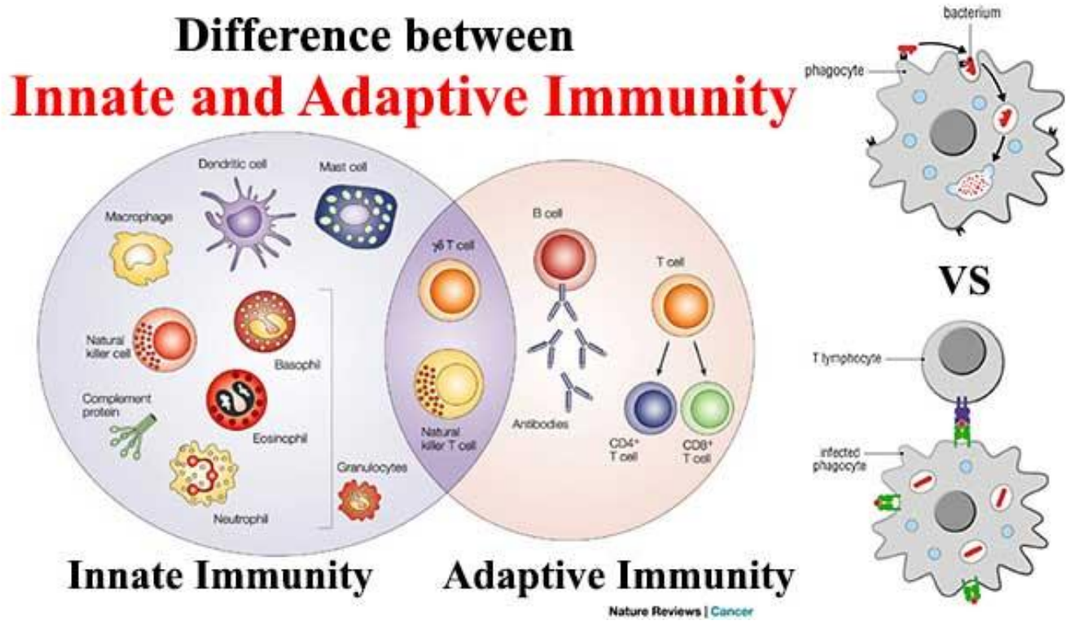
Innate Immunity



بسم الله الرحمن الرحيم

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Objectives

- Discuss the concept of innate immunity - features, importance.
- Explain how the innate immune system recognizes foreign antigens in general.
- Outline the components of the innate immune system.
- Discuss how these components combat various foreign antigens.

Introduction

- Protection against infections that relies on the mechanisms that exist before infection and are capable of rapid response to pathogens
- Innate immunity is the first line of defense against infection
- Characteristics:
  - set up at birth
  - non –specific
  - hereditable
  - no immune memory
  - Little individual difference

Innate (Nonspecific) Immunity	
First line of defense	**Second line of defense**
Intact skin Mucous membranes and their secretions Normal microbiota	Natural killer cells and phagocytic white blood cells Inflammation Fever Antimicrobial substances

Innate Host Defense Mechanisms

آليات الدفاع

- Physical factors
- Biochemical factors
- Microbiological factors
- Fever
- Innate Immune cells
- Cytokines
- Complement system
- Inflammation

1. Physical Factors

1. Skin: microbes sloughed off along with skin cells, Microbes must penetrate several layers
   - Stratified and cornified epithelium provides a mechanical barrier
   - Indigenous microbial flora competes with pathogens
   - Acid pH inhibits growth of disease producing bacteria
   - Bactericidal long chain fatty acids in sebaceous gland secretions
2. Mucous membranes: produce mucus to trap microbes, most lined with cilia

2. Biochemical Factors

1. **Low pH** in vaginal and urinary tracts, and stomach
2. **Defensins**: short antimicrobial peptides, insert into bacterial membranes and form pores.
3. **Lysozyme**: degrades peptidoglycan
   - Tears contain a high concentration of lysozyme (effective against gram positive microorganisms)
4. **Interferon**: are cytokines that trigger:
   - Macrophage activation
   - Production of substances to interfere with RNA viral reproduction

Antimicrobial Peptides/Defensins

- Originally isolated from frog skin based on their ability to kill bacteria
- Small polypeptides (<10kDa) secreted at mucosal surfaces
- Four hundred peptides described to date
- Defensins (four families in eukaryotes)
  - α-defensins (neutrophils and intestinal Paneth cells)
  - β-defensins (epithelial cells)
  - Insect defensins
  - Plant defensins
- Defensins appear to act by binding to outer membrane of bacteria, resulting in increased membrane permeability
- May also play a role in inflammation and wound repair

3. Microbiological Barriers

- **Normal Flora**: is not part of immune system, but are part of first line of defense
- Protection they provide is considerable
  - Competitive exclusion of invading microbes
  - Produce compounds that are toxic to other bacteria

4. Fever

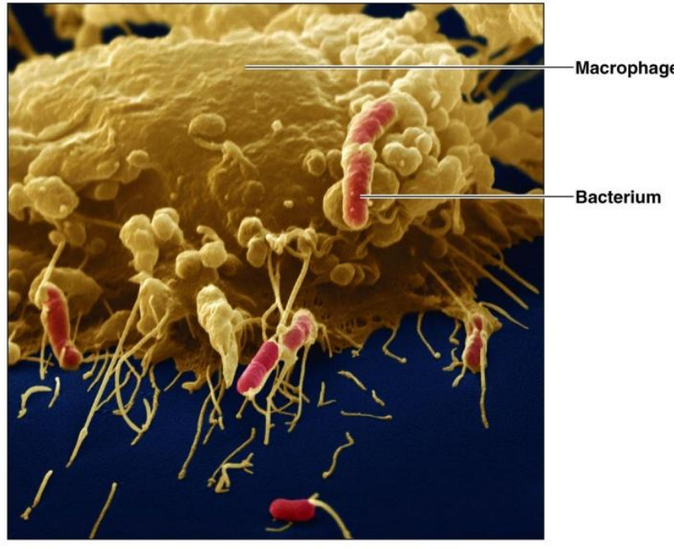
- **Mechanism of fever:**
  1. Higher body temperature occurs as a result of certain cytokines called pyrogens
  2. Cytokines carried in bloodstream to hypothalamus
  3. Hypothalamus responds by raising temperature
- Fever inhibits growth of many pathogens by at least two mechanisms:
  1. Elevates temperature above optimum growth temperature
  2. Activates and speeds up a number of other body defenses

5. Innate Immune Cells

Cell type	Pricipal function(s)
Monocytes/Macrophages	Phagocytosis, inflammation, T-cell activation, tissue repair
Neutrophils	Phagocytosis, inflammation
NK cells	Killing of infected or tumor cells
Dendritic cells	Phagocytosis, activation of naive T-cells
Mast cells	Inflammation
Eosinophils	Defense against parasites

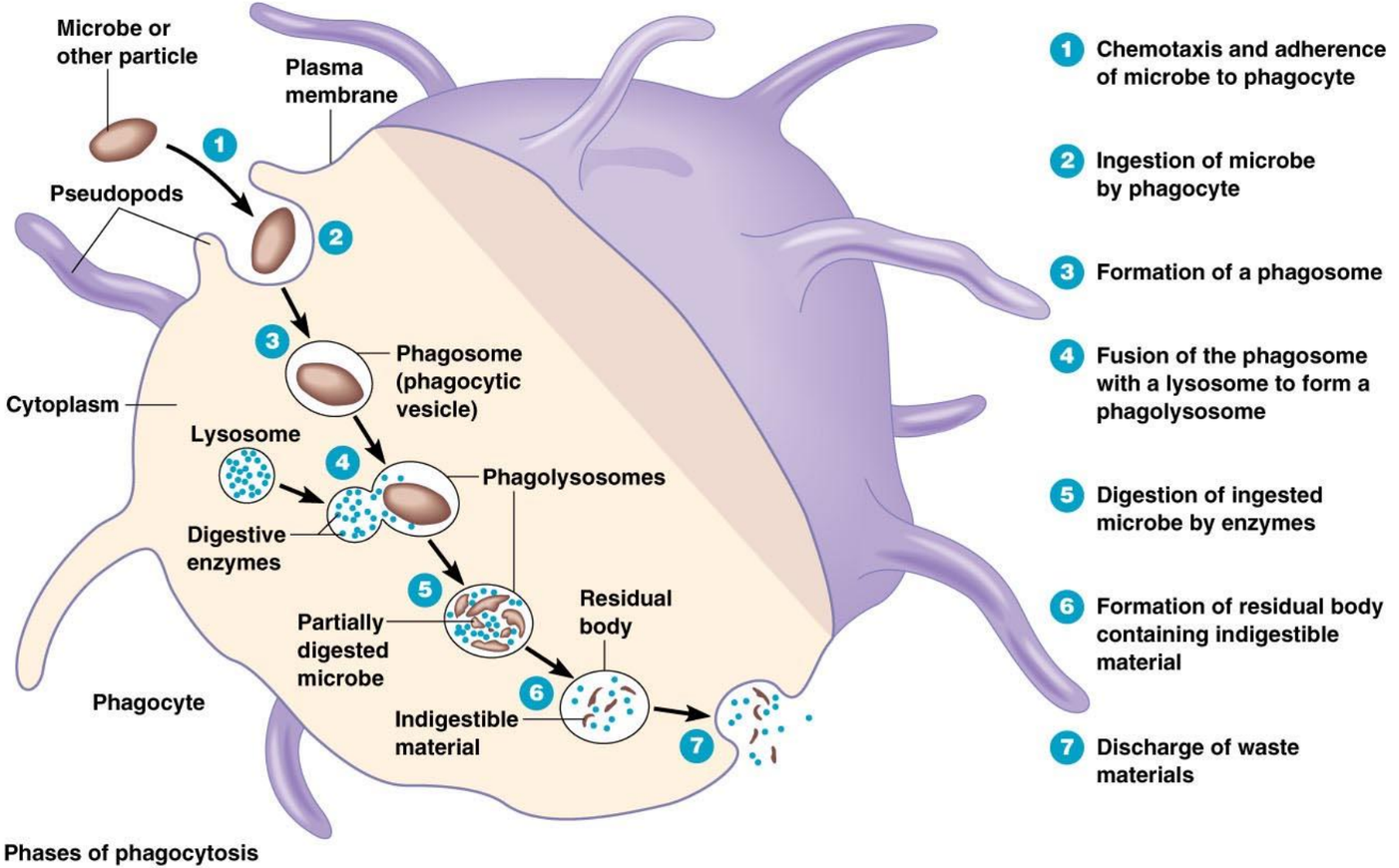
Phagocytes

- **Performed by Neutrophils and Macrophages**
  1. Phagocytosis is the capture and digestion of foreign particles
  2. Chemokines are cytokines that attract macrophages and neutrophils to infected tissues
  3. Opsonins attach to microbes to increase the ability of phagocytes to adhere (opsonization)



Steps of Phagocytosis

- Recognition
- Ingestion- pseudopods engulf microbe through endocytosis
- Vacuole Formation- vacuole contains microbe
- Digestion- vacuole merges with enzymes to destroy microbes
- Exocytosis- microbial debris is released



Phases of phagocytosis

Innate Immune Recognition

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- All multi-cellular organisms are able to recognize and eliminate pathogens
- Despite their extreme heterogeneity, pathogens share highly conserved molecules, called “pathogen-associated molecular patterns” (**PAMPs**)

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- Host cells do not share PAMPs with pathogens
- PAMPs are recognized by innate immune recognition receptors called pattern-recognition molecules/receptors (PRMs/PRRs)

Typical PAMPs

- **Typical PAMPs**:
  - Lipopolysaccharides
  - Peptidoglycans
  - Certain nucleotide sequences unique to bacteria
  - Other bacterial components

- **Binding of Innate immune receptors and PAMPs**:
  - Mediate inflammatory cytokines
  - Antigen-presenting cells recognize PAMPs

6. Cytokines

- In response to microbes, macrophage and other cells secrets proteins called cytokines that mediate many cellular reaction in innate immunity
- Cytokines act as
  - Inflammatory mediators
  - Communication between leukocytes and leukocytes and other cells
- 4 kinds:
  - **Chemokines**: important in chemotaxis of immune cells
  - **Interferons**: glycoproteins important in the control of viral infections; also help regulate cells involved in immune response
  - **Interleukins**: important in innate immunity, inflammation, and adaptive immunity
  - **Tumor necrosis factors**: help kill tumor cells, initiate programmed cell death (apoptosis)

6. Complement System

- The complement system is a collection of circulating and membrane associated proteins that are important in defense against microbes
- Many complement proteins are photolytic enzymes and complement activation involve the sequential activation of these enzymes called the enzymatic cascade
- Three pathways to activate the complement system
  - **Classical**: activated by antibody binding to microbes or antigen (adaptive part)
  - **Alternative**: directly activated by microbes (innate immunity)
  - **Lectin pathway** (binding to mannose-containing carbohydrates) (innate immunity- no need for antibodies)

6. Complement System

- Host cells have complement regulatory proteins on their surface that protect them from spontaneous activation of C3 molecules while microbes can activate the complement pathway but it has no regulatory proteins
- When pathogen activates the complement system this initiates innate immunity response by three main mechanisms:
  - Inflammation
  - Phagocytosis and lysis
  - Opsonization

Role of innate immunity in stimulation of adaptive immune response

- Adaptive immune system activation (T or B-cells) need two signals for activation
  - First signal: antigen recognition
  - Second signal: derived by innate immunity