IMMUNE SYSTEM II
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Reading: Gartner & Hiatt, Chapter 9; Sheedlo Chapter 12, p109

Learning Objectives:
• Describe the histologic organization of the spleen.
• Describe the histologic organization of the 3 types of tonsils.
• Know the types of unencapsulated lymphoid tissue and their respective locations in the body.

Key Words: Spleen, Tonsils, Unencapsulated Lymphoid Tissue, Appendix, Peyer’s Patches

I. SPLEEN

Spleen (G&H, p. 176)

A. Located in upper left quadrant of abdomen. Functions in defense against foreign microorganisms and a site of destruction of aged or abnormal red blood cells and platelets. Contains lymphocytes and can function as a major antibody production site.

B. General Organization
1. Enclosed by fibrous dense irregular connective tissue capsule which contains elastic fibers and occasional smooth muscle cells. Prominent trabeculae extend from the capsule into parenchyma.
2. Parenchyma composed of splenic pulp, which is further subdivided into red and white pulp. Supported by a network of reticular fibers.
3. The medial surface houses the hilum through which vessels and nerves pass into and out of the spleen. Lymphatic vessels are present in only 2/3 of all spleens.

C. Splenic Circulation

1. Splenic artery enters at hilum; branches into trabecular arteries, which follow the trabeculae.
2. Trabecular arteries branch repeatedly and eventually enter splenic pulp as central arteries. Become ensheathed by a cuff of lymphocytes, the periarterial lymphatic sheath or PALS. The cuff of lymphocytes may expand along the course of the artery to form actual lymphoid follicles. PALS and the follicles form the "white pulp."
3. Central arteries subdivide to form **penicillar arterioles** that eventually empty into capillaries.

4. **Capillaries** carry blood to the **spleenic sinusoids** by an incompletely understood mechanism.

5. Blood empties from sinusoids into pulp veins and then into **trabecular veins**. Trabecular veins empty into the **spleenic vein** that exits the spleen at the hilum.

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**D. White Pulp**

1. Composed of **diffuse and nodular** lymphoid tissue, primarily lymphocytes. In the fresh state, appears as small, round pale white or gray areas surrounded by dark red tissue. With H&E, it appears basophilic due to the concentration of lymphocytes.

2. The **peripheral lymphatic sheath** parallels the course of the central arteries. The PALS are primarily T-lymphocytes.

3. **Lymphoid nodules or follicles** may be present. Like lymphoid follicles in the lymph node, these are composed chiefly of B-lymphocytes. Germinal centers with mantle zones (B-cells) and marginal zones (B- and T-cells) may be present and result in the formation of large nodules known as **splenic nodules** or **Malpighian corpuscles**.

**E. Red Pulp**

1. In the fresh state, appears red due to the massive amount of **red blood cells**. Consists of **splenic cords** and **spleenic sinuses**. Makes up 75% of the volume of the spleen.

2. **Splenic cords** (or **cords of Billroth**) are a meshwork of reticular fibers containing reticular cells, lymphocytes, macrophages, red blood cells, plasma cells, and granulocytes.

3. **Spleenic sinuses** carry venous blood and are lined by special **endothelial cells**. These cells are very long and flat and run parallel to the direction of the vessel. They are surrounded by thick rings of reticular fibers, like a mesh.
   a. Since the endothelial cells are not tightly bound to each other at their lateral margins, small spaces exist, allowing blood cells (red blood cells, lymphocytes, etc.) and macrophages to pass easily into and out of the sinusoids. **Macrophages** associated with the sinusoids are highly phagocytic and function to filter out damaged cells and foreign particles.
II. TONSILS

A. Incompletely encapsulated aggregates of lymphoid nodules. They lie beneath the epithelium of the mouth and pharynx and are lined by the type of epithelium found in these areas.

1. Do not filter lymph (no afferent lymphatic vessels).

B. Palatine Tonsils

1. Paired masses of tissue located in the lateral wall of the oropharynx.
2. Lined by stratified squamous epithelium that forms multiple invaginations known as crypts. Contains dense collections of lymphoid nodules, many with germinal centers. Partially encapsulated at the basal surface.

C. Pharyngeal Tonsil

1. Single lymphoid structure located in posterior nasopharynx. Sometimes referred to as the adenoid. Typically present in children, but usually atrophies by adulthood.
2. Lined by ciliated pseudostratified columnar epithelium (respiratory-type epithelium) with occasional patches of stratified squamous epithelium. Mucosa is composed of pleats; there are no crypts.

D. Lingual Tonsils

1. Small, numerous lymphoid nodules at base of tongue.
2. Covered with stratified squamous epithelium; each has a single crypt into which empty the
ducts of minor salivary glands.

III. UNENCAPSULATED LYMPHOID TISSUE

A. Lymphoid follicles as well as diffuse aggregates of lymphocytes can be found in the lamina propria of the gastrointestinal tract, the upper respiratory tract, and the urinary tract. Generically referred to as **Mucosa-Associated Lymphoid Tissue** or **MALT**.

1. **No capsule** is present. Structure of the lymphoid follicles is same as in lymph nodes.
2. The major antibody produced by the plasma cells is **IgA**, which is secreted directly onto the mucosal surface.
3. Protects against exposure to foreign antigens that enter the respiratory or GI tract. Antigen-specific IgA can prevent adherence of certain microbes to the mucosa and neutralize various bacterial toxins and viruses.

B. Includes **GALT** (Gut-Associated Lymphoid Tissue) and **BALT** (Bronchus-Associated Lymphoid Tissue)

1. In the **ileum**, lymphoid aggregates are called **Peyer’s Patches**. Each patch is composed of approximately 10-200 lymphoid nodules; there are roughly 30 “patches” in the adult ileum.
   a. Covered with epithelium composed of **M (microfold) cells**. These cells have numerous membrane invaginations forming pits that contain lymphocytes. The M-cells take up microorganisms and foreign antigens and transport them to the underlying lymphocytes. The lymphocytes then migrate to the lymph nodes where an immune response can be initiated. This GALT also produces secretory IgA as a first line of defense.

C. **Appendix** (to be covered in depth in the GI lecture)

1. A small, finger-like blind pouch projecting off the cecum of the large intestine. Contains numerous lymphoid nodules in the mucosa and submucosa.

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**IMMUNE SYSTEM LABORATORY**

**Slide 59 - Thymus**

- Identification of the thymus can usually be done at low magnification. The presence of a cortex and medulla containing Hassall’s corpuscles (see #4) are the tip-offs.
- Examine the poorly-defined **capsule**, composed of a mixture of dense irregular and loose connective tissue. The trabeculae that extend from the capsule subdivide the thymus into indistinct **lobules**. Notice that the lobules contain a **cortex** and a **medulla**.
- In the lobules, examine the dark-staining basophilic **cortex**. It is composed of **epithelial reticular cells**, macrophages, and small **thymocytes**. The epithelial reticular cells have
large, pale-staining nuclei; sometimes they are difficult to distinguish from macrophage nuclei. Small capillaries are present. There are no lymphoid nodules.

- The medulla stains lighter and more eosinophilic than the surrounding cortex. It contains the same cells as the cortex, but they are less densely packed. In addition, there are Hassall's corpuscles. These are whorls of concentrically arranged epithelial reticular cells some of which show evidence of keratinization.

**Slide 20 - Lymph Node**

- Examine the tissue on low magnification. Notice that it is surrounded by a capsule that overlies a cortex and a medulla (start noticing how it is different from the thymus, which has the same features).
- The capsule is composed of dense irregular connective tissue intermingled with adipose tissue. Afferent lymphatics enter the capsule; efferent lymphatics and blood vessels exit via the hilum. Trabeculae extend from the capsule into the lymph node proper. Immediately below the capsule is the subcapsular sinus; this is continuous with the cortical or trabecular sinuses.
- The cortex contains lymphoid follicles. Find primary follicles (might be difficult) and secondary follicles (look for the lighter-staining germinal centers). The germinal center contains a mixture of medium and large B-lymphocytes, plasma cells, and dividing lymphocytes. Dendritic reticulum cells are also present in the cortex.
- The paracortex is the region between the lymphoid nodules and the medulla. This is a T-cell rich area. High endothelial venules are also found in this area.
- The medulla contains medullary cords, composed of macrophages, lymphocytes, and plasma cells, separated by lighter-staining areas, the medullary sinuses. The hilum may be apparent on some slides (large vessels can be seen in this area).

**Slide 3 - Spleen**

- Examine the entire section on low magnification. Notice that, unlike the thymus and lymph node, there is no cortex and medulla (this is a key identification feature). The main components are the red pulp and white pulp.
- The thick capsule is composed of dense irregular connective tissue (even though it really looks like dense regular, this is the wrong place to find that type of connective tissue). Extending from it are broad connective tissue trabeculae that may contain blood vessels.
- The red pulp makes up the majority of the parenchyma. It is composed of the venous sinuses and the splenic cords (cords of Billroth). The splenic cords are composed of reticular cells, plasma cells, macrophages, and circulating blood cells. The venous sinuses are lined by plump endothelial cells (whose nuclei often project out into the lumen) and contain mostly red blood cells (although in this section, many of the sinuses look empty due to processing of the tissue).
- The white pulp is composed of aggregates of lymphocytes. The central artery is typically surrounded by a thin sheath of lymphocytes, the periarterial lymphatic sheath (PALS). In some areas, the lymphatic sheath expands to form a lymphoid nodule. When this occurs, the central artery will be eccentrically placed in the nodule. In the lymphoid nodule, look for the germinal center, the mantle zone, and the marginal zone.

**Slide 60 - Tonsil**

- Examine the tissue on low magnification. A large portion of it is covered by stratified squamous epithelium (keratinized or nonkeratinized?) that dips into the underlying
Parenchyma to form crypts (the **tonsillar crypts**). A portion of the tissue also appears to be covered by dense irregular connective tissue with islands of muscle (what type?). Apparently the surgeon was intent on removing the ENTIRE TONSIL (including part of the throat), leaving nothing behind.

- Numerous lymphoid nodules are present in the walls of the crypts. Most nodules exhibit a germinal center (with simply gorgeous mitotic figures); you would call these what type of follicle?

**Unencapsulated Lymphoid Tissue**

Review the following slides for examples of unencapsulated lymphoid tissue. Recall what lymphocytes look like and then make sure you can recognize them whether they are “diffusely scattered” or present in “lymphoid nodules.”

**GALT**

**Slide 8 - Esophagus** - Look beneath the epithelium.

**Slide 6 - Ileum** - The lymphoid nodules (called **Peyer's patches**) are large and disrupt the epithelium. We will spend more time on this when we cover the GI tract.

**Slide 61 – Appendix** - Note stellate-shaped lumen of tissue cut in cross-section. It is lined by simple columnar epithelium that covers many lymphoid nodules. The wall is composed of muscle. Again, we spend more time on this when we cover the GI tract.

3. **BALT**

**Slide 12 – Trachea** - Look beneath the epithelium