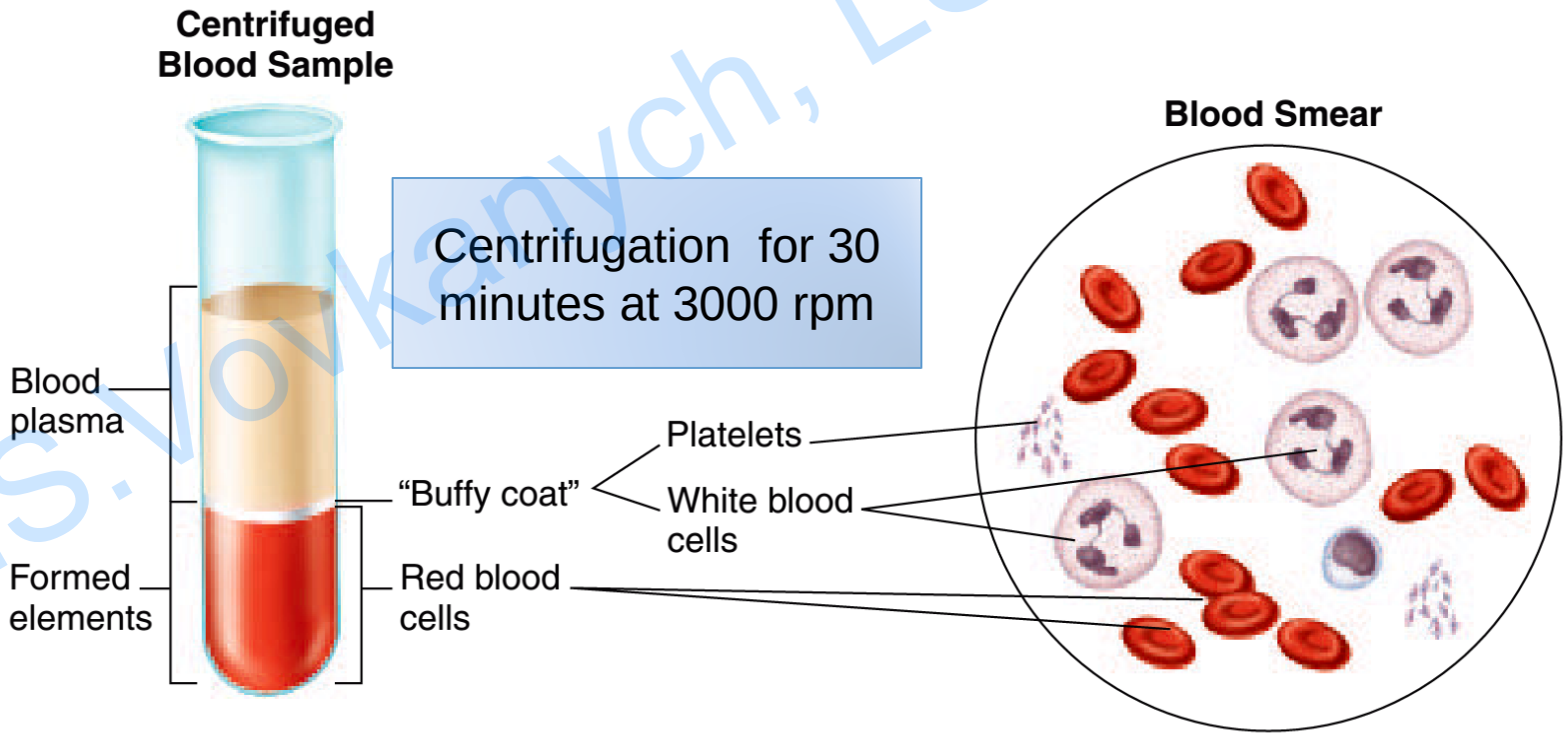
Three Types of Formed Elements

- **Red blood cells** (RBCs) or erythrocytes - transport oxygen
- **White blood cells** (WBCs) or leukocytes - part of the immune system
- **Platelets** - cell fragments involved in clotting



Hematocrit Value

- **Volume of red blood cells** expressed in percentage is called the hematocrit value or packed cell volume (PCV)
- Hematocrit value:
  - **female** - 37%–48%;
  - **male** - 45%–52%



Composition of Plasma

- **Water** – 90-92%
- **Gases** (oxygen, carbon dioxide, nitrogen etc.)
- **Solids**
  - **Organic** substances
    - Plasma **proteins** and **amino acids**
    - Non-protein **nitrogenous** substances
    - **Carbohydrates**
    - **Fats**
    - **Hormones**, **enzymes**, **antibodies**
  - **Inorganic substances** (sodium, calcium, potassium, magnesium, carbonate, chloride, phosphate, etc.)

Functions of Plasma Proteins

- **Transport** of various substances in the blood
- Maintenance of **osmotic pressure** in blood
- Regulation of **acid-base balance** (responsible for 15% of the buffering capacity of blood)
- Provide **viscosity** to the blood (important to maintain the blood pressure)
- Role in **suspension stability** of red blood cells (red blood cells remain suspended uniformly in the blood)
- **Coagulation** of blood (clot formation)
- **Defense** mechanism of body (as antibodies)
- **Reserve proteins** (utilized by the body tissues as the last source of energy)

Plasma Proteins

Albumins (60%, 4.7 g/100 ml)

- transport of fatty acids, thyroid and steroid hormones, osmotic pressure

Globulins (35%, 2.3 g/100 ml)

- **gamma globulins** - antibodies, also called immunoglobulins
- **alpha and beta globulins** - transport globulins (small molecules): hormone-binding proteins, metalloproteins, apolipoproteins (lipoproteins), and steroid-binding proteins
- normal albumin/globulin (A/G) ratio 2 : 1

Fibrinogen (4%, 0.3 g/100 ml)

- form **clots** and produce long, insoluble strands of **fibrin**
- plasma without fibrinogen is called **serum**

Other Plasma Proteins

- 1% of plasma
- enzymes, hormones, and prohormones

Normal Plasma Values

Organic Molecules

- Protein (total) 6.0–8.4 g/100 ml
- Cholesterol 120–220 mg/100 ml
- Glucose 70–110 mg/100 ml (fasting)
- Lactic acid 0.6–1.8 mmol/l
- Triglyceride 40–150 mg/100 ml
- Uric acid 3–7 mg/100 ml
- Creatinine 0.5–1.5 mg/100 ml
- Bilirubin 0.5–1.5 mg/100 ml

Ions

- Bicarbonate 24–30 mmol/l
- Calcium 2.1–2.6 mmol/l
- Chloride 100–106 mmol/l
- Potassium 3.5–5.0 mmol/l
- Sodium 135–145 mmol/l

Chemical and physical properties of the Blood

- **pH**: 7.4 (slightly alkaline and its pH in normal conditions)
- **Specific gravity**:
  - Specific gravity of total **blood** : 1.052 to 1.061 g/ml
  - Specific gravity **blood cells** : 1.092 to 1.101 g/ml
  - Specific gravity of **plasma** : 1.022 to 1.026 g/ml
- **Viscosity**: five times more viscous than water, mainly due to red blood cells and plasma proteins
- Blood **osmolality** 280–296 mOsm
- **Erythrocyte sedimentation rate** (ESR) shows the suspension stability of RBCs
  - In males: 3 to 7 mm in 1 hour
  - In females: 5 to 9 mm in 1 hour

pH homeostasis of the blood

The pH (negative logarithm of H^+ concentration) is another term for H^+ concentration

- increase in H^+ ion concentration decreases the pH (acidosis)
- reduction in H^+ concentration increases the pH (alkalosis)

- Changes in pH below 7.38 or above 7.42 will cause serious threats to many physiological functions

Acid-base Buffer System

- **Bicarbonate** buffer system (is not powerful, but plays an important role because the concentration of two components (HCO_3– and CO_2) of this buffer system is regulated separately by two different organs - by **kidney** and respiratory **system**)
- **Phosphate** buffer system (more powerful than bicarbonate)
- **Protein buffer system** (present both in the plasma and erythrocytes; hemoglobin is the most effective protein buffer and the major buffer in blood)

Osmotic Pressure

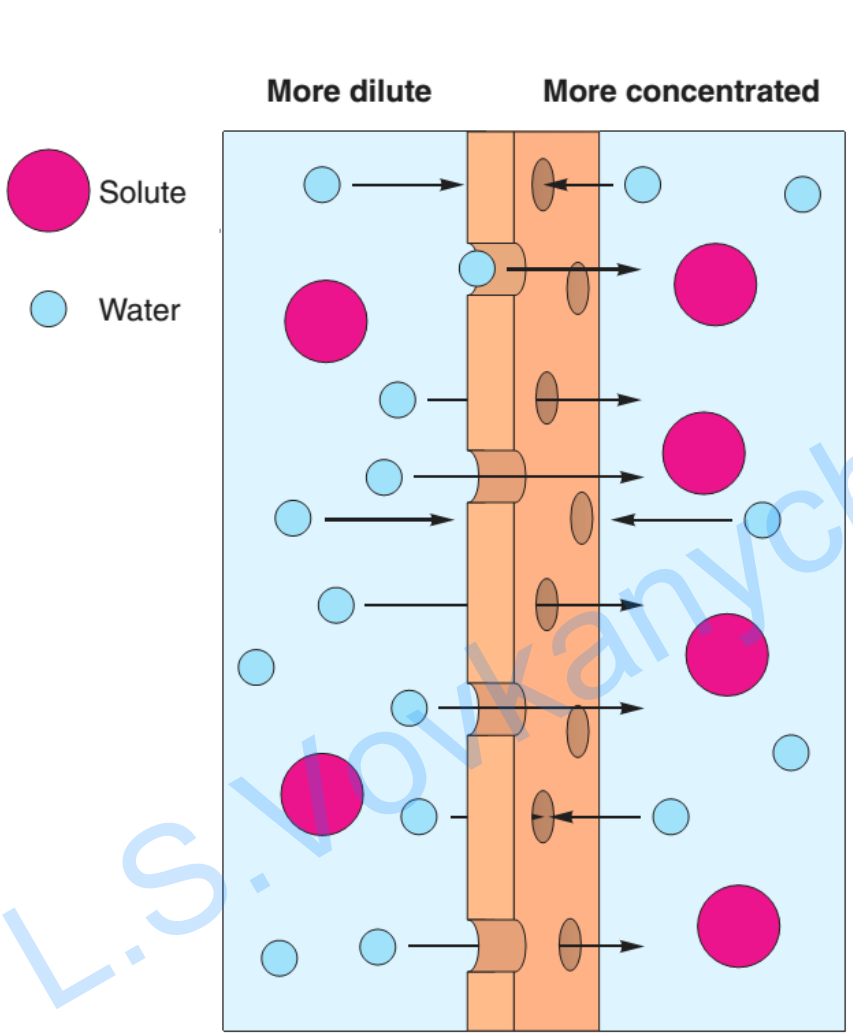
Osmotic pressure is the pressure created by the solutes in a fluid

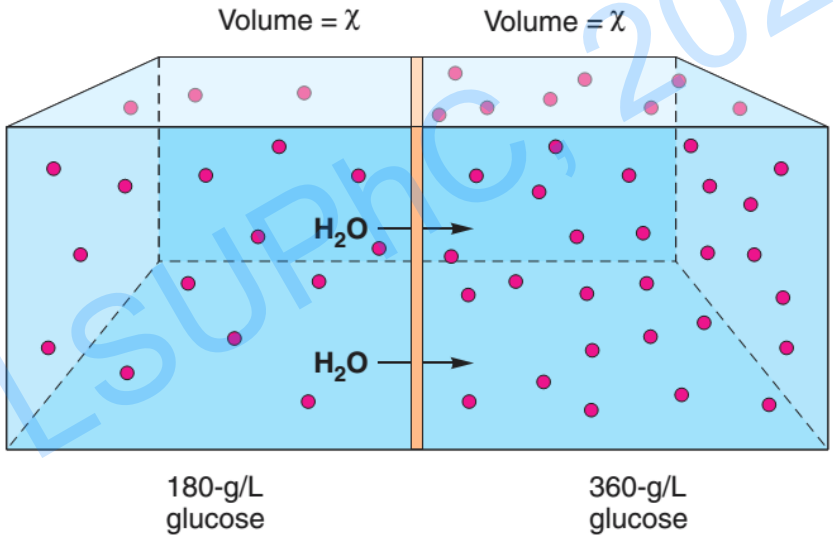
- **Osmosis** is passive transport, when water or any other solvent moves from the area of lower concentration to the area of higher concentration
- This **creates** a pressure which is known as **osmotic pressure**
- **Osmolality** depends on the concentration of osmotically active substance in the solution
- **Osmolarity** is the number of particles (osmoles) per liter of solution (osmoles/L)

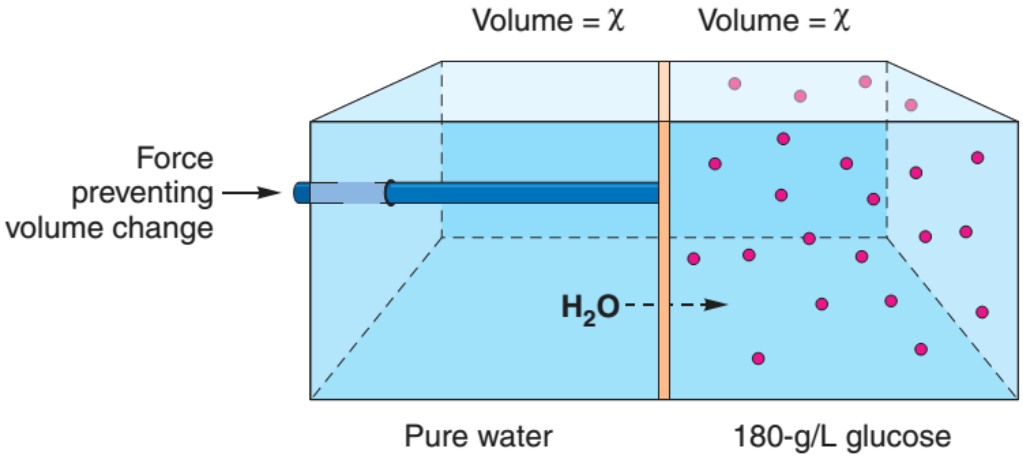
Tonicity is the measure of effective osmolality, the solutions can be classified into three categories:

- **Isotonic** fluid
- **Hypertonic** fluid
- **Hypotonic** fluid

A Model Of Osmotic Pressure

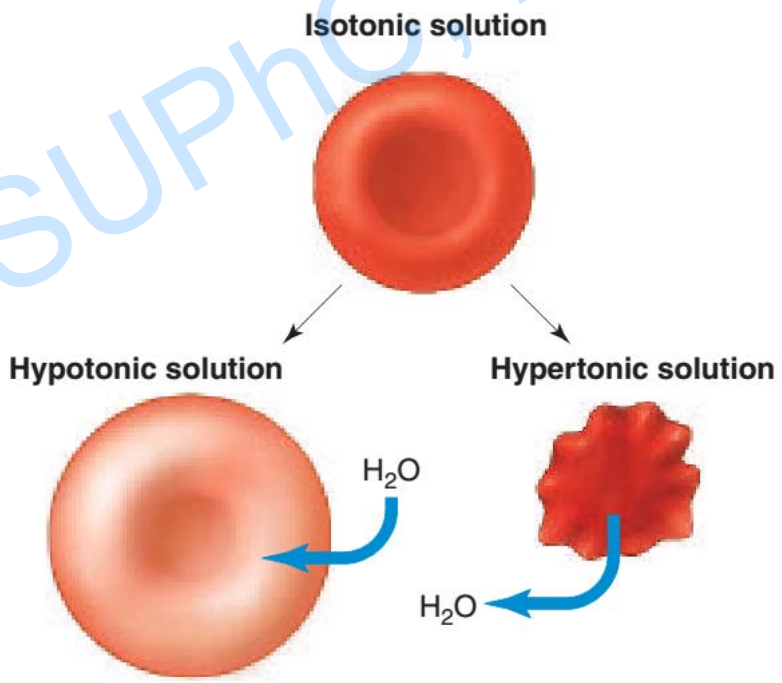




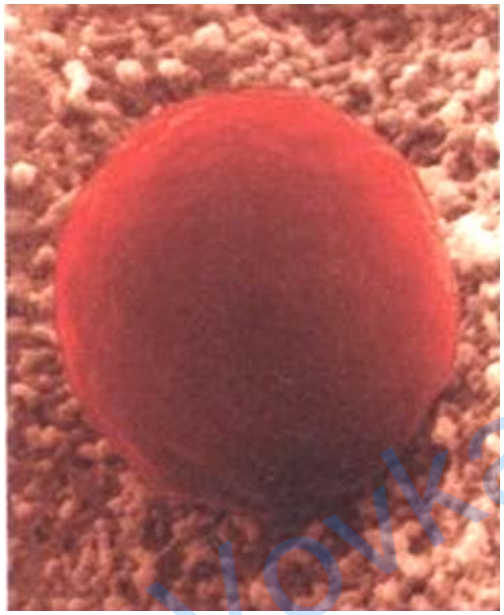


Red Blood Cells in Solutions with Different Tonicity

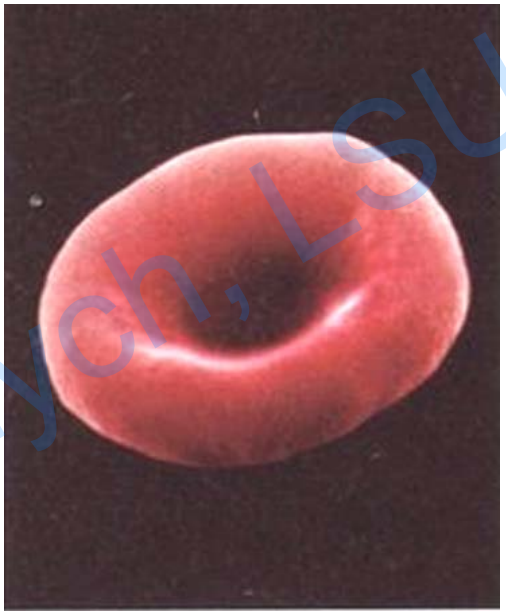
- **Isotonic fluids** have the **same** effective **osmolality** (tonicity) as body fluids (0.9% sodium chloride solution and 5% glucose solution). Red blood cells in isotonic fluid neither gain nor lose water
- **Hypertonic fluids** - greater effective osmolality, water moves out of the cells resulting in **shrinkage** of the cells
- **Hypotonic fluids** - with **less** effective osmolality, water moves into the cells and causes **swelling** and rupture (**hemolysis**)



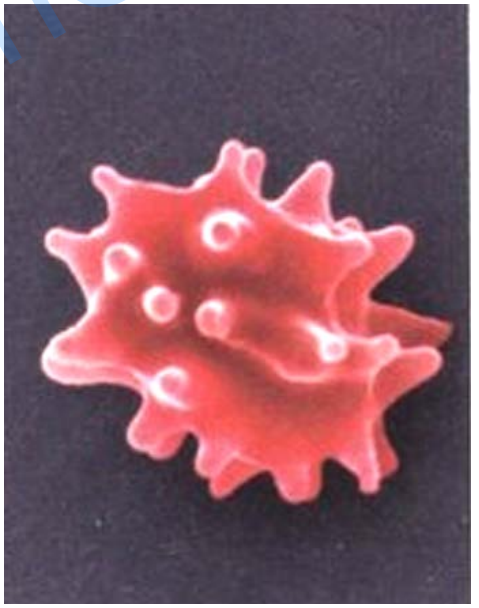
Red Blood Cells in Solutions with Different Tonicity



Isotonic fluid

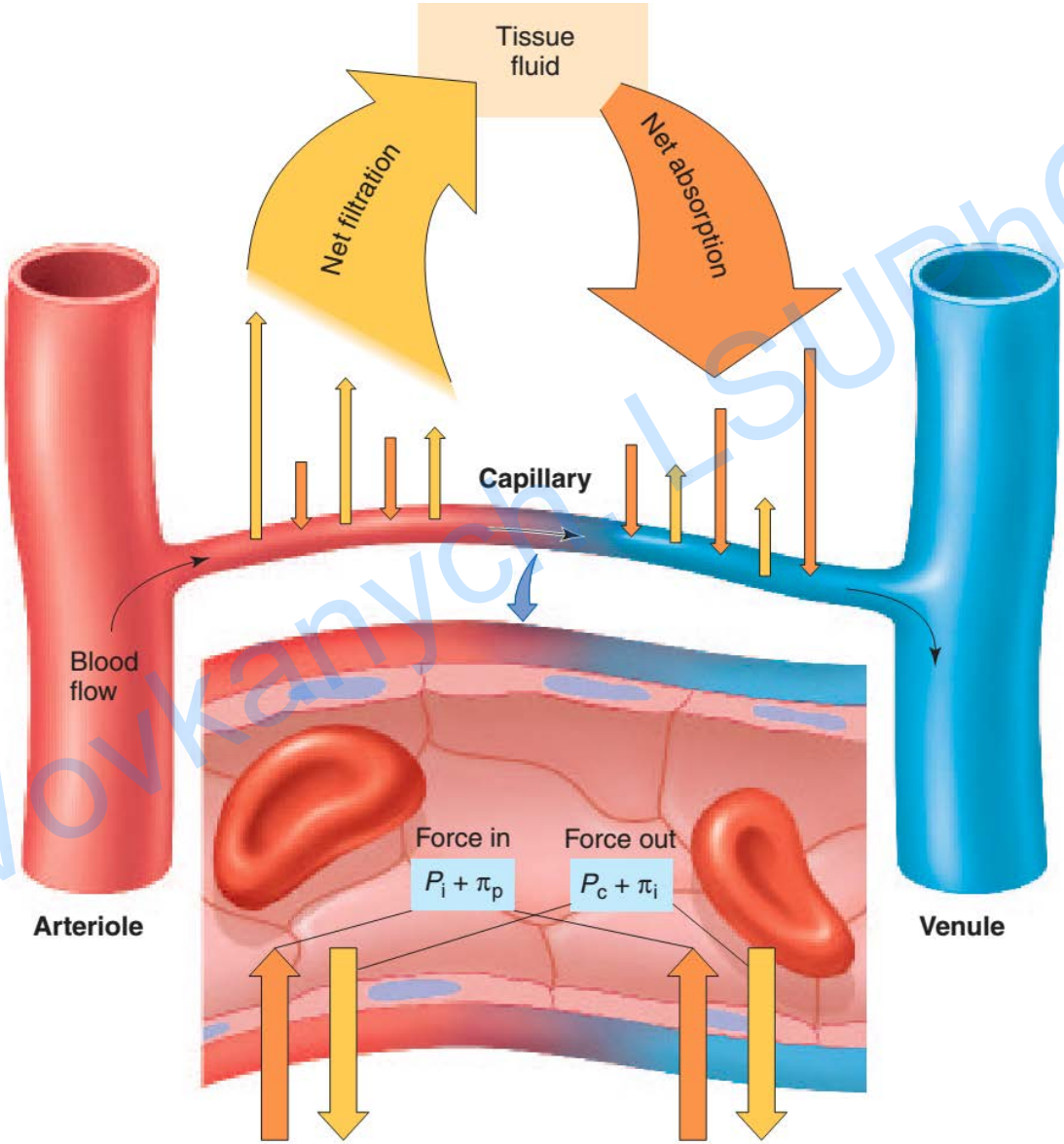


Hypotonic fluid



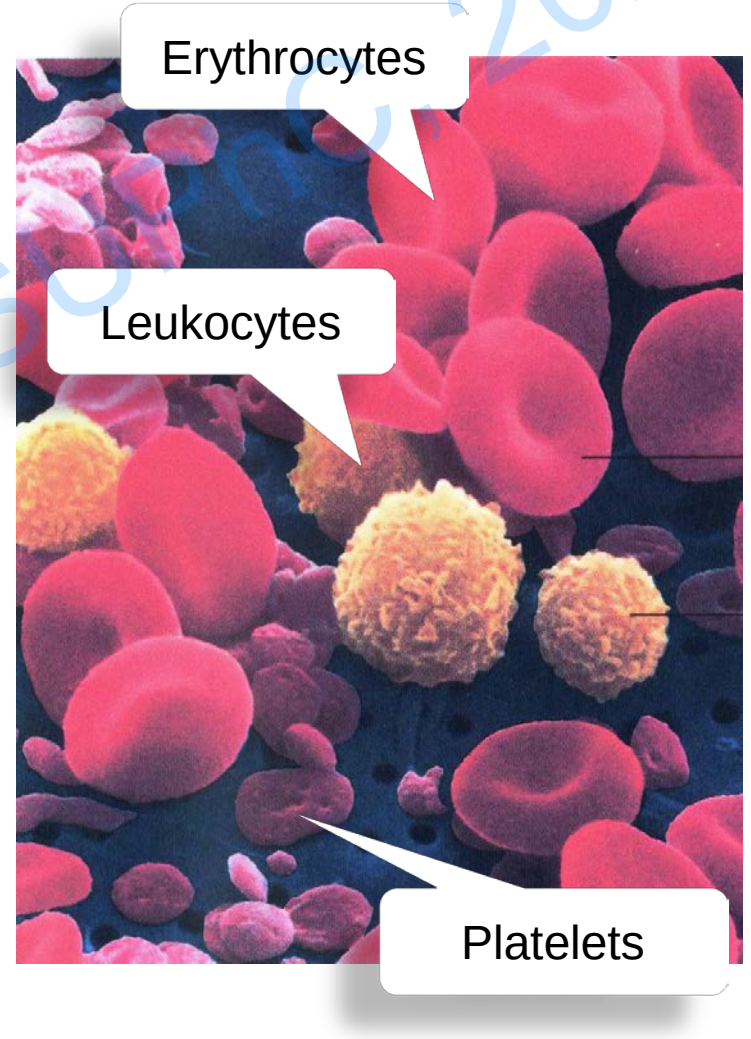
Hypertonic fluid

Osmotic Pressure and Water Transport



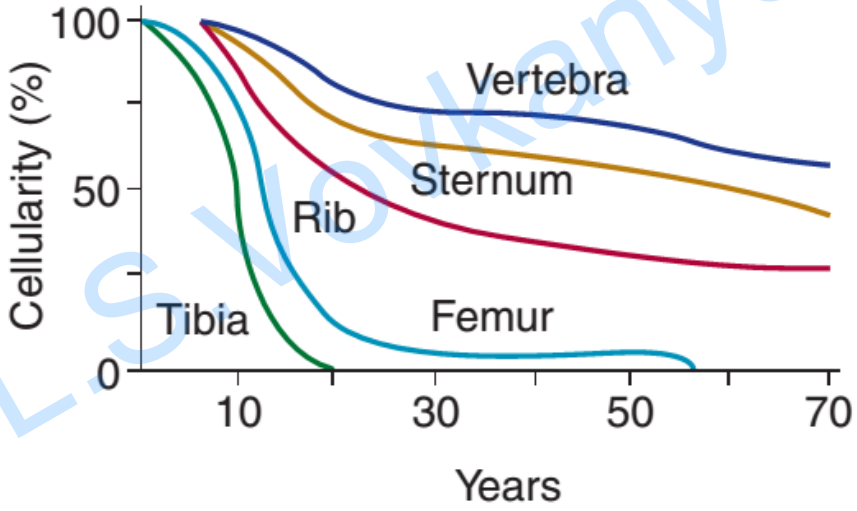
The Formed Elements (Cells) of Blood

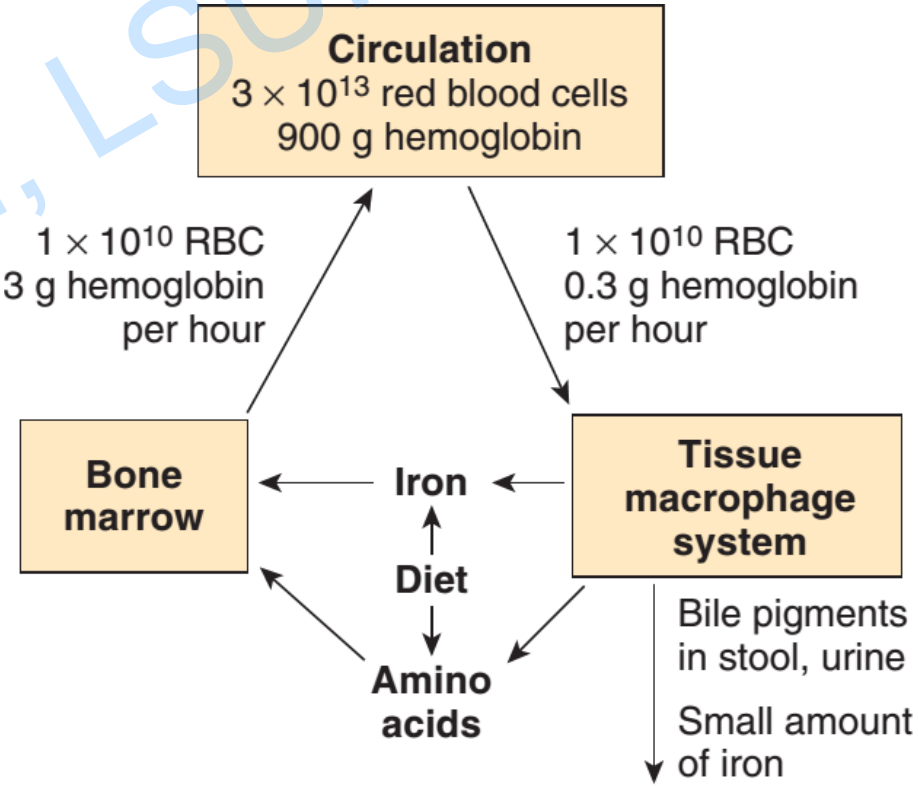
Cell	Cells/μL (average)	Normal Range (1/μL)
Erythrocytes • Males • Females	 5.4×10^6 4.8×10^6	
Leukocytes (white blood cells)	9000	4000–10,000
Granulocytes		
• **Neutrophils**	5400 (50-70%)	3000–6000
• **Eosinophils**	275 (1-4%)	150–300
• **Basophils**	35 (0.4%)	0–100
Lymphocytes	2750 (20–40%)	1500–4000
Monocytes	540 (2–8%)	300–600
Platelets	300,000	200,000–500,000



Red Blood Cells (Erythrocytes)

- In the adult, red blood cells, many white blood cells, and platelets **are formed in the bone marrow**
- Cellular marrow is called **red marrow**; inactive marrow that is infiltrated with fat is called yellow marrow

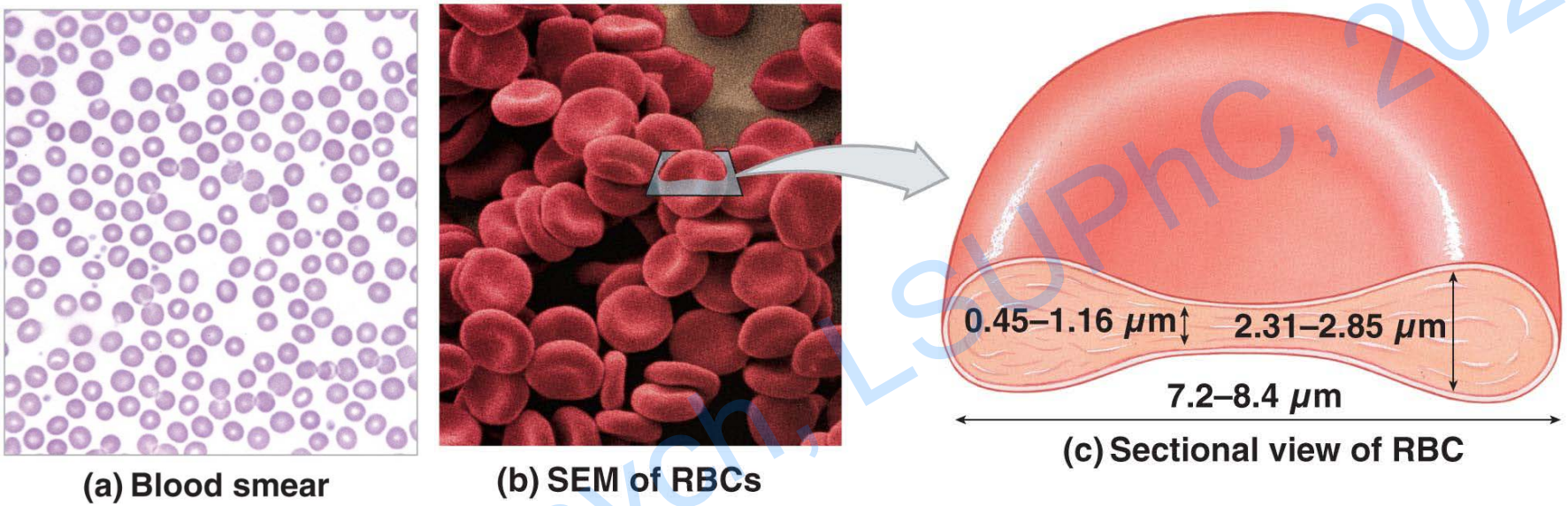




Red Blood Cells (Erythrocytes)

- RBCs are the **non-nucleated** formed elements in the blood
- **Diameter** : 7.2 µm (6.9 to 7.4 µm)
- **Red color** is due to the presence of the **hemoglobin**
  - Concentration of **Hemoglobin** (Hb) – 16-14 g/dL (male/female)
  - Mean **corpuscular hemoglobin** (MCH) – 29 pg
  - Totally 70-kg man has about **900 g** of hemoglobin
- Average **lifespan** of RBC: 120 days
- 3 million RBCs per second is formed
- Building red blood cells **requires**
  - Amino acids
  - Iron
  - Vitamins B12, B6, and folic acid:
- **Functions of red blood cells**
  - Transport of Oxygen and Carbon Dioxide
  - Buffering Action in Blood

Red Blood Cells (Erythrocytes)



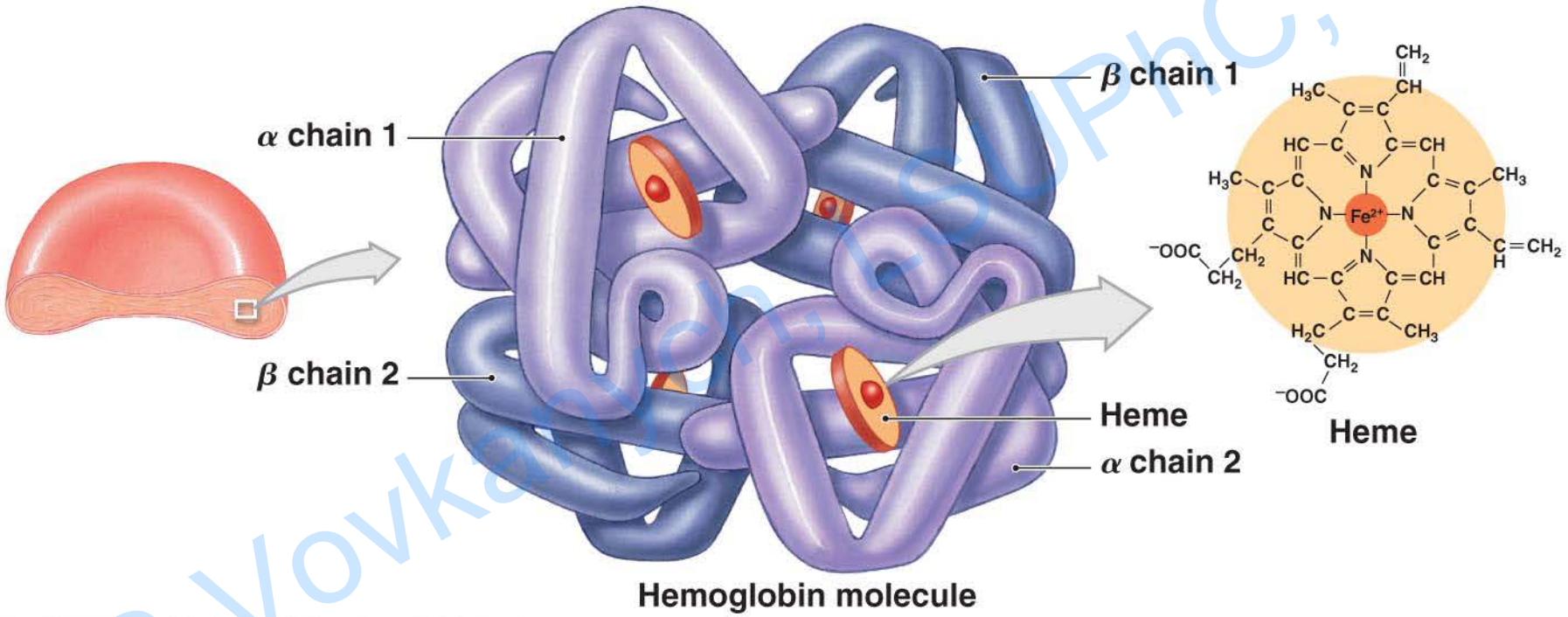
(a) Blood smear (b) SEM of RBCs (c) Sectional view of RBC

- RBCs are **disk shaped** and **biconcave** (dumbbell shaped)
  - helps **rapid diffusion** of oxygen into the interior of the cell
  - **large surface area** is provided
  - squeeze through the capillaries very easily discs form stacks called rouleaux (smooth the flow through narrow blood vessels)

Hemoglobin Structure

- Protein with complex **quaternary structure**
- **Four** globular protein **subunits**:
  - Each with one molecule of **heme**
  - Each heme contains one **iron ion**
- Associate easily with oxygen (**oxyhemoglobin**)
- Dissociate easily from oxygen (**deoxyhemoglobin**)
- Binds carbon dioxide (**carbaminohemoglobin**)
- **Abnormal** hemoglobin derivatives
  - **Carboxyhemoglobin** - complex with carbon monoxide
  - **Methemoglobin** - iron molecule of hemoglobin is oxidized

Hemoglobin Structure



White Blood Cells (Leukocytes)

- **Colorless** formed elements of blood
- Have **nucleus** of different shape
- Based on the presence or absence of granules in the cytoplasm, the leukocytes are **classified into two groups**:
  - **Granulocytes** which have granules
    - **Neutrophils** with granules taking both acidic and basic stains.
    - **Eosinophils** with granules taking acidic stain.
    - **Basophils** with granules taking basic stain
  - **Agranulocytes** which do not have granules
    - **Monocytes**
    - **Lymphocytes**

Properties of white blood cells

- **Diapedesis** - process by which the leukocytes squeeze through the narrow blood vessels
- **Amebic movement** - most pronounced in neutrophils, monocytes and lymphocytes
- **Chemotaxis** - attraction of WBCs towards the injured tissues by the chemical substances
- **Phagocytosis** – process, by which neutrophils and monocytes engulf (“eat up”) the foreign bodies

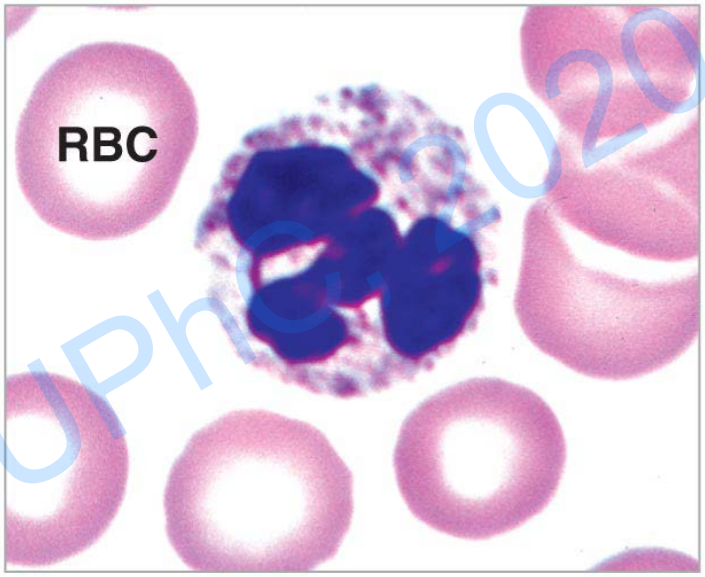
Neutrophils

Structure

- diameter - 10 to 12 µm
- small granules in the cytoplasm
- nucleus is multilobed
- in younger cells, the nucleus is not lobed.
- in older neutrophils, the nucleus has 2 to 5 lobes
- lifespan - 2-5 days

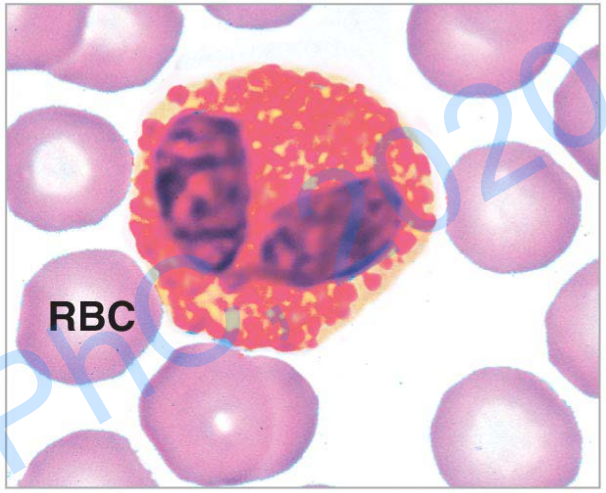
Function:

- neutrophils provide the first line of defense against the invading microorganisms, destroy them by means of phagocytosis
- release cytotoxic enzymes and chemicals



(a) Neutrophil

Eosinophils



(b) Eosinophil

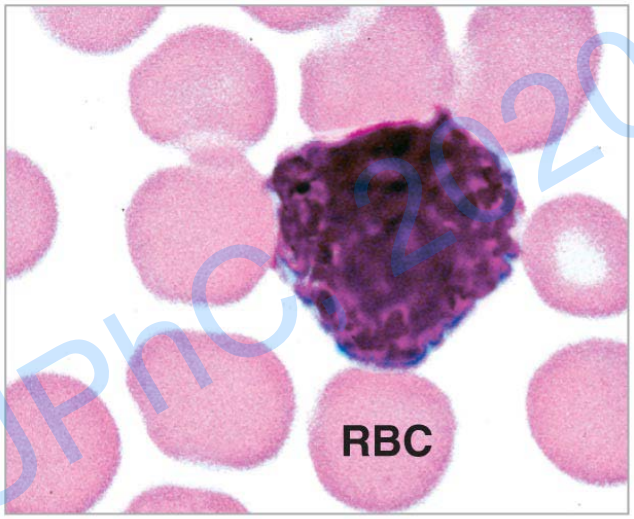
Structure

- diameter - 10 and 14 μm
- larger granules in the cytoplasm, which stain pink or red with eosin
- nucleus is bilobed
- lifespan: 7-12 days

Function

- play an important role in the defense mechanism of the body against the parasites
- increases also during allergic diseases
- are responsible for detoxification, disintegration and removal of foreign proteins
- release the cytotoxic substances present in their granules

Basophils



(c) Basophil

Structure

- diameter - 8 to 10 μm
- nucleus is bilobed
- have coarse granules in the cytoplasm
- stain purple blue with methylene blue
- lifespan: 5-12 days

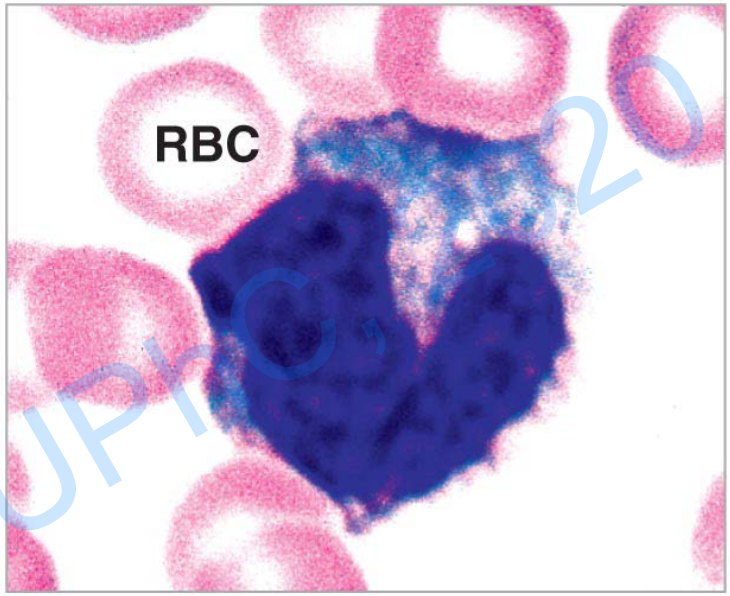
Function

- play an important role in healing processes and in allergy reactions
- releases:
  - heparin (essential to prevent the intravascular blood clotting)
  - histamine (causing vascular and tissue responses)
  - cytotoxic chemcals

Monocytes

Structure

- the largest leukocytes with diameter of 14 to 18 μm
- cytoplasm is clear without granules
- nucleus is round, oval, bean shaped or kidney shaped
- lifespan: 2-5 days



(d) Monocyte

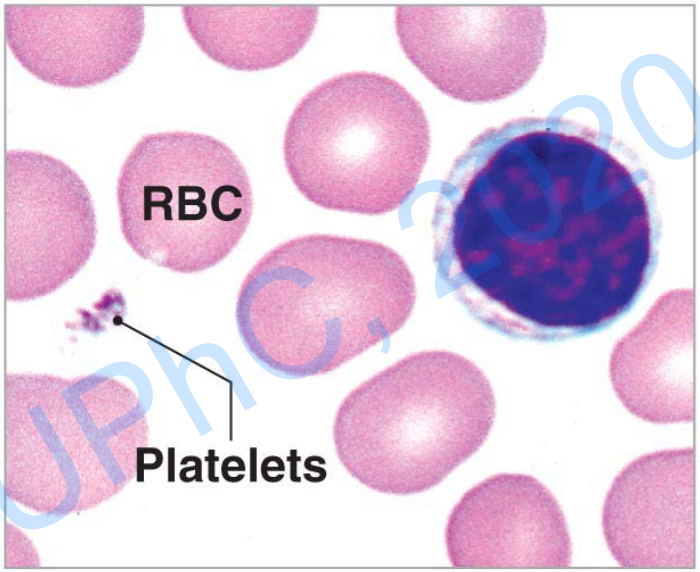
Function

- enter the tissues from the blood and become tissue macrophages
- neutrophils provide the first line of defense
- are motile and phagocytic in nature

Lymphocytes

Structure

- younger cells has a diameter of 10 to 12 μm, older cells – 7 to 10 μm
- do not have granules in the cytoplasm
- nucleus is oval, bean-shaped or kidney-shaped
- lifespan: approx. 1 day



(e) Lymphocyte

Function

- provide defense against the specific pathogens
- depending upon the function, lymphocytes are
- divided into two types:
  - **T lymphocytes**: cells concerned with cellular immunity
  - **B lymphocytes**: cells concerned with humoral immunity

Physiological Variations

- **Leukocytosis** is the increase in total WBC count
- **Leukopenia** is the decrease in total WBC count

Physiological changes in the stage of:

- **Exercise**: Increases slightly
- **Sleep**: Decreases
- **Emotional** conditions like anxiety: Increases
- **Pregnancy**: Increases

Pathological Variations

Leukocytosis

- Infections
- Allergy
- Common cold
- Tuberculosis
- Leukemia abnormal and uncontrolled increase in leukocyte count more than 1,000,000 µm

Leukopenia

- Anaphylactic shock
- Cirrhosis of liver
- Disorders of spleen
- Viral infections

Variation in Differential Leukocyte Count

Neutrophilia

- Acute infections
- Metabolic disorders
- Injection of foreign proteins
- Poisoning by chemicals

Eosinophilia - asthma and other allergic conditions

Basophilia – smallpox

Basopenia - stress

Monocytosis – tuberculosis, malaria

Lymphocytosis – diphtheria, infectious hepatitis etc.

Lymphocytopenia - AIDS

Platelets (Thrombocytes)

Structure

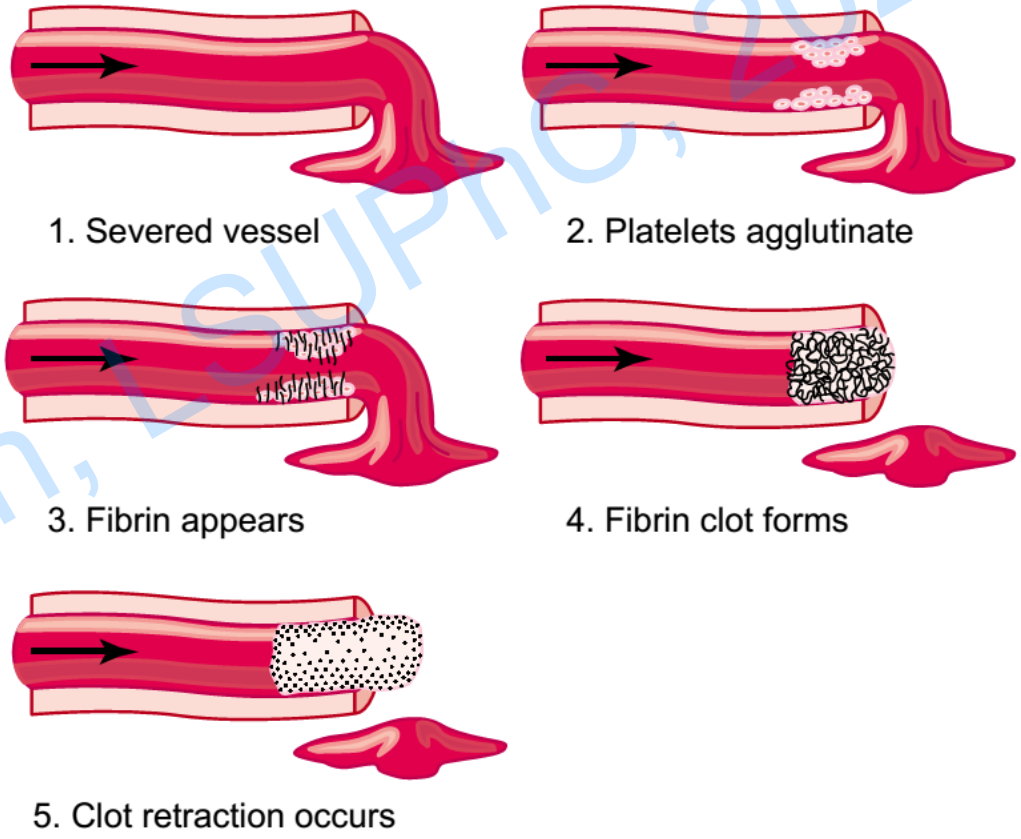
- diameter : 2.5 μm (2 to 4 μm)
- small colorless, non-nucleated bodies, are considered to be the fragments of cytoplasm
- lifespan: 10 days
- cytoplasm contains the cellular organelles and granules
  - **alpha granules** (clotting factors – fibrinogen etc.)
  - **dense granules** (serotonin, calcium etc.)
  - other proteins: fibrin-stabilizing factor, platelet-activating factor, thrombosthenin etc.

Function

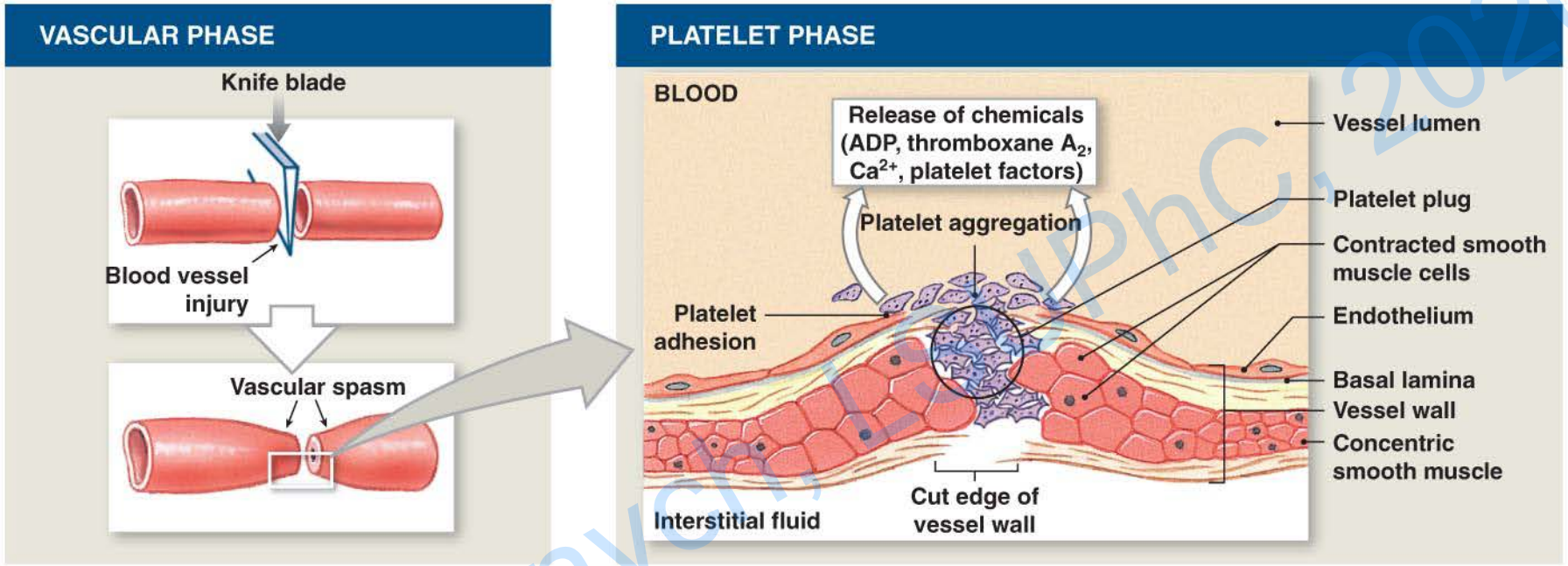
- are responsible for the formation of intrinsic prothrombin activator, responsible for the **onset of blood clotting**
- **release** important **clotting chemicals**, temporarily patch damaged vessel walls, actively contract tissue after clot formation

Hemostasis

- **Hemostasis** is the cessation of bleeding
- Consists of **three phases**
  - **Vascular phase** (vascular spasm that lasts 30 minutes)
  - **Platelet phase** (begins within 15 seconds after injury)
    - Platelet **adhesion** (attachment)
    - Platelet **aggregation** (stick together)
    - Forms **platelet plug**
  - **Coagulation** phase



Hemostasis



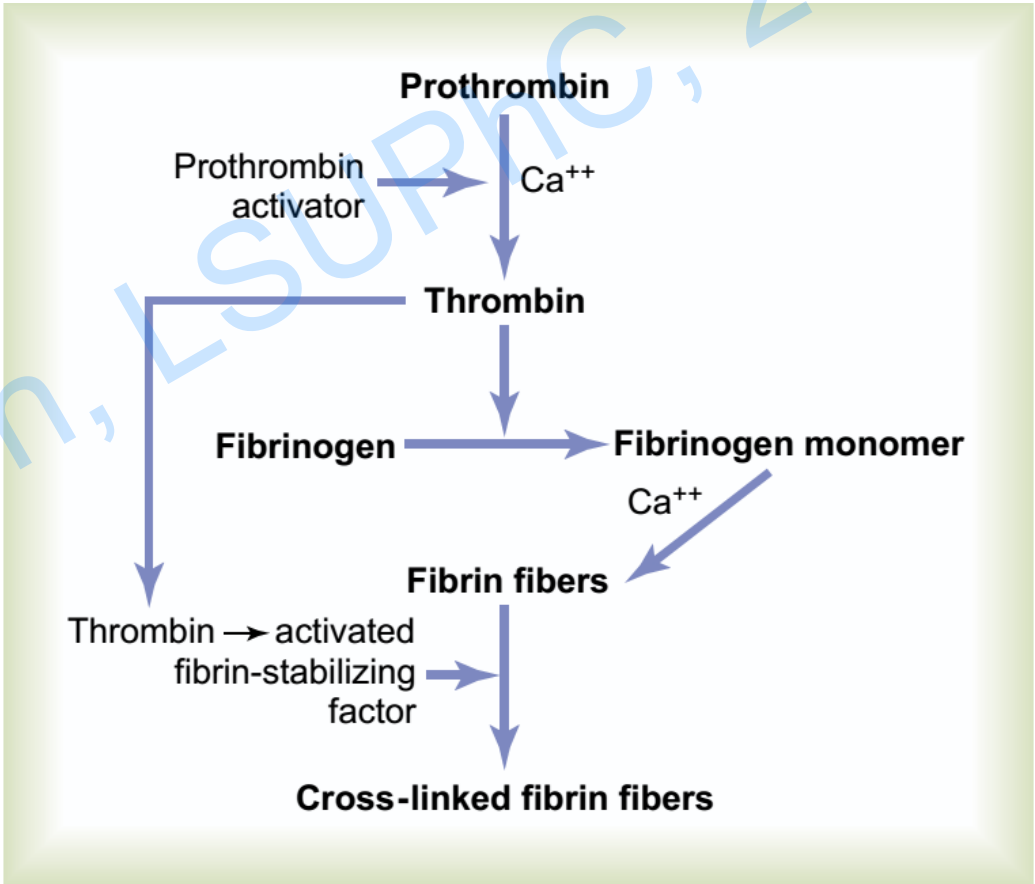
- Activated platelets release clotting compounds
  - Adenosine diphosphate (ADP)
  - Thromboxane A2 and serotonin
  - Clotting factors
  - Platelet-derived growth factor (PDGF)
  - Calcium ions

The Coagulation Phase

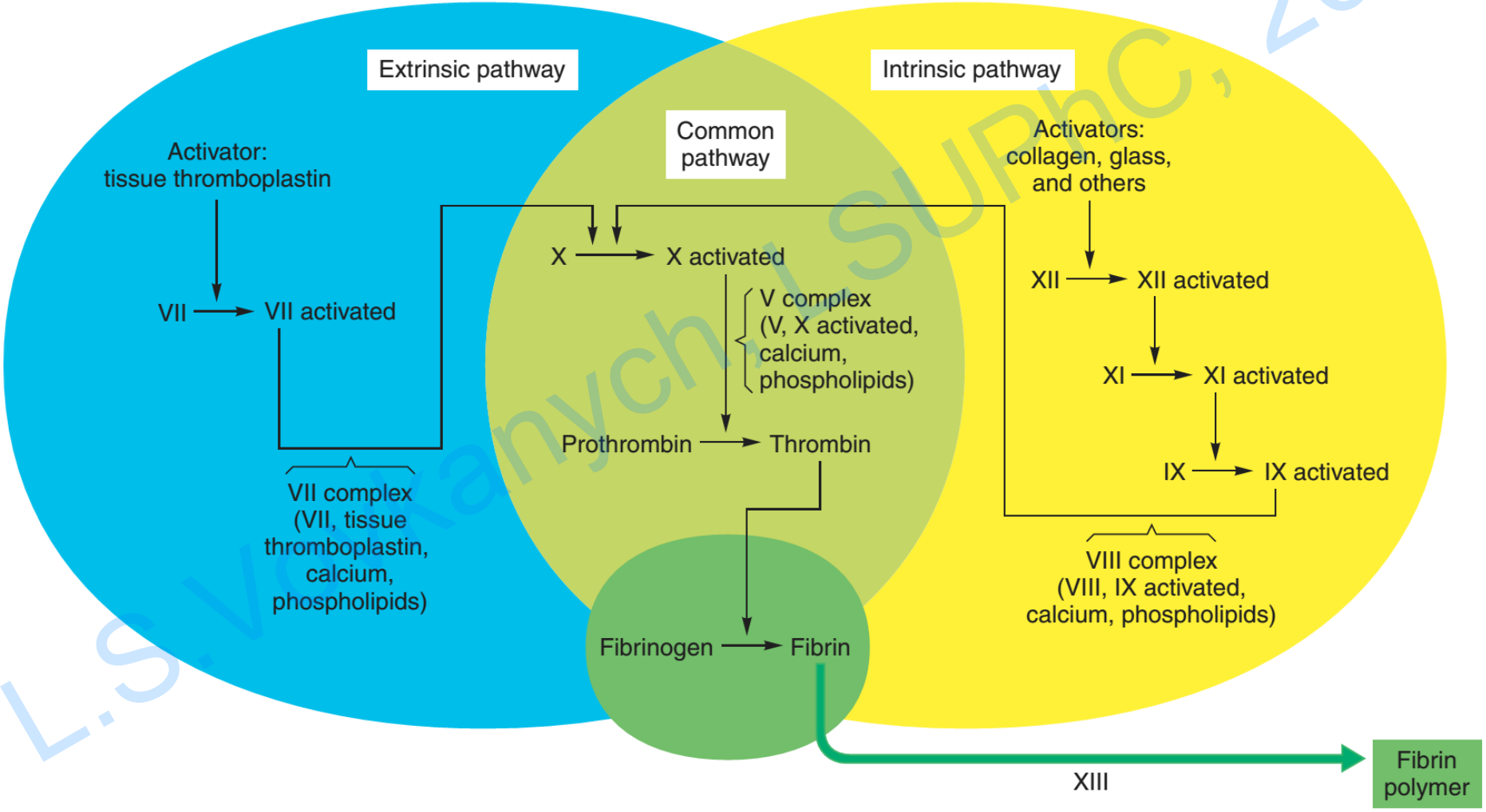
- Begins 30 seconds or more after the injury
- **Blood clotting** (coagulation) is the cascade reactions:
  - **chain reactions** of enzymes and proenzymes
  - form **three pathways**
  - convert **circulating fibrinogen** into insoluble **fibrin**
- **Clotting Factors** (13 of them), also called **procoagulants**
  - Proteins or ions in plasma
  - Required for normal clotting
- After clot has formed **platelets contract** and pull torn area together

Three Coagulation Pathways

- **Extrinsic pathway** - begins in the vessel wall
- **Intrinsic pathway** - begins with circulating proenzymes
- **Common pathway** – converge of both pathways:
  - Forms enzyme **prothrombinase**
  - Converts **prothrombin** to **thrombin**
  - Thrombin converts **fibrinogen** to **fibrin**



Extrinsic and Intrinsic Clotting Pathways



Anticoagulants

Substances which **prevent** or **postpone** coagulation of blood

- **Heparin** - naturally produced anticoagulant in the body
- **Coumarin** derivatives (dicoumoral and warfarin)
- **Ethylenediaminetetraacetic** acid (EDTA)
- **Oxalate** compounds
- **Citrates** of sodium, ammonium and potassium
- **Hirudin –** natural from the leach Hirudinaria manillensis

Anticlotting Mechanism in the Body

Under physiological conditions, **intravascular clotting does not occur**, because of:

- continuous circulation of blood
- smooth endothelial lining of the blood vessels
- presence of natural anticoagulant (heparin)
- production of thrombomodulin
- all the clotting factors are in inactive state

Thrombosis or intravascular blood clotting refers to coagulation of blood inside the blood vessels

Complications of **thrombosis**

- **embolus** - thrombus or part of it, which arrests the blood flow
- **ischemia** - insufficient blood supply to an organ or area of the body by the obstruction of blood vessels is called
- **necrosis** - tissue death caused by loss of blood supply

Fibrinolysis

- **Fibrinolysis** - lysis of blood clot inside the blood vessel
- It helps to **remove the clot** from lumen of the blood vessel
- This process requires a substance called **plasmin** or fibrinolysin
- Plasmin is formed from inactivated glycoprotein called **plasminogen**
- Reaction is **started during intravascular clotting**

Blood Types

- The membranes of human red cells contain a variety of **blood group antigens**, which are also called **agglutinogens**
- There are several groups of red blood cell antigens, but the **major groups** are known as the **ABO system** and **Rh system**
- The most important and best known of **blood group antigens** are the A, B and D (Rh) antigens
- **Plasma antibodies** attack and **agglutinate (clump) foreign antigens**

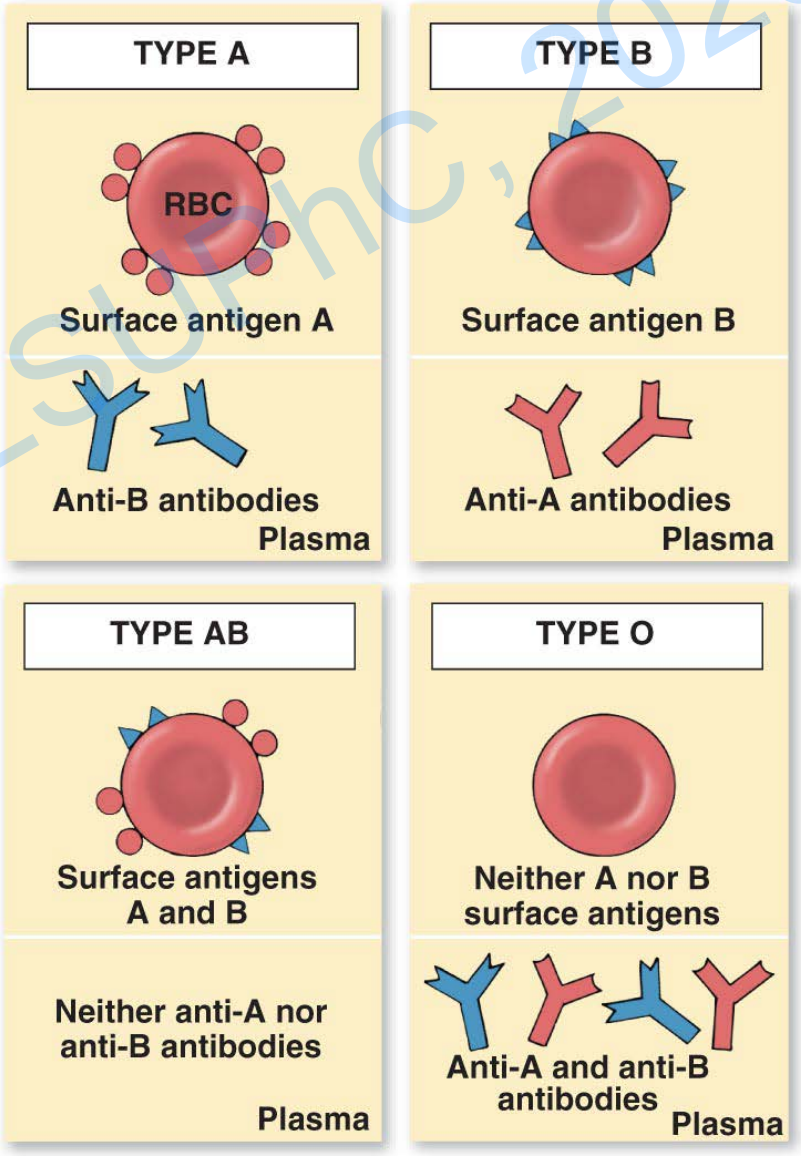
Main Blood Types

Four Basic Blood Types in **ABO system**

- A (surface antigen A)
- B (surface antigen B)
- AB (antigens A and B)
- O (neither A nor B)

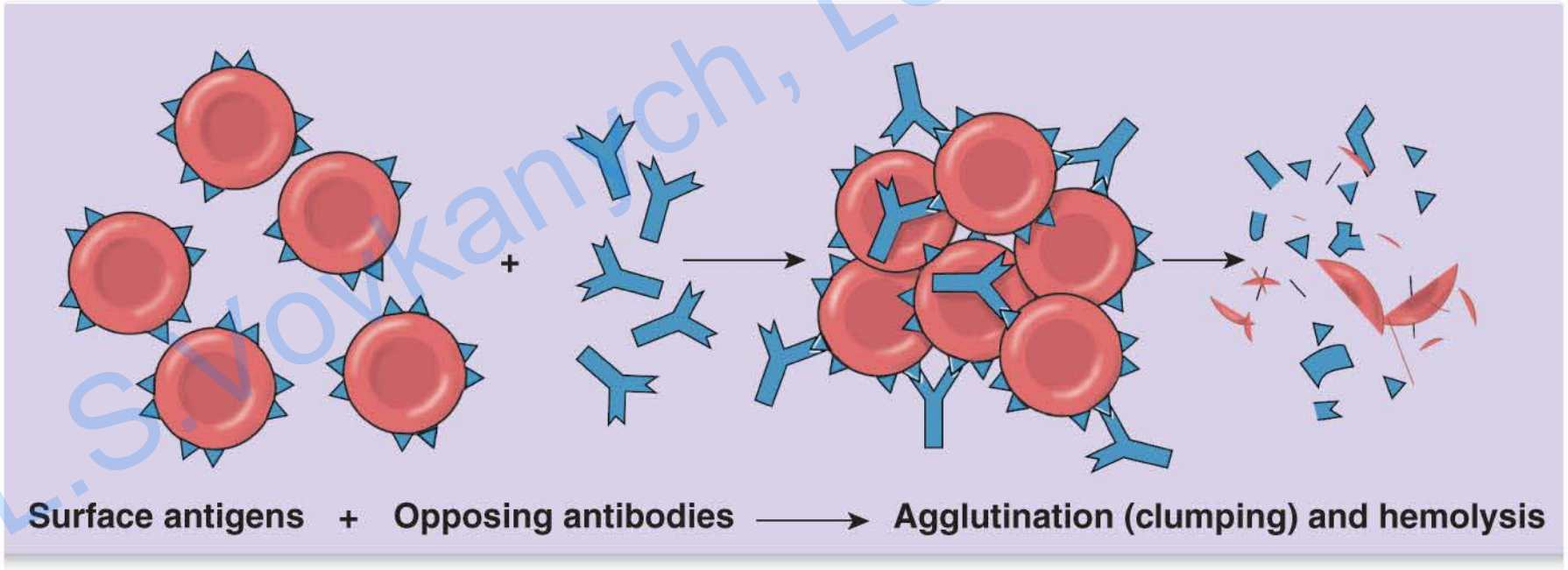
Two Basic Blood Types in **Rh System**

- Rh positive (Rh+)
- Rh negative (Rh-)
- Only sensitized Rh- blood has anti-Rh antibodies



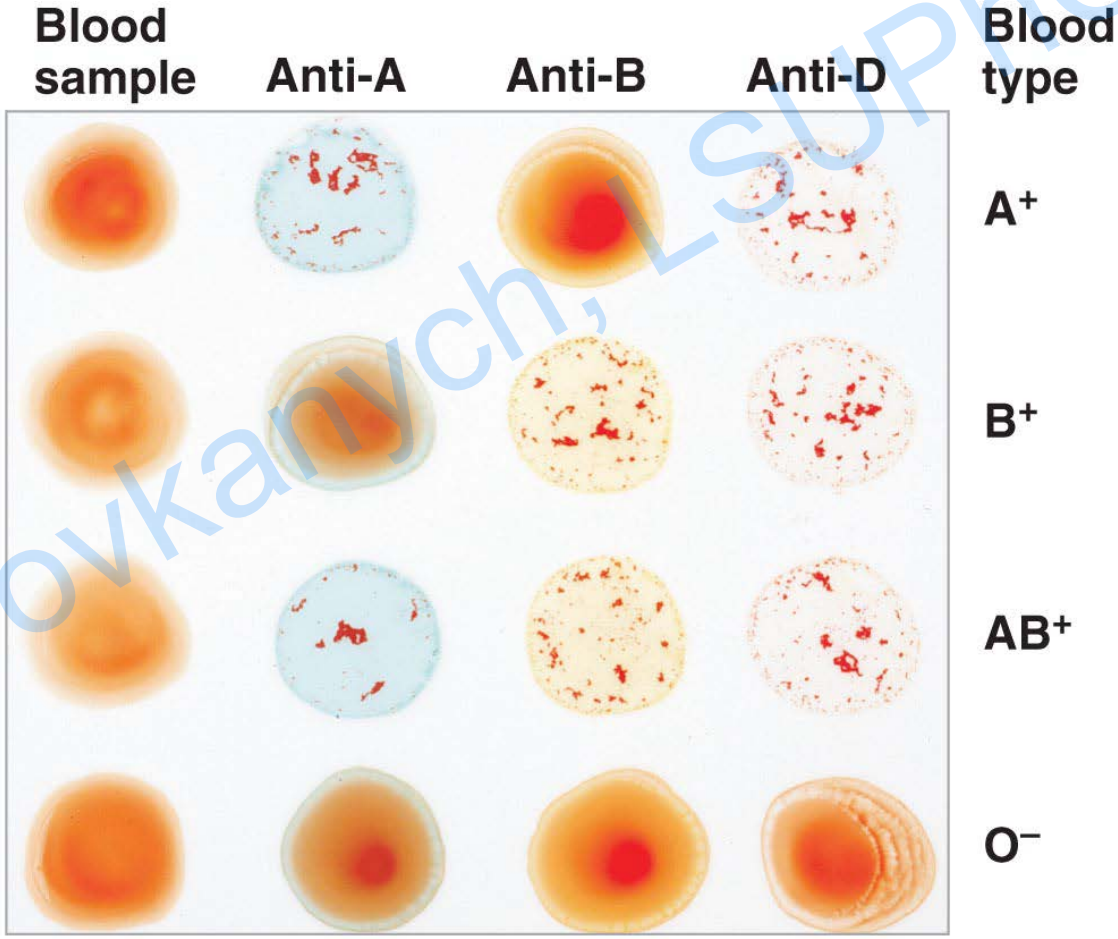
Cross-Reactions in Transfusions

- Plasma **antibody meets** its specific surface **antigen**
- Blood will **agglutinate** and **hemolyze**
- Occur if donor and recipient blood types **not compatible**



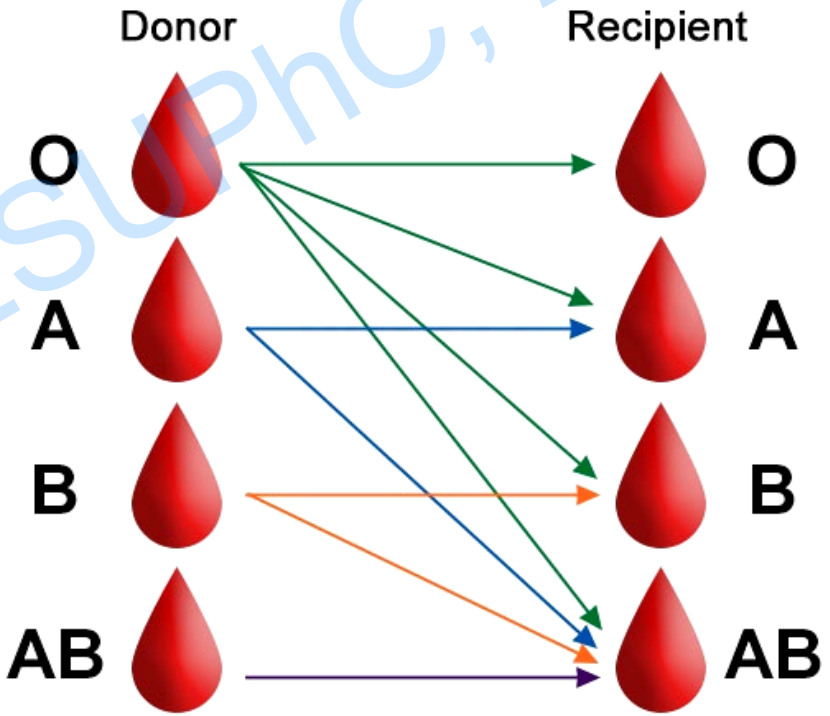
Determination of ABO Group

- Blood typing is done on the basis of agglutination with the standard serum



Blood transfusion

- only **compatible** blood must be used
- person who gives blood is called the **donor**
- person who receives the blood is called **recipient**
- compatibility is considered on
  - **antigen** of the **donor**
  - **antibody** of the **recipient**
- **cross-matching** is done by mixing the serum of the recipient and the RBCs of donor
- people with O group are called '**universal donors**'
- people with AB group are called '**universal recipients**'



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