

CHAPTER 2 CELLS AND ORGANS OF IMMUNE SYSTEM



Learning Objectives

Upon completion of this lesson the student will be able to:

- Describe cells and organs of immune system
- Describe lymphoid tissue by primary or secondary, locations of specialized tissues, cells produced and key role in immunity.
- Describe the morphology, source and role of macrophages, natural killer cells, cytotoxic, helper, suppressor or B lymphocytes and plasma cells.
- Discuss the role of surface markers in cells involved with immunity, referring to specific markers used to differentiate T and B lymphocytes.

Chapter Outline

- 2.1. Overview of the Immune System
- 2.2. Organs of the Immune System
- 2.3 Cells of the Immune System
- 2.4 Classification of Cells and Organs of the Immune system
- 2.5 Development of Immune Cells





Overview of the immune System

- The immune system is a <u>Host Defense System</u> comprising many biological structures and processes within an organism that protects against disease.
- It detects a wide variety of agents, known as pathogens, from viruses to parasitic worms, and distinguish them from the organism's own healthy tissue.
- It's classified into subsystems, such as the <u>Innate Immune System</u> versus the <u>Adaptive Immune System</u>

or *Humoral Immunity* versus *Cell-mediated Immunity*

In humans, the Blood–Brain Barrier, Blood–Cerebrospinal Fluid Barrier, and Similar Fluid–Brain Barriers separate the Peripheral Immune System from the Neuroimmune System, which protects the brain.





2.1. Organs of the immune system

INTRODUCTION:

- The immune system consists of many different organs and tissues that are found throughout the body.
- These organs can be classified functionally into two main groups:

•<u>THE PRIMARY LYMPHOID ORGANS</u>- which provide appropriate microenvironments for the development and maturation of lymphocytes. This includes **Thymus, Bone** *Marrow, Fetal Liver*

- THE SECONDARY LYMPHOID ORGANS- which trap antigen from defined tissues or vascular spaces and are sites where mature lymphocytes can interact effectively with that antigen.
- Blood vessels and lymphatic systems connect these organs, uniting them into a functional whole.
- These are:
 - Lymph nodes, Spleen
 - Mucosa Associated Lymph tissue (MALT)
 - Tonsils, Peyers patches, lamina propria (largest amount of lymphs), appendix collectively known Gut associated lymhoid tissue (GALT)
 - Bronchial associated lymphoid tissue (BALT)

2.1. Organs of the immune system

TERTIARY LYMPHOID TISSUES:

- They are tissues which normally contain fewer lymphoid cells than secondary lymphoid organs
- Can import lymphoid cells during an inflammatory response.
- Most prominent of these are:
 - Cutaneous-associated lymphoid Tissues (CALT).

Once mature lymphocytes have been generated in the primary lymphoid organs, they circulate in the blood and lymphatic system, a network of vessels that collect fluid that has escaped into the tissues from capillaries of the circulatory system and ultimately return it to the blood.

Classification of Organs of the Immune System



Primary Lymphoid System

Classification-Residence

- 1. **Primary** lymphoid tissue primary diff/maturation
 - 1. Thymus
 - 2. Bone marrow
 - 3. Fetal liver
- 2. **Secondary** Lymphoid tissue Ag exposure and final differentiation
 - 1. Lymph nodes, Spleen
 - 2. Mucosa Associated Lymph tissue (MALT)



Source: Kuby immunology 2007, 5th ed



Primary:

- Thymus
- Bone Marrow

Secondary:

- Spleen
- Lymph nodes
- Mucosal Associated Lymphoid Tissue

Blood Lymphatics

Primary lymphoid organs:

- Bone marrow - Thymus the cells of the immune system originate in and mature here

Secondary lymphoid organs:

- Spleen

- Lymphatic vessels
- Lymph nodes
- Adenoids and tonsils
- MALT (Mucosal Associated Lymphoid Tissue) GALT (Gut Associated Lymphoid Tissue) BALT (Bronchus Associated Lymphoid Tissue) SALT (Skin Associated Lymphoid Tissue) NALT (Nasal Associated Lymphoid Tissue)

not for cell development. (final differentiation, activation may be performed) The cells of the adaptive immune system recognize here the pathogens



Thymus

Lymphoid organ that lies behind the breastbone.

Directs the maturation of immature thymocytes into T-cells (T lymphocytes).

Spleen

Filters the blood and contains immune cells. Serves as a meeting ground where immune defenses confront antigens.

Bone marrow

The soft tissue in the hollow center of bones.

Is the ultimate source of all blood cells, including lymphocytes.

Lymph nodes

Contain specialized immune cells. Filter the antigens out of the lymph before returning it to the circulation.

Skin

Acts as a barrier betwen body and germs.

Is generally impermeable to bacteria and viruses.

- <u>Thymus</u> glandular organ near the heart where T cells learn their jobs
- <u>Bone marrow</u> blood-producing tissue located inside certain bones
 - blood stem cells give rise to all of the different types of blood cells
- <u>Spleen</u> serves as a filter for the blood
 - removes old and damaged red blood cells
 - removes infectious agents and uses them to activate cells called lymphocytes
- Lymph nodes small organs that filter out dead cells, antigens, and other "stuff" to present to lymphocytes
- Lymphatic vessels collect fluid (lymph) that has "leaked" out from the blood into the tissues and returns it to circulation

THYMUS:

- The site of t-cell development and maturation.
- Flat, bilobed organ situated above the heart.
- Each lobe is surrounded by a capsule and is divided into lobules.
- Each lobule is organized into two compartments:



 The outer compartment, or cortex, is densely packed with immature T cells, called thymocytes

 The inner compartment, or medulla, is sparsely populated with thymocytes.





Source: Kuby immunology 2007, 5th ed



Source: Kuby immunology 2007, 5th ed

- Both the cortex and medulla are crisscrossed by
 - a three-dimensional stromal-cell network composed of:
 - Epithelial cells,
 - Dendritic cells, and
 - Macrophages, which make up the framework of the organ and contribute to the growth and maturation of thymocytes (T cells)



Function of Thymus:

To generate and select a repertoire of T cells that will protect the body from infection.

As thymocytes develop, an enormous diversity of tcell receptors is generated by a random process that produces some t cells with receptors capable of recognizing antigen-mhc complexes.



Most of the T-cell receptors produced by this random process are incapable of recognizing antigen-MHC complexes and a small portion react with combinations of self antigen-MHC complexes.

More than 95% of all thymocytes die by apoptosis in the thymus without ever reaching maturity.

Bone marrow:

- Bone marrow is a semi-solid tissue which may be found within the spongy or cancellous portions of bones.
- Bone marrow is the primary site of new blood cell production or Hematopoiesis.
- It is composed of hematopoietic cells, marrow adipose tissue, and supportive stromal cells.
- In adult humans, bone marrow is primarily located in the ribs, vertebrae, sternum, and bones of the pelvis.



Bone Marrow:

- The site of B-cell origin and development.
- Immature B cells proliferate and differentiate within the bone marrow, and stromal cells within the bone marrow interact directly with the B cells and secrete various cytokines that are required for development.

Selection process within the bone marrow eliminates B cells with self-reactive antibody receptors.



Lymph Nodes:

- Lymph nodes are your immune system's first line of defence, protecting you from things like bacteria or viruses that could make you sick.
- You have hundreds of the small, round, or bean-shaped glands all over your body.
- Most are spread out, but some are found in groups in a few major places, like your neck, under your arm, and in your chest, belly, and groin.



Lymph Nodes

- These are sites where immune responses are mounted to antigens in lymph.
- Are encapsulated bean shaped structures containing a reticular network packed with
 - Lymphocytes,
 - Macrophages, and
 - Dendritic cells



Lymph Nodes:

Cont...

- The first organized lymphoid structure to encounter antigens that enter the tissue spaces.
- Morphology

lymph node can be divided into three

The Cortex:

- □ The outermost layer
- Contains lymphocytes (mostly B cells), macro-phages, and follicular dendritic cells arranged in primary follicles.
- After antigenic challenge, the primary follicles enlarge into secondary follicles, each containing a germinal center.



The Paracortex:

□ Beneath the cortex.

- Populated largely by T lymphocytes and
- □ Contains interdigitating dendritic cells
- These interdigitating dendritic cells express high levels of class II MHC molecules, which function as APC.

The Medulla:

 \Box The innermost layer .

More sparsely populated with lymphoidlineage cells; of those present, many are plasma cells actively secreting antibody molecules.





Source: Kuby immunology 2007, 5th ed

The spleen:

- It acts primarily as a blood filter. The word spleen comes from Ancient Greek (splén).
- The spleen plays important roles in regard to red blood cells (erythrocytes) and the immune system.
- It removes old red blood cells and holds a reserve of blood, which can be valuable in case of hemorrhagic shock, and also recycles iron.
- As a part of the mononuclear phagocyte system, it metabolizes hemoglobin removed from senescent red blood cells (erythrocytes).



The Spleen

The globinportion of hemoglobin is degraded to its constitutive amino acids, and the heme portion is metabolized to bilirubin, which is removed in the liver.

The spleen synthesizes antibodies in its white pulp and removes antibody-coated bacteria and antibody-coated blood cells by way of blood and lymph node circulation



Spleen:

- Plays a major role in mounting immune responses to antigens in the blood stream.
- Large, ovoid situated high in the left abdominal cavity.
- Specializes in filtering blood and trapping bloodborne antigens;
- Can respond to systemic infections.
- Two compartments:
 - The red pulp populated by MØs, RBCs and few lymphocytes
 - A site where old and defective RBCs are destroyed and removed
 - White pulp, is primarily populated by T cells and B cells



Structure of SPLEEN

Cont...



Source: Kuby immunology 2007, 5th ed

Cutaneous-Associated Lymphoid Tissue

- The skin is barrier to the external environment.
- Important in nonspecific defenses.
- Epithelial cells the outer layer of the skin (keratinocytes) secrete a number of cytokines that may function to induce a local inflammatory reaction.
Cont...

- Keratinocytes can be induced to express class II MHC molecules and may function as APC.
- The Langerhans cells migrate from the epidermis to regional lymph nodes, where they differentiate into interdigitating dendritic cells.
- These cells express high levels of class II MHC molecules and function as potent activators of naive TH cell

Organ Summary

- The cells that participate in the immune response are white blood cells.
- The lymphocyte is the only cell to possess the immunologic attributes of specificity, diversity, memory, and self/non self recognition
- The primary lymphoid organs provide sites where lymphocytes mature and become antigenically committed
- Secondary lymphoid organs- capture antigens and provide sites where lymphocytes become activated by interaction with antigens.

Development Of Immune Cells:

Hematopoiesis:

- All blood cells arise from a type of cell called the hematopoietic stem cell (HSC).
- Stem cells are cells that can differentiate into other cell types; they are self-renewing-they maintain their population level by cell division.
- In humans, hematopoiesis, the formation and development of red and WBCs, begins in the embryonic yolk sac during the first weeks of development.

Overview of Cells the Immune system

An effective immune response is mediated by a verity of cells including; <u>Neutrophils, lymphocytes, Natural killer (NK) cells,</u> <u>Eosinophils and Antigen-presenting cells.</u>

□ The immune system consist of two main group of cells:

- Lymphocytes and Antigen-presenting cell
 - The lymphocytes are mainly responsible for initiating adaptive immune response in the human body. All lymphocytes are produced in the bone marrow stem cells by a process known as <u>HAEMATOPOEISIS</u>
 - <u>Two main types of Lymphocytes:</u>

T-lymphocytes (develops in the thymus)
 B-lymphocytes (develops in the bone marrow)

B Lymphocytes

- It originates in the bone marrow where they continue to differentiate and mature
- Each B cell is genetically programmed to encode a unique antigen-building receptor on its membrane (*membrane-bound antibody molecule*)
- When a naïve B cell; which has not previously encountered antigen comes in contact with an antigen via its membrane-bound antibody, it multiplies and differentiates into PLASMA CELLS and MEMORY CELLS

T Lymphocytes

- It originates in the bone marrow but they migrate to the THYMUS to mature.
- During migration, each T cell acquires a specific receptor on its membrane termed as the <u>T cell receptor</u>
- A T-cell receptor does not recognize soluble antigen. It recognizes antigens only when they are associated with a protein complex *called the Major Histocompatibility Complex (MHC)*

Organs

 Primary lymphoid organs: 1.bone marrow.
 2.thymus gland
 Secondary lymphoid organs:

1.lumph nodes. 2.Spleen. 3.mucsa associated lymphoid tissue. CELLS

Lymphocytes:

 B lymphocytes.
 T lymphocytes.
 NK cells.

 Granulocytes:

 neutrophils.
 esinophils.
 basophils and mast cells.

Phagocytic cells:

monocytes.
 macrophages.
 dendritic cells.





















- Lymphocytes: (B cells and T cells): Lymphocytes are the central cells of the immune system, responsible for adaptive immunity and the immunologic attributes of diversity, specificity, memory, and self/non-self recognition.
- The other types of white blood cells play important roles, engulfing and destroying microorganisms, presenting antigens, and secreting cytokines such as Natural Killer cells (NKs), Nutrophils, Macrophage, Eosinophils, Basophilis, Mast cells and Dendritic cells.

Natural Killer Cells

- Natural killer cells (NKs), described in 1970s, were shown to be a small population of large, granular lymphocytes that display cytotoxic activity against a wide range of tumor cells in the absence of any previous immunization with the tumor.
- NK cells play an important role in host defense both against tumor cells and against cells infected with some though not all, viruses.

NK Cells...

Do not express the membrane molecules and receptors that distinguish T- and B-cell lineages.

Although NK cells do not have T-cell receptors or immunoglobulin incorporated in their plasma membranes, they can recognize potential target cells in two different ways:

NK cells...

- NK cells may employ receptors that distinguish abnormalities, notably a reduction in class I MHC molecules and the unusual profile of surface antigens displayed by some tumor cells and cells infected by some viruses.
- NK cells recognize potential target cells depends upon the fact that some tumor cells and cells infected by certain viruses display antigens against which the immune system has made an antibody response, so that antitumor or antiviral antibodies are bound to their surfaces



- Mononuclear Phagocytes:
 - □ The mononuclear phagocytic system consists of:
 - Monocytes
 - Macrophages all sorts
- Polymorphonuclear phagocytic cells (PMNs):
 - PMNs are capable of ingesting and digesting exogenous antigens, such as whole microorganisms and insoluble particles, and endogenous matter.

DCs...

Derived from myeloid progenitor (some lymphoid)

Immature DCs:

Migrate from blood to reside in tissues and are both phagocytic and micropinocytic (ingest large amount of the surrounding ECF)

Continuously migrate from the tissues bearing self Ags and induce tolerance as they lack co-stimulatory molecules

Upon encountering a pathogen, they readily mature, express costimulatory molecules, and migrate to lymph nodes

DCs...

Mature DCs:

- Specialized to take up Ag, process it, and display it for recognition by T Lymphocytes i.e., act as APCs to T cells initiating adaptive IR (express co-stimulatory molecules when encountering pathogen)
- Classified by location as follows:
 - Langerhans cells (epidermis/skin and mucous membranes)
 - □ Interstitial DCs (organs: heart, lungs, liver, kidney, GIT)





Source: Immunobiology 2001, 5th ed

Lymphocyte Recirculation

Lymphocytes are capable of recirculation, continually moving through the blood and lymph to the various lymphoid organs

Lymphocytes migrate from the blood into lymph nodes through specialized areas in post-capillary venules called high-endothelial venules (HEVs).

Lymphocyte recirculation



Source: Kuby immunology 2007, 5th ed

Cell-Adhesion Molecules

The vascular endothelium regulate the movement of
 blood-borne molecules and
 leukocytes into the tissues.

In order for circulating leukocytes to enter inflamed tissue or peripheral lymphoid organs, the cells must adhere to and pass between the endothelial cells lining the walls of blood vessels, a process called **extravasation**.

Endothelial cells express leukocyte-specific cell adhesionmolecules (CAM)

Cell-Adhesion Molecules

- Recalculating leukocytes bear receptors that bind to CAMs on the vascular endothelium,
 - \Box enabling these cells to extravasate into the tissues.

CAMs on leukocytes also serve to increase the strength of the functional interactions between cells of the immune system.

Neutrophil Extravasation

- Neutrophils first bind to inflamed endothelium and extravasate into the tissues.
- Neutrophils recognize the inflamed endothelium and adhere
 so that they are not swept away by the flowing blood.
- The bound neutrophils then penetrate the endothelial layer and migrate into the underlying tissue.
- Monocytes and eosinophils extravasate by a similar process,



Source: Kuby immunology 2007, 5th ed

Neutrophil Extravasation

Neutrophil extravasation has four sequential steps:

Rolling,

- □ Activation by chemoattractant stimulus,
- \Box Arrest and adhesion, and
- □ Transendothelial migration.

Neutrophil Extravasation



Neutrophil Extravasation

- Lymphocytes exhibit directed extravasation at
 inflammatory sites and
 - secondary lymphoid organs.

The recirculation of lymphocytes is carefully controlled
 to ensure appropriate populations of B and T cells are recruited into different tissues.

Neutrophil Extravasation

Extravasation of lymphocytes involves interactions among a number of cell-adhesion molecules.

Some regions of vascular endothelium in postcapillary venules of lymphoid organs are composed of specialized cells with a plump, cuboidal ("high") shape; such regions are called high-endothelial venules, or HEVs.

Neutrophil Extravasation

- Each of the secondary lymphoid organs, with the exception of the spleen, contains HEVs.
- HEVs express a variety of cell-adhesion molecules.
- Unlike neutrophils, various lymphocyte populations exhibit differential extravasation into various tissues.
- Trafficking, or homing receptors on lymphocytes interact with tissue-specific adhesion molecules, called vascular addressins, on high endothelial venules (HEVs) in lymphoid organs and on the endothelium in extra lymphoid tissues
Neutrophil Extravasation





Figure 6. Phagocytosis

The Inflammatory Process

Is a physiologic response to a variety of stimuli
Such as infections and tissue injury.

- An acute inflammatory response
 - □ Has a rapid onset
 - □ Lasts a short and
 - Accompanied by a systemic reaction known as the acute-phase response, which is
 - -characterized by a rapid alteration in the levels of several plasma proteins.

The Inflammatory Process

□ Chronic inflammation results in,

-Persistent immune activation

- Pathologic consequences
- Lead to formation of a granuloma
- The accumulation and activation of macrophages is the hallmark of chronic inflammation.

The Inflammatory Process

Two cytokines in particular, IFN- γ and TNF- α , play a central role in the development of chronic inflammation.

TH1 cells,NK cells, and TC cells release IFN- γ, while activated macrophages secrete TNF-α.

The Inflammatory Process

- Inflammatory Responses May Be Localized or Systemic
- The hallmarks of a localized acute inflammatory response, are
 - □ swelling (*tumor*)
 - □ redness(*rubor*)
 - □ heat (*calor*)
 - □ pain (*dolor*), and loss of function

The Inflammatory Process

The local inflammatory response is accompanied by a systemic response known as the acute-phase response, marked by

 \Box the induction of fever,

- increased synthesis of hormones such as ACTH and hydrocortisone,
- increased production of white blood cell (leukocytosis),
- production of a large number of acute-phase proteins (C-reactive protein) in the liver.

The Inflammatory Process

Many systemic acute-phase effects are due to the combined action of IL-1, TNF- and IL-6.

Summary of Cells and organs of the immune system

Organs of the immune system

- Primary lymphoid organs
 - The primary lymphoid organs provide appropriate microenvironments for the development and maturation of lymphocytes. This includes Thymus, Bone marrow, Fetal liver



Source: Kuby immunology 2007, 5th ed

Summary of Cells and organs of the immune system

The secondary lymphoid organs trap antigen from defined tissues or vascular spaces and are sites where mature lymphocytes can interact effectively with that antigen. These are,

□ Lymph nodes,

□ Spleen,

- □ Mucosa Associated Lymph tissue (MALT),
- Tonsils, Peyers patches, lamina propria (largest amount of lymphs), appendix collectively known Gut associated lymhoid tissue (GALT)
- □ Bronchial associated lymphoid tissue (BALT)

Summary of Cells and organs of the immune system

Tertiary lymphoid organs

Tertiary lymphoid tissues are normally contain fewer lymphoid cells than secondary lymphoid organs,

- Can import lymphoid cells during an inflammatory response.
- Most prominent of these are
- cutaneous-associated lymphoid Tissues (CALT).

Review questions

- Explain cells and organs of immune system
- Explain the role of surface markers in cells involved with immunity, referring to specific markers used to differentiate T and B lymphocytes
- Describe lymphoid tissue by primary or secondary, locations of specialized tissues, cells produced and key role in immunity.
- Describe the morphology, source and role of macrophages, natural killer cells, cytotoxic, helper, suppressor or B lymphocytes and plasma cells.

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