**Immunity** is defined as resistance to disease, specifically infectious disease.
**Immune system** The collection of cells, tissues, and molecules that mediate resistance to infections
**Immunology** is the study of the immune system, including its responses to microbial pathogens and damaged tissues and its role in disease.
**The most important physiologic function of the immune system is to prevent infections and to eradicate established infections,**

| Role of the immune system | Implications |
|---|---|
| Defense against infections | Deficient immunity results in increased susceptibility to infections; exemplified by AIDS<br>Vaccination boosts immune defenses and protects against infections |
| Defense against tumors | Potential for immunotherapy of cancer |
| The immune system recognizes and responds to tissue grafts and newly introduced molecules | Immune responses are barriers to transplantation and gene therapy |
| The immune system can injure cells and induce pathologic inflammation | Immune responses are the cause of allergic, autoimmune, and other inflammatory diseases |

**Importance of the immune system in health and disease**

## INNATE AND ADAPTIVE IMMUNITY

Host defense mechanisms consist of:

- Innate immunity, which mediates the initial protection against infections,
- Adaptive immunity, which develops more slowly and provides more specialized and effective defense against infections

**1.Innate immunity,** also called natural immunity or native immunity, is always present in healthy individuals (hence the term innate), prepared to block the entry of microbes and rapidly eliminate microbes that do succeed in entering host tissues.
**2.Adaptive immunity,** also called specific immunity or acquired immunity, requires expansion and differentiation of lymphocytes in response to microbes before it can provide effective defense; that is, it adapts to the presence of microbial invaders. Innate immunity is phylogenetically older, and the more specialized and powerful adaptive immune system evolved later.
The first line of defense in **innate immunity** is provided by:

1. **Epithelial barriers** and by cells and natural antibiotics present in epithelia, all of which function to block the entry of microbes.

2. If microbes do breach epithelia and enter the tissues or circulation, they are attacked by **phagocytes**,
   specialized lymphocytes called **natural killer cells**,
   and several plasma proteins, including **the proteins of the complement system**.

All these mechanisms of innate immunity specifically recognize and react against microbes. In addition to providing early defense against infections,

3. innate immune responses enhance adaptive immune responses against the infectious agents.

**The adaptive immune system:** consists of Lymphocytes and their products, such as antibodies. Adaptive immune responses often use the cells and molecules of the innate immune system to eliminate microbes, and adaptive immunity functions to greatly enhance these antimicrobial mechanisms of innate immunity.The two types of adaptive immunity:

- **humoral immunity**
- **cell-mediated immunity**

The two are mediated by different cells and molecules and provide defense against extracellular microbes and intracellular microbes, respectively . **Humoral immunity** is mediated by proteins called antibodies, which are produced by cells called B lymphocytes

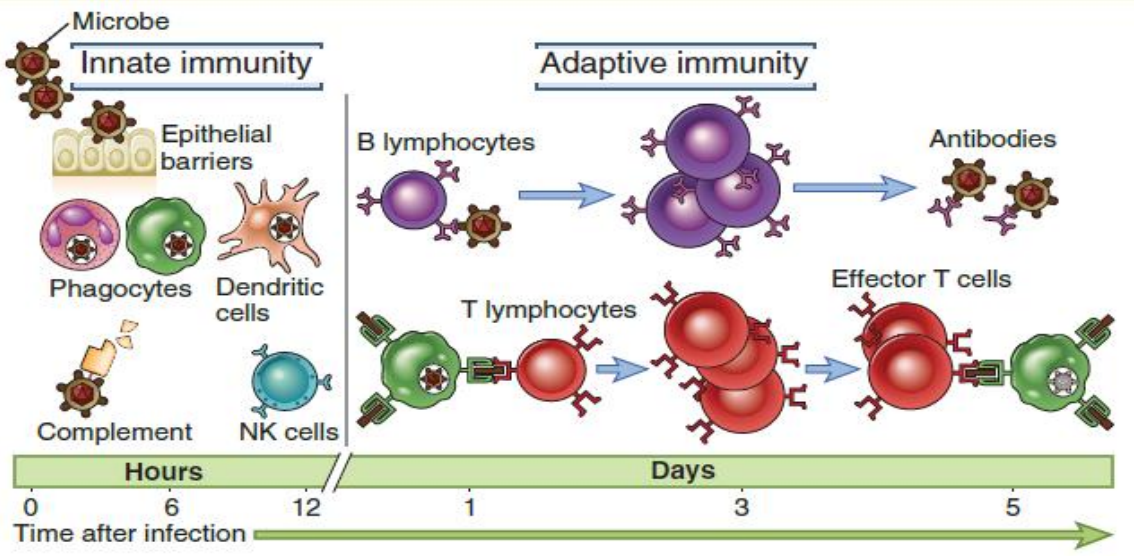
**The function of adaptive immune system:**

1-Secreted antibodies bind to (antigens) extracellular microbes, block their ability to infect host cells,and promote their ingestion and subsequent destruction by phagocytes.

2-Phagocytes ingest microbes and kill them, and helper T cells enhance the microbicidal abilities of the phagocytes.

3-Helper T cells recruit leukocytes to destroy microbes and enhance epithelial barrier function to eject microbes.

4-Cytotoxic T lymphocytes destroy cells infected by microbes that are inaccessible to antibodies.




**principal mechanisms of innate and adaptive immunity**

**Immunity**
**Lecture 2&3** **by: Dr. Ghasoun M.Ali wadai**

# CELLS OF THE IMMUNE SYSTEM:

The cells that serve specialized roles in innate and adaptive immune responses are phagocytes, dendritic cells, antigen-specific lymphocytes, and various other leukocytes that function to eliminate antigens. most of these cells are found in the blood, their responses to microbes

usually occur in lymphoid and other tissues and therefore may not be reflected by changes in their numbers in the circulation.

**TABLE 2-1 Normal Blood Cell Counts**

| | Mean Number per Microliter | Normal Range |
|---|---|---|
| White blood cells (leukocytes) | 7400 | 4500–11,000 |
| Neutrophils | 4400 | 1800–7700 |
| Eosinophils | 200 | 0–450 |
| Basophils | 40 | 0–200 |
| Lymphocytes | 2500 | 1000–4800 |
| Monocytes | 300 | 0–800 |

## Phagocytes

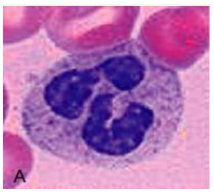
Phagocytes, including neutrophils and macrophages, are cells whose primary function is to ingest and destroy microbes and get rid of damaged tissues
The functional responses of phagocytes in host defense consist of sequential steps:

- recruitment of the cells to the sites of infection,
- recognition of and activation by microbes,
- ingestion of the microbes by the process of phagocytosis,
- and destruction of ingested microbes.
- In addition, through direct contact and by **secreting cytokines**, phagocytes communicate with other cells in ways that promote or regulate immune responses.

These functions of phagocytes are important in innate immunity, and also in the effector phase of some adaptive immune responses.

## 1.Neutrophils:

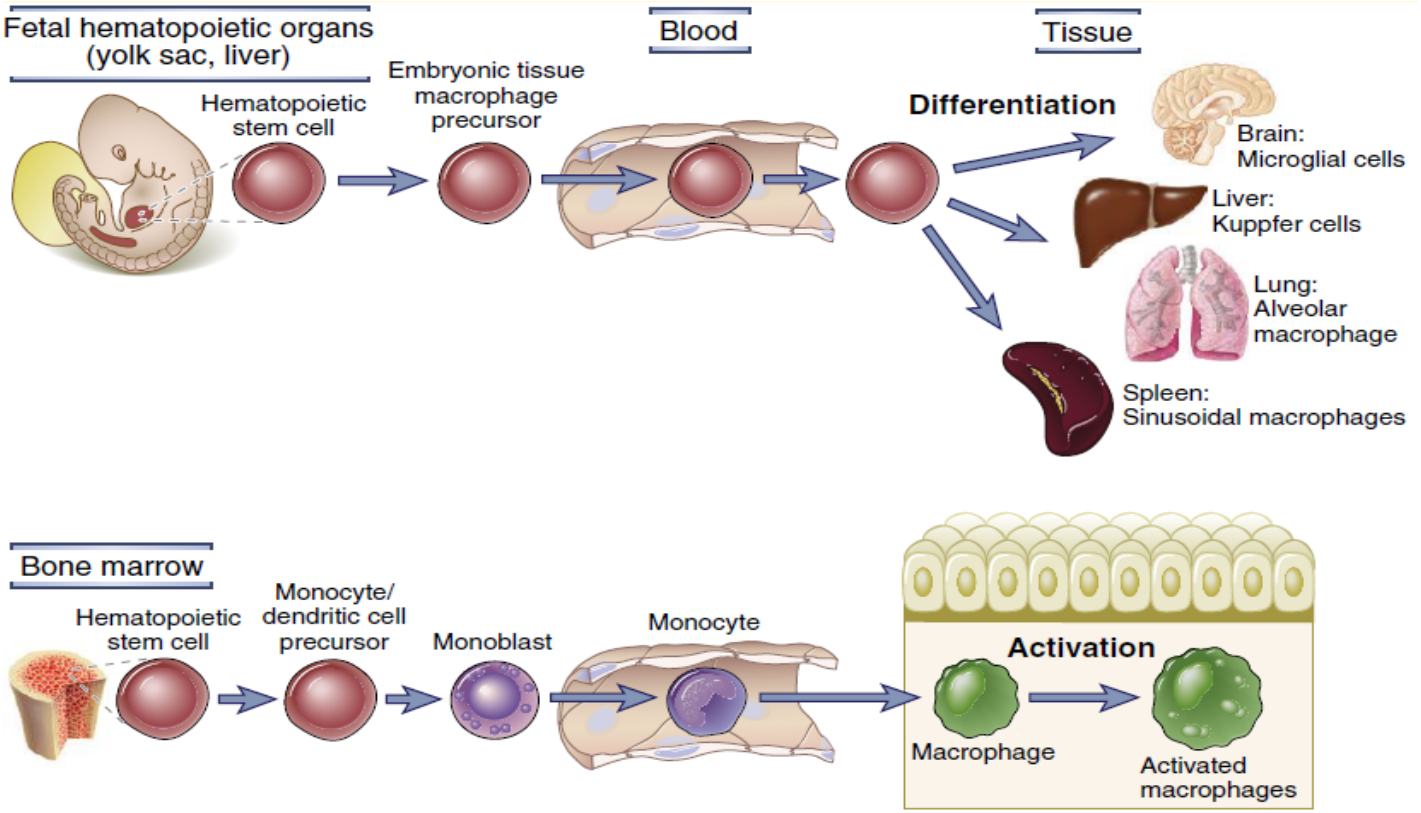
Neutrophils, also called polymorphonuclear leukocytes, are the most abundant population of circulating white blood cells and mediate the earliest phases of inflammatory reactions.
Neutrophils circulate as spherical cells about 12to 15 $\mu$ **m** in diameter with numerous membranous projections. The nucleus of a neutrophil is segmented into three to five connected lobules, hence the synonym polymorphonuclear leukocyte




**The light micrograph of a Wright-Giemsa–stained blood neutrophil shows the multilobed nucleus, because of which these cells are also called**

## *2.*Mononuclear Phagocytes:

**The mononuclear phagocyte system includes circulating cells called monocytes** and tissue resident cells called **macrophages**. Macrophages, which are widely distributed in organs and connective tissue, play central roles in innate and adaptive immunity. Many tissues are populated with long-lived resident macrophages derived from yolk sac or fetal liver precursors during fetal development, and they assume specialized phenotypes depending on the organ. Monocytes are 10 to 15 $\mu$ m in diameter, and they have bean-shaped nuclei and finely granular cytoplasm containing lysosomes, phagocytic vacuoles, and cytoskeletal filaments




**Maturation of mononuclear phagocytes**

Tissue macrophages perform several important functions in innate and adaptive immunity:

1. A major function of macrophages in host defense is **to ingest and kill microbes**. ingest dead host cells.
2. Activated macrophages secrete several different cytokines that act on endothelial cells lining blood vessels to enhance the recruitment of more monocytes and other leukocytes from the blood into sites of infections.
3. Macrophages serve as APCs that display antigens to and activate T lymphocytes. This function is important in the effector phase of T cell–mediated immune responses
4. Macrophages promote the repair of damaged tissues by stimulating new blood vessel growth.

## Mast Cells

Mast cells **are bone marrow–derived cells** present in the skin and mucosal epithelia, which contain abundant cytoplasmic granules filled with **histamine** and **other mediators**. Normally, mature mast cells are not found in the circulation but are present in tissues, usually adjacent to small blood vessels and nerves.

## Basophils

Basophils are blood granulocytes with many structural and functional similarities to mast cells. Like other granulocytes, basophils are **derived from bone marrow** progenitors , mature in the bone marrow, and circulate in the blood. Basophils constitute less than 1% of blood leukocytes. Although they are normally not present in tissues, basophils may be recruited to some inflammatory sites. Basophils contain granules that bind basic dyes.

## Eosinophils

Eosinophils are blood granulocytes that express cytoplasmic granules containing enzymes that are harmful to the cell walls of parasites but can also damage host tissues. Eosinophil granules contain basic proteins that bind role of dendritic cells as mediators of innate immunity and as APCs.

## Antigen-Presenting Cells:

**Antigen-presenting cells (APCs)** are cells that capture microbial and other antigens, display them to lymphocytes, and provide signals that stimulate the proliferation and differentiation of the lymphocytes.

## Lymphocytes

Lymphocytes, the unique cells of adaptive immunity, are the only cells in the body that express clonally distributed antigen receptors, each specific for a different antigenic determinant. Each clone of T and B lymphocytes expresses antigen receptors with a single specificity.

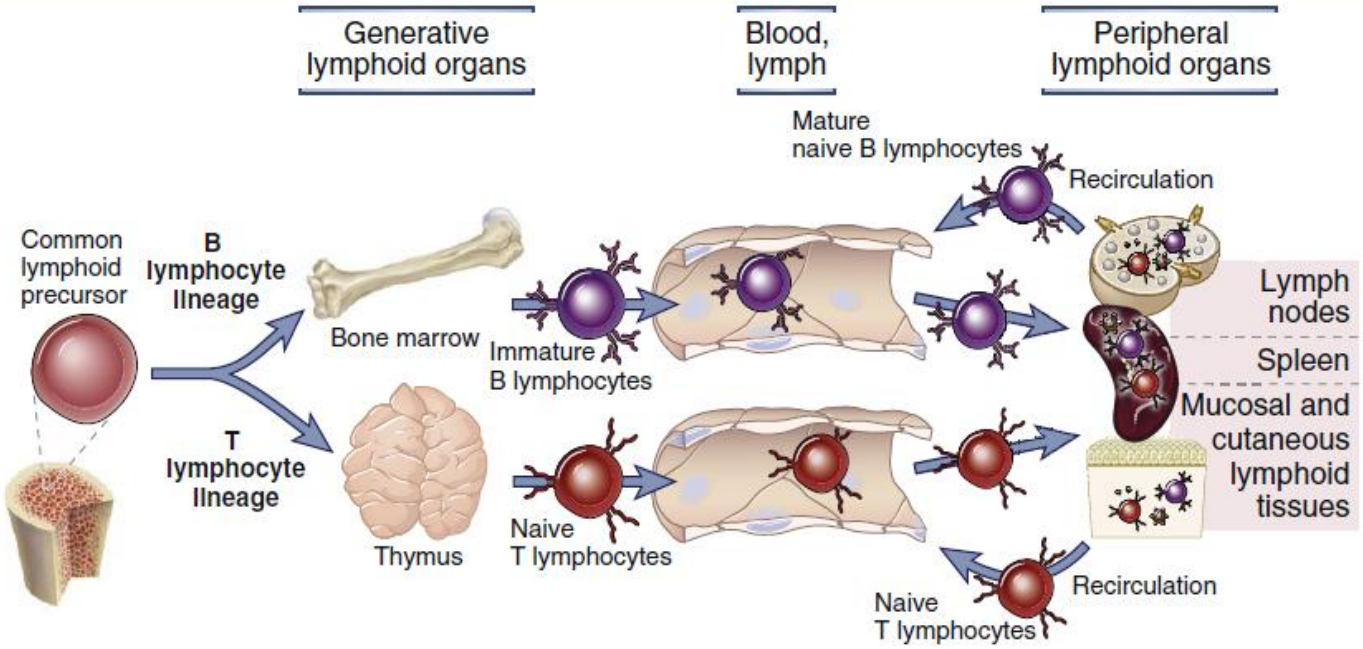
### Subsets of Lymphocytes

Lymphocytes consist of distinct subsets that are different in their functions and protein products:

**B lymphocytes:**

The cells that produce antibodies, were so called because in birds they were found to mature in an organ called the bursa of Fabricius. In mammals, no anatomic equivalent of the bursa exists, and the early stages of B cell maturation occur in the bone marrow. Thus, B lymphocytes now refer **to bone marrow–derived lymphocytes**.

**T lymphocytes:** The mediators of **cellular immunity**, arise in the bone marrow, and migrate to and mature in **the thymus**; T lymphocytes refer **to thymus-derived lymphocytes**.




**Maturation of lymphocytes**. Lymphocytes develop from bone marrow stem cells, mature in the generative lymphoid organs(bone marrow and thymus for B and T cells, respectively), and then circulate through the blood to secondary lymphoid organs (lymph nodes, spleen,regional lymphoid tissues such as mucosa-associated lymphoid tissues). Fully mature T cells leave the thymus, but immature B cells leave the bone marrow and complete their maturation in secondary lymphoid organs. Naive lymphocytes may respond to foreign antigens in these secondary lymphoid tissues or return by lymphatic drainage to the blood and recirculate through other secondary lymphoid organs.

## ANATOMY AND FUNCTIONS OF LYMPHOID TISSUES:

Many lymphocytes constantly recirculate and exchange between the circulation and the tissues. Lymphoid tissues are classified as:

1. **Generative organs**, also called **primary or central lymphoid organs**, where Lymphocytes first express antigen receptors and attain phenotypic and functional maturity. Included the bone marrow and the thymus, the sites of maturation of B cells and T cells, respectively.
2. **Peripheral organs**, also called **secondary lymphoid organs**, where lymphocyte responses to foreign antigens are initiated and develop, including spleen and lymph nodes, cutaneous immune system, and mucosal immune system.

## Bone Marrow

The bone marrow is the site of generation of most mature circulating blood cells, including red blood cells, granulocytes, and monocytes, and the site of early events in Bcell maturation.

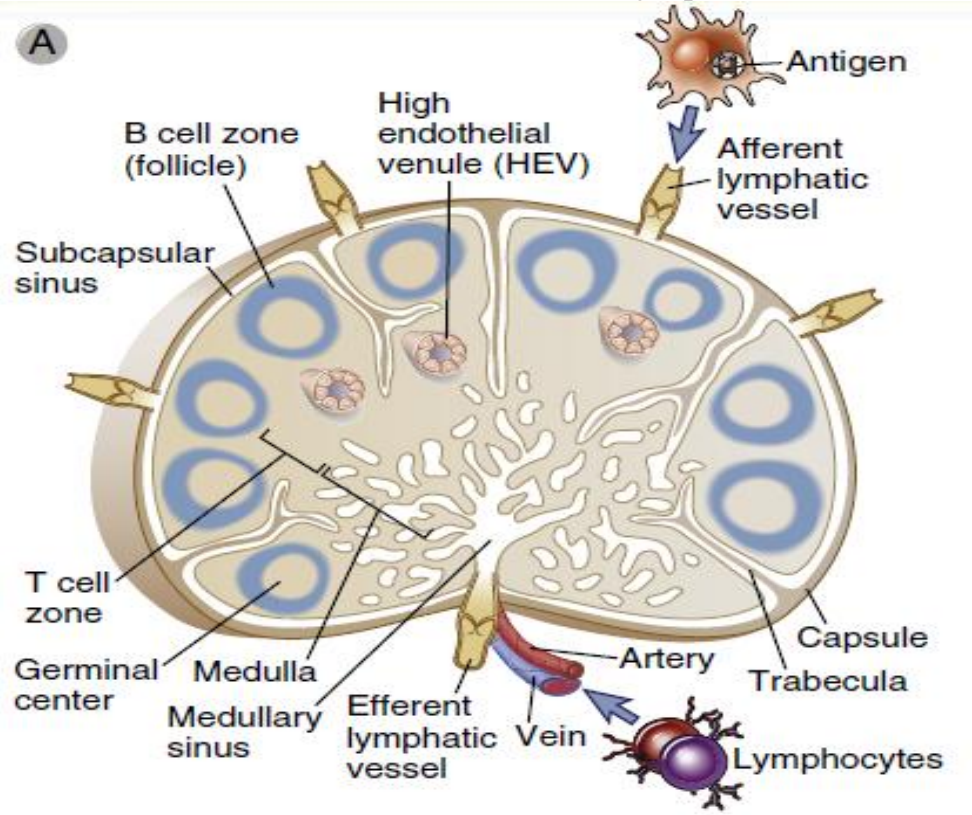
The generation of all blood cells, called hematopoiesis , occurs initially during fetal development in blood islands of the yolk sac and the para aortic mesenchyme, then shifts to the liver between the third and fourth months of gestation, and finally shifts to the bone marrow. At birth, hematopoiesis takes place mainly in the bones throughout the skeleton, but it becomes increasingly restricted to the marrow of the flat bones.

## Thymus

The thymus is the site of T cell maturation. The thymus is a bilobed organ situated in the anterior mediastinum. Each lobe is divided into multiple lobules by fibrous septa, and each lobule consists of an outer cortex and an inner medulla. The cortex contains a dense collection of T lymphocytes, and the lighter-staining medulla is more sparsely populated with lymphocytes.

## Lymph Nodes

Lymph nodes are encapsulated, vascularized secondary lymphoid organs with anatomic features that favor the initiation of adaptive immune responses to antigens carried from tissues by lymphatics Lymph nodes are situated along lymphatic channels throughout the body and therefore have access to antigens encountered at epithelia and originating in interstitial fluid in most tissues. There are about 500 lymph nodes in the human body.




**Morphology of a lymph node**.
A, Schematic diagram of a lymph node illustrating the T cell–rich and B cell–rich zones and the routes of entry of lymphocytes and antigen (shown captured by a dendritic cell).

## Spleen

The spleen is a highly vascularized organ whose major functions are to remove aging and damaged blood cells and particles (such as immune complexes and opsonized microbes) from the circulation and to initiate adaptive immune responses to blood-borne antigens. The spleen weighs about 150g in adults and is located in the left upper quadrant of the abdomen. The splenic parenchyma is anatomically and functionally divided into:

1-**red pulp**, which is composed mainly of blood-filled vascular sinusoids, The red pulp macrophages serve as an important filter for the blood, removing microbes, damaged cells, and antibody-coated (opsonized) cells and microbes.

2-and lymphocyte-rich **white pulp**

**The white pulp** contains the cells that mediate adaptive immune responses to blood-borne antigens

## The Lymphatic System

The lymphatic system consists of specialized vessels that drain fluid from tissues into and out of lymph nodes and then into the blood. It is essential for tissue fluid homeostasis and for immune responses. Interstitial fluid is constantly formed in all vascularized tissues by movement of a filtrate of plasma out of capillaries, and the rate of local formation can increase dramatically when tissue is injured or infected.

## Regional Immune Systems

All major epithelial barriers of the body, including the skin, gastrointestinal mucosa, and bronchial mucosa, have their own system of lymph nodes, nonencapsulated lymphoid structures, and diffusely distributed immune cells, which work in coordinated ways to provide specialized immune responses against the pathogens that enter at those barriers. The skin-associated immune system has evolved to respond to a wide variety of environmental microbes.

The **cutaneous immune system** and **mucosal immune system** are specialized collections of lymphoid tissues, APCs, and effector molecules located in and under the epithelia of the skin and the gastrointestinal and respiratory tracts, respectively. Although most of the immune cells in these tissues are diffusely scattered beneath the epithelial barriers, there are discrete collections of lymphocytes and APCs organized in a similar way as in lymph nodes.For example, pharyngeal tonsils and Peyer’s patches of the intestine are two anatomically defined mucosal lymphoid tissues