Innate Immunity

Innate immunity – mechanical & chemical factors
Review Questions

1. What is immunity? What are the outcomes of it? What are the types of immunity.
2. What are the components of innate immunity?
3. What are the physical factors of innate immunity? Write short notes on Anatomical barriers and mechanical removal.
4. What do know about the chemical factors? Write short notes on – Acute phase proteins.
5. Write down the role of skin & mucosal lining as innate immunity component.
6. What are the determinants of innate immunity?
7. What are cells of innate immunity?
8. What are the biological factors of innate immunity?
Types of immunity

The body has two immune systems:

The Innate immune system
The Acquired or adaptive immune system.
Innate (Nonspecific) Immunity - Innate immunity, refers to the basic resistance to disease that a species possesses - the first line of defense against infection.

Innate immunity refers to antigen-nonspecific defense mechanisms that a host uses immediately or within several hours after exposure to an antigen. This is the immunity one is born with and is the initial response by the body to eliminate microbes and prevent infection.

Innate immunity is the inherent immunity an individual born with and that is always present and is available at a very short notice, the action of which is nonspecific.
The characteristics of the innate immune response

The characteristics include the following:

– Present from birth
– Responses are Broad-Spectrum (Antigen non-specific)
– There is no memory or lasting protective immunity
– There is a limited role of recognition molecules
– The responses are phylogenetically ancient
Mechanisms of Innate Immunity

Respiratory Tract:
1. Mucus
2. Ciliated epithelium
3. Alveolar macrophage

GI Tract:
1. Acidity of stomach
2. Normal flora

Genitourinary Tract:
1. Washing action of urine
2. Acidity of urine
3. Acidity of vagina
4. Normal flora of vagina

Phagocytosis

1. Attachment
2. Engulfment
3. Degranulation
4. Killing and digestion

Fever
Components of innate immunity

1. Physical / Mechanical factors
1. Chemical factors
2. Biological / Cellular factors
Physical factors

• Bony encasements-
• Skin - Keratin & other layers of skin
• Mucosal lining- Intact mucosal lining of different organs
• Washing action of tears, saliva, urine
• Respiratory cillia – expels foreign substances
• Mucus layers over inner surfaces of the body – traps & expels foreign substances
• Mechanical removal by- Coughing, sneezing reflexes – expels foreign substances trapped in mucus layer.
1. Fatty acids, lactic acid
2. Pepsin & HCL gastric juice
3. Transferrin and lactoferrin.
4. Lysozyme,
5. Fibronectin
6. Complement components and their products
7. Acute phase proteins
8. TNF-alpha
9. Cryptidins
10. a-defensins
11. b-defensins
12. surfactant proteins A & D
13. Cytokines
14. Chemokines
15. Interferon
Cellular/ biological factors

- Phagocytosis – by neutrophils & macrophages
- Natural killer cells - tumors, viral infected cells
- Surface phagocytes - Alveolar macrophages
- Normal flora - can compete with pathogenic bacteria for nutrients & also produce antibacterial substance
- Fever
- Nutritional factors
Bony encasements, such as the skull and the thoracic cage, Vertebral column protect vital organs from injury and entry of microbes.
The skin, consisting of the epidermis and the dermis is dry, acidic, and has a temperature lower than 37 degrees Celsius (body temperature). These conditions are not favorable to bacterial growth. Resident normal flora of the skin also inhibit potentially harmful microbes. In addition, the dead, keratinized cells that make up the surface of the skin are continuously being sloughed off so that microbes that do colonize these cells are constantly being removed.
Hair follicles and sweat glands produce lysozyme and toxic lipids that can kill bacteria. (Finally, beneath the skin surface is skin-associated lymphoid tissue (SALT) that contains cells for killing microbes and sampling antigens on the skin to start acquired immune responses against them)
Mucus membrane

- Goblet cells
- Ciliated epithelial cells
- Fibroblasts of supporting CT
- BV
- Serous gland
- Mucous gland with Serous demi-lune
- Gland duct
Mucous membranes line body cavities that open to the exterior, such as the respiratory tract, the gastrointestinal tract, and the genitourinary tract. Mucous membranes are composed of an epithelial layer that secretes mucus, and a connective tissue layer.

The **mucus is a physical barrier that traps microbes**. Mucus also contains

- **Lysozyme** to degrade bacterial peptidoglycan,
- *(Secretory IgA that prevents microbes from attaching to mucosal cells and traps them in the mucousa)*
- **lactoferrin** to bind iron and keep it from being used by microbes, and
- **lactoperoxidase** to generate toxic superoxide radicals that kill microbes.
Resident normal flora of the mucosa also inhibit potentially harmful microbes. Constantly sloughing cells to remove microbes that have attached to the mucous membranes. Mucosa-associated lymphoid tissue (MALT) that contains cells for killing microbes and sampling antigens on the mucosa to start acquired immune responses against them.
Mechanical removal is the process of physically flushing microbes from the body.

**Methods include:**

a. mucus and cilia
   - **Mucus** traps microorganisms and prevents them from reaching and colonizing the mucosal epithelium.
   - **Cilia** on the surface of the epithelial cells propel mucus and trapped microbes upwards towards the throat where it is swallowed. This is sometimes called the tracheal toilet.

b. the cough and sneeze reflex
   - Coughing and sneezing removes mucus and trapped microbes

c. **Vomiting and diarrhea**
   - These processes remove pathogens and toxins in the gastrointestinal tract.

   d. **Physical flushing action of body fluids**
      - Fluids such as urine, tears, saliva, perspiration, and blood from injured blood vessels also flush microbes from the body.
• **Lactic and fatty acids**, found in perspiration and sebaceous secretions, inhibit microbes on the skin.

• **Hydrochloric acid** and enzymes found in gastric secretions destroy microbes that are swallowed.

• **Transferrin and lactoferrin** deprive organisms of iron.

• **Lysozyme**, in serum and tears, breaks down the bacterial cell wall (peptidoglycan).

• **Fibronectin** coats (opsonizes) bacteria and promotes their rapid phagocytosis.
Complement components and their products cause destruction of microorganism directly or with the help of phagocytic cells.

- **Acute phase proteins** (such as CRP) interact with the complement system proteins to combat infections.
- **TNF-alpha** suppresses viral replication and activates phagocytes.
- **Cryptidins and α-defensins** (produced in base of crypts of small intestine - damage cell membranes)
- **B-defensins** (produced within skin, respiratory tract - They forms pores in the cytoplasmic membrane of a variety of bacteria causing leakage of cellular needs.
- **Surfactant proteins A & D** (present in lungs - function as opsonins which enhance the efficiency of phagocytosis)
Cytokines are **pleiotropic, redundant, and multifunctional**.

**Pleiotropic** means that a particular cytokine can act on a number of different types of cells rather than a single cell type.

**Redundant** refers to the ability of a number of different cytokines to carry out the same function.

**Multifunctional** means the same cytokine is able to regulate a number of different functions.
Some cytokines are antagonistic in that one cytokine stimulates a particular defense function while another cytokine inhibits that function. Other cytokines are synergistic wherein two different cytokines have a greater effect in combination than either of the two would by themselves.

There are three functional categories of cytokines:

1. Cytokines that regulate innate immune responses,
2. Cytokines that regulate adaptive Immune responses, and
3. Cytokines that stimulate hematopoiesis.
Interferons are cytokines that prevent viral replication, activate a variety of cells important in body defense, and exhibit some anti-tumor activity. Produced by immune-activated cells or virus-infected cells in response to the double-stranded RNA (dsRNA) that many viruses produce as a part of their life cycle. Interferon induces uninfected cells to produce enzymes capable of degrading mRNA.
### Table 2. Physico-chemical barriers to infections

<table>
<thead>
<tr>
<th>System/Organ</th>
<th>Active component</th>
<th>Effector Mechanism</th>
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<tbody>
<tr>
<td>Skin</td>
<td>Squamous cells;</td>
<td>Sweat Desquamation; flushing, organic acids</td>
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<tr>
<td>GI tract</td>
<td>Columnar cells</td>
<td>Peristalsis, low pH, bile acid, flushing, thiocyanate</td>
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<td>Lung</td>
<td>Tracheal cilia</td>
<td>Mucociliary elevator, surfactant</td>
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<td>Nasopharynx and eye</td>
<td>Mucus, saliva, tears</td>
<td>Flushing, lysozyme</td>
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<tr>
<td>Circulation and lymphoid organs</td>
<td>Phagocytic cells</td>
<td>Phagocytosis and intracellular killing</td>
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<td></td>
<td>NK cells</td>
<td>Direct and antibody dependent cytolysis</td>
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<td></td>
<td>LAK cells</td>
<td>IL2-activated cytolysis</td>
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<tbody>
<tr>
<td>Serum</td>
<td>Lactoferrin and Transferrin</td>
<td>Iron binding</td>
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<td></td>
<td>Interferons</td>
<td>Antiviral proteins</td>
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<td></td>
<td>TNF-alpha</td>
<td>Antiviral, phagocyte activation</td>
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<td>Lysozyme</td>
<td>Peptidoglycan hydrolysis</td>
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<td></td>
<td>Fibronectin</td>
<td>Opsonization and phagocytosis</td>
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<td></td>
<td>Complement</td>
<td>Opsonization, enhanced phagocytosis, inflammation</td>
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Determinants of innate immunity

Important determinants

– Genetic factors:
– Age:
– Humoral and metabolic conditions of the individual:
– Nutritional status: