12.4: The Lymphoid System

Learning Objectives

1. Compare and give examples of the following:
   a. primary lymphoid organs
   b. secondary lymphoid organs

2. Define the following:
   a. plasma
   b. tissue fluid
   c. lymph
   d. lymph vessels
   e. MALT

3. Briefly describe the importance of the lymphoid system in adaptive immune responses and how microbes and other antigens encounter naive B-lymphocytes and T-lymphocytes.

The body uses the lymphoid system to enable lymphocytes to encounter antigens and it is here that adaptive immune responses are initiated. The lymphoid system consists of primary lymphoid organs, secondary lymphoid organs, and lymphatic vessels.

The bone marrow and the thymus constitute the primary lymphoid organs. Both B-lymphocytes and T-lymphocytes are produced from stem cells in the bone marrow. B-lymphocytes mature in the bone marrow while T-lymphocytes migrate to the thymus and mature there. After maturation, both naive B-lymphocytes and naive T-lymphocytes circulate between the blood and the secondary lymphoid organs.

Lymphatic vessels are responsible for flow of lymph within the lymphoid system and are a part of the body's fluid
recirculation system. The liquid portion of the blood, called plasma, constantly leaks out of capillaries to deliver oxygen and nutrients to cells of the surrounding tissue. Once in the tissue, the plasma is now called tissue fluid. While most of this tissue fluid re-enters capillaries and is returned directly to the bloodstream, some fluid enters lymph vessels as lymph. The lymph flows through regional lymph nodes and eventually enters the circulatory system at the heart to maintain the fluid volume of the circulation.

Secondary lymphoid organs

Adaptive immune responses require antigen-presenting cells, such as macrophages and dendritic cells, and ever changing populations of B-lymphocytes and T-lymphocytes. These cells gather to detect and present antigens in secondary lymphoid organs. The secondary lymphoid organs include highly organized lymphoid organs such as lymph nodes and the spleen, as well as less organized accumulations of lymphoid organs scattered strategically throughout the body.

Figure (Figure 1): Structure of a Lymph Nodes. Antigens enter lymph nodes through afferent lymphoid vessels. Antigen-presenting dendritic cells enter the lymph node through afferent lymphatic vessels while naive B-lymphocytes, and naive T-lymphocytes enter through high endothelial venules. Non-activated and effector lymphocytes leave the lymph node through efferent lymphatic vessels. Naive B-lymphocytes become activated, proliferate, and differentiate into plasma cells in the germinal centers of lymphoid follicles while naive T-lymphocytes become activated, proliferate and differentiate into T-effector lymphocytes in the T-cell area.

Lymph nodes (Figure (Figure 1)) contain many reticular fibers that support fixed macrophages and dendritic cells as well as ever changing populations of circulating B-lymphocytes and T-lymphocytes. When microorganisms and other antigens enter tissues, they are transported by tissue fluid into the lymph vessels. Lymph vessels, in turn, carry these antigens, now in the lymph, to regional lymph nodes. In addition, immature dendritic cells located under the surface epithelium of the skin and the surface epithelium of the mucous membranes of the respiratory tract, genitourinary tract, and the gastrointestinal tract capture antigens through pinocytosis and phagocytosis. The dendritic cells detach from their initial site, enter lymph vessels, and are carried to regional lymph nodes. Here the microbes and other antigens in the lymph encounter changing populations of B-lymphocytes, are filtered out and phagocytosed by the fixed macrophages and dendritic cells, and are presented to changing populations of T-lymphocytes (Figure (Figure 2)). Approximately 25 billion different lymphocytes migrate through each lymph node every day.
Figure \(\PageIndex{2}\): B-lymphocyte and T-Lymphocytes Recognizing Antigens in a Lymph Node. Opsonized antigens (those coated with C3b and Ced from the complement pathways) enter a lymph node through afferent lymphoid vessels. These opsonized antigens bind to and remain on the surface of specialized macrophages and follicular dendritic cells (FDCs). In addition, macrophages can transfer antigens to FDCs (see 4. above). Using their B-cell receptor (BCR), naive B-lymphocytes are able to recognize antigens directly (see 1. above), or more commonly, on the surface of FDCs (see 2. above), or on the surface of macrophages (see 3. above) in the germinal centers and lymphoid follicles of the lymph node. Meanwhile, naive T-lymphocytes are being activated by antigen-presenting dendritic cells in the T-cell areas of the lymph node (see 5. above). T4-effector cells and activated B-lymphocytes then interact with one another at the interface between the germinal centers and the T-cell areas.

Like the lymph nodes, the spleen contains many reticular fibers that support fixed macrophages and dendritic cells as well as ever changing populations of circulating B-lymphocytes and T-lymphocytes. When microorganisms and other antigens enter the blood, they are transported by the blood vessels to the spleen. Most of the spleen is referred to as red pulp. This area is involved in the disposal of old red blood cells. Scattered throughout the spleen are isolated areas called the white pulp (Figure \(\PageIndex{3}\)). Here antigens in the blood encounter macrophages, dendritic cells, and ever-changing populations of B-lymphocytes and T-lymphocytes.
Figure \(\PageIndex{3}\): Section of a Spleen Showing Red Pulp and White Pulp. The red pulp makes up the majority of the spleen. This is where old red blood cells are destroyed. Scattered throughout the spleen are areas of white pulp where microbes, cells, and antigens encounter macrophages, dendritic cells, and changing populations of B-lymphocytes and T-lymphocytes. Soluble antigens, blood-borne microbes, and antigen-antibody complexes are filtered out of the blood and phagocytosed by immature dendritic cells and macrophages within the marginal zone. After maturation, dendritic cells migrate to the periphery of the periarteriolar lymphoid sheath, The T-cell area of the white pulp, and present antigens bound to MHC molecules to the TCRs of T-lymphocytes. Secondary follicles consisting of germinal centers surrounded by a B-cell corona are where B-lymphocytes encounter microbes and soluble antigens.

Mucosal surfaces within the body, the most common sites of microbial invasion, are protected by the mucosal immune system consisting of the mucosa-associated lymphoid tissue or MALT, an extensive diffuse system of small concentrations of lymphoid tissue found in various sites of the body such as the gastrointestinal tract, thyroid, breast, lung, salivary glands, eye, and skin. MALT is populated by loose clusters of T-lymphocytes, B-lymphocytes, plasma cells, activated TH cells, and macrophages. MALT can be subdivided into:

- GALT (gut-associated lymphoid tissue, such as the Peyer's patches (Figure \(\PageIndex{4}\)) in the lining of the small intestines, as well as the adenoids, tonsils, and appendix)
- BALT (bronchial-associated lymphoid tissue in the bronchi)
- SALT (skin-associated lymphoid tissue beneath the epidermis)
- NALT (nose-associated lymphoid tissue)
- LALT (larynx-associated lymphoid tissue)
- CALT (conjunctiva-associated lymphoid tissue in the eye)

As can be seen, no matter how microbes and other antigens enter the body, they will eventually encounter the lymphoid system to initiate adaptive immune responses.

Figure \(\PageIndex{4}\): Diagram of a Peyer's Patch. Peyer's patches are part of the mucosa-associated lymphoid tissue (MALT) in the small intestines. Microbes and antigens enter through specialized epithelial cells called microfold (M) cells. Changing populations of naive B-lymphocytes and naive T-lymphocytes enter the Peyer's patch via blood vessels with B-lymphocytes entering the follicles and germinal centers and T-lymphocytes entering the T-cell area. Dendritic cells engulf and process antigens and present them by way of MHC molecules to the TCRs of naive T-lymphocytes.
Summary

1. The body uses the lymphoid system to enable lymphocytes to encounter antigens and it is here that adaptive immune responses are initiated.
2. The lymphoid system consists of primary lymphoid organs, secondary lymphoid organs, and lymphatic vessels.
3. The bone marrow and the thymus constitute the primary lymphoid organs.
4. While both B-lymphocytes and T-lymphocytes are produced from stem cells in the bone marrow, B-lymphocytes mature in the bone marrow and T-lymphocytes migrate to the thymus to mature.
5. After maturation, both naive B-lymphocytes and naive T-lymphocytes circulate between the blood and the secondary lymphoid organs.
6. Adaptive immune responses require antigen-presenting cells, such as macrophages and dendritic cells, and ever changing populations of B-lymphocytes and T-lymphocytes. These cells gather to detect and present antigens in secondary lymphoid organs.
7. The secondary lymphoid organs include highly organized lymphoid organs such as lymph nodes and the spleen, as well as less organized accumulations of lymphoid organs scattered strategically throughout the body.
8. Lymphatic vessels are responsible for flow of lymph within the lymphoid system and are a part of the body's fluid recirculation system. The lymph flows through regional lymph nodes and eventually enters the circulatory system at the heart to maintain the fluid volume of the circulation.

Contributors and Attributions

- Dr. Gary Kaiser (COMMUNITY COLLEGE OF BALTIMORE COUNTY, CATONSVILLE CAMPUS)