Nonspecific Defenses of the Host

- Susceptibility: Lack of resistance to a disease
- Resistance: Ability to ward off disease
- Nonspecific resistance: Defenses against any pathogen
- Specific resistance: Immunity, resistance (antibodies) to a specific pathogen

Mechanical Factors

Describe the role of the skin and mucous membranes in nonspecific resistance.

- Skin (works generally if intact)
- Epidermis consists of tightly packed cells with Keratin, a protective protein, waterproof

Differentiate between mechanical and chemical factors, and list five examples of each.

- Mucous membranes (overcome by large numbers)
- Ciliary escalator: Microbes trapped in mucus are transported away from the lungs
- Lacrimal apparatus: Washes eye, removes microbes
- Saliva: Washes microbes off teeth and gums, tongue
- Mucus traps microbes, moved up and out by ciliary escalator
- Urine: Flows out
- Vaginal secretions: Flow out
Ciliary escalator

- Microbes trapped in mucus produced by goblet cells, then propelled upward by cilia

Chemical Factors

- Fungistatic fatty acid (unsaturated) in sebum
- Sweat washes off skin (contains lysozyme)
- Low pH (3-5) of skin
- Lysozyme in perspiration, tears, saliva, and tissue fluids
- Low pH (1.2-3.0) of gastric juice prevents microbe growth (except *Helicobacter pylori*)
- Transferrins in blood bind iron removing this nutrient
- NO (nitrous oxide) inhibits ATP production of microbes

Normal Microbiota

Describe the role of normal microbiota in nonspecific resistance.

- Microbial antagonism/competitive exclusion: Normal microbiota compete with pathogens, preventing their growth on the host.
Phagocytosis

- Phago: eat
- Cyte: cell
- Ingestion of microbes or particles by a cell, performed by phagocytes (certain white blood cells)

Define phagocytosis and phagocyte.

Differential White Cell Count

Define differential blood cell count.

- Percentage of each type of white cell in a sample of 100 white blood cells

<table>
<thead>
<tr>
<th>Cell Type</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neutrophils</td>
<td>60-70%</td>
</tr>
<tr>
<td>Basophils</td>
<td>0.5-1%</td>
</tr>
<tr>
<td>Eosinophils</td>
<td>2-4%</td>
</tr>
<tr>
<td>Monocytes</td>
<td>3-8%</td>
</tr>
<tr>
<td>Lymphocytes</td>
<td>20-25%</td>
</tr>
</tbody>
</table>

White Blood Cells

- Leukocytes (white blood cells) divided into granulocytes (neutrophils, basophils, eosinophils), lymphocytes, and monocytes
- Granulocytes: (dominate early in infection)
  - Neutrophils: Phagocytic (most important)
  - Basophils: Produce histamine
  - Eosinophils: Toxic to parasites, some phagocytosis
- Lymphocytes: Involved in specific immunity
- Monocytes: Phagocytic as mature macrophages
- Fixed macrophages in lungs, liver, bronchi
- Wandering macrophages (enlarged monocytes) roam tissues

Principle kinds of leukocytes

Lymphatic system

Macrophage engulfing rod-shaped bacteria
Phagocytosis

Describe the process of phagocytosis, and include the stages of adherence and ingestion.

Microbial Evasion of Phagocytosis

<table>
<thead>
<tr>
<th>Microorganism</th>
<th>Evasion Strategy</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Coxiella burnetti</em></td>
<td>Survive in phagolysosome</td>
</tr>
<tr>
<td><em>HIV</em></td>
<td>Prevent phagosome-lysosome fusion</td>
</tr>
<tr>
<td><em>Shigella</em></td>
<td>Escape phagosome</td>
</tr>
<tr>
<td><em>Listeriamonocytogenes</em></td>
<td>Lyse phagocytes: Membrane attack complex</td>
</tr>
<tr>
<td><em>Staphylococcus aureus</em></td>
<td>Kill phagocytes: Leukocidins</td>
</tr>
<tr>
<td><em>Streptococcus pyogenes, S. pneumoniae</em></td>
<td>Inhibit adherence: M protein, capsules</td>
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</tr>
</tbody>
</table>

Inflammation – body response to cell damage

- Redness
- Pain
- Heat
- Swelling (edema)
- Acute-phase proteins activated (complement, cytokine, kinins) – short, intense
- Chronic inflammation is a prolonged response
- Vasodilation (histamine, kinins, prostaglandins, leukotrienes)
- Margination and emigration of WBCs
- Tissue repair

Inflammation

Chemicals Released by Damaged Cells

Describe the roles of vasodilation, kinines, prostaglandins, and leukotrienes in inflammation.

- 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
Describe phagocyte migration.

- Phagocytes can stick to lining of blood vessels
- They also can squeeze through blood vessels
- Pus is the accumulation of damaged tissue, dead microbes, granulocytes, macrophages

Fever: Abnormally High Body Temperature

- Hypothalamus normally set at 37°C
- Gram-negative endotoxin cause phagocytes to release interleukin 1
- Hypothalamus releases prostaglandins that reset the hypothalamus to a high temperature
- Body increases rate of metabolism and shivering to raise temperature
- When IL-1 is eliminated, body temperature falls. (Crisis - sweating)

Outcomes of Complement Activation System

- Serum proteins (liquid in blood) activated in a cascade.
- Activate one another in a cascade to destroy invading microorganisms

Effects of Complement Activation

List the components of the complement system.

- Cytolysis caused by complement
- Opsonization or immune adherence: enhanced phagocytosis
- Membrane attack complex: cytolysis
- Attract phagocytes

Effects of Complement Activation (inflammation)
Classical Pathway of complement activation

- Pathway initiated by antigen-antibody reaction
- Results in cytolysis, inflammation, and phagocytosis.

Describe three pathways of activating complement.

Alternative Pathway of complement activation

- Pathway initiated by contact between proteins and pathogen

Lectin Pathway of complement activation

- Mannose-binding lectin binds to mannose, enhancing phagocytosis via classical and alternative pathways

Some bacteria evade complement

- Capsules prevent C activation
- Surface lipid-carbohydrates prevent MAC formation
- Enzymatic digestion of C5a

Interferons (IFNs)

Define interferon.

Compare and contrast the actions of α-IFN, β-IFN, and γ-IFN.

- Alpha IFN & Beta IFN: Cause cells to produce antiviral proteins that inhibit viral replication
- Interferons are host-cell specific, but not virus-specific
- Gamma IFN: Causes neutrophils and macrophages to phagocytize bacteria

Viral RNA from an infecting virus enters the cell.

The infecting virus replicates into new viruses.

Interferons released by the virus-infected host cell bind to plasma membranes or nuclear membrane receptors on uninfected neighboring host cells, inducing them to synthesize antiviral proteins (AVPs). These include oligoadenylate synthase, and protein kinase.