

## Chapter 1: General Introduction

### 1. Definitions

**Immunology** is a branch of biology devoted to the study of the immune system, and also a field of medicine concerned with diseases of the immune system.

**Immunity** refers to the defense mechanisms of a living organism against foreign agents, particularly infectious agents, or against internal threats, notably tumor transformation, which may compromise its proper functioning or survival. All organs and tissues, cells, and molecules involved in resisting infections constitute what is called the **immune system**.

**Immunogenicity**: the ability of an antigen to induce an immune response in a given individual under defined conditions. Some antigens are highly immunogenic, whereas others are weakly immunogenic.

**The immune system** consists of a complex set of distinct organs and tissues between which cells of the innate and adaptive immune systems continuously circulate.

This organization as a communication network gives the immune system three essential properties:

- **A strong capacity for information exchange**, through direct intercellular membrane contacts or through the release of soluble mediators. These exchanges occur between components of the immune system (for example, interactions between innate immune cells and adaptive immune cells), but also with other systems (for example, neuro-immuno-endocrine interactions).
- **An efficient effector arm** capable of protecting the integrity of the organism.
- **Tight regulation**, which is crucial to maintain, at all times and in all locations, the balance of the immune system (homeostasis) and to ensure an appropriate immune response.

Disruption of any of these systems can lead to pathological disorders such as immunodeficiencies, autoimmune diseases, or hypersensitivity states.

Several immunocompetent cells have long been recognized as such, including lymphocytes, granulocytes, monocytes/macrophages, and dendritic cells. These cells originate from a common precursor, the **pluripotent hematopoietic stem cell**, located in the bone marrow, which is capable of self-renewal and differentiation into more committed stem cells and then into progenitor cells.

Classically, progenitors are divided into two major families:

- those derived from a **myeloid stem cell**, which give rise to granulocytes, monocytes/macrophages, and dendritic cells;
- those derived from a **lymphoid stem cell**, which give rise to T, B and NK (Natural Killer) lymphocytes, ILCs (Innate Lymphoid Cells), NKT cells (Natural Killer T cells), and MAIT cells (Mucosal-associated invariant T cells).

More recently, a role in immunity has also been recognized for other cell types, such as epithelial cells, endothelial cells, and even platelets.

## **2. The Immune Response**

### **A. The two types of immune response**

The immune response corresponds to the defense mechanisms of the body that distinguish what belongs to the self from what does not, that is, the “self” from the “non-self”. Two immune responses can be distinguished over time.

→ **Innate immunity** is the first line of defense against the infectious and pathogenic agents that surround us. It is activated immediately (rapid response), is non-specific, initiates the adaptive immune response, and also plays a role in homeostasis (elimination of dead and tumor cells).

It involves different defense modules:

- constitutive modules such as the skin and mucosal barriers, and
- induced modules such as phagocytosis and the inflammatory response, which require phagocytic cells, cytokines and the complement system.

#### **1. Constitutive modules**

The **cutaneous and mucosal barrier** is in contact with viruses, parasites and bacteria. It prevents their adhesion through mechanical, chemical and biological mechanisms, and consists of two main components: the skin and the mucous membranes.

##### **A. The skin**

The skin is a stratified keratinized epithelium covering the entire external surface of the body and represents a very effective barrier against all types of invasion. It therefore acts as:

- **A mechanical barrier** against bacterial, viral and parasitic development, due to its low permeability and continuous desquamation.

- **A chemical barrier**, through the presence of antimicrobial proteins and peptides. These peptides act through three main mechanisms: disruption of bacterial membranes, enzymatic degradation of bacterial membranes, and sequestration of essential nutrients.
- **A biological barrier**, provided by the commensal flora, which consists of bacteria located on the skin and plays an important protective role. Sweat and sebaceous glands secrete sebum rich in lipids; these lipids are degraded by lipases released by the commensal microflora (e.g. staphylococci and streptococci) into fatty acids, which lowers the skin pH and inhibits microbial growth.

## **B. Mucous membranes**

Mucous membranes possess a single-layered or stratified non-keratinized epithelium and are therefore more sensitive to infectious attacks. They have developed an additional defense mechanism: **mucus**.

- **Mechanical barrier**: the ciliary movement in the bronchi carries mucus loaded with dust and bacteria toward the upper airways.
- **Chemical barrier**: mucus contains sugars called mucins. It also plays a mechanical role by forming a viscous substance that traps foreign elements, which are then eliminated by expectoration.

In addition, the presence of enzymes in tears and saliva (lysozyme, phospholipase A), hydrochloric acid in the stomach, and bile salts contributes to the destruction of antigens.

- **Biological barriers**: the presence of lactobacilli in the vaginal mucosa lowers the vaginal pH, creating unfavorable conditions for pathogen development. Some cells also synthesize antimicrobial molecules such as defensins: Paneth cells of the intestinal mucosa secrete  $\alpha$ -defensins, while epithelial cells of the respiratory and urogenital tracts secrete  $\beta$ -defensins.

→ Adaptive immune response, which is delayed. It is characterized by the involvement of lymphocytes, which tailor their response specifically to a given pathogen.

## **B. The cell types involved**

### **B-1) In the innate immune response:**

**a) Phagocytes**: Phagocytes act as the body's "clean-up crew" by engulfing (endocytosis) bacteria, dead cells, and other debris — a process called **phagocytosis**.

- **Monocyte:** an immature cell that gives rise to **macrophages** and **dendritic cells**.
- **Macrophage:** the prototypical phagocyte, whose main role is to clean up the organism.
- **Dendritic cell:** has cytoplasmic extensions called dendrites. It functions as a phagocyte and also as a cell that activates the adaptive immune response.
- **Polymorphonuclear cells (granulocytes):**
  - Neutrophils:** phagocytes attracted to infection sites by molecular signals released by macrophages or other resident cells.
  - **Basophils:** play a key role in allergy.
  - **Eosinophils (acidophils):** act against parasites by releasing the contents of their granules onto them.

#### b) Mast cells

Mast cells play a **key role in allergies**, similar to basophils. They are usually located in **connective tissues** and also help **activate and amplify the inflammatory response**.

#### c) Other cells

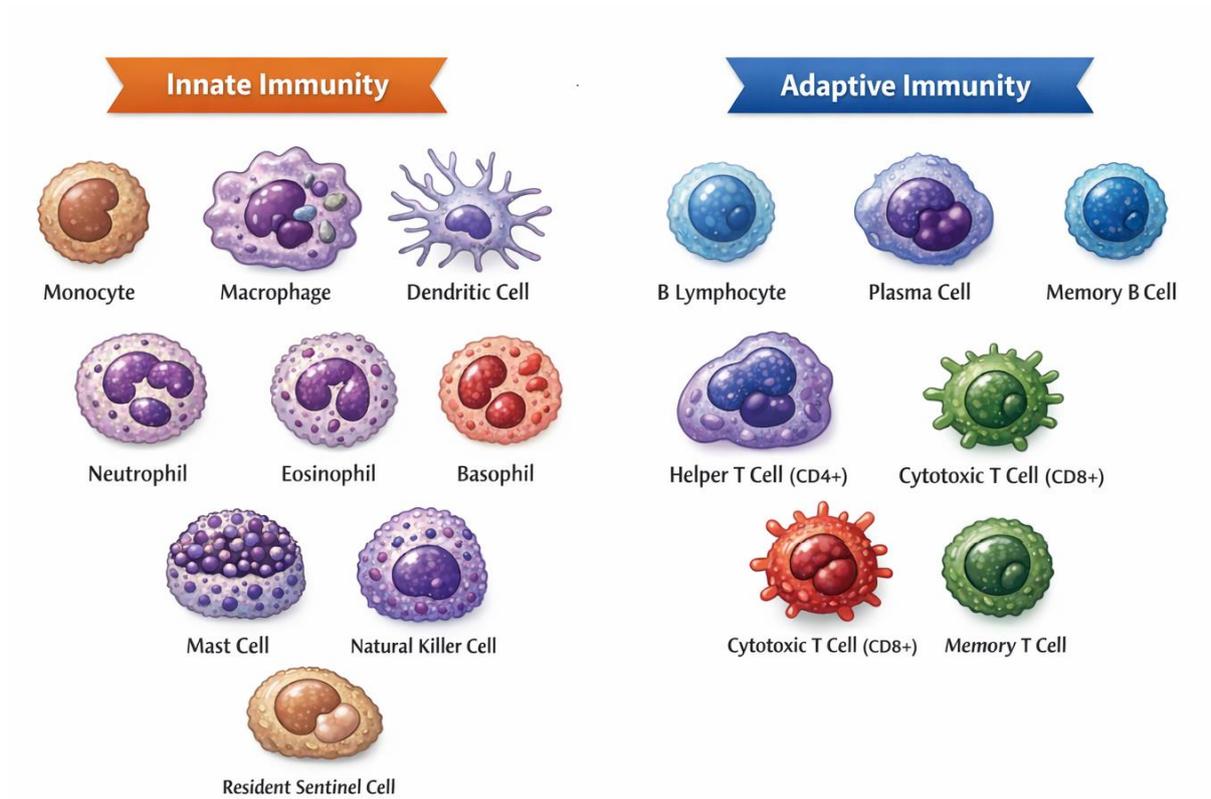
Other cells involved include:

- **Natural Killer (NK) cells**, which can eliminate diseased or infected cells.
- **Resident cells**, which act as **tissue sentinels**, capable of detecting potential threats.

#### B-2) In the adaptive immune response:

Lymphocytes are the cells involved in the adaptive immune response. There are two main types:

- B lymphocytes (B cells): (“B” stands for Bursa of Fabricius, the organ in birds where these cells mature). In humans, B cells mature in the bone marrow. They can differentiate into plasma cells or memory B cells. Plasma cells produce antibodies that specifically target antigens.
- T lymphocytes (T cells): (“T” stands for Thymus, the human organ where they mature). They recognize membrane receptors. Several subpopulations of T cells exist:
  - Helper T cells (T CD4 or T4), which coordinate the activities of different immune cells involved in the immune response.
  - Cytotoxic T cells (T CD8), which selectively destroy infected cells.
  - Memory T cells, which provide long-term immune memory.



### C. Lymphoid organs

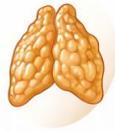
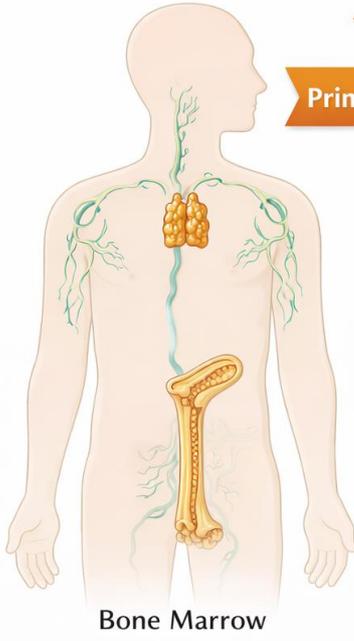
**Lymphoid organs and tissues** are the sites where lymphocytes and other immune system cells reside. They are classified into two groups:

- **Primary lymphoid organs:** these organs produce and/or allow the proliferation and maturation of lymphocytes. They include the **bone marrow** and the **thymus**.
- **Secondary lymphoid organs:** these organs are sites where the **adaptive immune response** is activated. Examples include **lymph nodes** and the **spleen**.

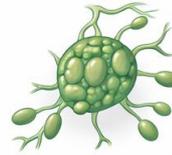
## Lymphoid Organs

### Primary Lymphoid Organs

### Secondary Lymphoid Organs



Thymus



Lymph Nodes



Tonsils



Spleen



Peyer's Patches