Part 2. Immunology

SECTION OUTLINE

1. Immunity, Components of Immune System, Immune Response
2. Antigen, Antibody and Complement
3. Antigen-Antibody Reaction
4. Hypersensitivity Reactions
5. Immunoprophylaxis and Immunization Schedule

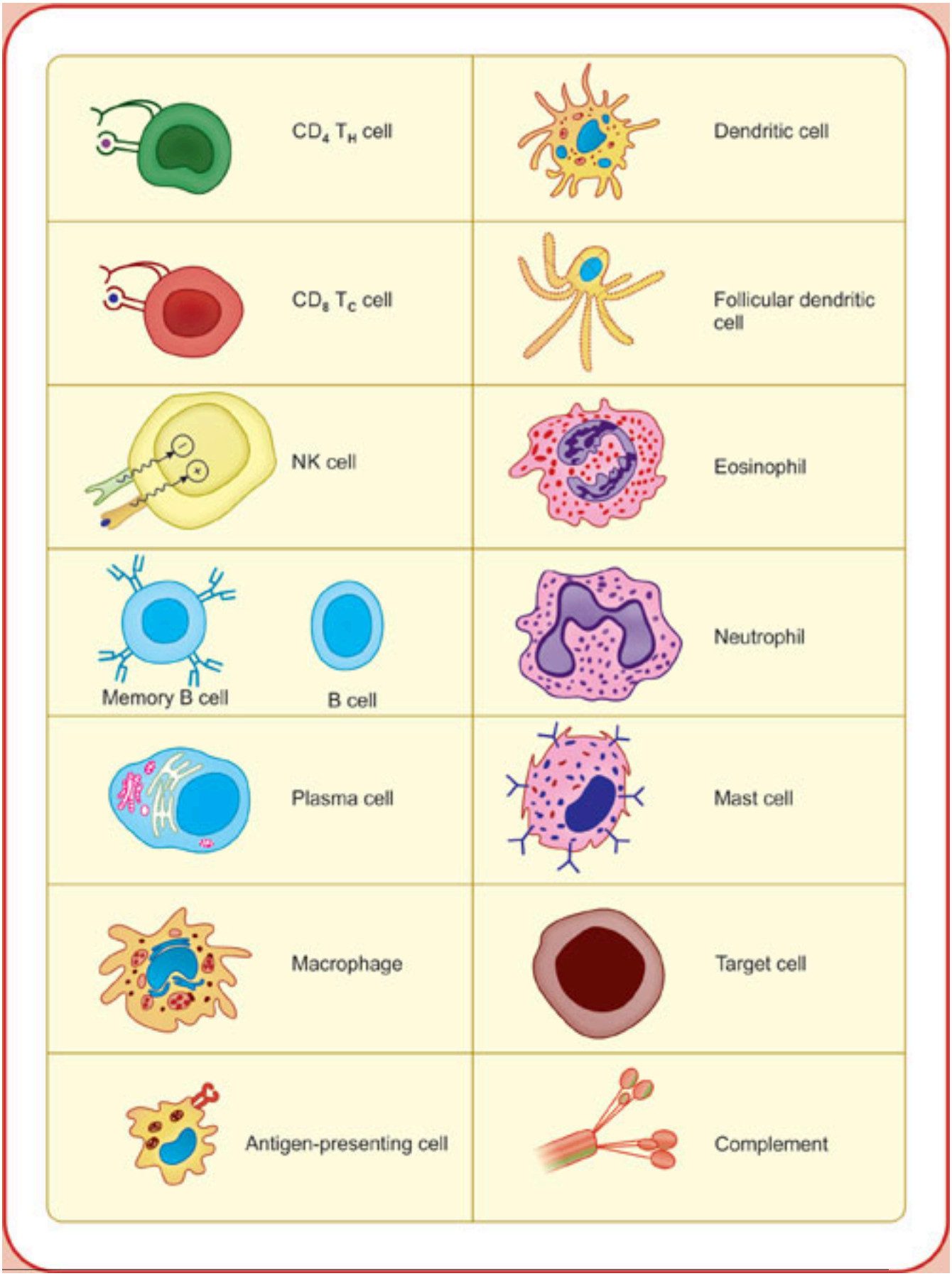

Table of Contents

Chapter 7. Immunity, Components of Immune System, Immune Response

CHAPTER PREVIEW

- Innate Immunity
- Acquired Immunity
- Components of Immune System
- Immune Response

The term “immunity” is defined as the resistance offered by the host against microorganism(s) or any foreign substance(s). Immunity can be broadly classified into two types:

1. Innate immunity—present right from birth
2. Acquired/adaptive immunity—acquired during the course of life.

INNATE IMMUNITY

Innate immunity is the inborn resistance against infections that an individual possesses right from birth, due to his genetic or constitutional makeup.

Innate immunity has certain unique properties by which it can be differentiated from acquired immunity **(Table 7.1)**.

- **Acts in minutes:** Innate immunity is the **first line of host defense** against infections; occurs immediately after the microbial entry
- **Prior microbial exposure is not required:** Innate immunity is independent of prior exposure to the microbes; presents even before the first entry of the microorganism
- **Non-specific:** Cells of innate immunity are non-specific in their action; can be directed against any microbial antigen(s)
- **No memory:** Innate immunity does not have a memory component. Response to a repeat infection is identical to the primary response.

Mechanism of Innate Immunity

Following the exposure to microorganisms, several mediators of innate immunity are recruited to the site of infection. The first step that takes place is **attachment,** which involves binding the surface molecules of organisms to the receptors on the cells of innate immunity (e.g. Toll-like receptors).

Components of Innate Immunity

There are several mediators of innate immunity.

- **Anatomical barriers:** Such as skin and mucosal surfaces have a spectrum of antimicrobial activities
  - Mechanically prevents entry of microbes
  - Mucosa produces mucus which entraps microbes
  - Cilia present in the lower respiratory tract propel the microbes outside.
- **Physiological barriers** are also capable of inhibiting certain microbes; examples include:
  - Normal body temperature
  - Gastric acidity
  - Secretory products of mucosa such as saliva, tears, trypsin and bile salts, etc.

Table 7.1. Differences between innate and acquired immunity.

Properties	***Innate immunity***	***Acquired/Adaptive immunity***
Resistance to infection that an individual	Possesses right from birth	Acquires during his lifetime
Duration	The immune response occurs in minutes	The immune response occurs in days
Prior exposure to the antigen	Not required	Required
Immunological memory	Absent	Present
Host cell receptors	Non-specific, e.g. toll-like receptor	Specific, e.g. T cell receptors and B cell immunoglobulin receptors
Important components of innate immunity	• Anatomical and physiological barriers • Host immune cells: Phagocytes, NK cells, mast cells, dendritic cells, etc. • Complement pathways—alternative and mannose-binding pathways • Normal resident flora	T cell B cell Classical complement pathway

- **Host immune cells:** Several immune cells such as phagocytes, NK cells, mast cells, and dendritic cells play a crucial role in innate immunity
  - *Phagocytes* such as neutrophils, and macrophages are the main components of innate immunity. They are rapidly recruited to the site of infection and mediate phagocytosis (i.e. engulfment of microbes and subsequent microbial killing
  - *Natural killer (NK) cells:* They are a class of lymphocytes that kill intracellular pathogens, virus-infected cells, and tumor cells
  - *Mast cells:* They are present in the epithelial lining of respiratory and other mucosa and are capable of killing the microbes by releasing several inflammatory meditators
  - *Dendritic cells:* They respond to microbes by producing numerous cytokines that initiate inflammation.

- **Complement pathways:** Alternative and mannose-binding pathways are the chief mediators of innate immunity
- **Normal resident flora** lining the intestinal, respiratory, and genital tract can compete with the pathogens for nutrition. They also produce antibacterial substances
- **Acute phase reactant proteins (APRs):** They are the proteins synthesized by liver at a steady concentration, but their synthesis increases exponentially during acute inflammatory conditions. Examples of APR include: C-reactive protein, serum amyloid A, complement proteins, coagulation protein, and mannose-binding protein.

C-Reactive Protein (CRP)

It is one of the most common markers of acute inflammation, used in most diagnostic laboratories.

- The level of CRP rises in acute inflammatory conditions including bacterial infection
- CRP is so named because it precipitates with the C-carbohydrate antigen of pneumococcus. However, it is not an antibody against the C-antigen of pneumococcus; it is nonspecific, can be raised in any inflammatory conditions
- It can be detected by latex agglutination test using latex particles coated with anti- CRP antibodies.

The differences between innate and acquired immunity are depicted in **Table 7.1**.

ACQUIRED IMMUNITY

Acquired immunity is defined as the resistance against the infecting foreign substance that an individual acquires or adapts during the course of his life.

- **Mediators: T cells and B cells** are the chief mediators of acquired immunity. Other mediators include:
  - Classical complement pathway
  - Antigen-presenting cells
  - Cytokines (IL-2, IL-4, IL-5).
- **The response occurs in days:** Acquired immunity involves activation of T and B cells against the microbial antigens; which takes several days to weeks to develop, following the microbial entry
- **Requires prior microbial exposure:** Acquired immunity develops only after exposure to the microbes
- **Specific:** Acquired immunity is highly specific; directed against specific antigens of the microbes
- **Memory present:** Acquired immunity does have a memory component. A proportion of T and B cells become memory cells following primary contact with the microbe, which play an important role when the microbe is encountered subsequently
- **Host cell receptors** of acquired immunity are specific for a particular microbial antigen. Examples include T cell receptors and B cell immunoglobulin receptors.

Types of acquired immunity: Acquired immunity can be classified in two ways:

1. Active and passive immunity
2. Artificial and natural immunity.

Active Immunity

Active immunity is the resistance developed by an individual towards an antigenic stimulus.

- Here, the host's immune system is actively involved against the antigenic stimulus; leading to the activation of T and B cells, and the production of specific antibodies
- Active immunity may be induced naturally or artificially
  - **Natural active immunity** occurs following exposure to microbial infection (e.g. measles virus infection)
  - **Artificial active immunity** develops following exposure to an immunogen by vaccination (e.g. measles vaccine). Vaccines are discussed in Chapter 11.
- As the host's immune apparatus is actively involved, active immunity often fails to develop when the host is immunocompromised
- Active immunity **develops slower**; as there is an initial **lag phase**, required for activation of the T and B cells
- **Long-lasting:** Active immunity usually lasts for longer periods, but the duration varies depending on the type of pathogen.

Types of immune response in active immunity vary depending on the microbial exposure that occurs for the first time (called primary immune response) and subsequent time (called secondary immune response).

Passive Immunity

Passive immunity is defined as the resistance that is transferred passively to a host in a “readymade” form without the active participation of the host's immune system.

- Passive immunity can also be induced naturally or artificially
  - **Natural passive immunity** involves the IgG antibody transfer from mother to fetus across the placenta
  - **Artificial passive immunity** develops following the readymade transfer of commercially prepared immunoglobulin (e.g. Rabies immunoglobulin).
- Passive immunity plays a very important role in:
  - Immunodeficient individuals (as the host's immune apparatus is not effective), and
  - Post-exposure prophylaxis; when an immediate effect is warranted.
- Passive immunity **develops faster**; there is no lag phase
- There is no **immunological memory** as the memory cells are not involved
- **Booster doses are not effective:** As the memory component is absent, the effect produced following subsequent immunoglobulin administration is the same as the effect produced after the primary dose.

Table 7.2. Differences between active and passive immunity.

Properties	***Active immunity***	***Passive immunity***
Mechanism	Produced actively by host immune system	Immunoglobulins received passively

Properties	*Active immunity*	*Passive immunity*
Induced by	• Infection (natural) • Vaccination (artificial)	• Mother to fetus IgG transfer (natural) • Readymade antibody transfer (artificial)
Duration	Long-lasting	Short-lasting
Lag period	Present	No lag period
Memory	Present	No memory
Booster doses	Useful	Less effective
In Immunodeficient individuals	Not useful	Useful
Post-exposure prophylaxis	Less useful	Useful

The differences between active and passive immunity are listed in **Table 7.2**.

OTHER TYPES OF IMMUNITY

Local (or Mucosal) Immunity

Local or mucosal immunity is the immune response that is active at the mucosal surfaces such as intestinal or respiratory or genitourinary mucosa.

- It is mediated by a type of IgA antibody called secretory IgA, which prevents the entry of microbes at the local site itself
- Local immunity can only be induced by natural infection or by live vaccination, e.g. live oral polio vaccine (but not by killed vaccines).

Herd Immunity

Herd immunity is defined as the overall immunity of a community (or herd) toward a pathogen.

- It plays a vital role in preventing epidemic diseases
- If herd immunity is good, that means a large population of the community is immune to a pathogen. Hence, epidemics are less likely to occur and eradication of the disease may be possible
- Herd immunity develops following effective vaccination against some diseases like:
  - Diphtheria and pertussis vaccine
  - Measles, mumps, and rubella (MMR) vaccine
  - Polio (oral polio vaccine)
  - Smallpox vaccine.

COMPONENTS OF THE IMMUNE SYSTEM

The immune system comprises lymphoid organs, cells of the immune system (lymphoid cells and other cells) and their soluble products called cytokines.

Lymphoid Organs

Lymphoid organs consist of central and peripheral lymphoid organs.

Central or Primary Lymphoid Organs

The central lymphoid organs are the site for the development of immune cells. Examples include:

- **Thymus:** It is the site of proliferation and maturation of T cells
  - It has an outer cortex and an inner medulla
  - Any defect in the thymus leads to a defect in the maturation of T-lymphocytes that in turn results in severe life-threatening immunodeficiency disorders.
- **Bone marrow:** It is the site of the development of B cells
  - Almost all the cells in the blood have originated from pluripotent hematopoietic stem cells of bone marrow and the process is called hematopoiesis
  - The progenitor T and B cells originate in the bone marrow. Further development of B cells occurs in the bone marrow itself, whereas the progenitor T cells migrate to the thymus for further proliferation.

Peripheral or Secondary Lymphoid Organs

They host the T cells and B cells. Examples include:

- **Lymph node:** They are small bean-shaped organs; distributed along the lymphatic vessels
  - They host the mature B cells and T cells
  - Divided into the outer cortex, inner medulla, and in-between there is a paracortical area
  - Cortex is rich in lymphoid follicles containing B cells, whereas the paracortical area is rich in T cells
  - They act as physiological barriers; filter the microbial antigens carried to the lymph node by activating the T and B cells.
- **Spleen:** Spleen is the largest secondary lymphoid organ. It acts as a physiological barrier similar to the lymph node in clearing the microbial antigens through the stimulation of T and B cells
- **Mucosa-associated lymphoid tissue (MALT):** The group of lymphoid tissues lining the mucosal sites (e.g. respiratory or intestinal) is collectively known as MALT
  - They are present either as loose clusters of lymphoid cells or as organized structures such as tonsils, appendix, and Peyer's patches
  - They provide immunity at the local sites by encountering the pathogen entry.

Lymphoid Cells

Lymphoid cells consist of lymphocytes such as T cells, B cells, and NK cells.

T Lymphocytes

They constitute 70–80% of blood lymphocytes. They bear specialized surface receptors called T cell receptors (TCR). T cell development takes place in the thymus. There are two types of effector T cells—(1) $CD4^+$ helper T cells and (2) $CD8^+$ cytotoxic T cells.

- **Helper T cells:** Helper T cells (T_H) possess CD4 molecules as surface receptors
  - They recognize the antigenic peptides that are processed by antigen-presenting cells and presented along with MHC-II molecules (major histocompatibility complex)
  - Following antigenic stimulus, the helper T cells differentiate into either of the two types of cells—(1) T_H1, and (2) T_H2 subset
  - T_H1 cells secrete specific cytokines such as IL-2, interferon-gamma which modulate the cellular humoral immune response
  - T_H2 cells secrete specific cytokines such as IL-4, IL-5, and IL-6 which modulate the humoral immune response.
- **Cytotoxic T cells:** In contrast to T_H cells, cytotoxic T cells (T_C) possess CD8 molecules and recognize the intracellular antigens (e.g. viral antigens or tumor antigens) that are processed by any nucleated cells and presented along with MHC-I. In general, T_C cells are involved in the destruction of virus-infected cells and tumor cells.

B Lymphocytes

B lymphocytes are the mediators of humoral immunity; constitute 10–15% of blood lymphocytes. B cells proliferate through various stages, first in bone marrow, then in peripheral lymphoid organs. B cells produce five classes of antibodies, which in turn have various biological functions (discussed in Chapter 8).

NK Cells

Natural killer (NK) cells are large granular lymphocytes that constitute 10–15% of peripheral blood lymphocytes. They are derived from a separate lymphoid lineage. Similar to cytotoxic T cells, NK cells also are involved in the destruction of virus-infected cells and tumor cells.

Other Cells of the Immune System

Other cells of the immune system include phagocytes, such as

- **Macrophages:** They play a vital role in host defense by performing two important functions—
  1. *Phagocytosis:* The process by which the microbes are ingested and subsequently killed through producing various lysosomal enzymes and free radicals
  2. *Antigen presentation:* Macrophages capture the antigen, process it into smaller antigenic peptides, and present the antigenic peptides along with the MHC class II molecules to the helper T cells; thus facilitating helper T cell activation.

     Examples of macrophages present in various body sites include—(i) Kupffer cells in liver, (ii) microglial cells in brain, (iii) alveolar macrophages in lungs, etc.
- **Microphages:** Examples include granulocytes such as neutrophils, eosinophils, and basophils. They are the principal phagocytes; the mechanism of microbial killing is similar to that of macrophages
- **Dendritic cells:** They are non-phagocytic in nature. They help in antigen presentation; their main function is to capture, process, and present the antigenic peptides on their cell surface to the helper T cells

- **Mast cells:** They are present in various body sites, such as skin and respiratory mucosa. They contain cytoplasmic granules rich in histamine and other active substances and play an important role in the development of certain allergic (type I hypersensitivity) reactions.

Cytokines

They are the soluble products secreted from various cells of the immune system. They include interleukins (IL), interferons (IFN- α, β, γ), tumor necrosis factors (TNF), colony-stimulating factors (CSF), etc.

Major Histocompatibility Complex (MHC)

They are a group of host cell surface molecules that bind to peptide fragments derived from pathogens and display them on the host cell surface for recognition by the appropriate T cells.

- **MHC-I:** MHC-I proteins are located on the surface of all nucleated cells. They present the peptide antigen to CD8 T cells
- **MHC-II:** MHC-II proteins are located on the surface of antigen-presenting cells. They present the peptide antigen to CD4 T cells.

IMMUNE RESPONSE

Immune response refers to the highly coordinated reaction of the cells of the immune system and their products. It has two arms.

Cell-mediated Immune Response (CMI)

It plays a crucial role in protecting against intracellular microbes as well as tumor cells. Although CMI is mainly T cell-mediated (especially cytotoxic T cells); however, various other effector cells such as natural killer (NK) cells, macrophages, and granulocytes are also components of CMI.

Humoral or Antibody-mediated Immune Response (AMI)

It protects the host by secreting *antibodies*; that can bind and neutralize microbial antigens circulating free or present on the surface of the host cells and in the extracellular spaces, but have no role against intracellular antigens.

EXPECTED QUESTIONS

1. **I. Write an essay on:**
    1. Define immunity. Describe in detail about the properties and mediators of innate immunity.
2. **II. Write short notes on:**
    1. Herd immunity.
    2. Differences between innate and acquired immunity.
    3. Differences between active and passive immunity.
3. **III. Multiple Choice Questions (MCQs):**
    1. **Which is not a mediator of innate immunity?**

a. T cells

b. NK cell

c. Phagocytes

d. Neutrophil

2. **Which of the following about innate immunity is wrong?**

a. The immune response occurs in minutes

b. Non-specific

c. It is first line of defense

d. Need prior contact with the antigen

3. **Which of the following about active immunity is correct?**

a. No lag phase

b. Booster doses are useful

c. Useful in immunodeficient people

d. No memory cells

4. **The type of immunity that develops after infection is:**

a. Artificial immunity

b. Acquired immunity

c. Passive immunity

d. Combined immunity

5. **The immunity develops after the vaccination is an example for:**

a. Natural active immunity

b. Artificial active immunity

c. Natural passive immunity

d. Artificial passive immunity

Answers

1. a	**2.** d	**3.** b	**4.** b	**5.** b