White blood cells
for
first year MBBS students

DR RIFFAT SULTANA

White blood cell,

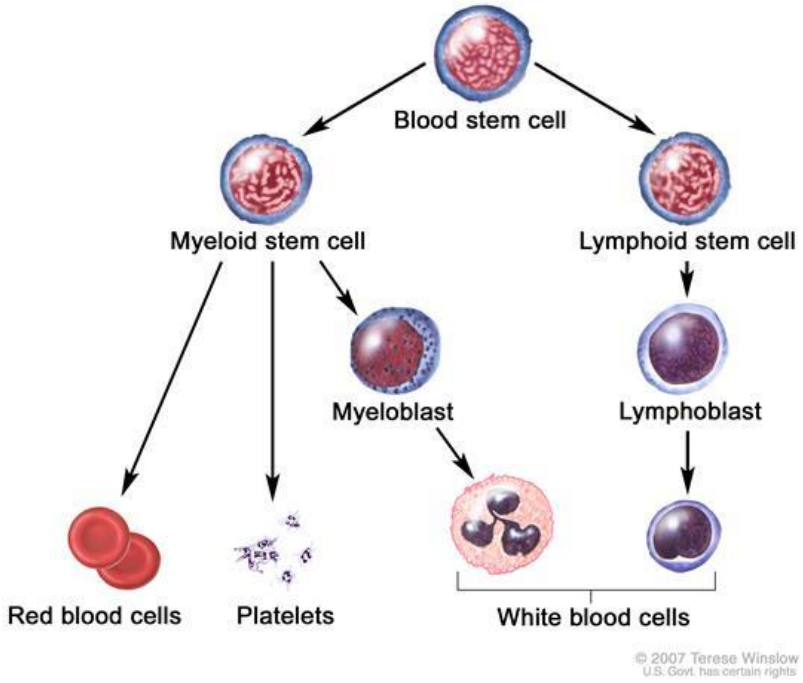
- also called **leukocyte** or **white corpuscle**, a cellular component of the blood.
- lacks hemoglobin,
- has a nucleus,
- is capable of motility,
- and defends the body against infection and disease by ingesting foreign materials and cellular debris, by destroying infectious agents , or by producing antibodies.

Definition

The tissues and organs that produce, store, and carry white blood cells that fight infections and other diseases.

This system includes the

- Bone Marrow
- Spleen
- Thymus



- The granulocytes and monocytes are formed only in the bone marrow.
- Lymphocytes and plasma cells are produced mainly in the various lymphogenous tissues- especially the lymph glands
- spleen
- Thymus
- Tonsils
- various pockets of lymphoid tissue such as bone marrow
- and in payer patches underneath the epithelium in the gut wall.

Leucopoiesis

Definition

The process of development and maturation of white blood cells(leucocytes), is called leucopoiesis.

Definition

- ***White blood cells*** *or* ***leukocytes*** are cells of the immune system which defend the body against both infectous disease and foreign materials.

➢ ***Characters of WBCs:***

1. Whenever a germ or infection enters the body the white blood cells have a variety of ways by which they can attack. Some will produce protective antibodies that will overpower the germ. Others will surround and devour the bacteria.

- A healthy adult human has between 4,500 and 11,000 white blood cells per cubic millimetre of blood.

Leukocytosis

- Fluctuations in white cell number occur during the day; lower values are obtained during rest and higher values during exercise. An abnormal increase in white cell number is known as leukocytosis
- White cell count may increase in response to intense physical exertion, convulsions acute emotional reactions, pain, pregnancy, labour (physiological leukocytosis)and certain disease states, such as infections and intoxications.(pathological leukocytosis).

- Although white cells are found in the circulation, most occur outside the circulation, within tissues, where they fight infections; the few in the bloodstream are in transit from one site to another.
- White cells, containing a nucleus and able to produce ribonucleic acid (RNA) can synthesize protein
- White cells are highly differentiated for their specialized functions
-

White blood cells

- On the basis of their appearance under a light microscope, white cells are grouped into three major classes—lymphocytes, granulocytes, and monocytes—each of which carries out somewhat different functions.

lymphocytes

- mostly stored in the various lymphoid tissues except for a small number that are temporarily being transported in the blood.
- Lymphocytes which are further divided into B cells and T cells, are responsible for the specific recognition of foreign agents and their subsequent removal from the host.
- B lymphocytes secrete antibodies, which are proteins that bind to foreign microorganisms in body tissues and mediate their destruction.

  Typically, T cells recognize virally infected or cancerous cells and destroy them, or they serve as helper cells to assist the production of antibody by B cells.
- Also included in this group are natural killer (NK) cells, so named for their inherent ability to kill a variety of target cells. In a healthy person, about 25 to 33 percent of white blood cells are lymphocytes

Their common functions are

1. **NK Cells:**

   Usually have cytotoxic activity against a wide range of tumor cells and also against some cells infected with viruses.

2. **T-Lymphocytes**

   They identify and bind to antigenswhich are bound to MHC complex,a self antigen on the surface of T-cells.

3. **B-Lymphocytes**

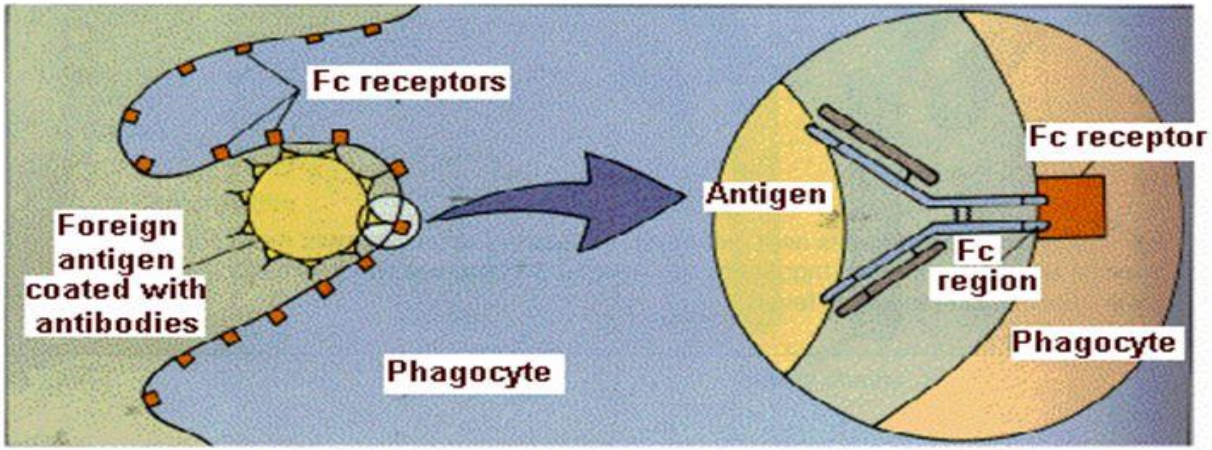
   Produce antibodies against a given antigen.The Abs act as receptors.

T cells

T cells or **T lymphocytes** are a type of lymphocytes (itself a type of white blood cells) that play a central role in cell-mediated immunity. They can be distinguished from other lymphocytes, such as B cells and natural killer cells (NK cells), by the presence of a *T-cell receptor* (TCR) on the cell surface. They do not have antigen-presenting They are called *T* cells because they mature in the thymus.

Opsonization and Inactivating an Antigen

Opsonization: Certain bacterial cells have so many AG determinants that the antibodies coat the bacteria cell. The constant regions stick out (called the FC region). The phagocytes have FC receptors. This interaction allows the phagocyte to roll over the pathogen and phagocytosis occurs.



Granulocytes

- most numerous of the white cells, rid the body of large pathogenic organisms such as protozoans or helminths and are also key mediators of allergy and other forms of inflammation
- These cells contain many cytoplasmic granules, or secretory vesicles, that harbour potent chemicals important in immune responses.
- They also have multilobed nuclei, and because of this they are often called polymorphonuclear cells.

Granulocytes--- subdivided into three categories

- : **NEUTROPHILS, EOSINOPHILS** and **BASOPHILS.**
- The most numerous of the granulocytes—making up 50 to 80 percent of all white cells—are neutrophils.
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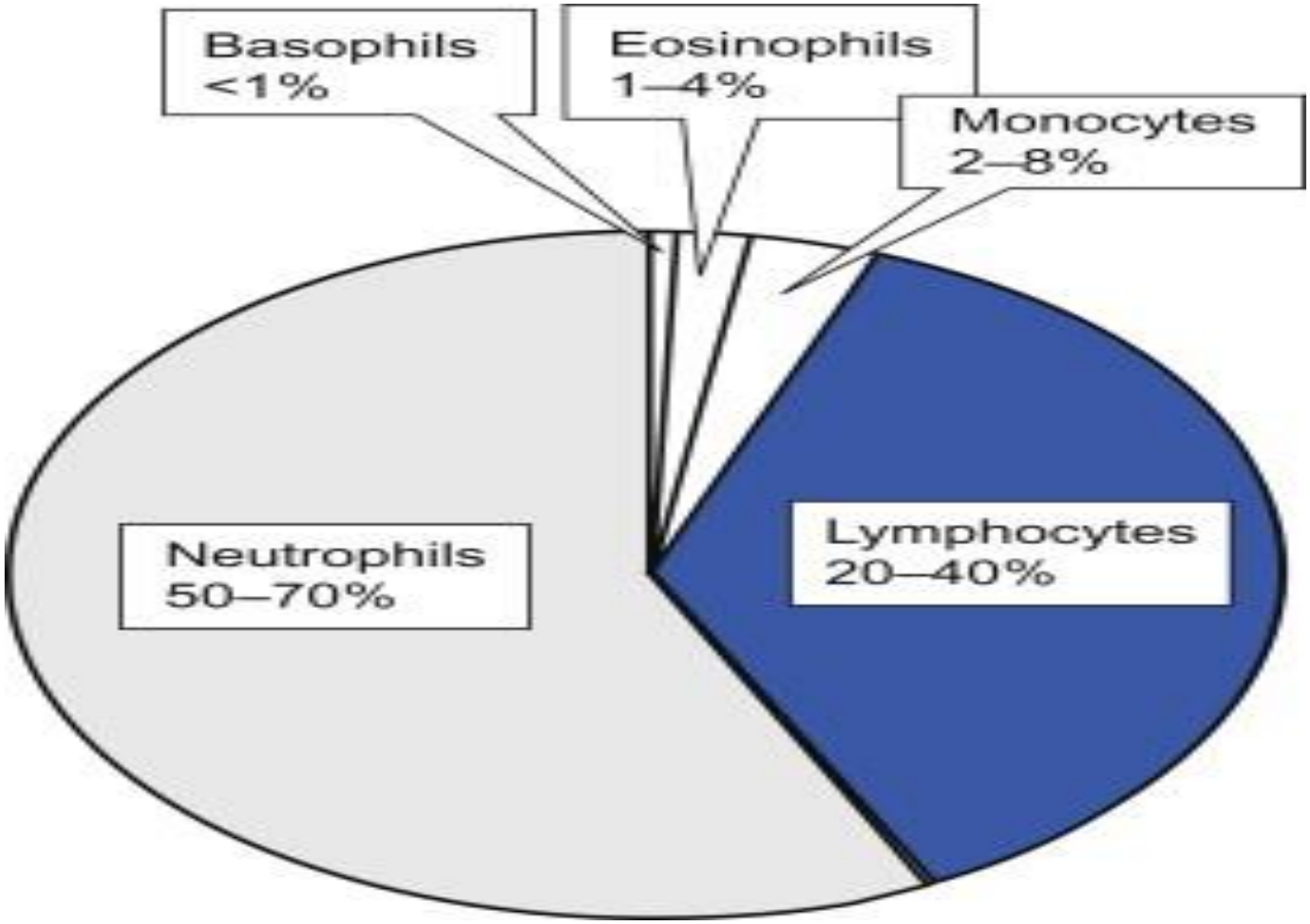
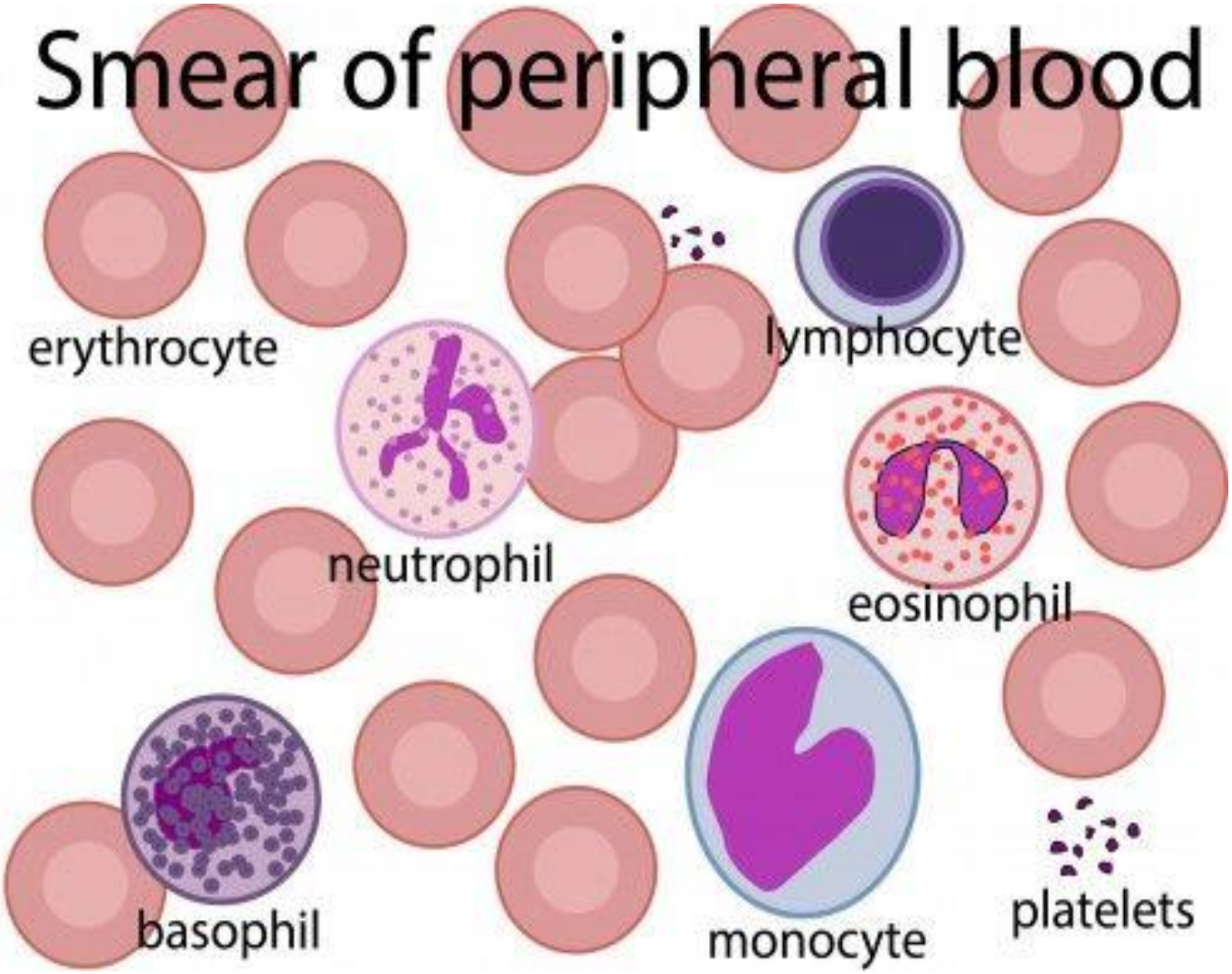

Basophils
<1%
Eosinophils
1–4%
Monocytes
2–8%
Lymphocytes
20–40%
Neutrophils
50–70%

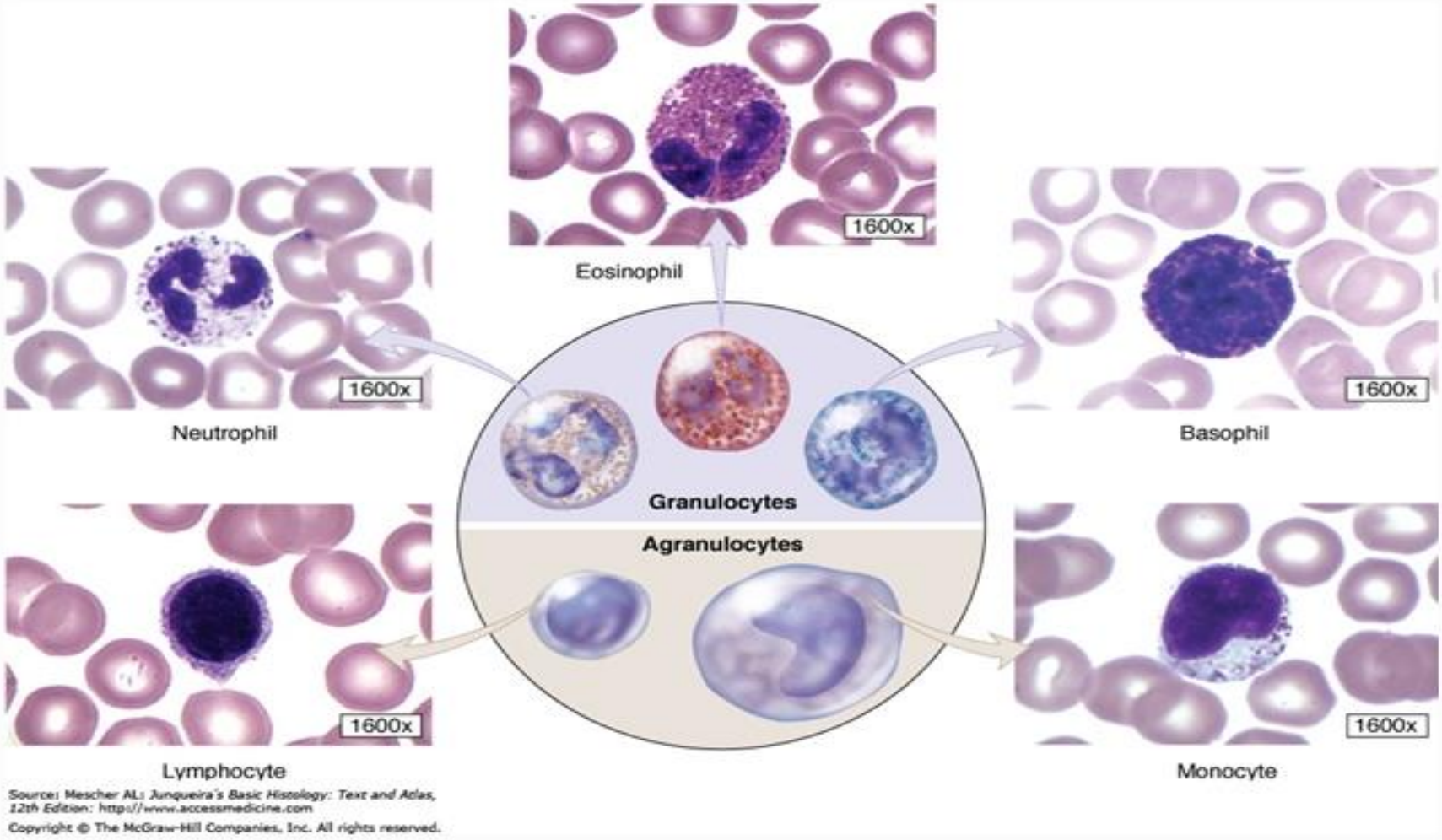
- Eosinophils and basophils, as well as the tissue cells called mast cells, typically arrive later.
- The granules of basophils and of the closely related mast cells contain a number of chemicals, including **histamine** and **leukotrienes**, that are important in inducing allergic inflammatory responses.
- Eosinophils destroy parasites and also help to modulate inflammatory responses.

- **MONOCYTES** which constitute between 4 and 8 percent of the total number of white blood cells in the blood, move from the blood to sites of infection, where they differentiate further into **MACROPHAGES.**
- These cells are scavengers that phagocytose whole or killed microorganisms and are therefore effective at direct destruction of pathogens and cleanup of cellular debris from sites of infection.
- macrophage are more powerful phagocytes than neutrophils.

Smear of peripheral blood



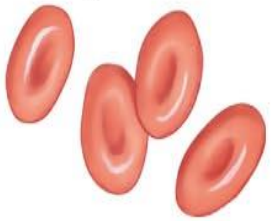
Wbcs serve as Sanitary engineers cleaning up dead cells and tissue debris that otherwise accumulate to and lead to problems.



The formed elements in blood, a fluid connective tissue with a watery matrix called plamsa

Red Blood Cells

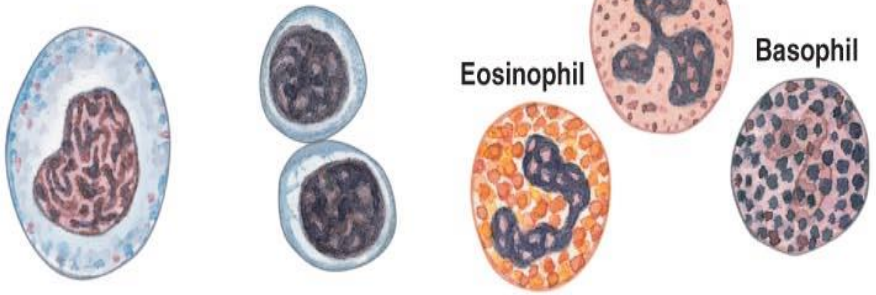
Red blood cells are formed elements responsible for the transport of oxygen (and, to a lesser degree, of carbon dioxide) in the blood.



Red blood cells account for roughly half the volume of whole blood and give blood its color.

White Blood Cells

White blood cells are formed elements that help defend the body from infection and disease.



Monocytes are phagocytes similar to the free macrophages in other tissues.

Lymphocytes are uncommon in the blood but they are the dominant cell type in lymph, the second type of fluid connective tissue.

Eosinophils and **neutrophils** are phagocytes. **Basophils** promote inflammation much like mast cells in other connective tissues.

Platelets

Platelets are formed elements consisting of membrane-enclosed packets of cytoplasm.

These cell fragments are involved in the clotting response that seals leaks in damaged or broken blood vessels.

Life Span Of WBC

- Not constant.
- ❑ Neutrophils -> 2-5 days
- ❑ Eosinophils -> 7-12 days
- ❑ Basophils -> 12-15 days
- ❑ Monocytes -> 2-5 days
- ❑ Lymphocytes -> ½-1 day

Life span of white blood cells

- Granulocytes after being released from the bone marrow is normally 4 to 8 hours circulating in the blood and another 4 to 5 days in tissues where they are needed.
- In case of serious tissue infection it is shortened to only few hours because the granulocytes proceed even more rapidly to the infected area perform their functions and in the process are themselves destroyed.

- Monocytes life span is 10 to 20 hours in the blood before wandering through the capillary membranes into the tissues.
- Once in the tissues they swell to much larger sizes(60 -80 micron the size that can barely be seen by the naked eye) to become tissue macrophage system which provides continuing defense against infection.

Lymphocytes

- Lymphocytes enter the circulatory system continually along with drainage of lymph from the lymph nodes and other lymphoid tissues.
- After few hours they pass back into the tissues by diapedesis..
- then they re enter the lymph and return to the blood again and again thus there is continual circulation of lymphocytes through the body.
- Lymphocytes have life span of weeks or months depending on the body need for these cells.

- **Neutrophils and macrophages are the main phagocytic cells of the body,**
- but macrophages are much larger and longer-lived than neutrophils.
- Some macrophages are important as antigen-presenting cells, cells that phagocytose and degrade microbes and present portions of these organisms to T lymphocytes, thereby activating the specific acquired immune response.

- Specific types of cells are associated with different illnesses and reflect the special function of that cell type in body defense.
- In general, newborns have a high white blood cell count that gradually falls to the adult level during childhood.
- An exception is the **lymphocyte count**, which is low at birth, reaches its highest levels in the first four years of life, and thereafter falls gradually to a stable adult level.

Leukopenia

- whereas an abnormal decrease in number is known as Leukopenia.
- The count may decrease in response to certain types of **infections** or **drugs** or in **association with certain conditions, such as chronic anemia**, **malnutrition**, or anaphylaxis

Table 4. Selected Conditions Associated with Elevations in Certain White Blood Cell Types

White blood cell line	*Conditions that typically cause elevations*
Basophils	Allergic conditions, leukemias
Eosinophils	Allergic conditions, dermatologic conditions, eosinophilic esophagitis, idiopathic hypereosinophilic syndrome, malignancies, medication reactions, parasitic infections
Lymphocytes	Acute or chronic leukemia, hypersensitivity reaction, infections (viral, pertussis)
Monocytes	Autoimmune disease, infections (Epstein-Barr virus, fungal, protozoan, rickettsial, tuberculosis), splenectomy
Neutrophils	Bone marrow stimulation, chronic inflammation, congenital, infection, medication induced, reactive, splenectomy

Neutrophil recruitment

- Neutrophils make up the first wave of cells that cross blood vessel wall to enter inflammatory site
- Four steps:

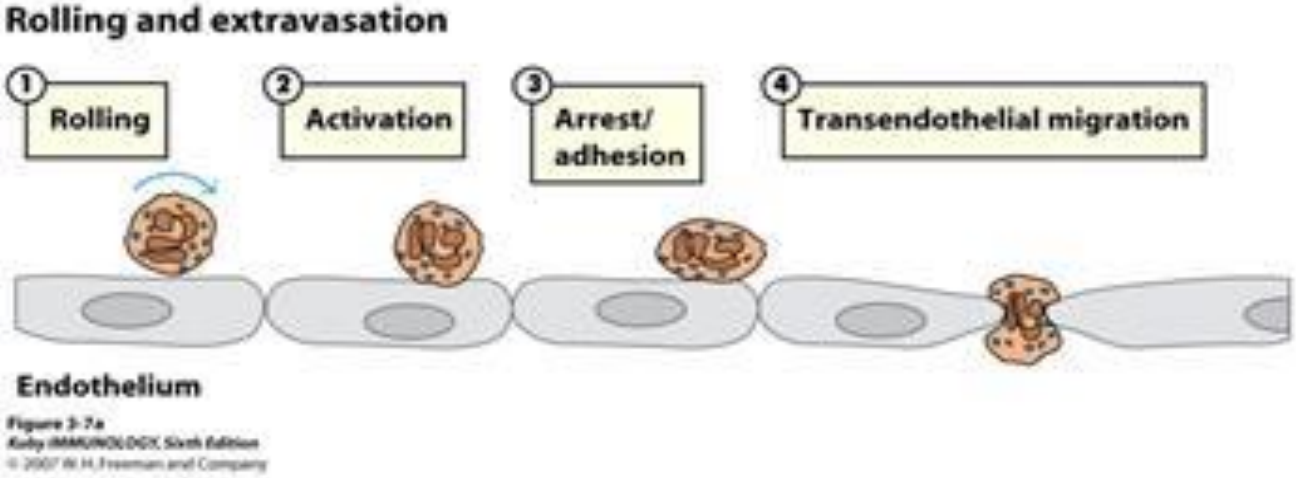


Figure 3-7a
Kuby IMMUNOLOGY, Sixth Edition
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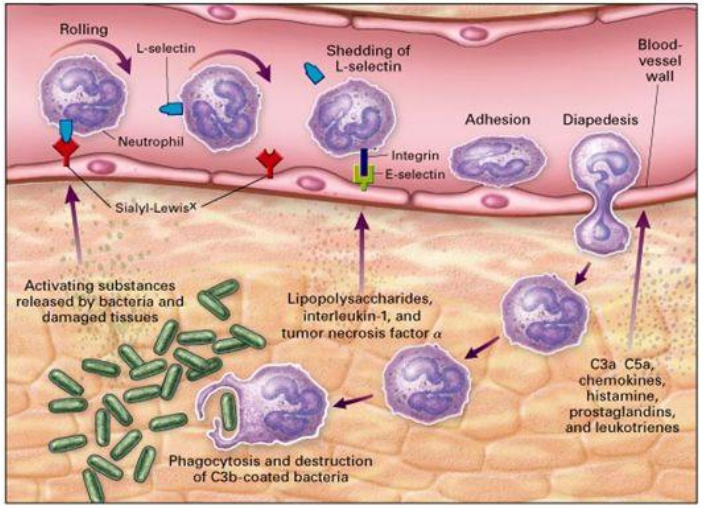
http://www.youtube.com/watch?v=xKoncIMFPtg

Neutrophil function

The main function of neutrophils – internalization of microorganisms

Phagocytosis - three phases:

1. Migration and diapedesis (outward passage of cells through intact vessel walls)
2. Opsonization and recognition
3. Ingestion, killing and digestion (phagocytosis)



Diapedesis

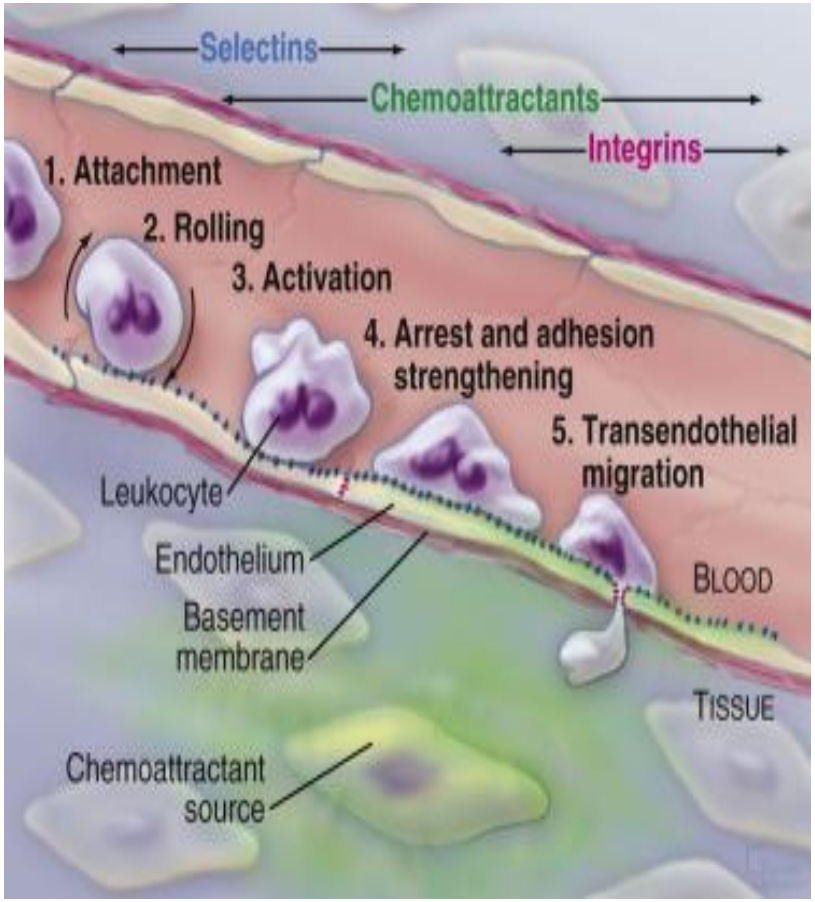
- Neutrophils and monocytes can squeez through the pores of the blood capillaries by Diapedesis.
- That is even through the pores is much smaller then the cell a small portion of the cell slide through the pore at a time, the portion sliding through is momentarily constricted to the size of pore.

ameboid motion

- White blood cells move through tissues spaces by ameboid motion.
- Both neutrophils and macrophages can move through the tissues by ameboid motion.
- Some cells move at velocities of 40 micro meter/min a distance great as their own length each minute.

margination

- When the inside of the capillary wall is altered the neutrophils stick to the capillary walls.This is called as margination.



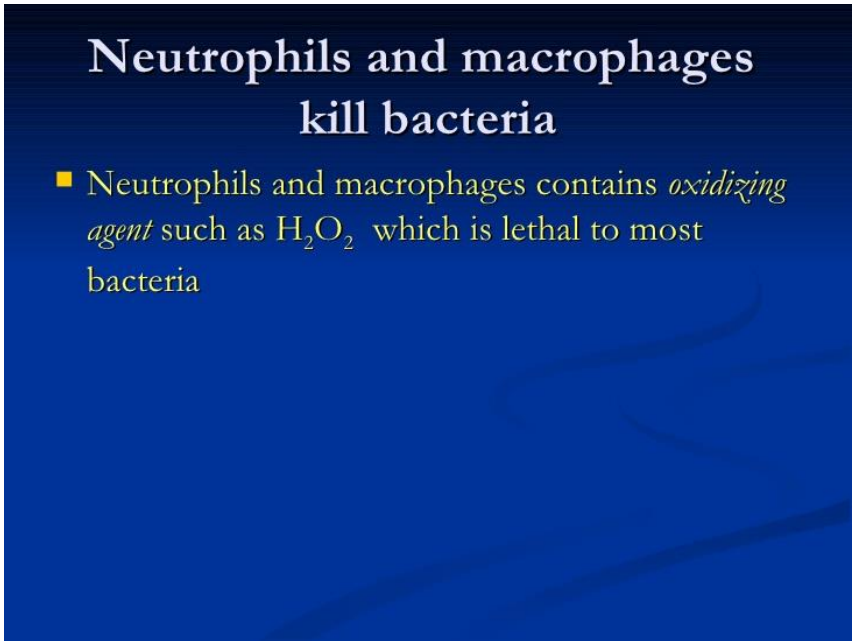
Chemotaxis

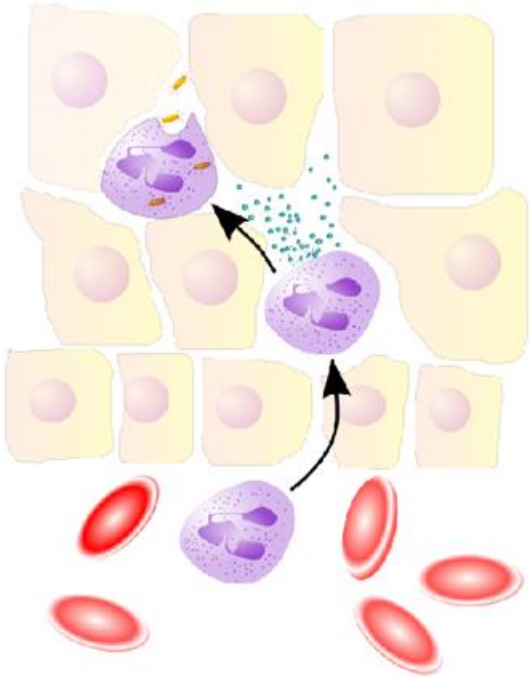
- Many different chemical substances in the tissues cause both neutophils and macrophages to move towards the source of the chemical .this phenomenon is called as Chemotaxis.They include
- some of the bacterial or viral toxins
- Degenerative products of the inflammed tissues.
- Several reaction products of the plasma clotting in the inflamed area.
- Chemotaxis depends upon the concentration gradient of chemotaxic substances.

PHAGOCYTOSIS or cellular ingestion of the offending agent

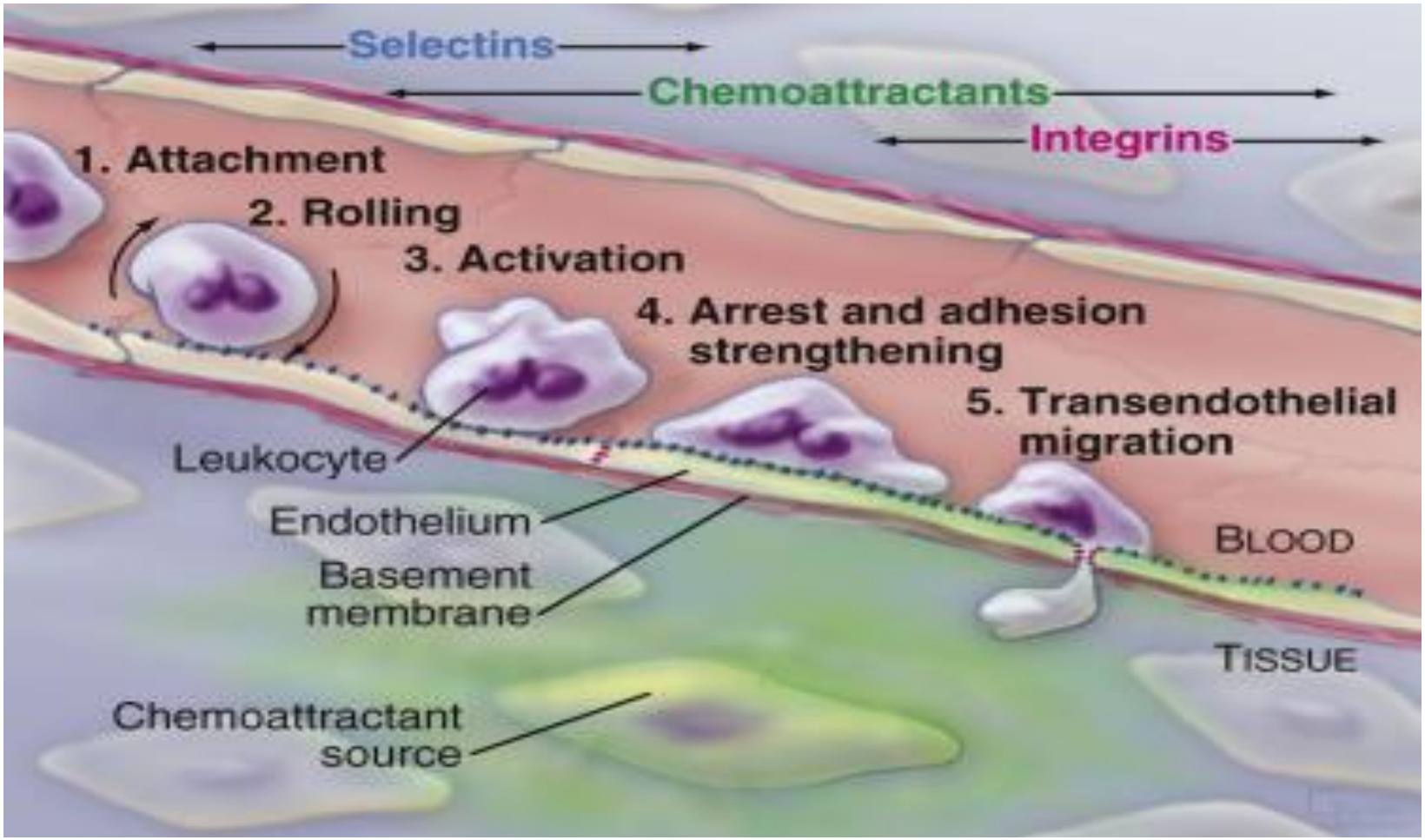
- Neutrophils are first cell types to arrive at a site of infection, where they engulf and destroy the infectious microorganisms through a process called **PHAGOCYTOSIS**,
- phago meaning eating cyte meaning vessel and osis meaning process.
- The likelihood of phagocytosis is increased
- if the surface is rough
- the particles is dead
- foreign particles
- as the natural substances in the tissues have smooth protein coats which repel phagocytosis.

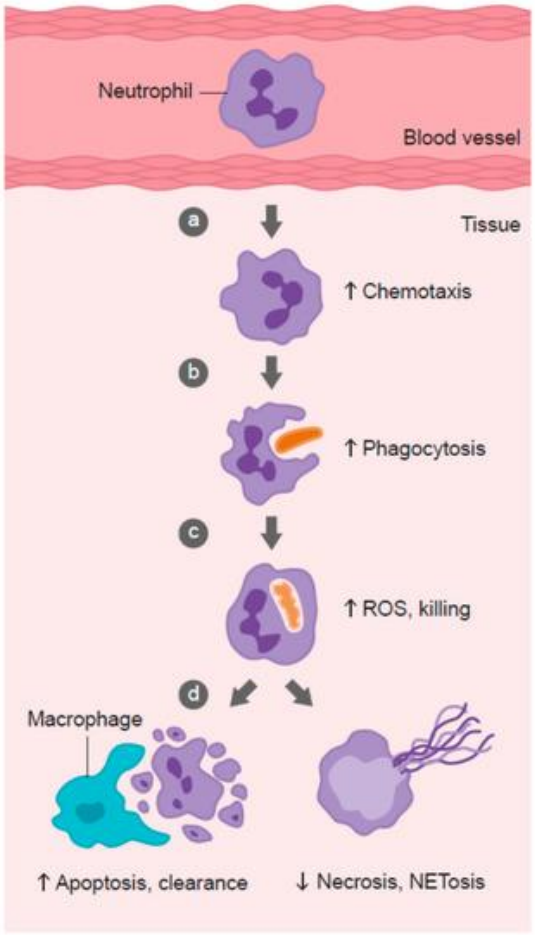
- Lysosome in the neutrophils and macrophages come in contact with the phagocytic vesicles and digestion of phagocytized particles begin.
- Both neutrophils and macrophages contain proteolytic enzymes
- The lysosome in the macrophages contain lipases





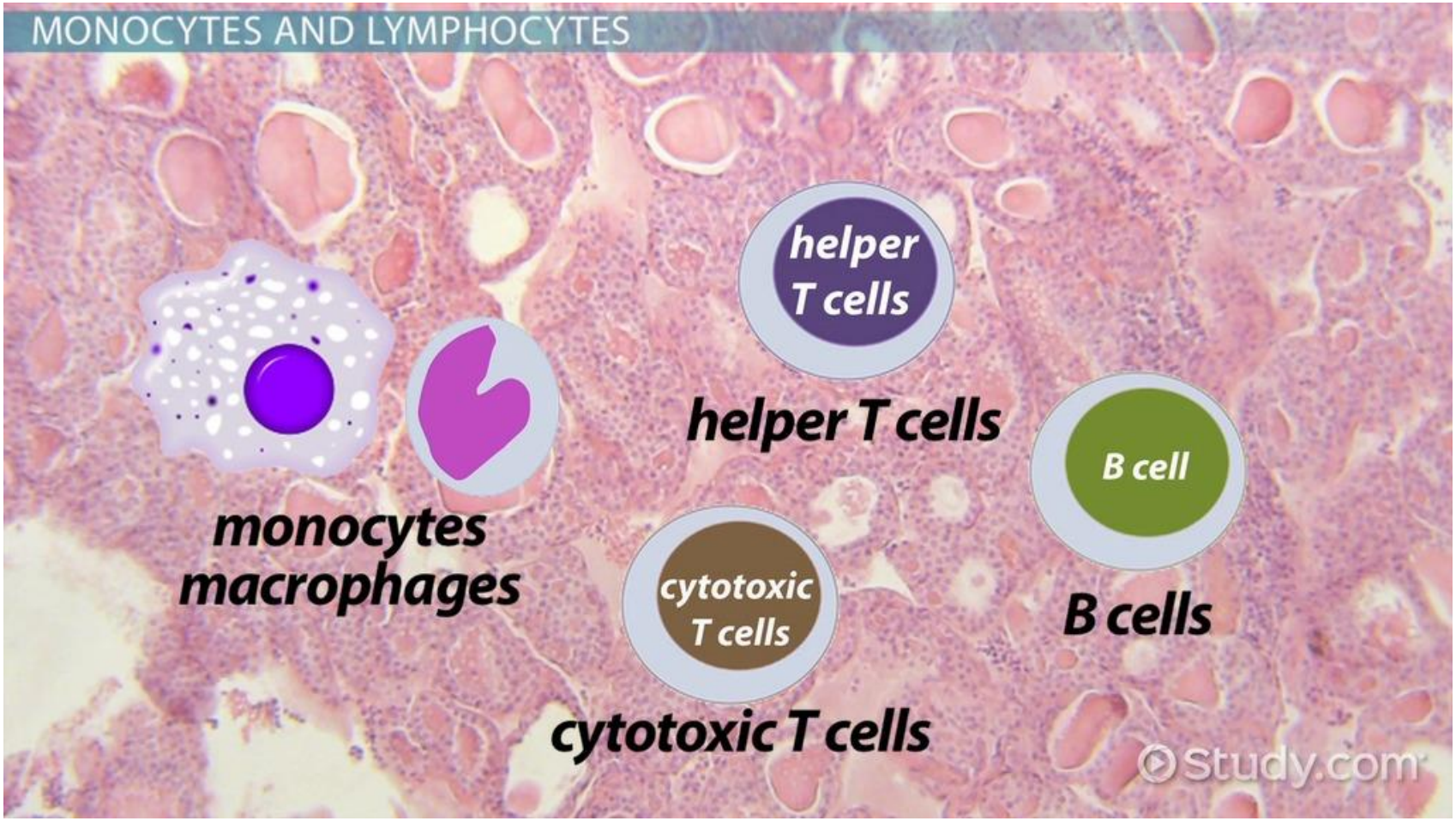
Neutrophils migrate from blood vessels to the inflamed tissue via chemotaxis, where they remove pathogens through phagocytosis and degranulation


Selectins
Chemoattractants
Integrins
1. Attachment
2. Rolling
3. Activation
4. Arrest and adhesion strengthening
5. Transendothelial migration
Leukocyte
Endothelium
Basement membrane
BLOOD
TISSUE
Chemoattractant source


Neutrophil
Blood vessel
Tissue
a
↑ Chemotaxis
b
↑ Phagocytosis
c
↑ ROS, killing
d
Macrophage
↑ Apoptosis, clearance
↓ Necrosis, NETosis

Monocyte-Macrophage Cell System

- The combination of monocytes, mobile macrophages, fixed tissue macrophages and specialized endothelial cells in the bone marrow, spleen and lymph nodes is called Monocyte-Macrophage cell system or *reticuloendothelial* system


MONOCYTES AND LYMPHOCYTES
helper T cells
helper T cells
B cell
B cells
monocytes
macrophages
cytotoxic T cells
cytotoxic T cells
Study.com

- Tissue macrophage provide a **first line of defence**.
- Neutrophil invasion of the inflamed area is a **second line of defence**.
- Second macrophage invasion into the inflamed tissue is a **third line of defence.**
- Increased production of granulocytes and monocytes by the bone marrow is a **fourth line of defence**.

leukaemia

- a malignant progressive disease in which the bone marrow and other blood-forming organs produce increased numbers of immature or abnormal leucocytes. These suppress the production of normal blood cells, leading to anemia and other symptoms.