IMMUNE (LYMPHOID) SYSTEM

The primary functions of the lymphoid organs (thymus, spleen, lymph nodes) are protective or immunologic in nature. These organs are the source of immunocompetent cells, which have the capacity to react with and neutralize foreign substances (antigens) to which the body may be exposed. Whether these substances are pathogens, such as bacteria and viruses or endogenous abnormal constituents, such as those found in tumors, the body can normally eliminate whatever foreign antigens are presented to it. Lymphocytes, plasma cells, and macrophages perform direct immunologic functions that effectively neutralize these antigens. Other cells, such as reticular cells and granulocytic white blood cells, perform more specialized ancillary functions in certain types of reactions. These cells and their precursors form the primary cellular populations of the lymphoid organs. The cellular population of any lymphoid organ is highly variable and largely reflects the organ’s functional role in the development of the immune system or its state of immune reactivity.

The term lymphoid system includes not only the cells within distinct (i.e., encapsulated) lymphoid organs but also the widely and more abundantly distributed lymphoid cells found in the peripheral circulation and in the loose connective tissue and epithelial tissues of various organs (e.g., gut, lung). The term immune system includes lymphoid cells and accessory cells, such as macrophages, and their secretory products (e.g., antibodies, cytokines, etc.).

PRIMARY (CENTRAL) LYMPHOID ORGANS

THYMUS

The thymus has a cortex and medulla (see below) and is partially divided into lobules by connective tissue septa derived from the gland capsule. Most of the cells (thymocytes) are small, immature T-lymphocytes. There are a few interspersed reticular cells, which are large cells having large pale staining nuclei. There is a blood-thymic barrier in the cortex. The barrier is formed by the continuous blood capillaries, reinforced by epithelial reticular cells and macrophages.

There are fewer cells in the medulla compared to cortex and the lymphocytes here are mostly immunocompetent but naive (virgin) T cells that have passed the selection process. The medulla is also more heterogeneous in appearance, containing in addition to lymphocytes many macrophages, “reticular cells”, abundant blood vessels and usually some thymic (Hassall’s) corpuscles. The latter are balls of squamoid epithelial cells that are usually keratinized and often contain keratohyaline granules. They probably are formed from defunct reticular cells, but their function, if any, is still unknown.
In the adult thymus, the lymphoid tissue is substantially less abundant and is typically replaced by fibroadipose tissue. Most important for histological identification is the fact that Hassall’s corpuscles persist.

ENCAPSULATED SECONDARY (PERIPHERAL) LYMPHOID ORGANS

A lymph node (“gland”) is an encapsulated lymphoid organ. Afferent lymphatics enter a subcapsular sinus by penetrating the capsule. There are many macrophages stationed in this sinus and is a site where metastatic cells may be lodged and start to proliferate. The cortex is divided into a superficial (containing lymphoid nodules) and a deep portion (paracortex). The superficial zone is “B cell-dependent”, since these cells represent a high proportion of the lymphocytes, while the paracortex has a predominance
of “T cells”. Many of the active follicles of the superficial cortex have germinal centers (and are secondary follicles). The largest cells in these follicles are macrophages and follicular dendritic cells. These are antigen-presenting cells and in the cytoplasm of some of these cells there are small particles of foreign material (“tingible bodies”). The paracortex also contains unusual vessels, the high endothelial venules (HEV), which are the site where most circulating lymphocytes enter the node.

The medulla is characterized by medullary cords and sinuses. The sinuses contain lymph and transmit lymph toward the efferent lymphatics at the hilus. The efferent lymph vessels and blood vessels enter and leave the node at the hilus.

The spleen has a capsule and trabeculae. Note that the largest trabeculae contain both arteries and veins whereas those of intermediate size contain only veins. There is scattered smooth muscles cells within the capsule and the substance of the trabeculae. The parenchyma of the organ is supported by a reticular cell stroma that provides support for the central regions of the spleen.

White pulp of the spleen is arranged so as to surround small (central) arteries thus forming a periarterial lymphatic sheath (PALS). The PALS is mainly populated by T cells. In places lymphoid nodules with germinal centers may develop next to the PALS, in which case the central artery appears eccentrically-located. As in lymph nodes, these nodules are the focus of B cells. In the intervening red pulp you will see cellular strands, the splenic cords (of Billroth) separating large, thin-walled sinusoids. These sinusoids have characteristic elongated endothelial cells (“stave cells”) through which red blood cells and white blood cells in the parenchyma of the red pulp squeeze to enter the sinusoid. These then coalesce into veins.
UNENCAPSULATED (aggregated and diffuse) SECONDARY LYMPHOID TISSUE

TONSILS

The **tonsils** (palatine, pharyngeal, and lingual) are incompletely encapsulated aggregates of lymphoid nodules that surround the entrance to the oral pharynx (tonsillar ring of Waldeyer). They are interposed in the path of both airborne and ingested pathogens. Not infrequently in young people they are “reactive” (enlarged) due to lymphocyte response to antigenic challenge. In the pre-antibiotic era surgical removal of chronically enlarged, inflamed tonsils was almost a routine office procedure. The epithelium covering the palatine tonsil is the stratified squamous, nonkeratinized epithelium of the oral cavity, while the pharyngeal tonsils (“adenoids”) are covered by respiratory epithelium. The palatine tonsil has well-developed “crypts”. The adenoids are located in the region of the auditory tubes and can block them when enlarged. This can lead to recurrent ear infections.
The substance of the tonsils is dominated by lymphoid nodules. The nodules are B cell domains, while the internodular zones are T cell dominated. Tonsils typically have efferent but no afferent lymphatic vessels.

GASTROINTESTINAL TRACT

There is extensive lymphoid tissue in the gastrointestinal tract to prevent invasion by the enormous numbers of bacterial located in the lumen. Much of this tissue is located in the lamina propria of the mucosal layer of the GI tract and has been termed GALT (gut-associated lymphoid tissue). In some areas (particularly the ileum and appendix) this lymphoid tissue can appear as follicles. In the ileum these are termed the Peyer’s patches located within the antimesenteric mucosa of the ileum.
CHECK LIST

Understand the role of each lymphoid organ and lymphoid tissue in the function of the immune system. Be able to distinguish these structures from one another.

THYMUS: Know the changes in the thymus with age. Identify and define:
- capsule
- medulla
- thymocytes
- Hassall’s (thymic) corpuscles
- involuted thymus

LYMPH NODE (GLAND): The structure of a lymph node is complex. Study the diagram in the lab manual. Understand the flow of lymph and blood within the node. Identify and define:
- capsule, trabeculae
- subcapsular sinus, cortical sinus, medullary sinus
- hilum
- afferent and efferent lymph vessels
- superficial (outer) cortex, follicles with germinal centers, B lymphocytes
- follicular dendritic cells
- paracortex (inner cortex), T lymphocytes
- high endothelial venules (HEV)
- medullary cords- reticular cells
- macrophages
- plasma cells

SPLEEN: Recognize the importance of the spleen and the relationship of its structure to its functions. Identify and define:
- capsule, trabeculae
- white pulp
- central arteries
- macrophages
- reticular cells
- periarterial lymphatic sheath (PALS), T lymphocytes
- secondary follicles, germinal center, B lymphocytes

UNENCAPSULATED LYMPHOID TISSUE: GALT & MALT.
- Tonsils covered with stratified squamous epithelium
  - lymphoid nodules, B lymphocytes
  - internodular zones, T lymphocytes
  - ring of Waldeyer
  - crypts
- Appendix with epithelial crypts (no villi)
  - lymphoid nodules (may have germinal centers)
- Peyer’s patches