Natural Defense Mechanisms

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Reference

Kuby Immunology 7th Edition

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Chapter 4 Pages 105-110

Chapter 5 Pages 141-176

Chapter 6 Pages 187-200 & page 213

Objectives

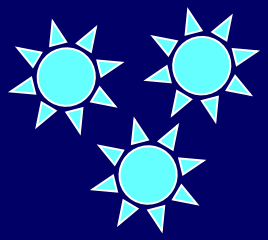
- + To know First (non-specific immunity) and second (adaptive immunity) lines of defense
- + To understand the Complement system, its activation and how it involves in pathogen killing.
- + To recognize the importance of accumulation of inflammatory cells for clearance of infection
- + To know the role of cytokines as mediators which regulate inflammation

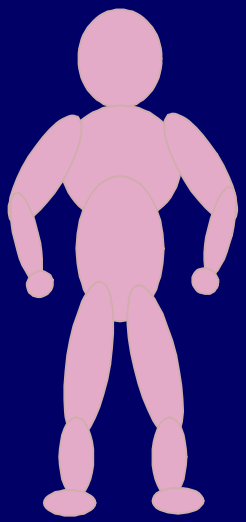
The main function of the immune system is to protect from infections:

Viruses e.g.

Influenza

Polio

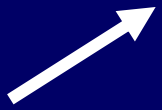


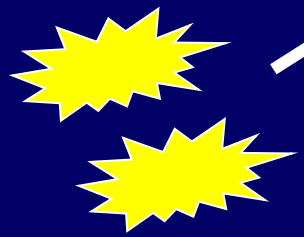


Parasites e.g.

Tapeworms

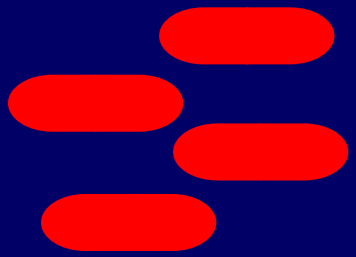
Malaria





Fungi e.g.

Candida albicans

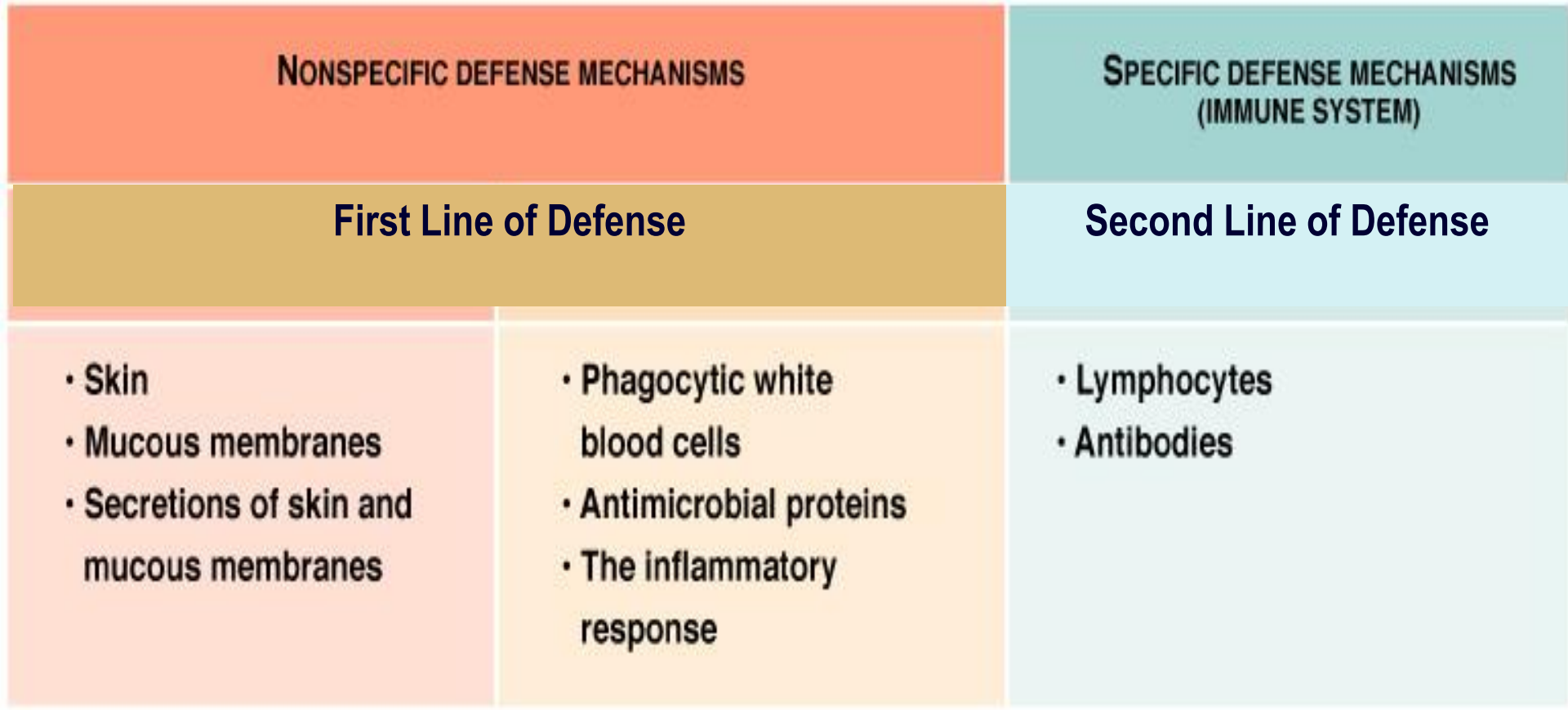


Bacteria e.g.

Tubercule bacillus

Staphylococci

First and the second lines of defense:



First line of defense :

- Natural (Innate) Immunity
- Physical (skin/ mucous membranes)
- Mechanical (Coughing, sneezing, vomiting, action of cilia in trachea)
- Biochemical barriers (antimicrobial peptides, lung secretions, mucus, saliva, tears)

Physical and mechanical barriers

- Skin, impermeable to microbes.
- Mucous membranes lining the gastrointestinal, genitourinary and respiratory tracts.

- Other protective mechanisms:
  - Shedding of outer skin layers.
  - Coughing and sneezing.
  - Flushing of urine.
  - Vomiting.
  - Mucus and cilia in respiratory tract.

Biochemical barriers

- Body secretions contain anti-bacterial substances e.g. saliva, tears and sweat.
- Antimicrobial peptides (e.g., defensins, hepcidins)
- Normal bacterial flora.
  (Compete with pathogenic bacteria for nutrients)

Inflammation:

- Inflammation is the first response of the immune system to infection or irritation.

- It consist of a series of vascular & cellular changes that occur in response to various stimuli

e.g. infections, injury, radiation etc.

Microbial infections initiate inflammation

As bacteria possess an array of pro-inflammatory molecules:

- e.g. Lipopolysaccharides (LPS)

Inflammation

- Goals

  - Prevent and limit infection and further damage
  - Interact with adaptive immune system
  - - For example Monocytes / Macrophages serve as a link between the adaptive and innate immunity by antigen presentation
  - Prepare the area of injury for healing

The Complement system

- Consists of a group of serum proteins initially present in inactive form

- Activation occurs in cascade (one component or more activating another) after enzymatic cleavage. Once components become activated they produce important biological effects that initiate inflammation.
- This system plays an important role in linking Innate & Adaptive immunity

The complement system:

3 Pathways of activation :

* Classical. (Requires antigen-antibody binding)

- (**C1,C4,C2,C3,C5,C6,C7,C8,C9)**

* Lectin. (Activated by mannan binding protien binding manose groups of bacterial carbohydrates)

- (**-C4,C2,C3,C5,C6,C7,C8,C9)**
- Alternative.(Activated by bacterial products)
- (**- C3,C5,C6,C7,C8,C9)**

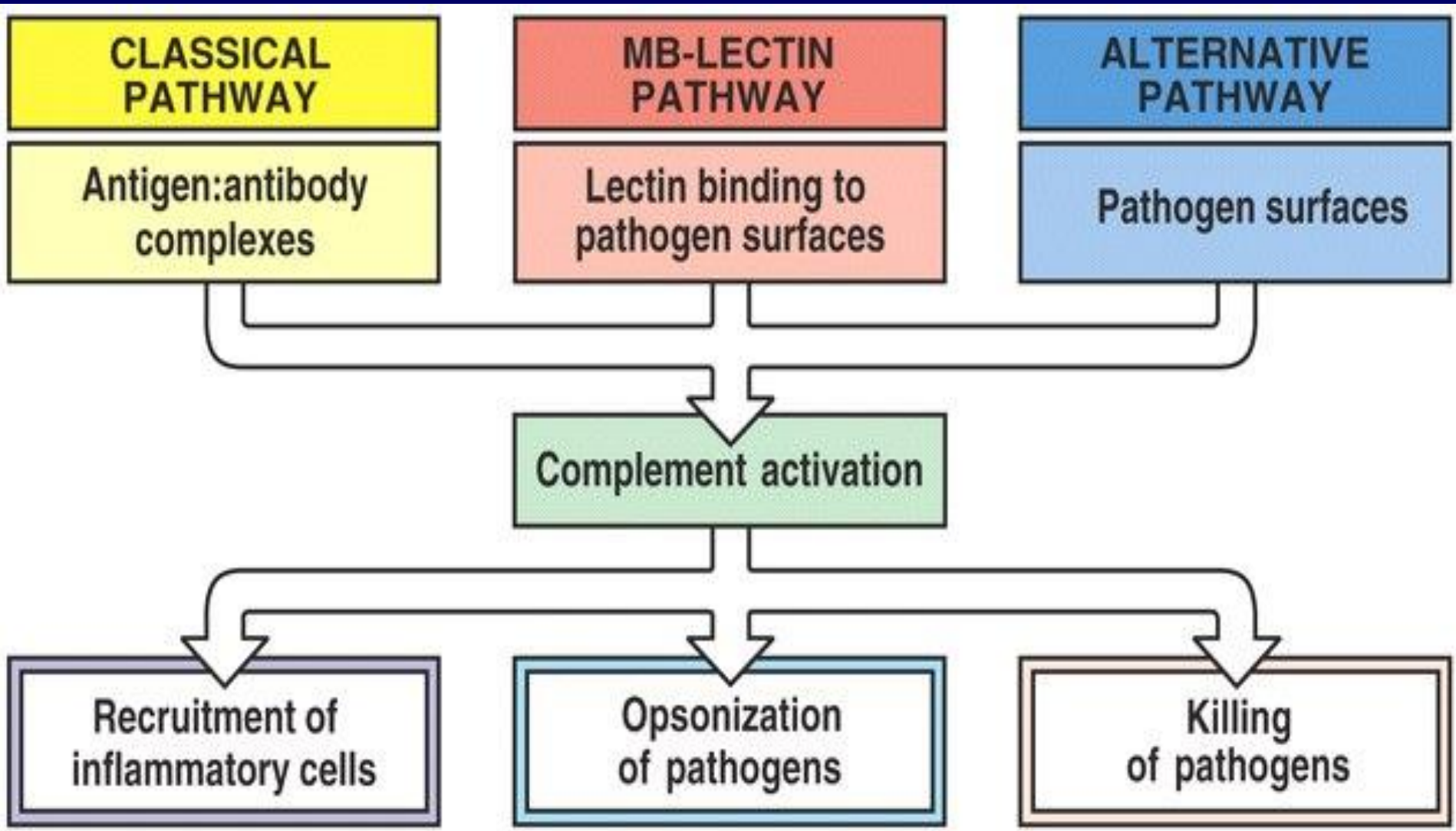
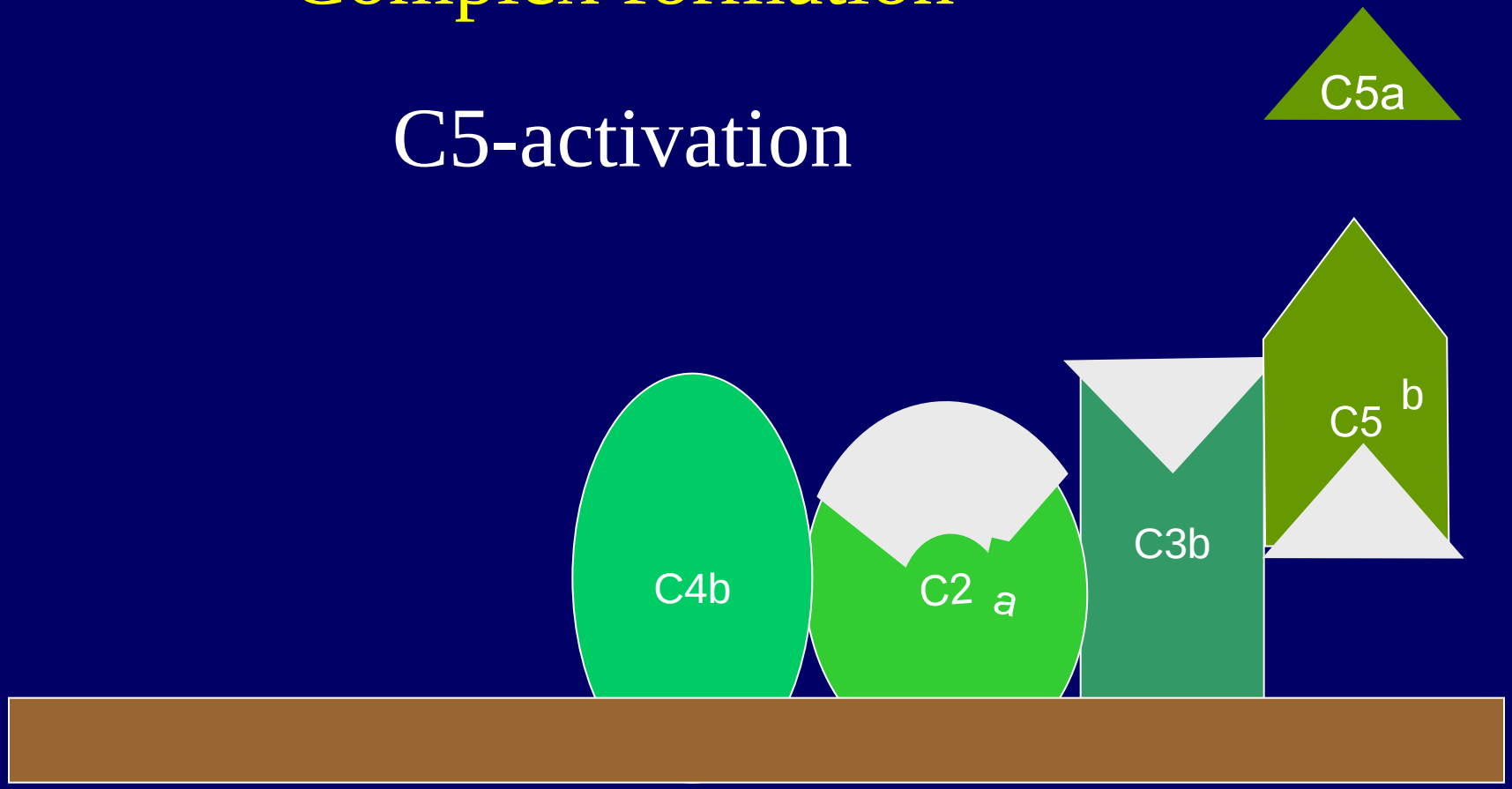


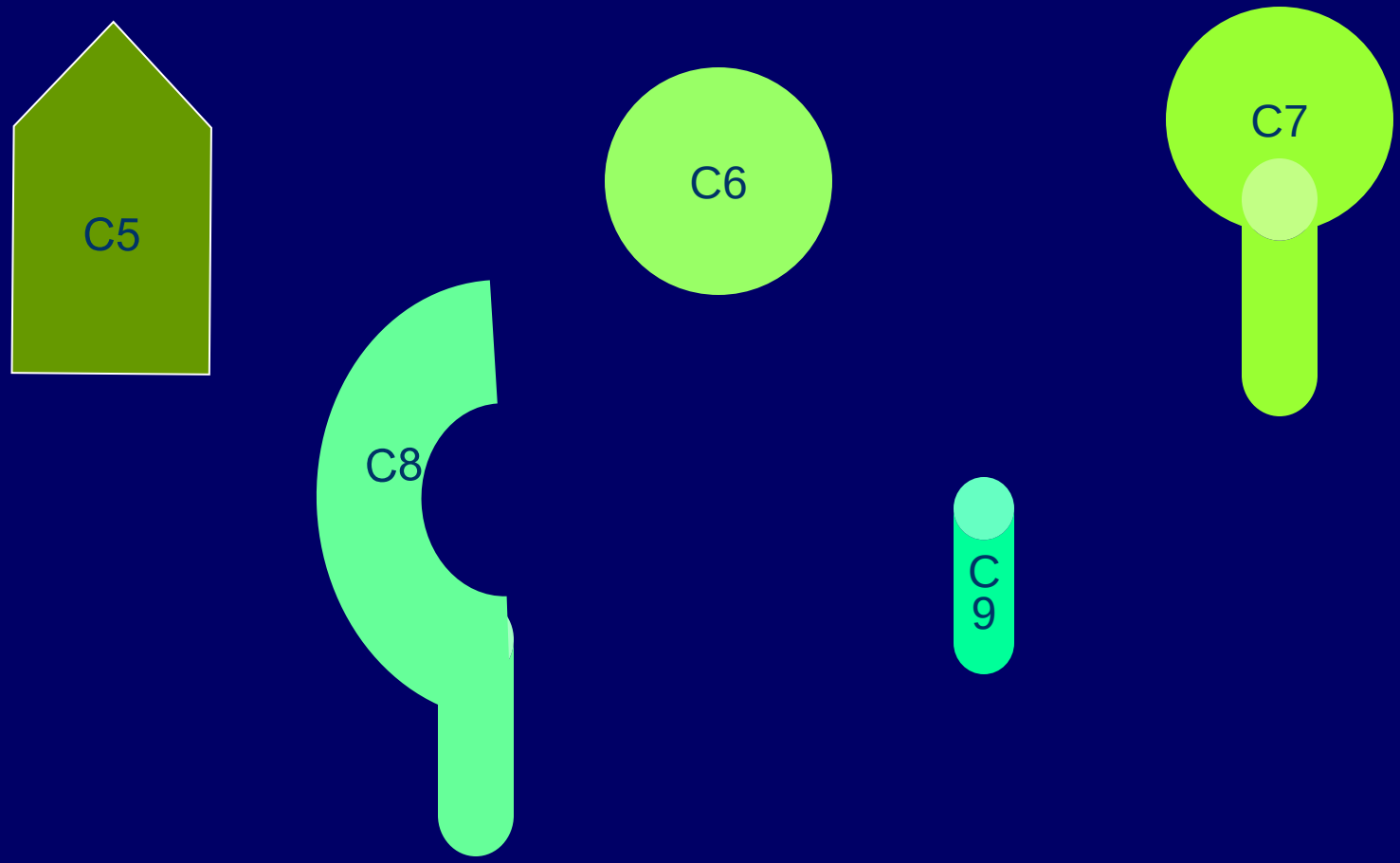
Figure 2-18 Immunobiology, 6/e. (© Garland Science 2005)

Membrane Attack Complex formation

C5-activation

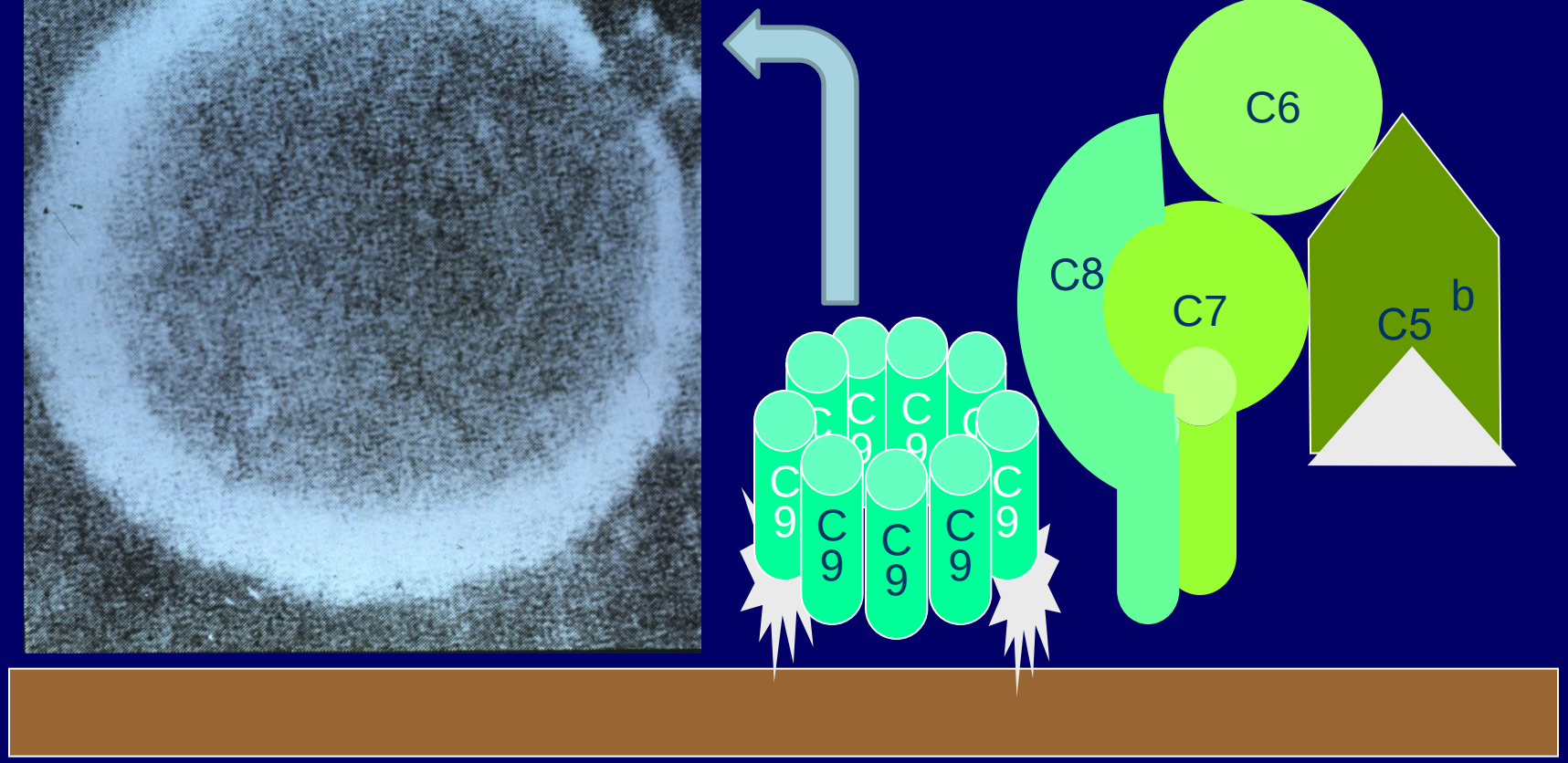


Components of the Membrane Attack Complex



Membrane Attack Complex components Assembly

Membrane Attack Complex formation：
insertion of lytic complex into cell membrane



Biological effects of complement activation

1. Anaphylatoxin functions (e.g. C3a, C5a):

- Trigger degranulation (release of substances) of endothelial cells, mast cells or phagocytes.

- Induce smooth muscle contraction and increased vascular permeability.

- Attract additional inflammatory cells to the site of activation.

2. Opsonization: C3b is the main opsonin and to a lesser extent C4b.

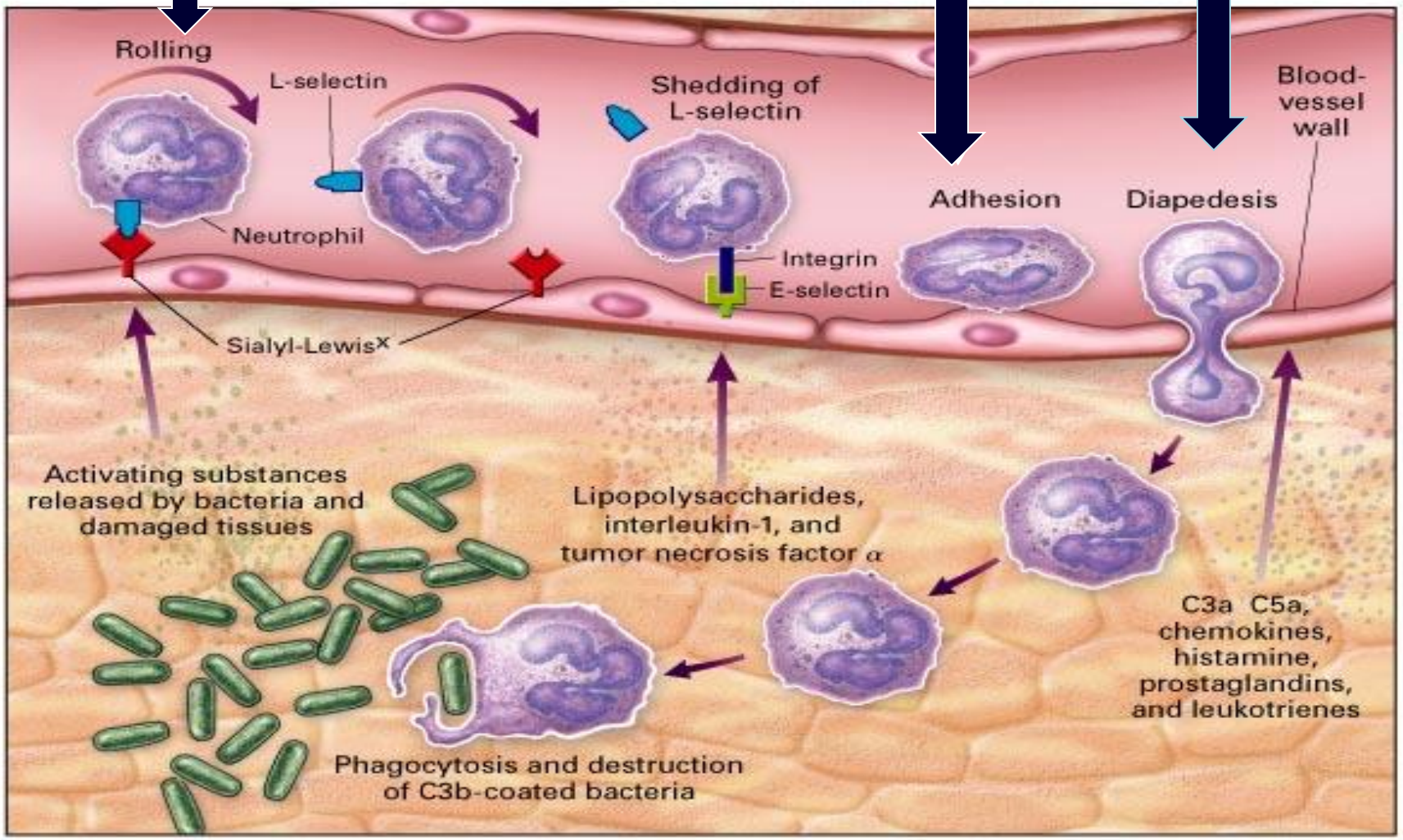
- Coating of bacteria enhances phagocytosis

3. Direct cell lysis:

- Destruction of bacteria.

Process of chemotaxis:

Rolling on vessel wall. Adhesion (attach) Pass through. :



Types of Cells attracted to the site of infection that mediate inflammation :

Monocytes :

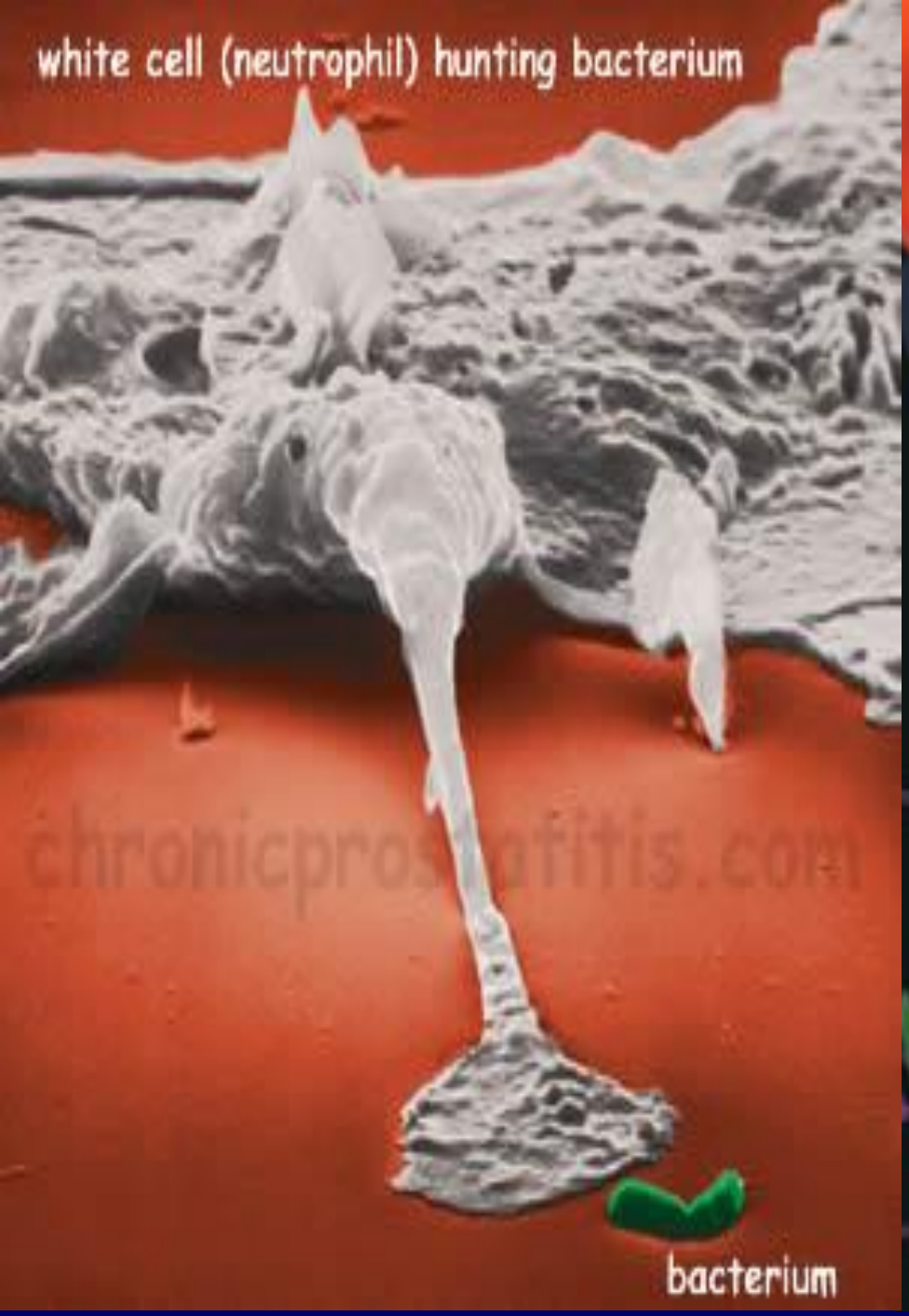
- Become Macrophages when they leave the blood and enter the tissues.

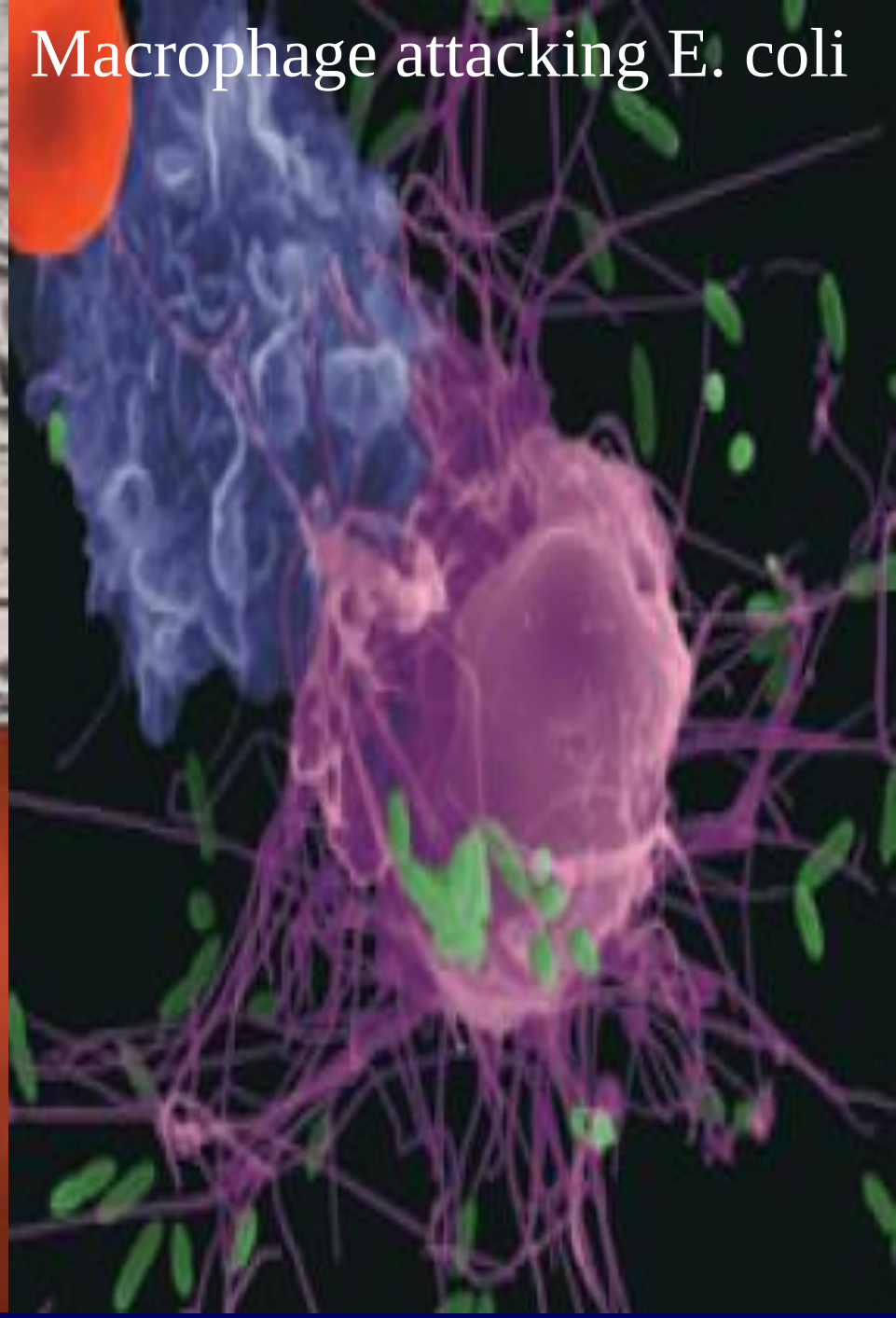
Neutrophils: (Phagocytic cells)

Eosinophils: (Allergy and Parasitic infections)

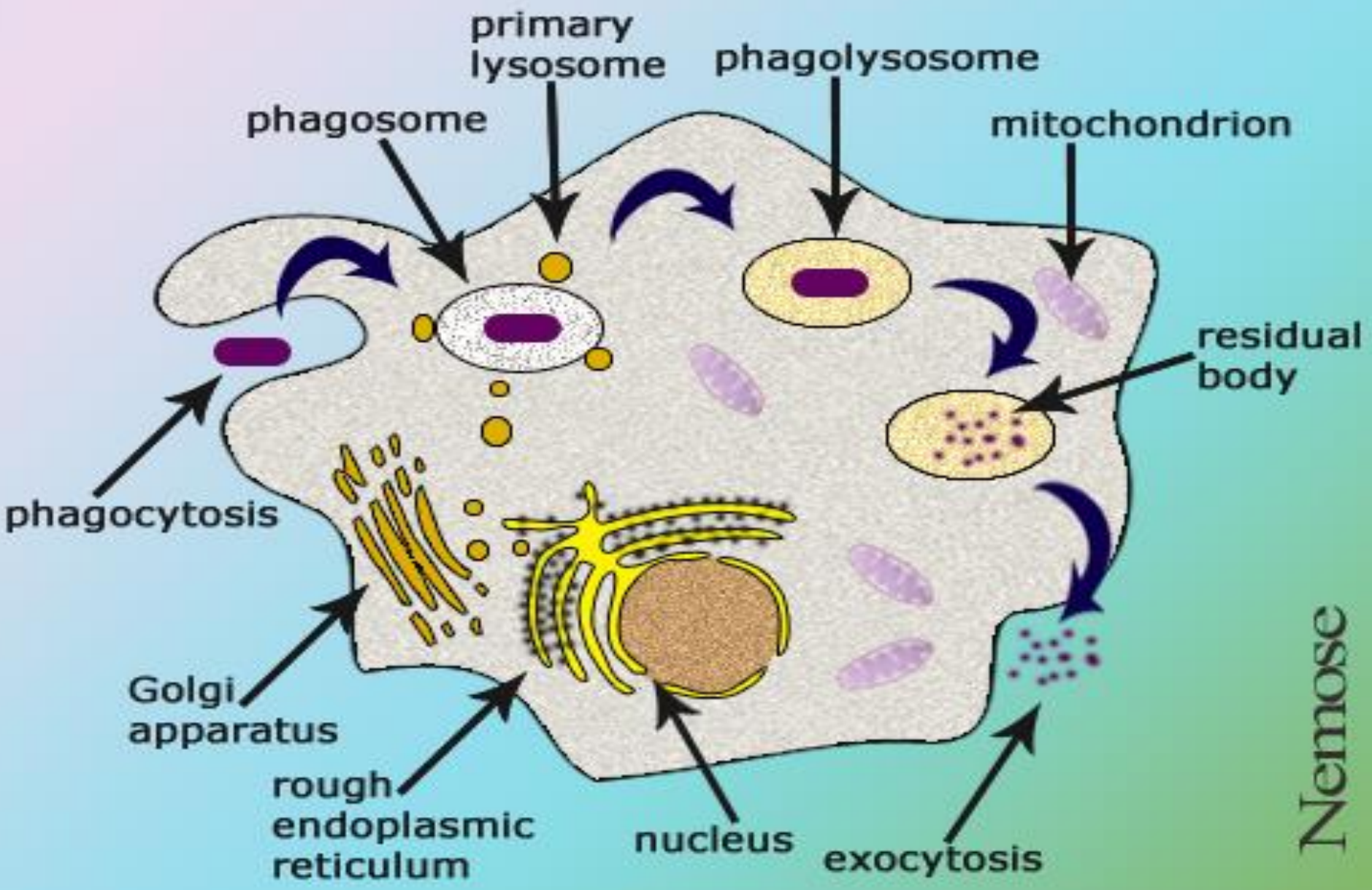
Natural Killer (NK) cells: (Kill tumor cells and virus infected cells)

Phagocytic cells (neutrophils & macrophages) at site of infection start the process of phagocytosis which is the process by which a cell engulf a solid particle such bacteria to form internal vesicle known as phagosome


white cell (neutrophil) hunting bacterium
bacterium


Macrophage attacking E. coli

Phagocytosis



Cytokines

Soluble molecules, produced by different cells, that control cell functions e.g. differentiation, proliferation activation or inhibition.

e.g. Interleukins

- Produced primarily by macrophages and lymphocytes in response to a pathogen.
- Many types
- Examples

IL-1, IL-2, IL-3…….

Cytokines

- Interferons:
  - Protects against viral infections
  - Produced and released by virally infected cells in response to viral infections.

Cytokines

- Tumor necrosis factor (TNF)
  - Secreted by macrophages.

    - Induces fever by acting as an endogenous pyrogen (a substance released from inside the body that produces fever)
      - - Increases synthesis of inflammatory serum proteins
      - - Increase expression of adhesion molecules on endothelial cells and vascular permeability

Take home message

- 1. Non-specific (innate immunity) acts as a first line of defense against invading pathogens
- 2. Innate immunity is an important initial step for generation of adaptive immune response
- 3. Inflammation is vital for controlling infection and limiting tissue damage