Immunology

Lecture- 1

Blood Cells

- Monocyte
- Lymphocyte
- Neutrophil
- Eosinophil
- Basophil
- Macrophage
- Erythrocyte
- Platelets
Immunology and Immune System

- **Immunology**: Study of the components and function of the immune system

- **Immune System**: a network collected from cells, tissues organs and soluble factors that work together and provide non-specific and specific protection to defend body against attacks by
  - Foreign pathogenic microbes
  - Microbial toxins
  - Tumor cells
  - Crucial to human survival

**All systems are integrated**

- **Recticulo-endothelial system (RES)** Network of connective tissue fibers (Reticulum)
  Interconnects cells
  - Allows immune cells to bind and move outside the blood & lymphatic system

- **Extracellular fluids system (ECF)** The spaces surrounding tissue cells and RES-
  - Enables immune cells to move

- **Blood, vascular (circulatory) system** transport system
- **Lymphatic system** transport system

**Immunity:**
- State of non-specific and specific protection
**Immune System (The Human Battle against pathogenic Microbes)**

**The Structure of Immune System**

- The organs of the immune system are positioned throughout the body.
  They are called *lymphoid organs* because they are home to *lymphocytes*, *small white blood cells* that are the *key players in the immune system*.

- All parts of the body that help in the recognition and destruction of foreign material; White blood cells, phagocytes and lymphocytes, bone marrow, lymph node, tonsils, thymus and spleen, all are part of immune system

  - **Lymphoid organ**: Primary (central) lymphoid organs - Bone marrow and thymus
    - where lymphocytes are generated (maturation site)
  
  - **Secondary (peripheral) lymphoid organs** - where adaptive immune responses are initiated (spleen, lymph nodes, lymphocyte proliferation, etc.)

**Bone marrow**, the soft tissue on the hollow center of bones, is the ultimate source of all blood cells, including white blood cells destined to become immune cells. B-cell mature in Bone marrow

**Thymus** is an organ that lies behind the breastbone; lymphocytes known as T lymphocyte or T cells mature in the thymus.

**Innate and Adaptive immunity result from the actions of cells that circulate in the blood and lymph, body fluids that directly or indirectly with every major organ system. All of the cells involved in immunity develop from common precursors called Stem cells, found in bone marrow.**
Distribution Parts of the immune system

**Primary**
- Development and maturation of lymphocytes
- Bone Marrow (B cells) and thymus gland (T cells)

**Secondary**
- Mature lymphocytes meet pathogens
- Spleen, adenoids, tonsils, appendix, lymph nodes, Peyer’s patches, mucosa-associated lymphoid tissue (MALT)
The Immune system (Defense Mechanisms)

Immune System

Innate (non specific)
- Anatomical (Physical) components
- Humoral components
- Cellular Components

Acquired (Specific)
- Cellular components
- Humoral components

Innate response
- Mucous membranes
- Physical barriers

Acquired response
- Cellular response
- Humoral response

Bacteria
- Viruses

Cytokines
- Cilia
- Antimicrobial secretions

Macrophages
- Macrophages present antigens

T cells
- Cytotoxic T cells
- Plasma cells

B cells
- Memory B cells

Antibodies

Designed by Dr. T.V. Rao MD
Non specific defenses: Innate Host defenses against infection

1- Anatomical (physical) Barriers
   - Mechanical factors
   - Chemical factors
   - Biological factors

2- Humoral components
   - Complement
   - Coagulation system
   - Cytokines (non specific immune response)

3- Cellular components (Leukocytes)
   - Neutrophils
   - Monocytes/macrophages
   - Eosinophils
   - Basophiles
   - Natural killer cells (large granular lymphocytes)
### Anatomical (Physical) barriers - a) mechanical and Chemical factors

**First line of host defense (surface defenses)**

<table>
<thead>
<tr>
<th>System of organ</th>
<th>Factor</th>
<th>Mechanism</th>
</tr>
</thead>
<tbody>
<tr>
<td>Skin (intact)</td>
<td>Squamous epithelium Anti-microbial fatty acid Low pH Lysozyme Sweat Keratin</td>
<td>Desquamation Inhibit non acid tolerance microbes destroy bacterial cell wall</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Protective protein</td>
</tr>
<tr>
<td>Mucous membrane</td>
<td>Non ciliated epithelium (e.g. gastrointestinal tract) (ciliated epithelium (e.g. respiratory tract) Epithelium (e.g. nasopharynx)</td>
<td>Peristalsis Mucociliary elevator</td>
</tr>
<tr>
<td></td>
<td>Lysozyme</td>
<td></td>
</tr>
<tr>
<td>Respiratory tract</td>
<td>Nasal hairs Ciliated epithelium Coughing Sneezing Mucous secretion Sufactants (lung)</td>
<td>filters and traps microbes Cilia–propels debris away from the respiratory tract. Eliminating microbes- traps microbes opsonin</td>
</tr>
<tr>
<td>Eyes</td>
<td>Blinking mechanically Tears lysozyme</td>
<td>removes microbe Flushes and Washes the surface of eyes</td>
</tr>
</tbody>
</table>
Cilia

Non- Ciliated Epithelium

Ciliated Epithelium

Intestinal Epithelium

Small intestine

Colon

Villus
Basolateral surface
Enterocyte
Crypt
Paneth cell

Enteroendocrine cell

Apical surface

Epithelial stem cell

Peyer's patch

Follicle-associated epithelial cell

Lamina propria

TLR1, TLR2, TLR3, TLR4, TLR5, TLR8, TLR9

Nature Reviews | Immunology
### Anatomical (Physical) barriers - a) mechanical and Chemical factors

**First line of host defense (surface defenses)**

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<tr>
<th>System of Organ</th>
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<tbody>
<tr>
<td>Mouth &amp; Intestinal Tract</td>
<td>Saliva (lysozyme &amp; Phospholipase A)</td>
<td>Phospholipase A destroy bacterial cell membranes</td>
</tr>
<tr>
<td></td>
<td>Low pH (HCL)- gastric juice</td>
<td>Kills or inhibit microbes</td>
</tr>
<tr>
<td></td>
<td>Bile salt</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Alkaline pH (lower intestine)</td>
<td>Prevent some microbes</td>
</tr>
<tr>
<td></td>
<td>Flushing action (intestine)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Mucous</td>
<td>Eliminate microbes which have not succeed to colonization</td>
</tr>
<tr>
<td>Urogenital tract</td>
<td>Urine (acidity)</td>
<td>low pH cleanses the urinary tract</td>
</tr>
<tr>
<td></td>
<td>Flushing action (urine-vagina secretions)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Acidic pH of vagina</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Mantle of vagina</td>
<td>inhibits growth of microbes</td>
</tr>
</tbody>
</table>
1- Anatomical barriers- c) Biological factors

<table>
<thead>
<tr>
<th>System of organ</th>
<th>component</th>
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</tr>
</thead>
</table>
| Non-sterile body sites such as: Skin and Mucous membranes | Normal flora | Antimicrobial substances  
Competition for colonization and nutrition  
Create an environment unfavorable for pathogens by changing pH  
Promote overall health by providing vitamins to host. |
# 2- Humoral Components

<table>
<thead>
<tr>
<th>Component</th>
<th>Mechanism</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complement</td>
<td>- Lysis of bacteria and some viruses&lt;br&gt;- Opsonin&lt;br&gt;- Increase in vascular permeability&lt;br&gt;- Recruitment and activation of phagocytic cells</td>
</tr>
<tr>
<td>Coagulation system</td>
<td>Increase vascular permeability&lt;br&gt;Recruitment of phagocytic cells&lt;br&gt;B- lysin from platelets – a cationic detergent in kills bacteria</td>
</tr>
<tr>
<td>Lactoferrin and Transferrin</td>
<td>Compete with bacteria for iron</td>
</tr>
<tr>
<td>Lysozyme</td>
<td>Breaks down bacteria cell walls</td>
</tr>
<tr>
<td>Cytokines</td>
<td>Various effects</td>
</tr>
<tr>
<td>Interferons</td>
<td>Antiviral proteins</td>
</tr>
</tbody>
</table>
COMPONENTS OF THE IMMUNE SYSTEM

Cellular components of the immune system

<table>
<thead>
<tr>
<th>Lymphocytes</th>
<th>Phagocytes</th>
<th>Granulocytes</th>
<th>Others</th>
</tr>
</thead>
<tbody>
<tr>
<td>B-cell</td>
<td>Mononuclear phagocyte</td>
<td>Basophil</td>
<td>Platelets</td>
</tr>
<tr>
<td>T-cell</td>
<td>Neutrophil</td>
<td>Mast cell</td>
<td></td>
</tr>
<tr>
<td>Large granular lymphocyte</td>
<td>Eosinophil</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Soluble mediators of the immune system

Antibodies  Cytokines  Complement  Inflammatory mediators
Cells in Immune System
3- Cellular Components - Second line of defenses (internal defenses)

- **phagocyte** a white blood cell that attracts (by chemotaxis), adheres to, engulfs, and ingests foreign bodies in blood stream and tissues

- Also known Polymorph nuclear leukocytes (PMN’s)

- Phagocytic cells

- Innate Lymphocyte cell (Natural killer cell, NK)
  - T-cell
  - B-cell (antibodies)
  - Non phagocytic

- Macrophages

- Dendritic cell

- Phagocytic cells
Neutrophil

- Principal phagocytic cell of innate immunity (Present in high numbers in blood and tissue)
- Nuclei (horse shoe or polymorphic nuclei)
- 10- 12µm
- Motile (circulate in blood stream and roam at sites of injury or infections)
- Comprise 40- 75% of blood leukocytes
- Primary function: phagocytosis, ingest and destroy invader (main target: bacteria)
- Primary responders to bacterial infections and components of pus
- Early responders to Inflammation and tissue damage (First arrive during an inflammatory immune response)
- Contain small granules (granules are digestive enzymes)
Eosinophils

- White blood cells primary responders to parasitic infections (Killing of certain intestinal parasites)
- Less abundant than neutrophil
- 8-10µm
- Product toxic proteins
- Some phagocyte foreign compound or pathogen that have been coated with antibodies
- 1-5% of blood leukocytes
- granulocytes
- recruited in the third line of defense.
- Modulate and control mechanism of allergic inflammatory responses
**Basophiles**

- Granulocytes (contain large cytoplasmic granules which obscure the cell nucleus under the microscope when stained, when unstained, the nucleus is visible and it usually has two lobes.
- 12-15µm
- Present in low in number in the body
- Function is similar to eosinophils and mast cell.
- Localized basophils are called mast cells.
- produce histamine (a chemical that is secreted when the cell stimulated, promote blood flow to tissues)
- Like all circulating granulocytes, basophils can be recruited out of the blood into a tissue when needed.

**Mast Cell**

- Granulocyte, is similar with basophiles in appearance and function. Mast cells are tissue resident, *e.g.*, in mucosal tissues, while basophils are found in the blood.
- contains many granules rich in histamine and heparin
- Major effector cell in allergy
- Modulation of initial immune response- activation T- cells
- usually do not circulate in the blood stream, but instead are located in connective tissue and mucous membrane.
- play an important protective role in wound healing and defense against pathogen
Monocytes

- Leukocytes with bean shaped or brain-like nuclei
- A granulocytes (having clear cytoplasm)
- 7-10\(\mu\)m
- Motile (can move quickly (8–12 hrs.) to sites of infection in the tissues)
- Largest of all leukocytes
- 3-7% of blood leukocytes
- Part of innate immunity in humans
- Phagocytosis
- Circulate in blood with half life of 8 hours
- Differentiate and divide into macrophages (circulation, lymphatics and tissues) and dendritic cells (tissue associated)
- Promonocytes are made in the bone marrow, after which they are released into the blood, called circulating monocytes, they circulate for a few days then migrate into tissues.
- In the tissue they further mature into macrophages. Tissue macrophages are extremely heterogeneous response to inflammation signals.
Macrophages (big eaters)

- Type of white blood cell that engulfs and digests dead cells, foreign substances, microbes, in a phagocytosis process
- 21μm
- Derive from blood monocytes after they migrate into tissues.
- Participate in innate and adaptive immunity (activation T-cells)
- Phagocytosis and intracellular and extracellular killing
- Tissue repair (Are essential in wound healing)
- Antigen presentation for specific immune response
- Active against fungi
- Some macrophages are fixed (immobile) and concentrated in specific tissue or organs, such as the lungs (alveolar macrophages), liver (Kupffer macrophages), synovial (synovial macrophages).
- In addition to fixed macrophages, there are wandering macrophages (free) (adhere to the inner linings of blood and lymph vessels and various organs, move throughout the body, arrived at sites of an injury or infection.
Macrophages

Microbe Killing
Fever, inflammation (via IL-1 and prostaglandins)
Activation of Lymphocytes

Tumour Killing
Activates Neutrophils (via IL-8 and TNF-α)

Tissue Repair/Reorganisation (via collagenase)
Tissue Damage (side effect)

Stem cells differentiate into macrophages in the bone marrow and peripheral blood, and then either migrate or take residence in a specific location.
Dendritic cell

• Cells with dendriform (star shaped) morphology
• Main function: Antigen-presenting cell (Capture and present antigens to T lymphocytes surface).
• Recognize pathogen
• Active against viruses
• They act as messengers between the innate and the adaptive immune system.
• Several types, present in those tissues that are in contact with the external environment, such as: skin, (a specialized dendritic cell type called the Langerhans cell) and the inner lining of the nose, lungs, stomach and intestines.
Natural Killer cell

- Type of **cytotoxic lymphocyte** (group of innate granular lymphocyte cell)
- critical to the innate immune system (The role NK cells play is analogous to that of cytotoxic T cells in the vertebrate adaptive immune response)
- lyse and kill virus-infected body cells- rapid responses to viral-infected cells (acting around 3 days after infection)
- **Not antigen specific, but can recognize “self” cells.**
- **Trigger cytokines release.**
- **NK cells are not phagocytic**
  - they perforate microbial cell membranes
- known to differentiate and mature in the bone marrow, lymph nodes, spleen, tonsils, and thymus.
Cells of the Immune System

- Stem Cell
  - Lymphoid Stem Cell
    - Lymphocytes
    - T Cell Progenitor
      - Natural Killer Cell
    - Neutrophils
    - Eosinophils
    - Basophils
    - Mast Cell
    - Monocyte
  - Myeloid Progenitor
    - Granulocytes
    - Macrophage

Phagocytes in the Body

- Brain: microglial cells
- Lung: alveolar macrophages
- Liver: Kupffer cells
- Kidney: mesangial phagocytes
- Lymph node: resident and recirculating macrophages
- Spleen: macrophages
- Blood: monocytes
- Precursors in bone marrow
- Joint: synovial A cells