

# Natural Defense Mechanisms

Immunology Unit  
Dept. of Pathology  
College of Medicine  
KSU

**Lecture 2/6**  
**Foundation**  
**block**

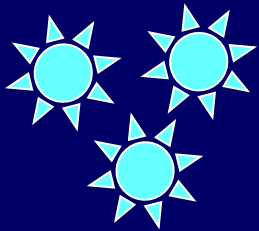
# Objectives

- ❑ 1. First (non-specific immunity) and second (adaptive immunity) lines of defense
- ❑ 2. Complement activation provides protection by killing pathogens
- ❑ 3. Accumulation of inflammatory cells important for clearance of infection
- ❑ 4. Cytokines as mediators regulate inflammation

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

## Viruses e.g.

Influenza  
*Polio*



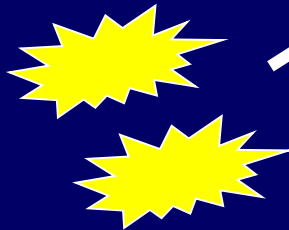
## Parasites e.g.

Tapeworms  
Malaria



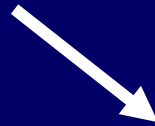
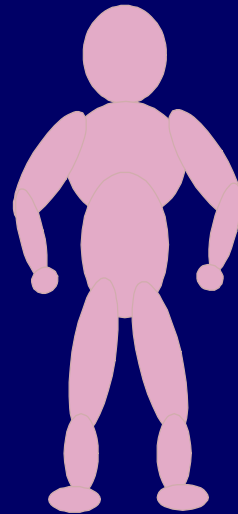
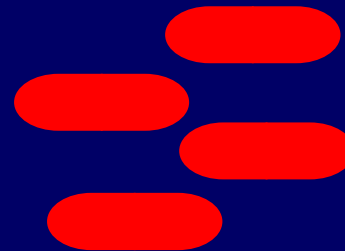
## Fungi e.g.

*Candida albicans*



## Bacteria e.g.

*Tubercule bacillus*  
*Staphylococci*



# First and the second lines of defense:



## NONSPECIFIC DEFENSE MECHANISMS

## SPECIFIC DEFENSE MECHANISMS (IMMUNE SYSTEM)

### First Line of Defense

### Second Line of Defense

- Skin
- Mucous membranes
- Secretions of skin and mucous membranes

- Phagocytic white blood cells
- Antimicrobial proteins
- The inflammatory response

- Lymphocytes
- Antibodies

# 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

- Consist of a group of serum proteins circulate in inactive form once they 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 protein 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)

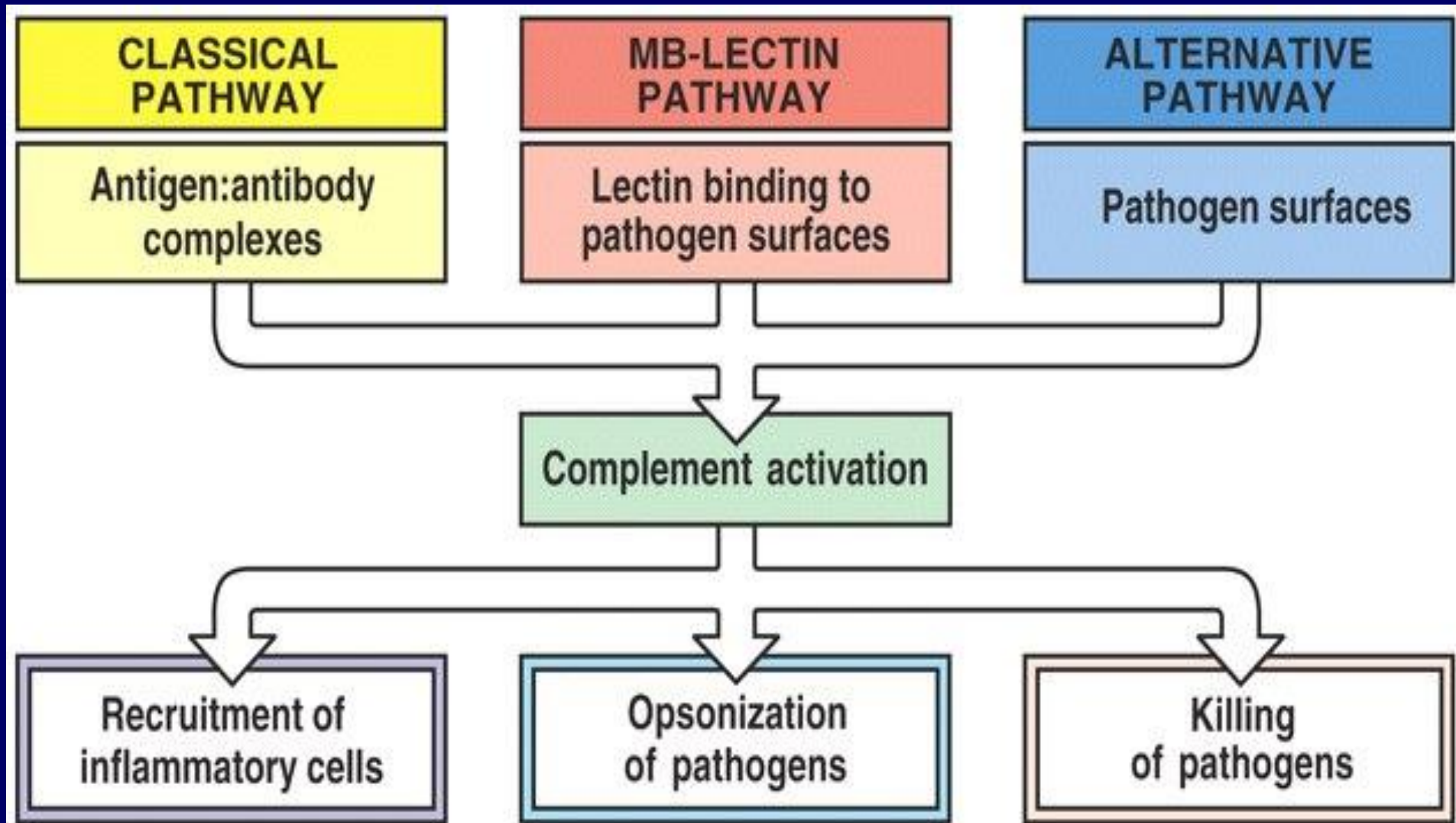
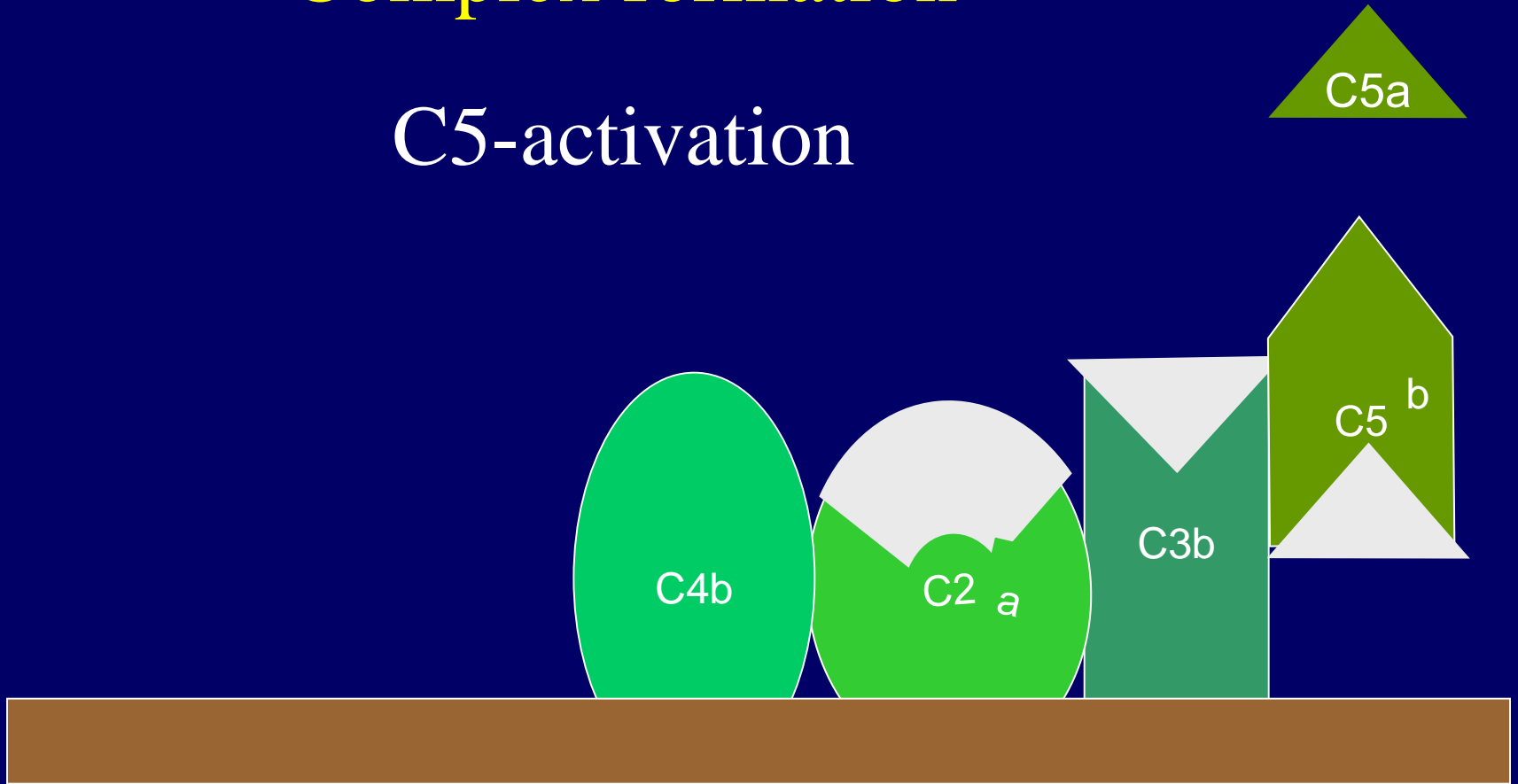


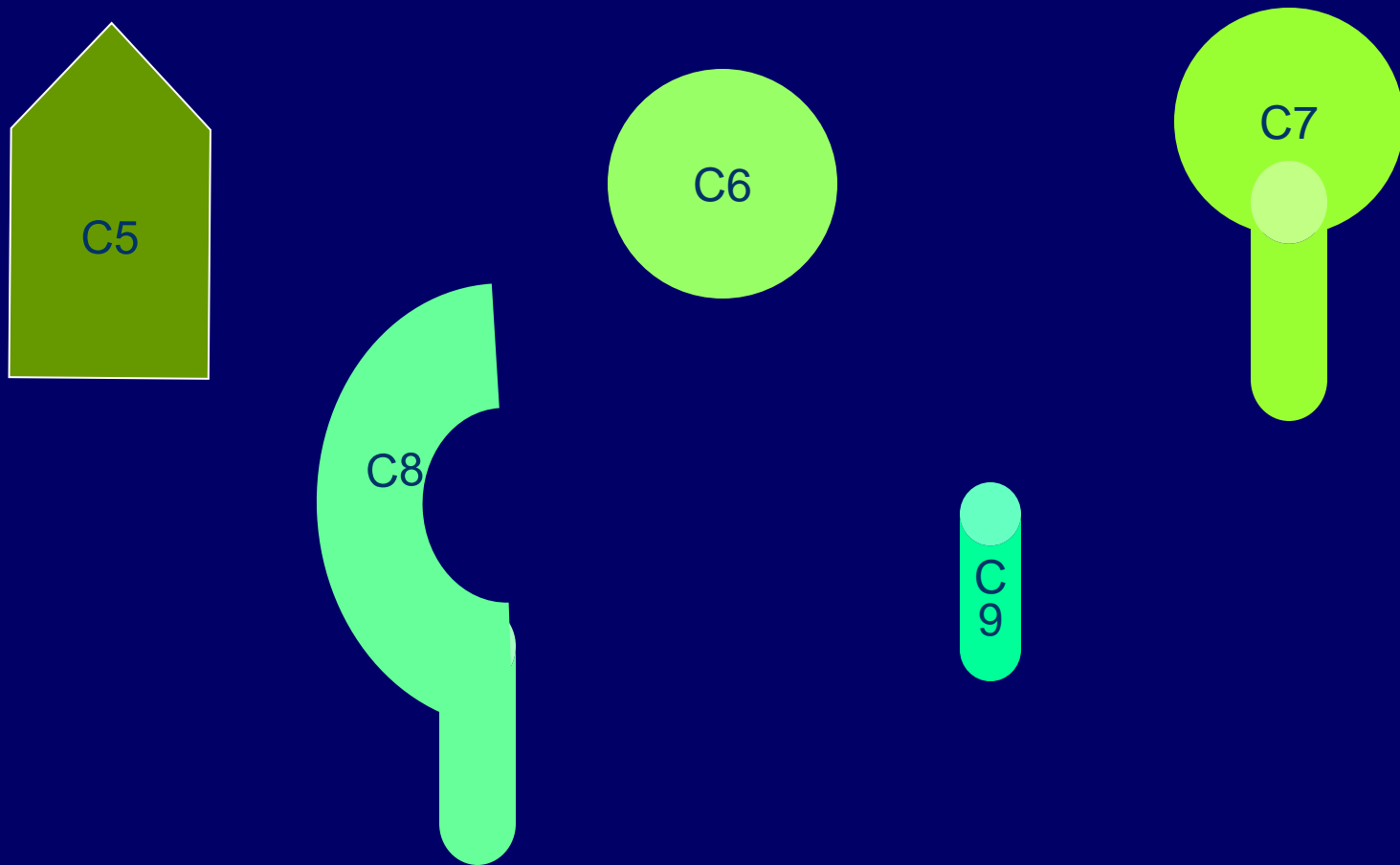
Figure 2-18 Immunobiology, 6/e. (© Garland Science 2005)

# Membrane Attack Complex formation

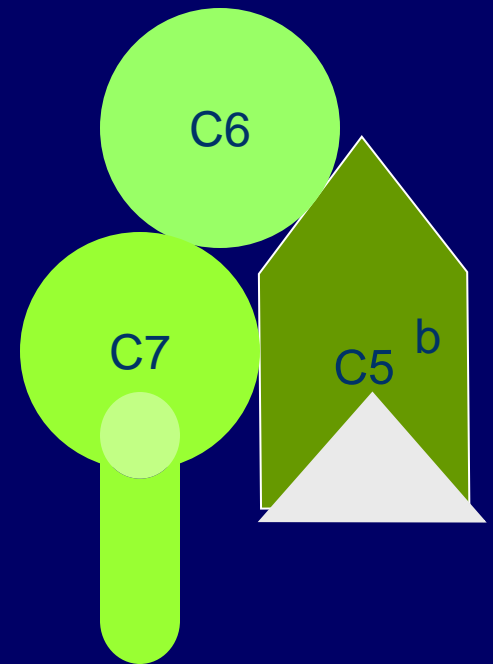
C5-activation



# Components of the Membrane Attack Complex

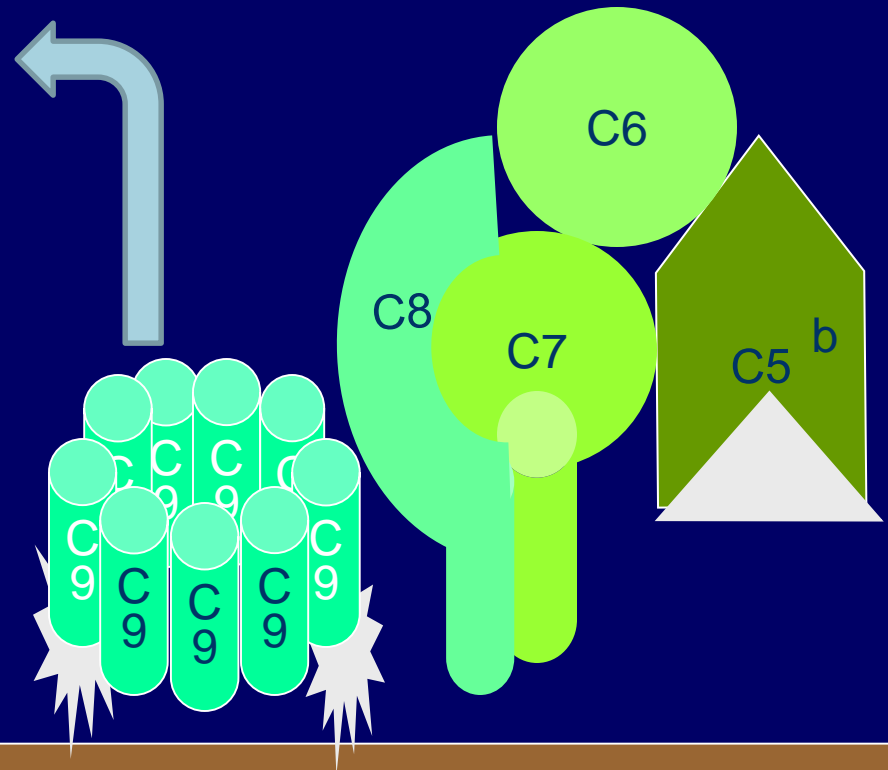
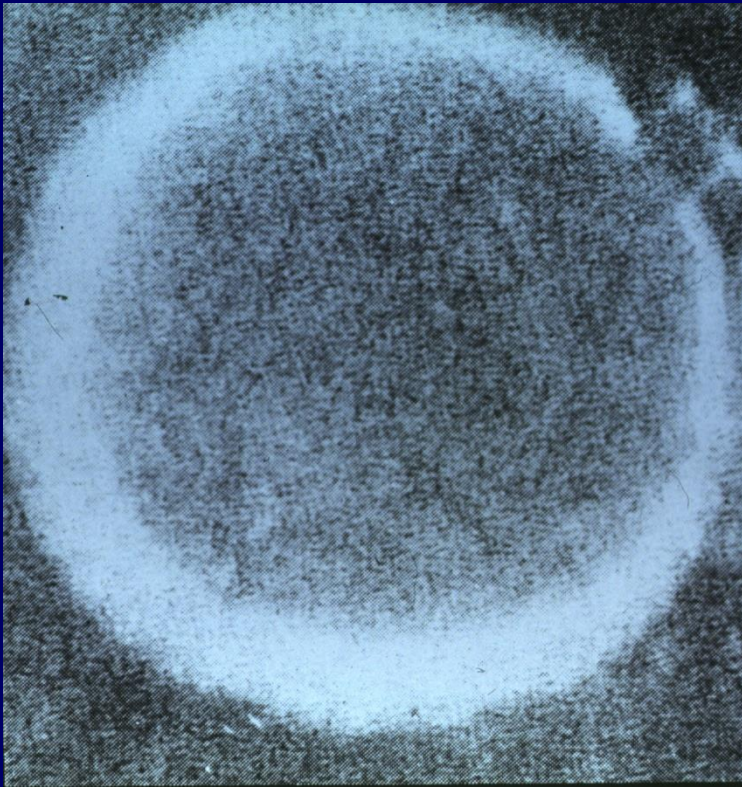


# Membrane Attack Complex components Assembly





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



# Biological effects of complement activation

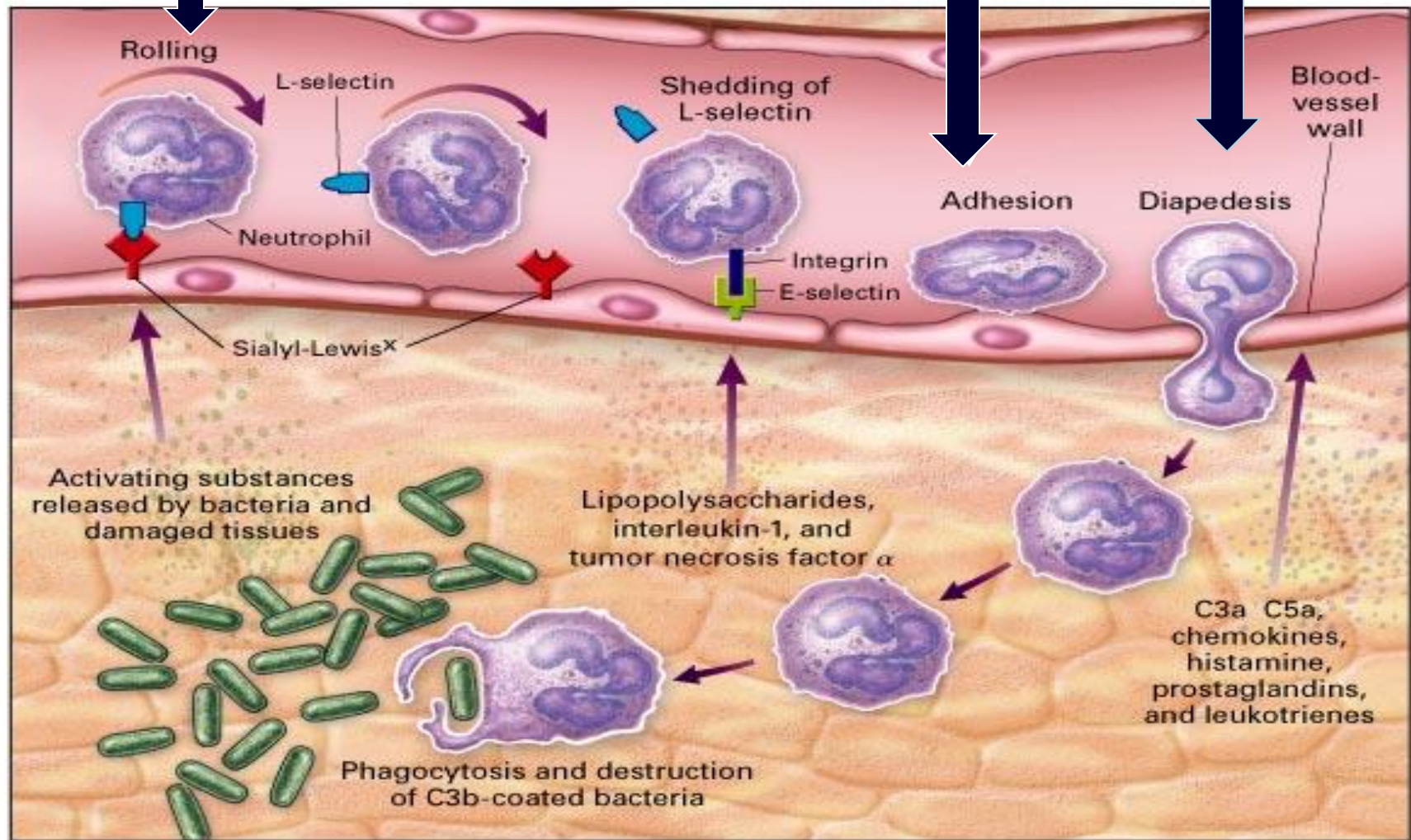
1. Anaphylatoxin (C3a, C5a)
  - Induce histamine release from mast cells.  
release chemotactic agents.
2. Opsonization: (opsonin, C3b )
  - Coating of bacteria enhances phagocytosis
3. Cause direct cell lysis
  - Destruction of bacteria.

# Process of chemotaxis:

Rolling on vessel wall.

Adhesion (attach)

Pass through.



# Types of Cells attracted to 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)

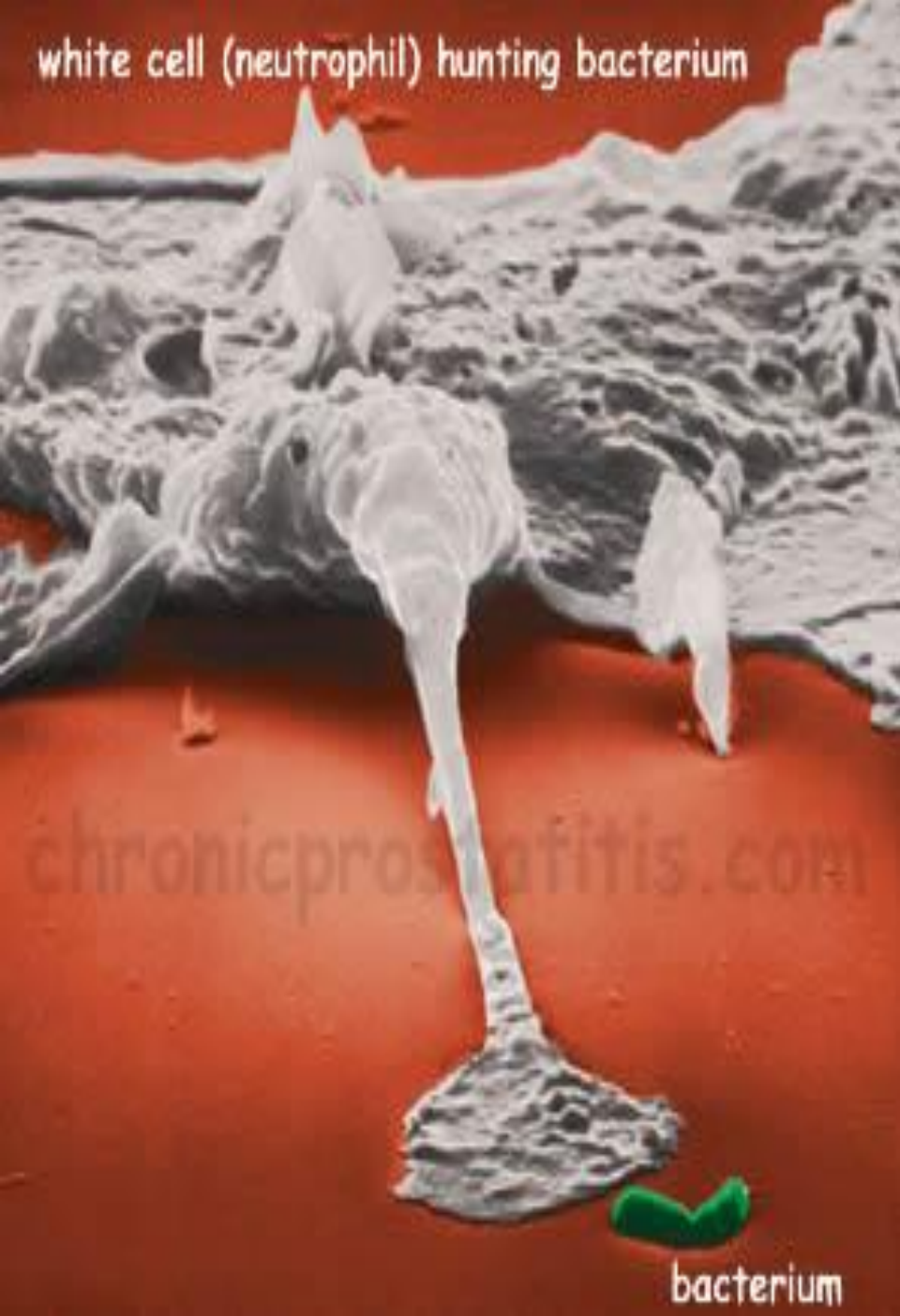
**Natural Killer (NK) cells:** (Kill tumor cells and virus infected cells)

Phagocytic cells (neutrophils & macrophages) at site of infection start the process of **phagocytosis**

The process by which a cell ingests and destroy foreign material

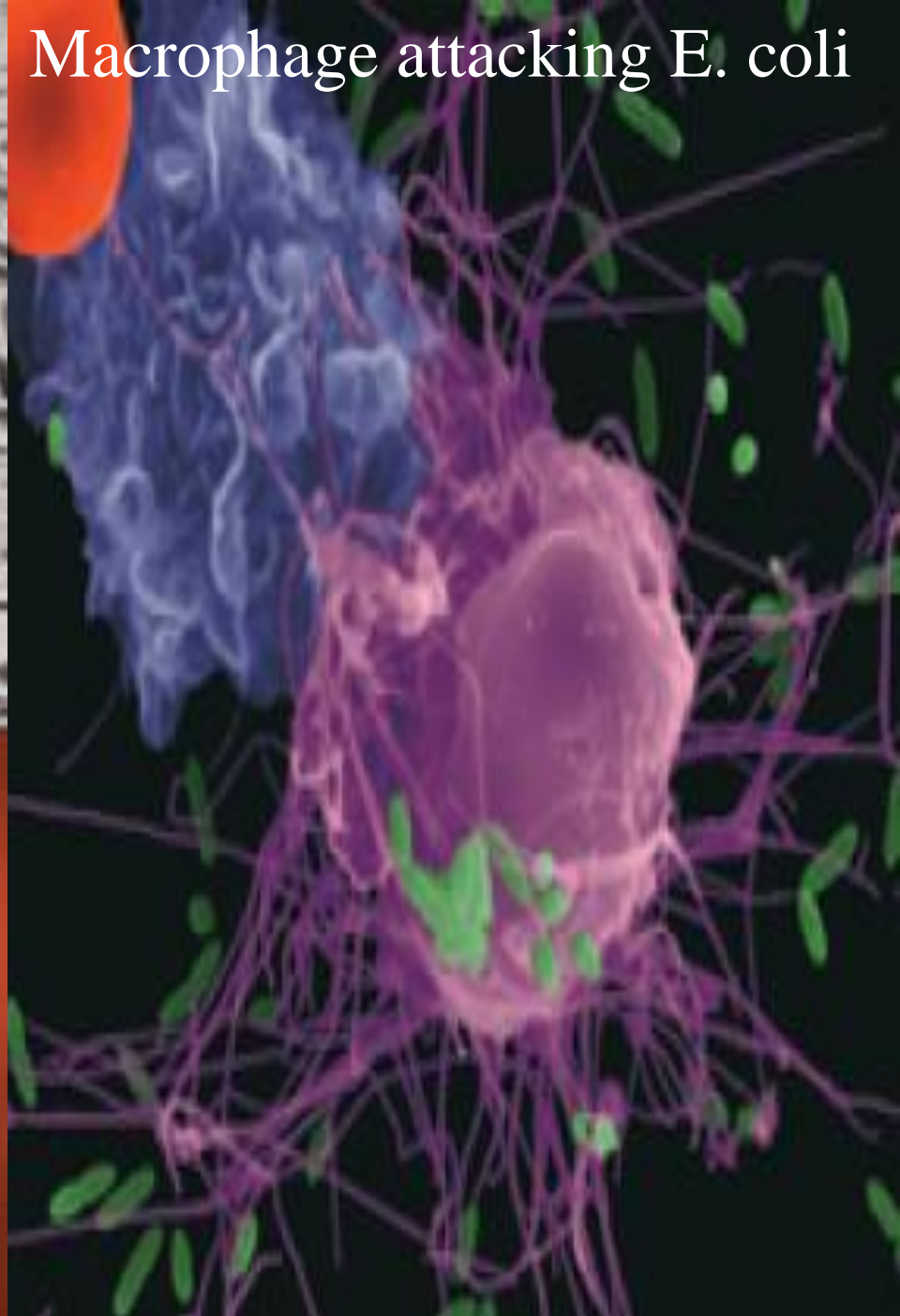


white cell (neutrophil) hunting bacterium

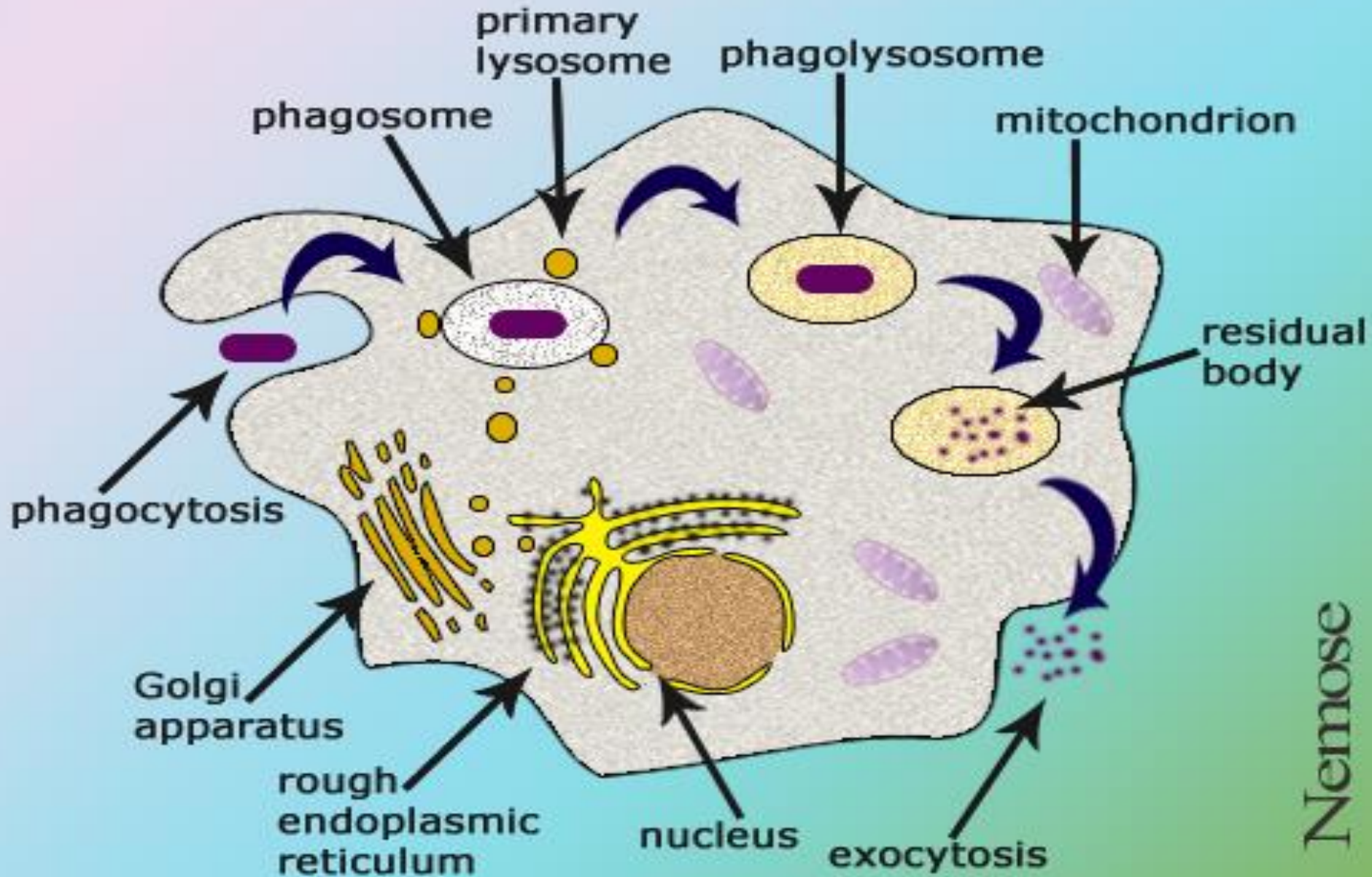


bacterium

Macrophage attacking E. coli



# Phagocytosis



# Cytokines

Soluble molecules, produced by different cells, that control cell functions e.g. 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

# 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