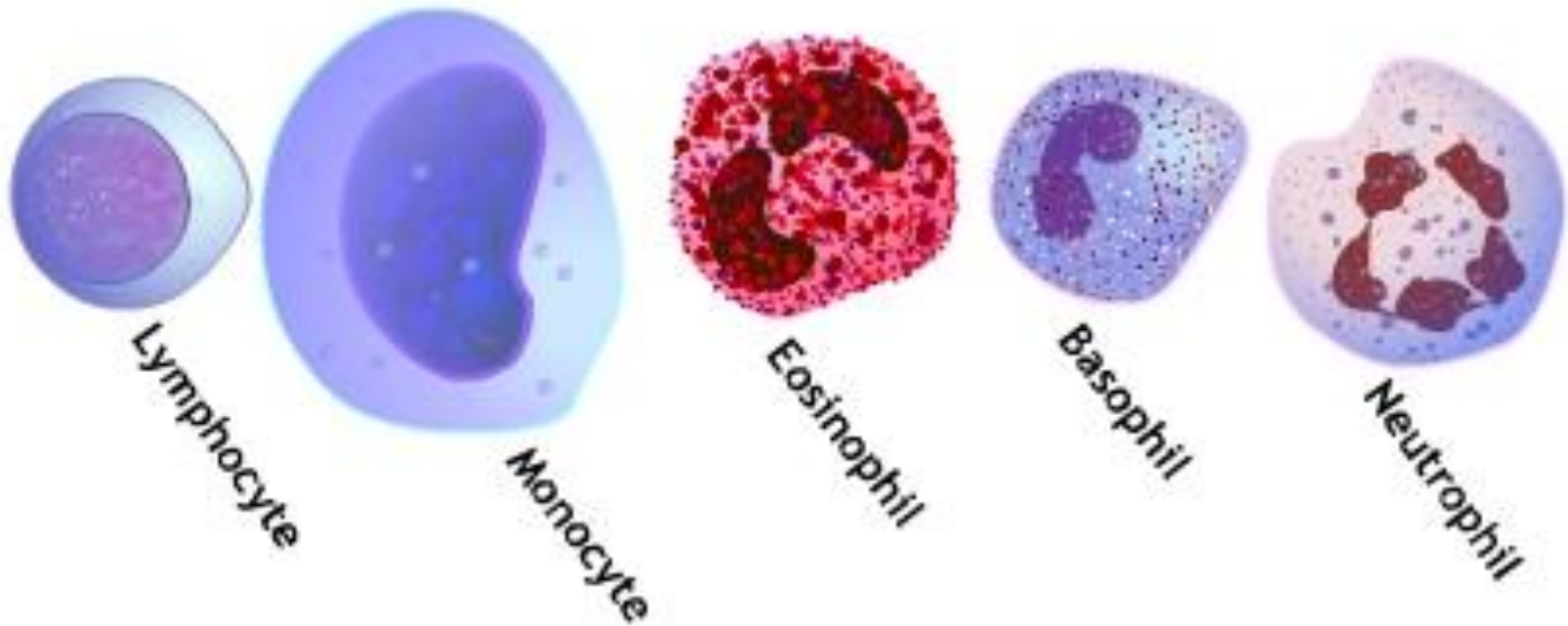


White Blood Cells



HANDOUTS 2016

DR SYED SHAHID HABIB
MBBS DSDM PGDCR FCPS
Professor & Consultant Clinical Neurophysiology
College of Medicine & KKHU

OBJECTIVES

At the end of this lecture you should be able to:

- ▶ Describe different types and formation of WBC
- ▶ Recognize the general functions of WBC
- ▶ Describe stages of neutrophil formation
- ▶ Describe role of neutrophils in defending against infections
- ▶ Explain the process of phagocytosis.

IMMUNITY

```
graph TD; A[IMMUNITY] --> B["Innate immunity  
(non specific)"]; A --> C["Acquired immunity  
(specific, adaptive)"]; B --> D["Phagocytes  
(Neut, Mono, NK)"]; B --> E["Complement"]; B --> F["Barriers"]; C --> G["Cell mediated  
T lymphocytes"]; C --> H["Humoral  
Antibody  
mediated  
B lymphocytes"];
```

Innate immunity

(non specific)

Examples:

- Phagocytes
(Neut, Mono, NK)
- Complement
- Barriers

Acquired immunity

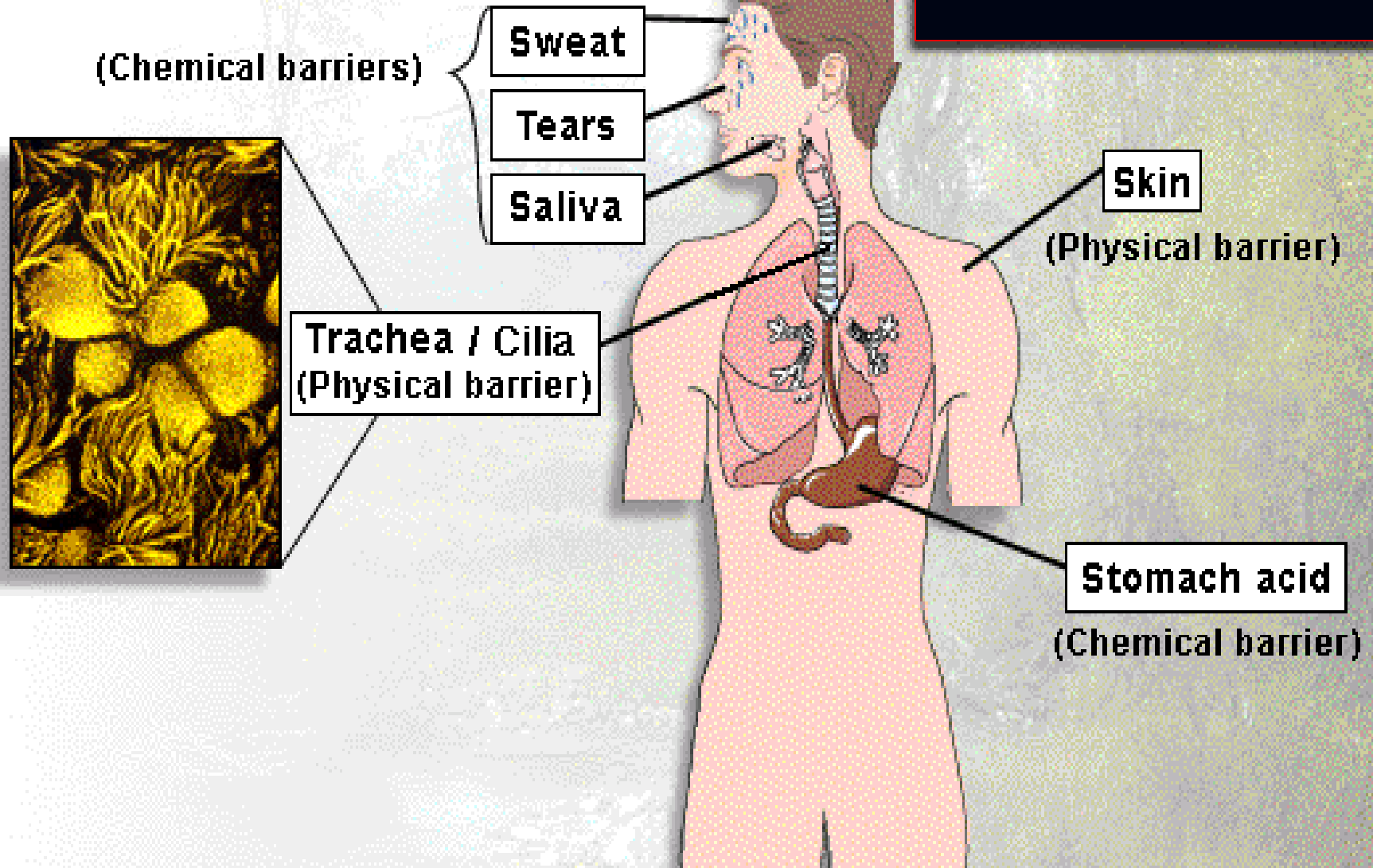
(specific, adaptive)

Cell mediated
T lymphocytes

Humoral
Antibody
mediated
B lymphocytes

Note: Macrophages are key components of the innate immunity and activate adaptive immunity by transforming into Antigen Presenting Cells

BARRIERS

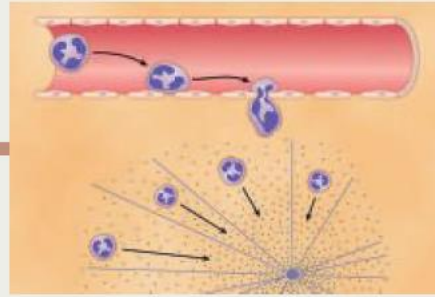


**Innate
immunity**

(non specific)

Examples:

- Phagocytes
- Complement
- Barriers



CHAPTER 34

**Resistance of the Body to Infection:
I. Leukocytes, Granulocytes, the
Monocyte-Macrophage System, and Inflammation**

UNIT VI

Acquired immunity
(specific, adaptive)



CHAPTER 35

**Resistance of the Body to Infection:
II. Immunity and Allergy**

UNIT VI

WBC TYPES (CLASSIFICATION)

■ Granulocytes

- Polymorphonuclear leukocytes (PMNs)
 - **Neutrophils** (10-16um, 2-5lobes of Nucleus)
 - **Eosinophils** (12-18um, Bilobed, coarse red granules)
 - **Basophils** (10-14um, rarely segmented Nucleus hidden by large round bluish granules)

■ Agranulocytes

- **Lymphocytes** (Round Nucleus, Small [5-8um] & large [9-15um])
 - T lymphocyte
 - B lymphocyte
- **Monocytes** (15-20um, Kidney shaped Nucleus) →
make macrophage system

WBCs Concentration (Normal Counts)

| Cells | Approximate Normal range (/μL) | Percentage of Total WBC | Life Span |
|--|--|--|---|
| Total WBC | 4000-11000 | - - - | |
| Granulocytes • Neutrophils • Eosinophils • Basophils | 3000-6000 150-300 0-100 | 50-70% 1-4% 0.4 | 4-8 hours in blood and 4-5 days in tissues |
| Lymphocytes | 1500-4000 | 20-40% | Weeks-months |
| Monocytes (macrophages) | 300-600 | 2-8% | 10-20 hours (months) |

| | |
|-------------------------------|-------|
| Polymorphonuclear neutrophils | 62.0% |
| Polymorphonuclear eosinophils | 2.3% |
| Polymorphonuclear basophils | 0.4% |
| Monocytes | 5.3% |
| Lymphocytes | 30.0% |

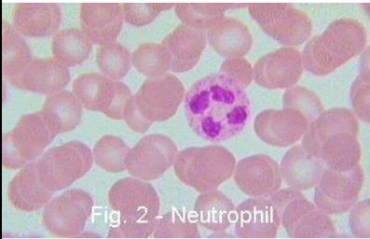


Fig. 2 - Neutrophil

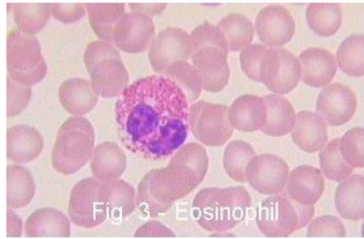


Fig. 3 - Eosinophil

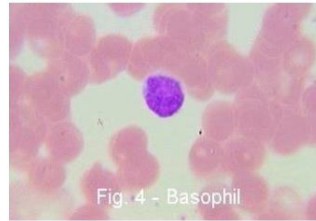


Fig. 4 - Basophil

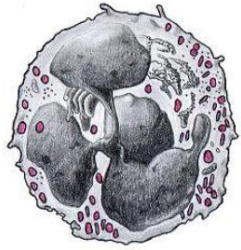


Fig. 8 - Neutrophil

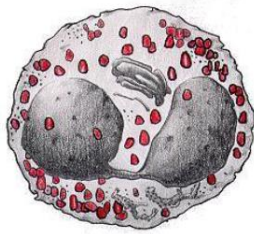


Fig. 9 - Eosinophil

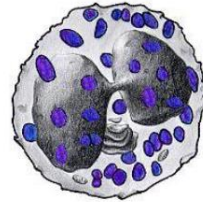


fig. 10 - Basophil

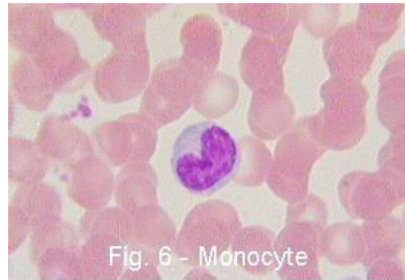


Fig. 6 - Monocyte

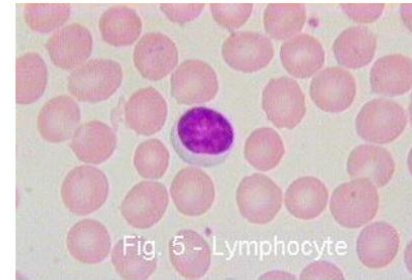


Fig. 5 - Lymphocyte

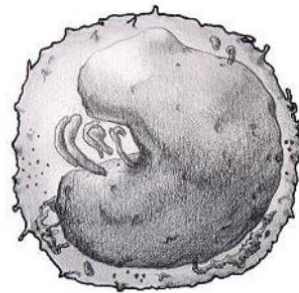


Fig. 12 - Monocyte

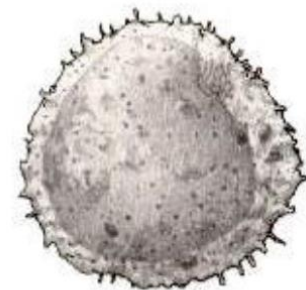


Fig. 11 - Lymphocyte

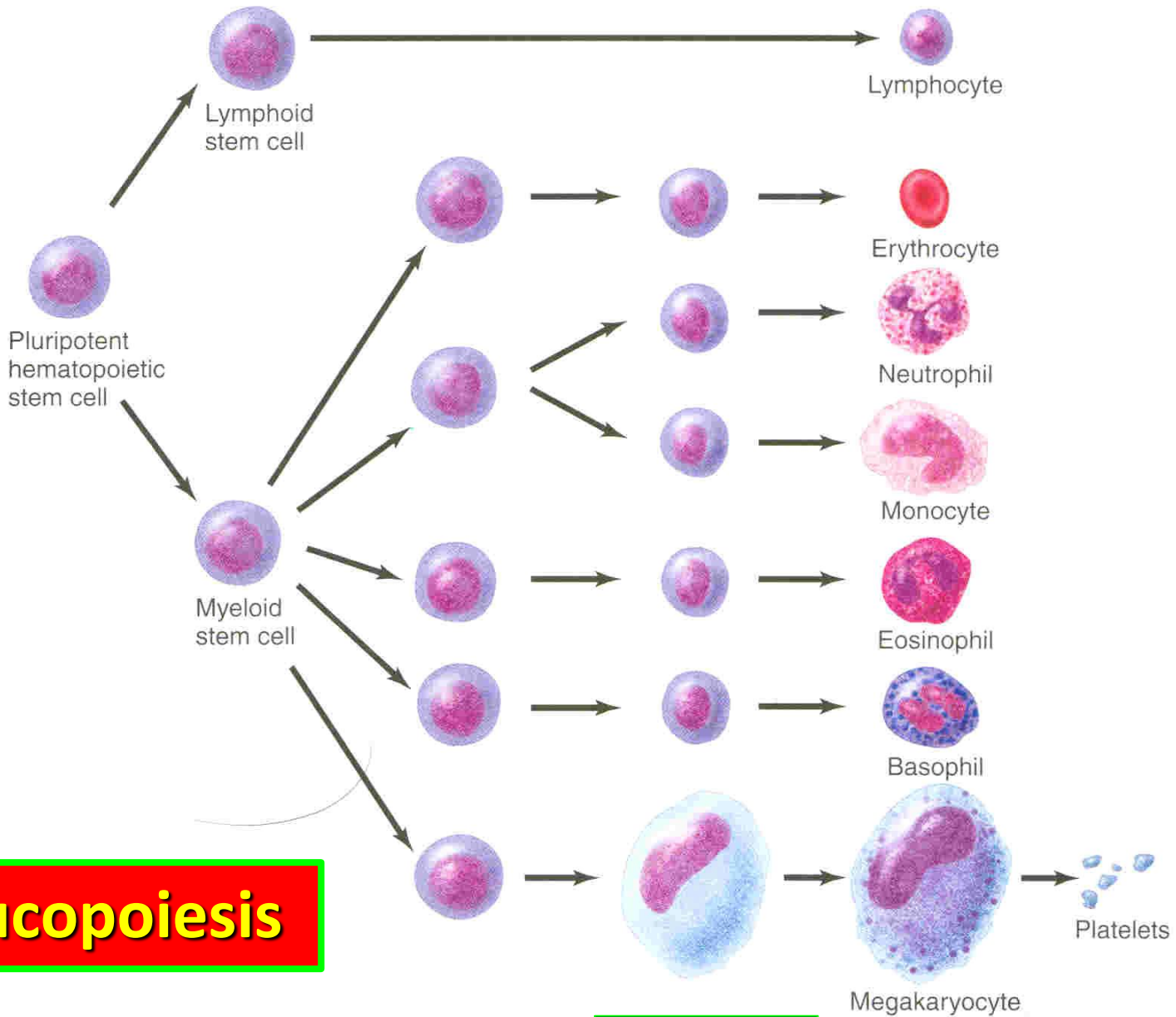
Leucopoiesis

Two major lineage of WBCs are formed:

- 1. Myelocytic: Granular, monocytes**
- 2. Lymphocytic: Lymphocytes**

Sites of WBC Formation

- **Granulocytes (neutrophil, basophil, eosinophil) in bone marrow**
- **Monocytes- bone marrow**
- **lymphocytes- bone marrow, thymus, lymphoid tissues**

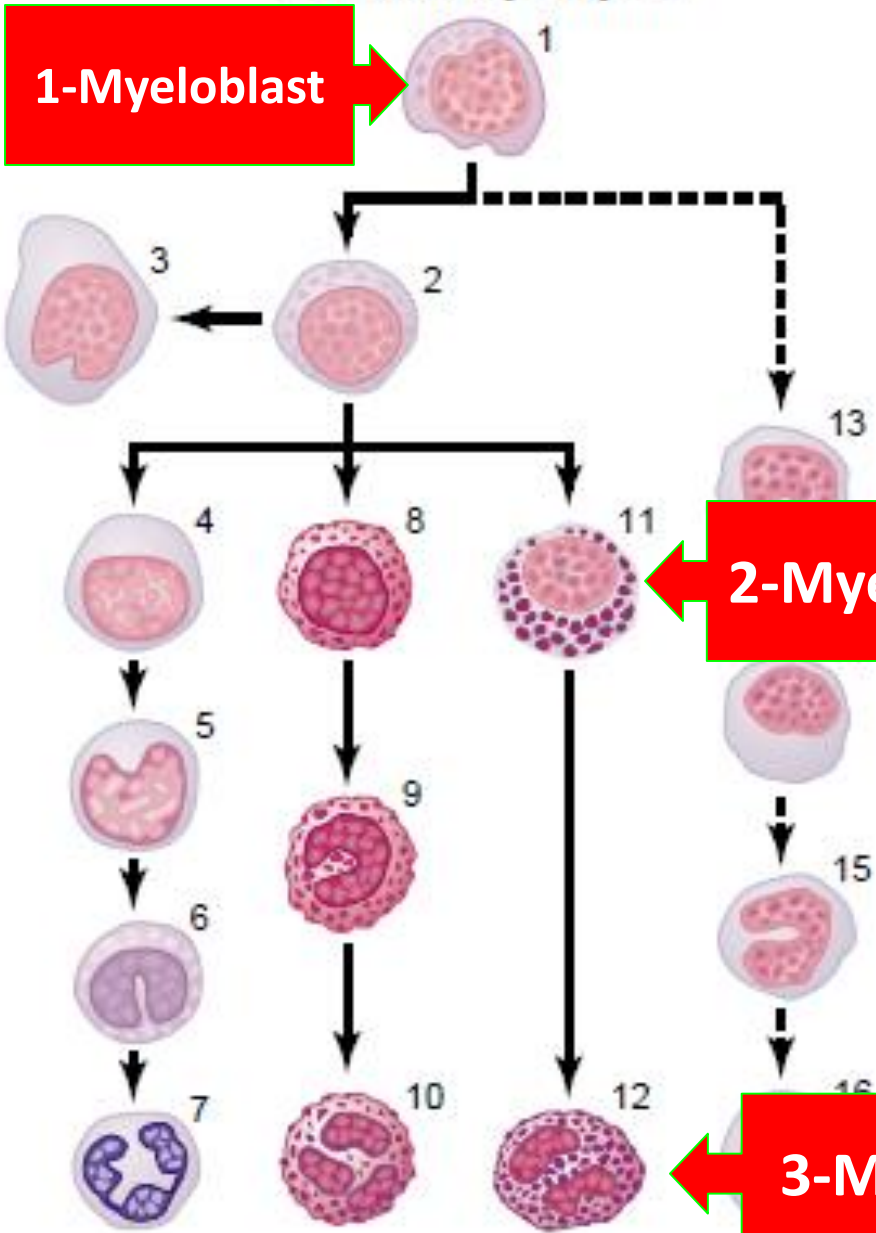


Leucopoiesis



Genesis of Myelocytes

1-Myeloblast



2-Myelocytes

3-Mature Cells

LEUCOPOIESIS

Genesis of white blood cells. The different cells of the myelocyte series are 1, myeloblast; 2, promyelocyte; 3, megakaryocyte; 4, neutrophil myelocyte; 5, young neutrophil metamyelocyte; 6, "band" neutrophil metamyelocyte; 7, polymorphonuclear neutrophil; 8, eosinophil myelocyte; 9, eosinophil metamyelocyte; 10, polymorphonuclear eosinophil; 11, basophil myelocyte; 12, polymorphonuclear basophil; 13-16, stages of monocyte formation.

Responses During Inflammation

Macrophage and Neutrophil

- ❑ **1st** line of defense – Tissue macrophages & Physical Barriers
- ❑ **2nd** line of defense – Neutrophil Invasion of the inflamed area
- ❑ **3rd** line of defense – Monocytes –macrophage invasion of inflamed area
- ❑ **4th** line of defense – Increased production of granulocytes and Monocytes by Bone marrow

NEUTROPHILS

- Most Abundant WBCs 60-70 %
- Size: 15-20 μm
- Nucleus: Multilobed 2-5 lobes
- Life span: 6-8 hours

NEUTROPHIL GRANULES

■ Primary Granules (Non Specific, Azurophilic, lysosomes) [33%]:

Acid hydrolases, MPO, HOCl, Defensins

■ Secondary Granules (Specific) [67%]:

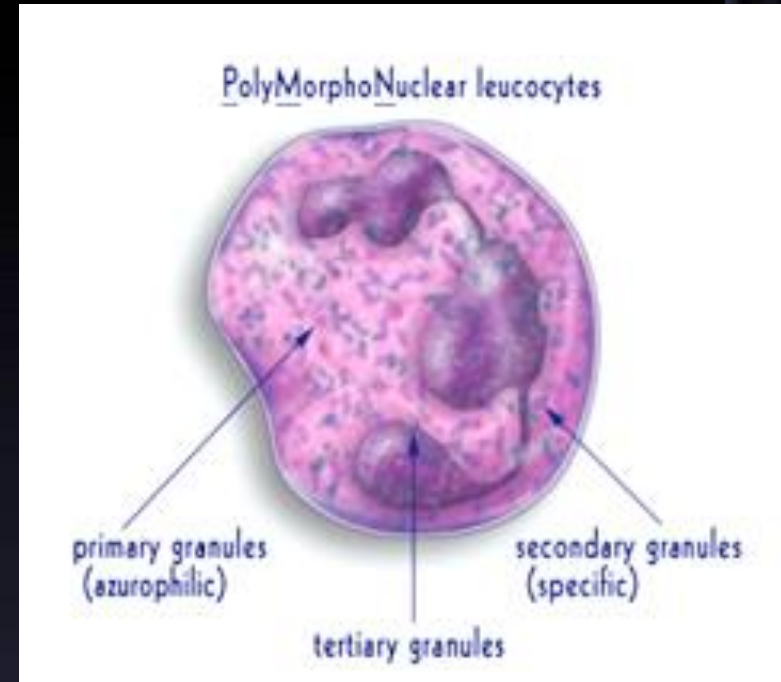
Lysozyme, Lactoferrin, Alkaline Phosphatase, Gelatinase, Bacteriostatic & Bactericidal products.

■ Tertiary Granules : (help to digest tissues)

Collagenase, Hyaluronidase and Gelatinase.

POOLS:

Bone Marrow, Circulating and Marginated Pool



Glycogen granules: for anaerobic glycolysis.

PMNs (Antimicrobial system)

RESPIRATORY BURST

- O₂ Free Radicals (O₂⁻, H₂O₂, -OH)
- NADPH-oxidase
- Myeloperoxidase
- Cl⁻ → HOCl: Hypochlorous acid “very toxic”

REACTIVE OXYGEN METABOLITES

Superoxide anion: O₂⁻



Hydrogen peroxide: H₂O₂



Hydroxyl radical: OH[•]



Hypochlorous acid: HOCl



Myeloperoxidase = MPO

DEFENSIVE PROPERTIES OF MACROPHAGES & NEUTROPHILS

- **Margination:** WBC Roll, Bind and then stick along the walls of blood capillaries
- **Diapedesis:** WBC squeezes itself through endothelial holes leaving blood capillaries
- **Chemotaxis:** WBC move by amoeboid motion towards inflammation area following chemotactic substances (Bacterial toxins, Complement [C5a], LKB4) are released from site of infection
- **Phagocytosis:** Upon reaching the site of infection neutrophils start to engulf infecting organism

Chemotaxis

- **The attraction of the neutrophils to inflamed area following chemotactic substances are released from infected site:**
- **Chemotactic substances:**
 - Bacterial toxins
 - Degenerative products of inflamed tissue
 - Complement system (C5a)
 - Reaction product of plasma
 - clotting

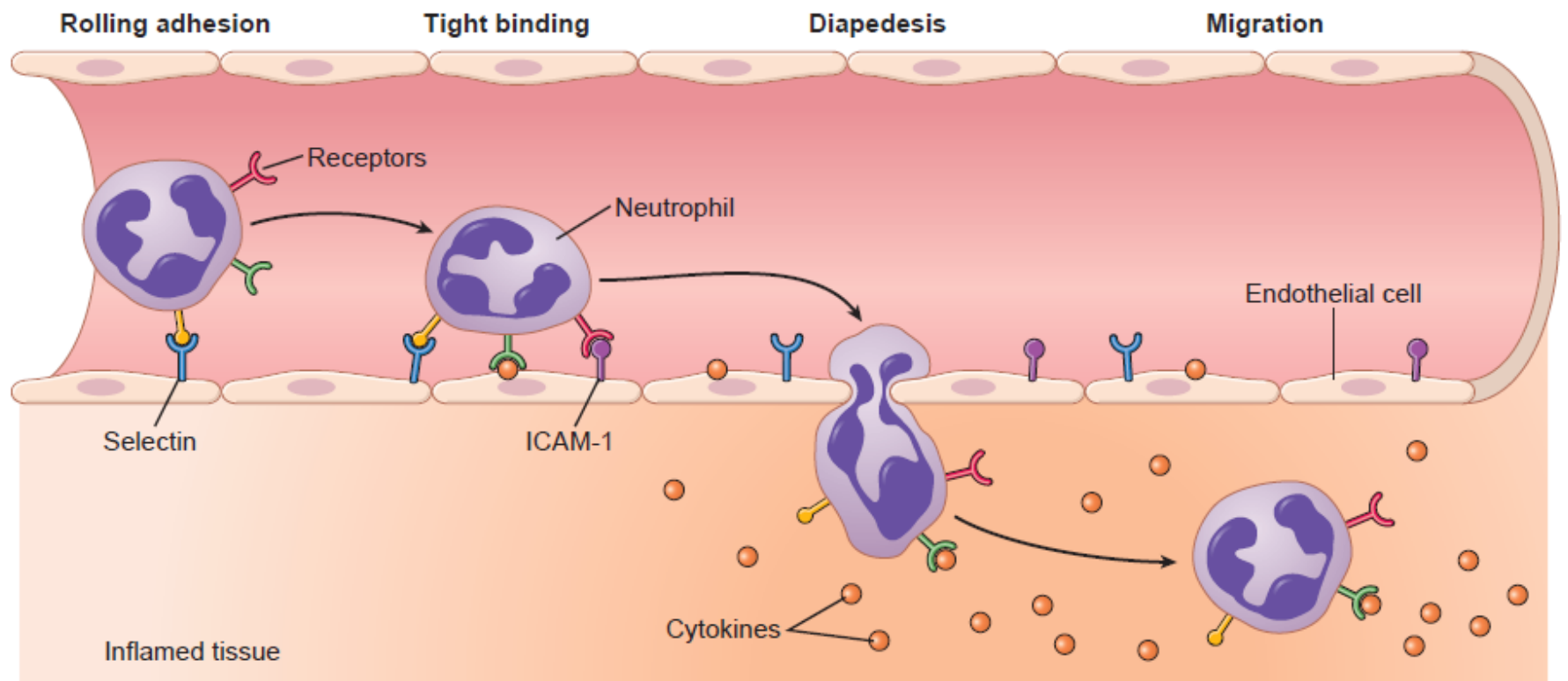


Figure 34-6. Migration of neutrophils from the blood into inflamed tissue. Cytokines and other biochemical products of the inflamed tissue cause increased expression of selectins and intercellular adhesion molecule-1 (*ICAM-1*) in the surface of endothelial cells. These adhesion molecules bind to complementary molecules/receptors on the neutrophil, causing it to adhere to the wall of the capillary or venule. The neutrophil then migrates through the vessel wall by diapedesis toward the site of tissue injury.

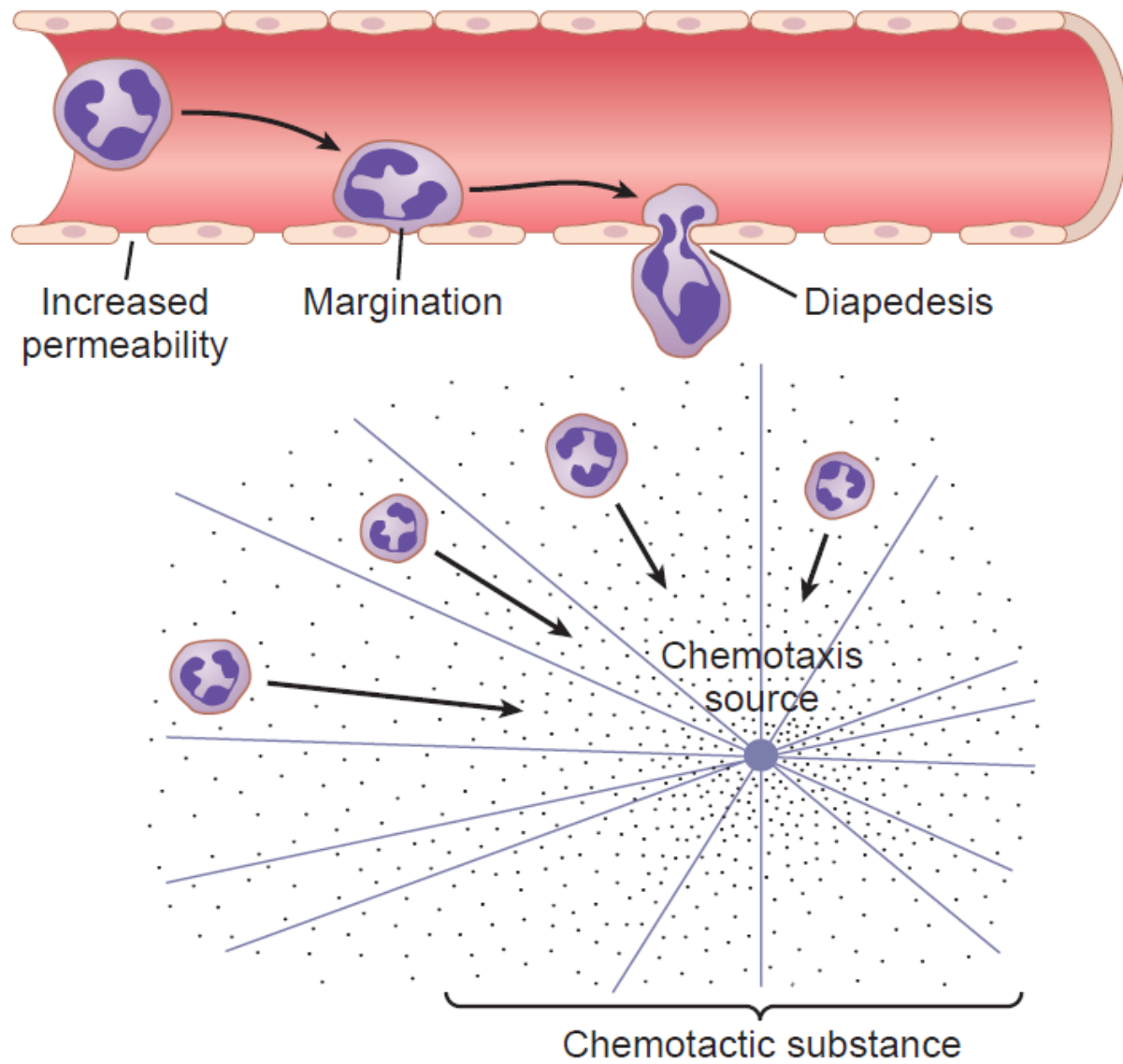
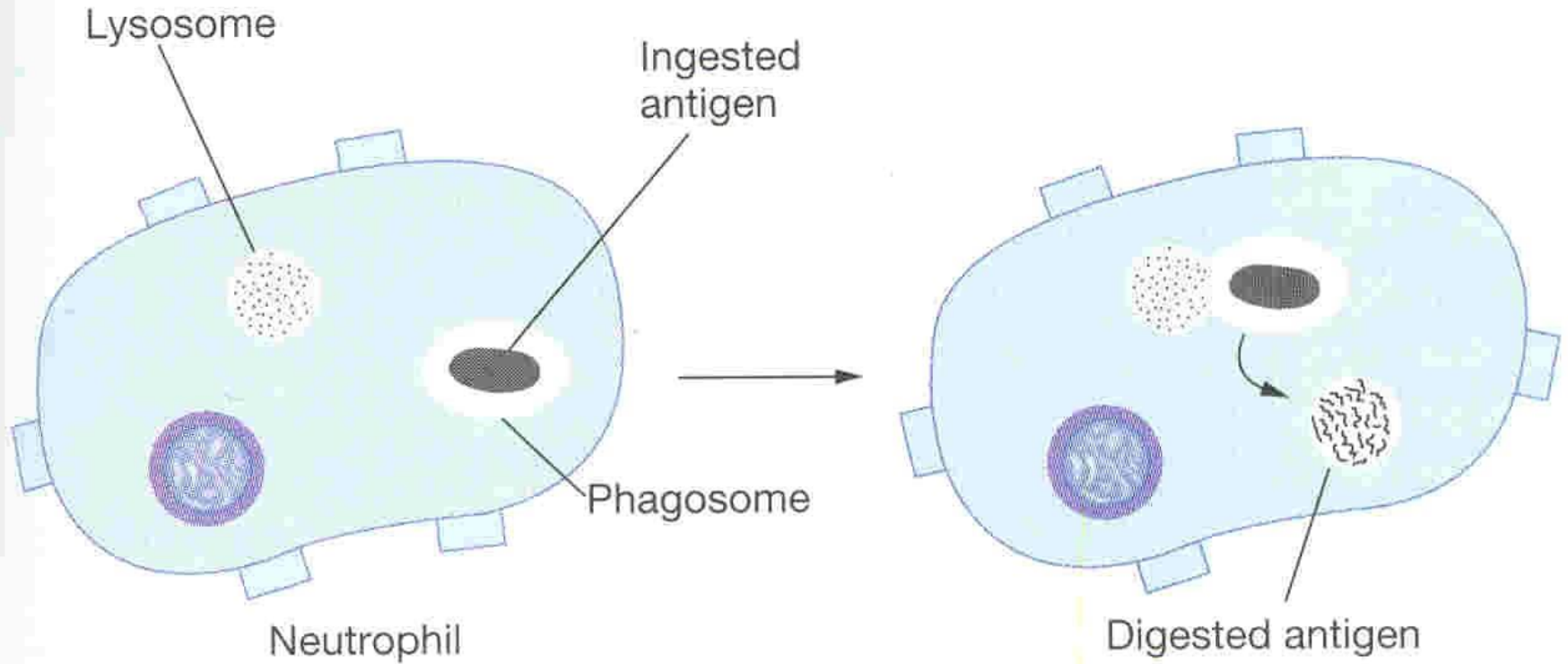


Figure 34-2. Movement of neutrophils by *diapedesis* through capillary pores and by *chemotaxis* toward an area of tissue damage.

Phagocytosis & Digestion



Phagocytosis

Selective process: **foreign substance recognize** by:

1. Rough surface

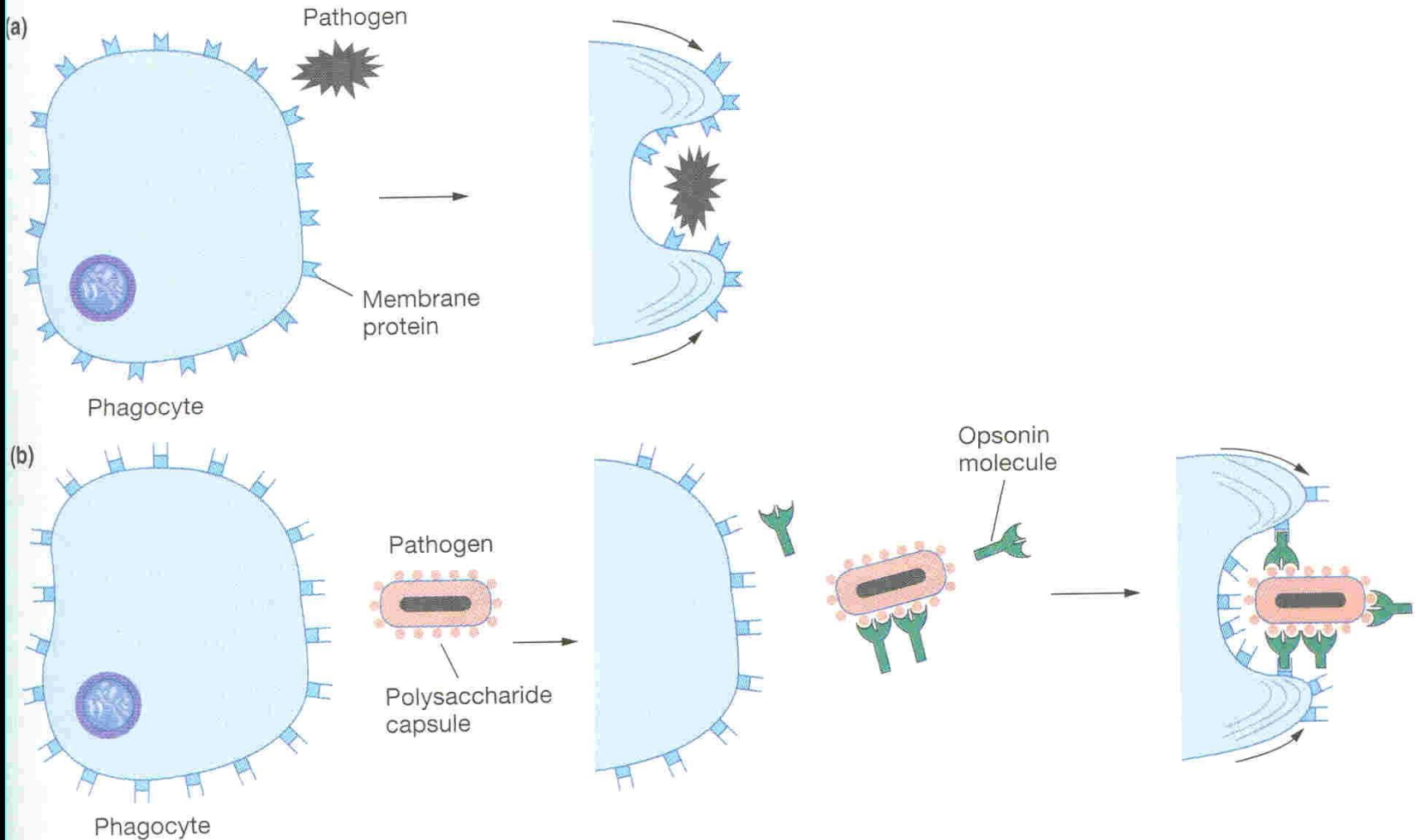
2. No protective protein coat, which prevents phagocytosis

3. Increased by certain substances e.g (OPSONINS)

- Complement 3b or antibodies like IgG making them ready for killing a process known as opsonization.

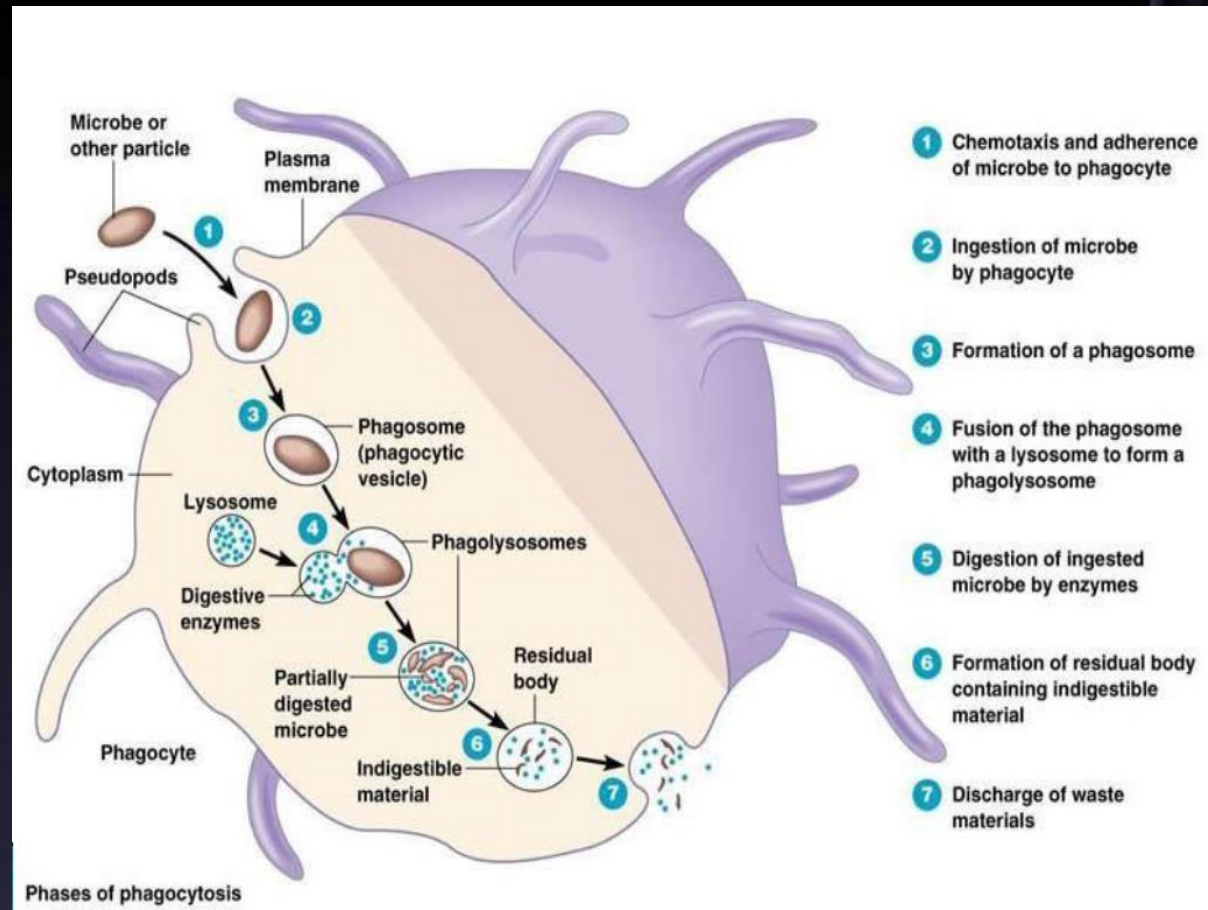
- Neutrophils encircle the bacteria with pseudopodia and engulf it inside into a vacuole (phagosome), can kill 3-20 bacteria

Opsonization & Phagocytosis

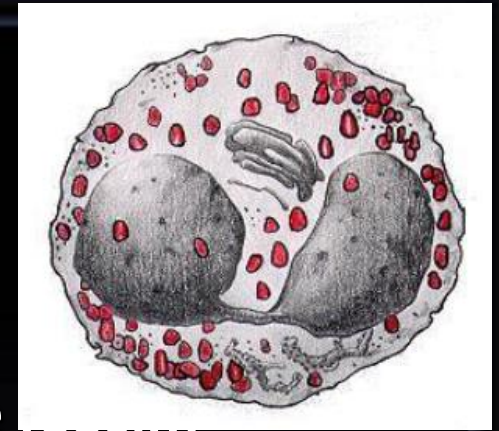
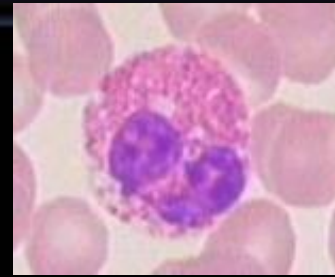


Microbial killing

- Digestion of organism inside the phagosome
- Fusion of intracellular lysosomes with phagosome vacuole
- **Lysosomes discharge its proteolytic enzymes such as myeloperoxidase, catalase into the vacuole, killing and digesting the engulfed bacteria.** and or Release of bactericidal such as superoxide, hydrogen peroxide to kill the bacteria

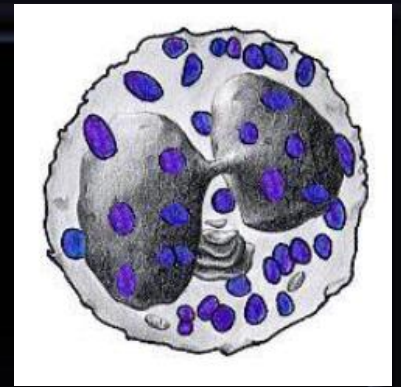


EOSINOPHILS



- **Size:** 10-14 μm in diam. 1-6%
- **Life span;** 4-5 hours in circulation.
- **Granules** are arginine rich, which take acid dye (eosin)
- **Weak phagocytes:** Exhibit **Chemotaxis:** attracted towards chronic inflammation: (1) by releasing hydrolytic enzymes from their granules (modified lysosomes); (2) release highly reactive forms of oxygen (3) release a highly larvacidal polypeptide called major basic protein.
- Increased in **PARASITIC INFECTIONS** eg; schistosomiasis, hook worm, Ascaris and in **ALLERGIES** eg; asthma & Rhinitis **DRUG REACTIONS** and **SKIN ALLERGIES**. Neutralises allergic products such histamine, 5-HT, Ag-Ab complex, bradykinin (allergic disease of skin & lungs)

BASOPHILS



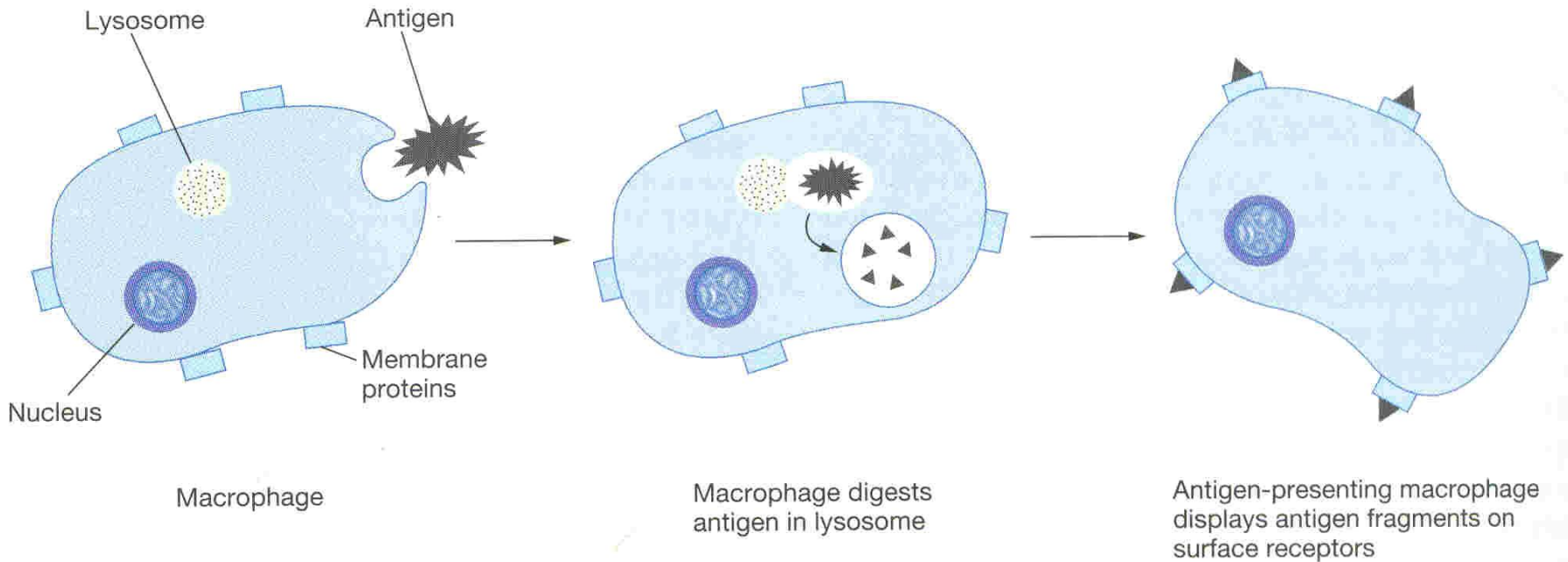
- **Size:** 10-14 μm in diam Count < 1%
- **Weak phagocytic** cells
- **Granules** contain polysaccharide granules > base methylene blue color.
- Both mast cells and basophils **liberate** histamine, heparin, bradykinin, Serotonin (5HT) , slow-reacting substance of anaphylaxis (a mixture of three leukotrienes) and a number of lysosomal enzymes.
- Increased in **allergic reactions**: immediate-type hypersensitivity (allergic) reactions

MONOCYTES



- **Size:** 15-20 μm (active cells 60-80 μm)
- **Small Granules (Prim) & Vacoules**
- **More Efficient than Neutrophils** (100 bacteria vs 3-20 by Neutr, larger particles like RBCs & malarial parasites)
- **Life span:** 10-20 hours in blood...& in tissues?
- **Two types:** Mobile & Fixed
- **Lysosomes contain lipases** unlike Neut.
- **Acts as Antigen Presenting Cells**

Antigen Presenting Cells



Reticuloendothelial System

Monocytes/Macrophage System

▪ Monocytes when enter the tissues they transform themselves into macrophages this system of phagocytes is called as **Monocyte-Macrophage Cell System**

Examples are: -

1. Skin and Subc tissues (Histiocytes)
2. Lymph Nodes
3. Alveolar macrophages
4. Liver sinuses (Kupffer Cells)
5. Spleen & Bone marrow
6. Microglia in Brain
7. Kidneys (Mesangial Cells)
8. Bone (Osteoclasts)

Tissue macrophages

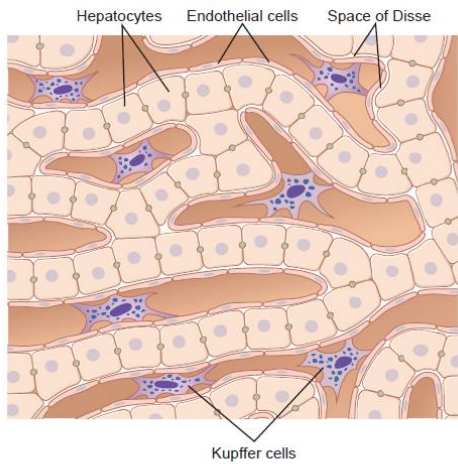


Figure 34-4. Kupfer cells lining the liver sinusoids, showing phagocytosis of India ink particles into the cytoplasm of the Kupfer cells.

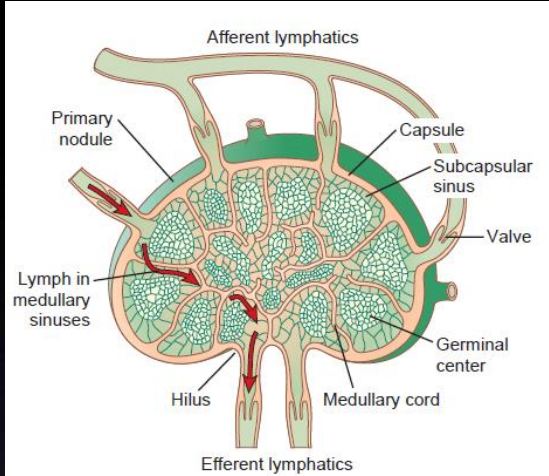
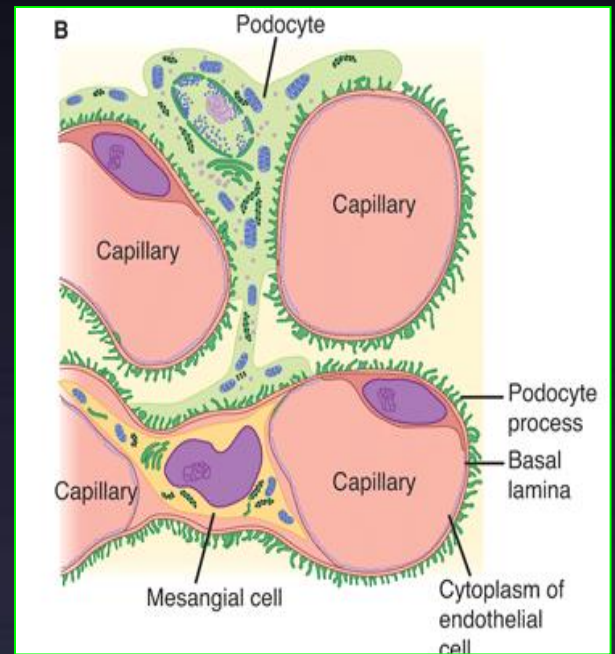
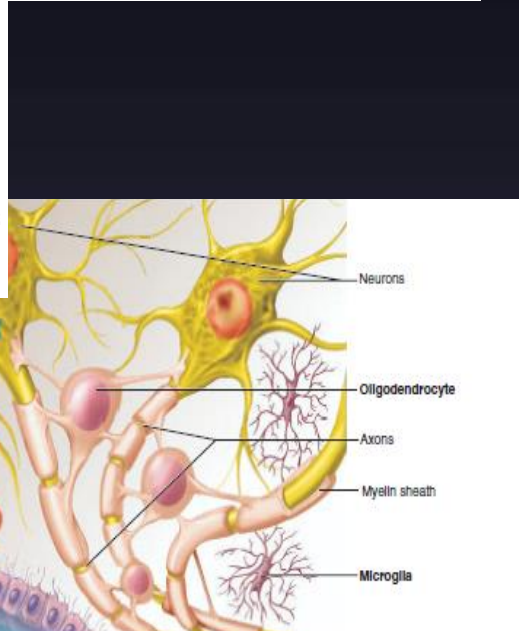
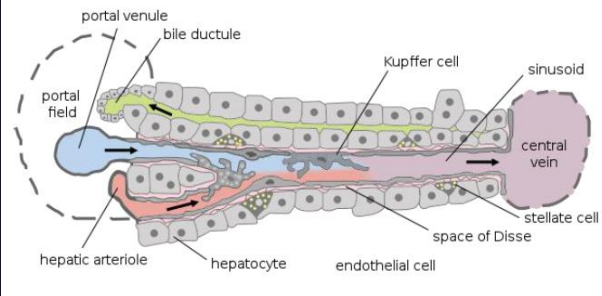
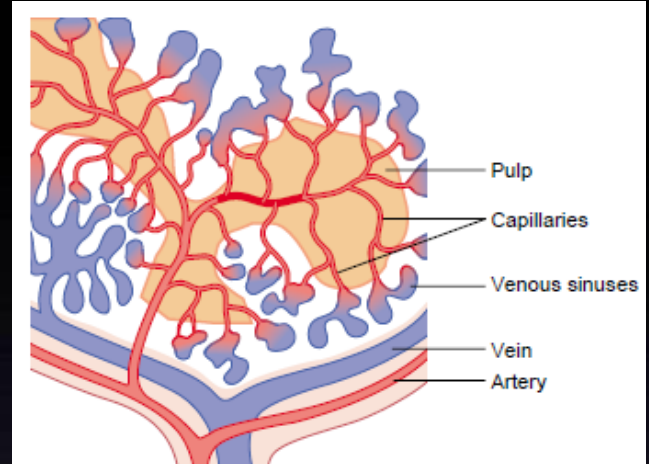


Figure 34-3. Functional diagram of a lymph node.



IMPORTANT TERMS

- **Pus** (necrotic tissue, dead neutrophils, dead macrophages and tissue fluid → Autolyze)
- **Leukocytosis**
- **Neutrophilia**
- **Leukopenia**
- **Leukemias**

THANKS

