

Chapter 16 Innate Immunity: Nonspecific Defenses of the Host

First Line of Defense – Skin and Mucous

- Physical factors
- Chemical factors
- Microbiota

Second Line of Defense – Defense cells and reactions

- Formed elements of blood
- Lymph system and phagocytosis
- Inflammation
- Fever
- Antimicrobial substances – the compliment system

The Concept of Immunity

- Susceptibility: Lack of resistance to a disease
- Immunity: Ability to ward off disease
- Innate immunity: Defenses against any pathogen
- Adaptive immunity: Immunity, resistance to a specific pathogen
- Host Toll-like receptors (TLRs) attach to
- Pathogen-associated molecular patterns (PAMPs)
- TLRs induce cytokines that regulate the intensity and duration of immune responses

Physical Factors

- Skin
- Epidermis consists of tightly packed cells with
 - Keratin, a protective protein

Physical Factors

- Mucous membranes
- Mucus: Traps microbes
- Ciliary escalator: Microbes trapped in mucus are transported away from the lungs

Physical Factors

- Lacrimal apparatus: Washes eye
- Saliva: Washes microbes off
- Urine: Flows out
- Vaginal secretions: Flow out

Chemical Factors

- Fungistatic fatty acid in sebum
- Low pH (3–5) of skin
- Lysozyme in perspiration, tears, saliva, and urine
- Low pH (1.2–3.0) of gastric juice
- Low pH (3–5) of vaginal secretions

Normal Microbiota and Innate Immunity

- Microbial antagonism/competitive exclusion: Normal microbiota compete with
 - pathogens or alter the environment
- Commensal microbiota: One organism (microbe) benefits and the other (host) is unharmed
 - May be opportunistic pathogens

Formed Elements in Blood

- See Table 16.1

Differential White Cell Count

- Percentage of each type of white cell in a sample of 100 white blood cells
 - = Neutrophils = 60-70%
 - = Lymphocytes = 20-25%

The Lymphatic System

Phagocytosis

- Phago: From Greek, meaning eat
- Cyte: From Greek, meaning cell
- Ingestion of microbes or particles by a cell, performed by phagocytes

Phagocytosis

- Neutrophils
- Fixed macrophages
- Wandering macrophages

Microbial Evasion of Phagocytosis

- Inhibit adherence: M protein, capsules
 - *Streptococcus pyogenes*, *S. pneumoniae*
- Kill phagocytes: Leukocidins
 - *Staphylococcus aureus*
- Lyse phagocytes: Membrane attack complex
 - *Listeria monocytogenes*

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- Escape phagosome
 - *Shigella*, *Rickettsia*
- Prevent phagosome-lysosome fusion
 - HIV, *Mycobacterium tuberculosis*
- Survive in phagolysosome
 - *Coxiella burnetii* (Q fever)

Inflammation

- Acute-phase proteins activated (complement, cytokine, and kinins)
- Vasodilation (histamine, kinins, prostaglandins, and leukotrienes)
- Redness
- Swelling (edema)
- Pain
- Heat

Functions

- Destroy agent causing injury (and remove its by-products)
- Limit effects of agent on body by containing the damage
- Repair damage from agent or its by-products

Steps in inflammation

- Vasodilation and blood vessel permeability
- Phagocyte migration and phagocytosis
- Tissue repair

Chemicals Released by Damaged Cells

- Histamine - Vasodilation, increased permeability of blood vessels
- Kinins - Vasodilation, increased permeability of blood vessels
- Prostaglandins - Intensity histamine and kinin effect
- Leukotrienes - Increased permeability of blood vessels, phagocytic attachment

Fever

- Abnormally high body temperature
- Hypothalamus normally set at 37°C
- Gram-negative endotoxin cause phagocytes to release interleukin-1 (IL-1)
- Hypothalamus releases prostaglandins that reset the hypothalamus to a high temperature

- Body increases rate of metabolism and shivering which raise temperature
- Vasodilation and sweating: Body temperature falls (crisis)
- Advantages
 - Increases transferrins
 - Increases IL-1 activity
 - Produces Interferon
- Disadvantages
 - Tachycardia
 - Acidosis
 - Dehydration
 - 44–46°C fatal

The Complement System

- Serum proteins activated in a cascade
- Activated by
 - Antigen-antibody reaction
 - Proteins C3, B, D, P and a pathogen
- C3b causes opsonization
- C3a + C5a cause inflammation
- C5b + C6 + C7 + C8 + C9 cause cell lysis

Effects of Complement Activation

- Opsonization or immune adherence: Enhanced phagocytosis
- Membrane attack complex: Cytolysis
- Attract phagocytes

Some Bacteria Evade Complement

- Capsules prevent C activation
- Surface lipid-carbohydrates prevent membrane attack complex (MAC) formation
- Enzymatic digestion of C5a

Interferons (IFNs)

- IFN- α and IFN- β : Cause cells to produce antiviral proteins that inhibit viral replication
- Gamma IFN: Causes neutrophils and macrophages to phagocytize bacteria

Innate Immunity

- Transferrins = Bind serum iron
- Antimicrobial peptides = Lyse bacterial cells