Introduction to Immunology

The Immune System - includes all parts of the body that help in the recognition and destruction of foreign materials. White blood cells, phagocytes and lymphocytes, bone marrow, lymph nodes, tonsils, thymus, and your spleen are all part of the immune system.

Immunity refers to protection against infection. The immune system is the collection of cells, tissues and molecules that functions to defend us against infectious microbes. The coordinated reaction of the immune system against infections (and other foreign substances) is known as the immune response.

Cells and Organs of the Immune System

Immune responses are mediated by a variety of cells and by the soluble molecules that they secrete. Leukocytes (WBCs) are central to all immune responses. Other cells in the tissues, such as macrophages and cytokines liberated by lymphocytes, also contribute to the immune response.

A number of morphologically and functionally diverse organs and tissues function in the development of immune responses.

These can be divided as Primary Lymphoid Organs and Secondary Lymphoid Organs.
Primary Lymphoid Organs include (Thymus and Bone marrow)
Secondary Lymphoid Organs include (Tonsil, Lymph node, Spleen, Peyer’s patches, Appendix and Tissue lymphatic)

The immune system is typically divided into two categories innate and adaptive

**Innate immunity (non specific immunity)**

- **Innate Immune System / First-Line Defenses** - The body’s first line of defense against pathogens uses mostly physical and chemical barriers such as
  - **Skin** — acts as a barrier to invasion
  - **Sweat** — has chemicals which can kill different pathogens.
  - **Tears** - have lysozyme which has powerful digestive abilities that render antigens harmless.
  - **Saliva** — also has lysozyme.
  - **Mucus** - can trap pathogens, which are then sneezed, coughed, washed away, or destroyed by chemicals.
  - **Stomach Acid** — destroys pathogens

- **Second-Line Defenses** - If a pathogen is able to get past the body’s first line of defense, and an infection starts, the body can rely on its second line of defense. This will result in what is called an **Inflammatory response** causes
  - **Redness** - due to capillary dilation resulting in increased blood flow
  - **Heat** - due to capillary dilation resulting in increased blood flow
  - **Swelling** — due to passage of plasma from the blood stream into the damaged tissue
  - **Pain** — due mainly to tissue destruction and, to a lesser extent, swelling.
Adaptive (Acquired) immunity (Specific Mechanisms of Defense)

Adaptive immunity refers to antigen-specific immune response. The adaptive immune response is more complex than the innate.

- **Third-Line Defenses** - Sometimes the second line of defense is still not enough and the pathogen is then heading for the body’s last line of defense, the immune system.
  - The immune system recognizes, attacks, destroys, and remembers each pathogen that enters the body. It does this by making specialized cells and antibodies that render the pathogens harmless.

  - Unlike the first line and second line defense the immune system differentiates among pathogens.
  - For each type of pathogen, the immune system produces cells that are specific for that particular pathogen.
Active Immunity or Passive Immunity

Active immunity is the resistance developed by an individual, as a result of an antigenic stimulus. This involves the active functioning of a person’s immune system, leading to the synthesis of antibodies and/or the production of immunologically active cells. Active immunity sets in only after a latent period, which is required for the immunological machinery to be set in motion.

The resistance that is transferred to a recipient in a ready-made form is known as passive immunity. Here, the recipient’s immune system plays no active role. There is no antigenic stimulus. Instead, pre-formed antibodies are administered.
Antigen

Any substance (usually foreign) that binds specifically to an antibody, or a T cell receptor, is referred to as an ‘antigen’.

A substance capable of inducing a specific immune response is called an antigen.

- **Antigens** are macromolecules that elicit an immune response in the body. The most common antigens are proteins and polysaccharides.

Antigens can enter the body from the environment. These include

- inhaled macromolecules (e.g., proteins on cat hairs that can trigger an attack of asthma in susceptible people)
- ingested macromolecules (e.g., shellfish proteins that trigger an allergic response in susceptible people)
- molecules that are introduced beneath the skin (e.g., on a splinter or in an injected vaccine)
Antigenic determinants.

The chemical groups on the antigen molecules that determine their immunogenicity are called antigenic determinants, also known as epitopes. Antigenic determinants may consist of several amino acids of a protein molecule or several monosaccharide units of a polysaccharide. Each species of living thing is chemically and antigenically unique because of differences in its proteins, carbohydrates, and other organic substances.

Types of antigens. Certain types of antigens are distinctive. Autoantigens, for example, are a person's own self antigens. Alloantigens are antigens found in different members of the same species (the red blood cell antigens A and B are examples). Heterophile antigens are identical antigens found in the cells of different species.

Antibody

A protein (immunoglobulin) that recognizes a particular antigen and binds specifically to it is called an ‘antibody’.

Antibodies are produced by B cells.

* Classification of Antibodies (Immunoglobulins)
  * Immunoglobulin M (IgM)
  * Immunoglobulin G (IgG)
  * Immunoglobulin A (IgA)
  * Immunoglobulin D (IgD)
  * Immunoglobulin E (IgE)
Humoral and Cellular Immunity

The immune system comprises of two parallel, but interrelated, systems: these are: Humoral immune response and Cellular immune response.

In the humoral immune response, soluble proteins called antibodies (immunoglobulins) function as recognition elements and they bind specifically to antigens. Antibodies are secreted by plasma cells that are derived from B-lymphocytes (B cells).

In the cellular immune response, cells called cytotoxic T-lymphocytes kill cells that display foreign motifs on their surfaces. The cellular immune response is mediated by specific receptors that are expressed on the surface of the T cells.

Another class, called helper T-lymphocytes, contributes to both humoral and cellular immune responses by stimulating the differentiation and proliferation of appropriate B cells and T cells. The site of infection and type of pathogen largely determine which immune response will be effective.
Immunization

- **Passive immunization** (patient is given preformed antibodies form of immunotherapy)

- **Active immunization** (patient is vaccinated with a microbe or its antigens providing a form of advance protection)

**DISORDERS OF THE IMMUNE SYSTEM**

1. Hypersensitivity Reactions
   * Over-reaction of adaptive immune response to harmless antigens
   * Four Types of reactions (I-IV)

2. Autoimmunity
   * Misdirected adaptive immune response
   * Results from a loss of self-tolerance
   * Three Types (II, III, IV) of reactions

3. Immunodeficiencies
   * Components of immune system either absent or defective
   * Genetic or acquired etiology

**Hypersensitivity**

Disorders caused by pathologic immune responses are called **hypersensitivity diseases**. This term is derived from the idea that an individual who has previously encountered an antigen is “sensitive” to a second encounter with that antigen (i.e. mounts a stronger response upon the second encounter); “hypersensitivity” denotes an abnormal, or pathologic, reaction. There are four types of hypersensitivity, which differ in their pathogenesis, effector mechanisms, and clinical and pathological manifestations.
Types of hypersensitivity diseases. (It is preferable to use the descriptive terms rather than the less informative numerical classification.)

<table>
<thead>
<tr>
<th>Type of Hypersensitivity</th>
<th>Pathologic Immune Mechanisms</th>
<th>Mechanisms of Tissue Injury and Disease</th>
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<tr>
<td>Immediate hypersensitivity: Type I</td>
<td>IgE antibody</td>
<td>Mast cells and their mediators (vasoactive amines, lipid mediators, cytokines)</td>
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<td>Antibody mediated: Type II</td>
<td>IgM, IgG antibodies against cell surface or extracellular matrix antigens</td>
<td>Opsonization and phagocytosis of cells</td>
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<td>Complement- and Fc receptor-mediated recruitment and activation of leukocytes (neutrophils, macrophages)</td>
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<td>Abnormalities in cellular functions, e.g., hormone receptor signaling</td>
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<td>Immune complex mediated: Type III</td>
<td>Immune complexes of circulating antigens and IgM or IgG antibodies</td>
<td>Complement- and Fc receptor-mediated recruitment and activation of leukocytes</td>
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<td>T cell mediated: Type IV</td>
<td>1. CD4+ T cells (delayed-type hypersensitivity)</td>
<td>1. Macrophage activation, cytokine-mediated inflammation</td>
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<td></td>
<td>2. CD8+ CTLs (T cell-mediated cytolysis)</td>
<td>2. Direct target cell killing, cytokine-mediated inflammation</td>
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Abbreviations: CTL, cytolytic T lymphocyte