

Non Specific Immune Responses (Chapter 16)

First Line of Defense:

Physical Barriers:

Intact Skin: Largest organ and protects epidermis (outer thinner layer) and dermis (inner, thicker layer of connective tissues)

Many tightly packed layers

Dryness (protective keratin protein)

Shedding

Mucus Membranes: less protective than skin; lines GI, respiratory, genitourinary tracts; secretes viscous glycoprotein (mucus)

Lacrimal Apparatus: produces and drains away tears (contains lysozyme)

Saliva: dilutes and washes (contains lysozyme)

Ciliary escalator: Cells with cilia in the lower respiratory tract propels inhaled dust and microbes that are trapped in mucus upwards toward throat.

Mucus hairs of nose filters and trap microbes

Chemical Barriers:

Sebaceous (oil) glands: Sebum lowers pH of skin (some bacteria metabolize sebum → fatty acids → acne)

Sweat glands: perspiration contains lysozyme; maintains body temperature; eliminates wastes

Gastric juice of stomach: HCL (pH 1.2 -3.0) toxic to bacteria and most toxins (except Clostridium botulinum and Staph aureus)

Some bacteria will be protected by food

Helicobacter pylori: neutralizes acids and allows bacteria to grow → ulcers

Microbial Barriers:

Normal Flora: Prevents growth of pathogens (competitive exclusion)

Opportunistic: usually harmless bacteria that can cause infections when their environment changes

Antimicrobial Substances:

1. **NO** (nitric oxide) released from blood vessels and macrophages: appear to kill microbes and tumor cells

2. **Complement**: 30 interacting blood proteins produced in the liver which destroy microorganisms by Cytolysis (C3b → C5b → C6 and C7 → C8 and C9: membrane attack complex punches holes in cell membrane → lysis)

Inflammation (cause release of histamine from mast cells to increase blood vessel permeability)

Opsonization (immune adherence: C3b coats surface) to enhance **phagocytosis**

Activates in a cascade/C3 activation begins cascade (C3b binds to surface of microorganism)

Complement Activation:

A. Classical: Antibody-Antigen complex on surface of cell binds and activates C1 → activates C2 and C4 (splits into fragments a and b) → C4b and C1b activate C3

B. Alternative Activation: (does not involve antigen)

Proteins B, D, F factors in blood bind to pathogen and activate C3

C. Lectin pathway: Macrophage that ingestions pathogens release chemical to stimulate liver to produce lectin (proteins that bind to carbohydrates). One type of lectin binds to mannose (MBL) in cell wall of bacteria and MBL functions as opsonin and to activate C2 and C4
Complement is inactivated quickly so host cell are not destroyed also

3. **Interferons (IFNs)**: Three types of glycoproteins (antiviral proteins) produced by animal cells after viral infection: **host cell specific**

Alpha: diffuses to neighboring cells to prevent infection

Beta: induces mRNA to synthesize enzymes to disrupt viral multiplication

Gamma: produced by lymphocytes to induce phagocytic cells to kill bacteria

IFNs to treat disease: recombinant interferons can be produced:

α IFN: treat Kaposi's sarcoma, genital herpes, Hep B and C, Hairy Cell Leukemia

β IFN: slows progression of MS

4. Transferrins: iron-binding proteins in blood that inhibit bacteria by reducing the amount of available iron. Iron overload increases risk of infection.

Blood Cells:

WBC (leukocytes): Leukocytosis and Leukopenia

Granulocytes: Neutrophils (Segs, Polymorphonuclear, Polys): phagocytic

Eosinophils : produce toxic proteins against parasites/helminthes; ↑ in allergies

Basophils: release histamine

Monocytes: not phagocytic in blood but go into body tissue and become macrophages

Lymphocytes: (B and T cells): not phagocytic; involved in specific immune response

Phagocytosis (ingestion of cells)

Neutrophils

Monocytes: enlarge and develop into macrophages (Fixed in tissue or Wandering macrophage)

In Bacterial infections: first increase and dominance of neutrophils and then macrophages increase

Steps of Phagocytosis:

1. Chemotaxis: attraction of phagocytes to microorganisms
2. Adherence: phagocyte membrane attaches to surface of microorganism
3. Ingestion: WBC plasma membrane forms pseudopod and engulfs microorganism
4. Digestion: fusion of phagosome and lysosome → phagolysosome; releases enzymes
5. Residual body discharged from cell

How some organisms evade phagocytosis:

Inhibit adherence: capsules of *Strep pneumoniae* and *Haemophilus influenzae*

Prevents fusion of lysosome: *Mycobacterium TB*

Survives in phagocyte: *Yersinia pestis*

Produces leukocidins that destroy phagocyte: *Staph aureus*

Inflammation:

Symptoms: redness, pain, heat, swelling

Purpose of inflammation: 1. contain site of infection

2. localize response

3. restore tissue function

Inflammation activates and increases concentration of acute phase proteins such as CRP

Process:

1. **Vasodilation:** increased blood flow (redness and heat); increase permeability of vessels (edema) caused by chemicals released from damaged tissue: histamine, kinins, prostaglandins)
2. **Phagocytic Migration:** chemotaxis—attracted to site by cytokines (chemical messengers)
3. **Phagocytosis:** Pus results from death of cells and phagocytic waste
4. **Tissue Repair:** tissue replaces dead cells

Fever: enhances natural defenses

Stimulates phagocytosis

Accelerates reaction rates

Intensifies Interferon

Reduces Iron content of body

Increases T cell production

Hypothalamus of brain set body temp at 37°C

Pyrogens: fever inducing agents: endogenous (cytokines) or exogenous (bacterial endotoxins/LPS of cell wall)

Pyrogens cause phagocytes to produce **Interleukin-I** (Il-I) → hypothalamus releases prostaglandins

Prostaglandins reset thermostat at higher temp → fever

When Il-I gone, temp is reset at 37°C

