LYMPHOID ORGANS

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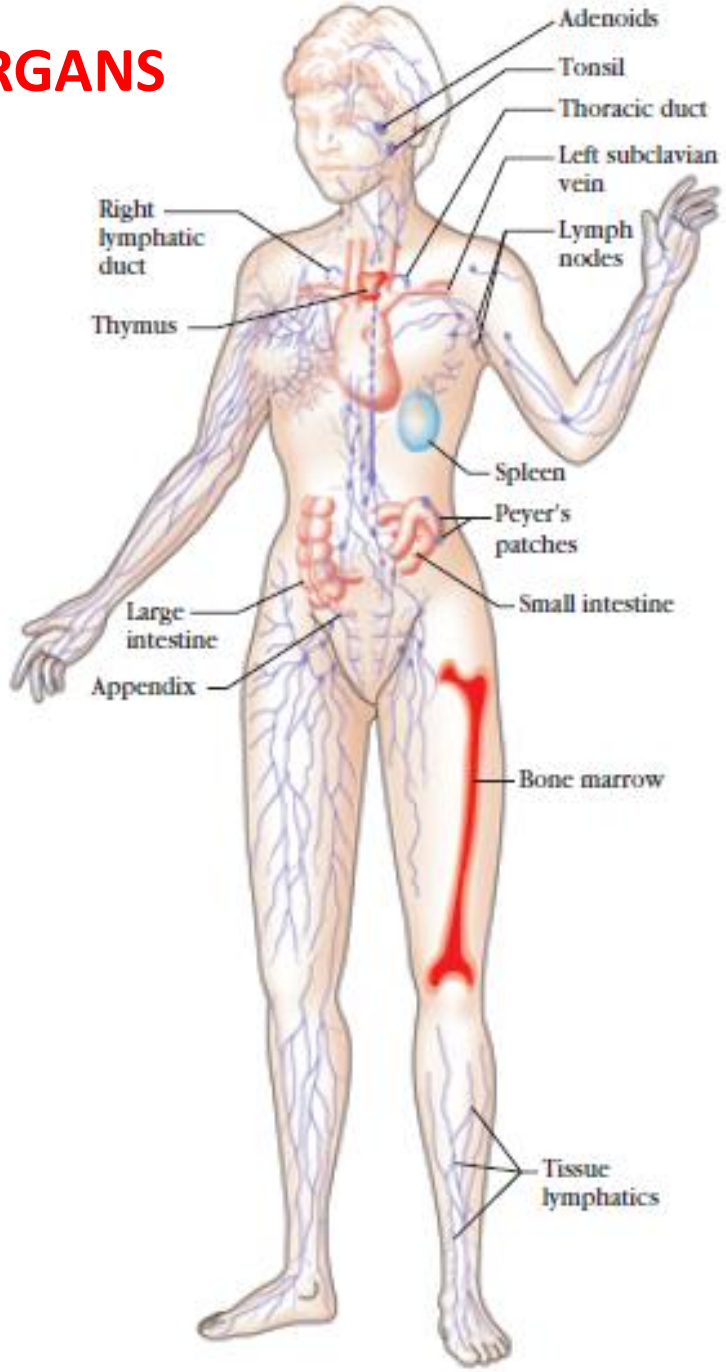
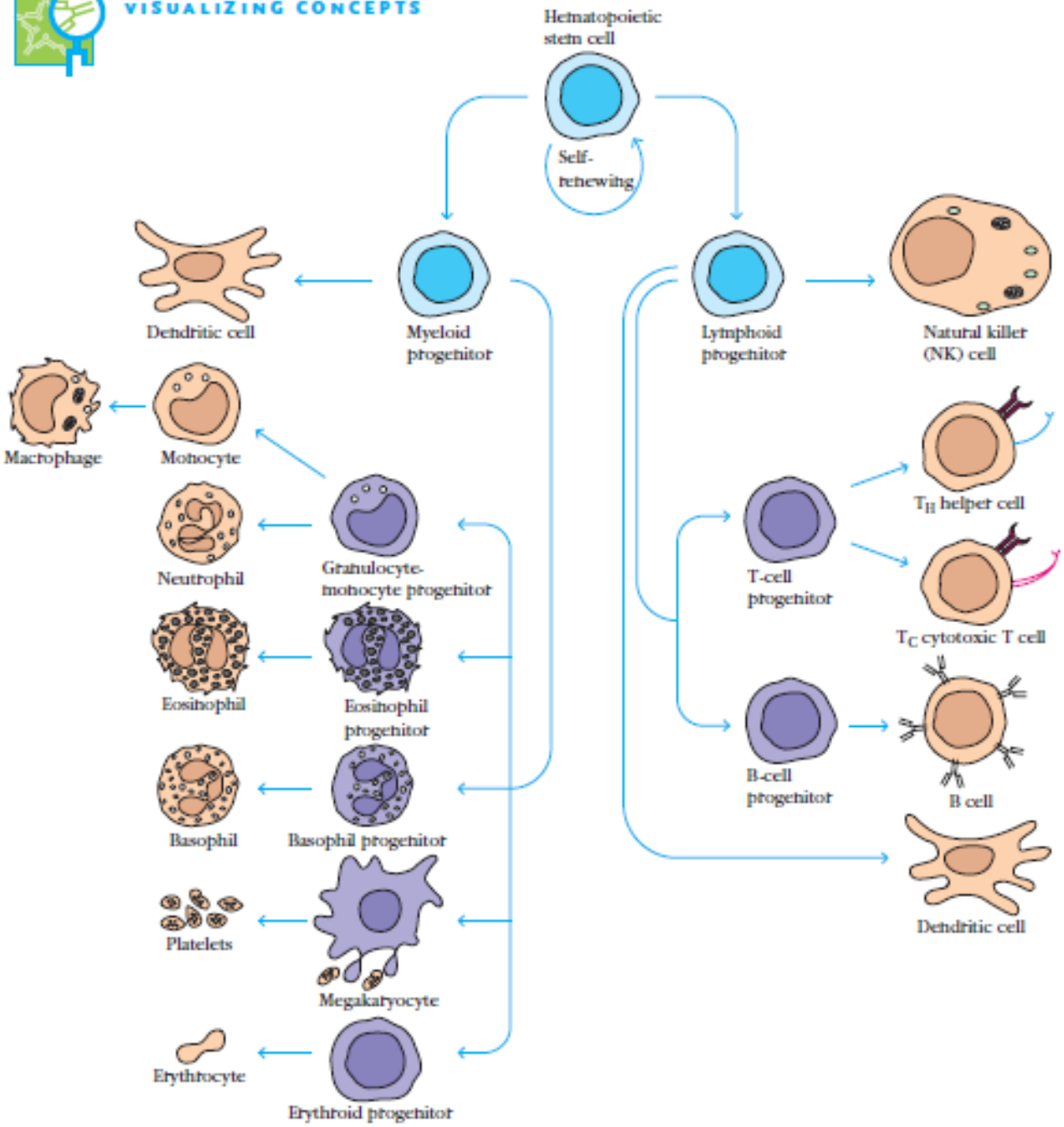


VISUALIZING CONCEPTS



Organs of the Immune System

A number of morphologically and functionally diverse organs and tissues have various functions in the development of immune responses. These can be distinguished by function as the **primary and secondary lymphoid organs**.

The thymus and bone marrow are the primary lymphoid organs, where maturation of lymphocytes takes place.

The lymph nodes, spleen, and various mucosalassociated lymphoid tissues (MALT) such as gut-associated lymphoid tissue (GALT) are the secondary (or peripheral) lymphoid organs, which trap antigen and provide sites for mature lymphocytes to interact with that antigen.

In addition, **tertiary lymphoid 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. 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.

Primary Lymphoid Organs

Immature lymphocytes generated in hematopoiesis mature and become committed to a particular antigenic specificity within the primary lymphoid organs. Only after a lymphocyte has matured within a primary lymphoid organ is the cell **immunocompetent (capable of mounting an immune response).**

T cells arise in the **thymus, and in many** mammals—humans and mice for example—B cells originate in **bone marrow.**

THYMUS

The thymus is the site of T-cell development and maturation.

It is a flat, bilobed organ situated above the heart. Each lobe is surrounded by a capsule and is divided into lobules, which are separated from each other by strands of connective tissue called trabeculae.

Each lobule is organized into two compartments:
the outer compartment, or ***cortex,*** *is densely packed* with immature T cells, called thymocytes, whereas the inner compartment, or ***medulla****, is sparsely populated with thymocytes.*

FUNCTION OF THE THYMUS

The function of the thymus is to generate and select a repertoire of T cells that will protect the body from infection.

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

However, 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.

The thymus induces the death of those T cells that cannot recognize antigen-MHC complexes and those that react with self-antigen– MHC and pose a danger of causing autoimmune disease.

THE THYMUS AND IMMUNE FUNCTION

Other evidence of the importance of the thymus comes from studies of a congenital birth defect in humans **(DiGeorge's syndrome) and in certain mice (nude mice) in which the thymus fails to develop. In both** cases, there is an absence of circulating T cells and of cell-mediated immunity and an increase in infectious disease.

Aging is accompanied by a decline in thymic function. This decline may play some role in the decline in immune function during aging in humans and mice.

The thymus reaches its maximal size at puberty and then atrophies, with a significant decrease in both cortical and medullary cells.

BONE MARROW

In humans and mice, bone marrow is the site of B-cell origin and development.

Arising from lymphoid progenitors, 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.

Like thymic selection during Tcell maturation, a selection process within the bone marrow eliminates B cells with self-reactive antibody receptors.

Bone marrow is not the site of B-cell development in all species. In birds,
a lymphoid organ called the bursa of Fabricius, a lymphoid tissue associated with the gut, is the primary site of B-cell maturation.

In mammals such as primates and rodents, there is no bursa and no single counterpart to it as a primary lymphoid organ. In cattle and sheep, the primary lymphoid tissue hosting the maturation, proliferation, and diversification of B cells early in gestation is the fetal spleen.

Later in gestation, this function is assumed by a patch of tissue embedded in the wall of the intestine called the ileal Peyer's patch,which contains a large number of B cells

Lymphatic System

As blood circulates under pressure, its fluid component **(plasma) seeps through the thin wall of the capillaries into** the surrounding tissue.

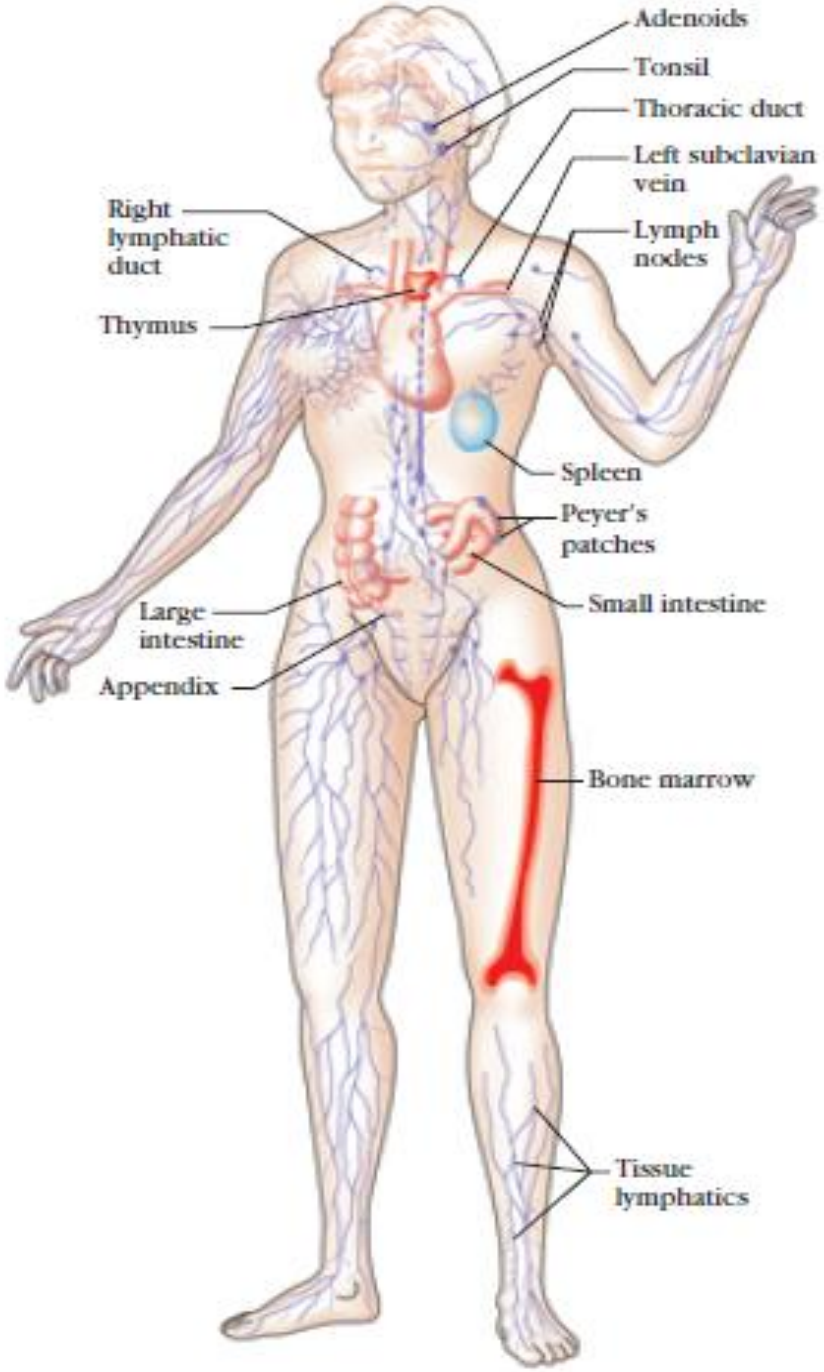
Much of this fluid, called **interstitial fluid, returns to the blood through the capillary membranes.** The remainder of the interstitial fluid, now called **lymph,** flows from the spaces in connective tissue into a network of tiny open lymphatic capillaries and then into a series of progressively larger collecting vessels called **lymphatic vessels.**

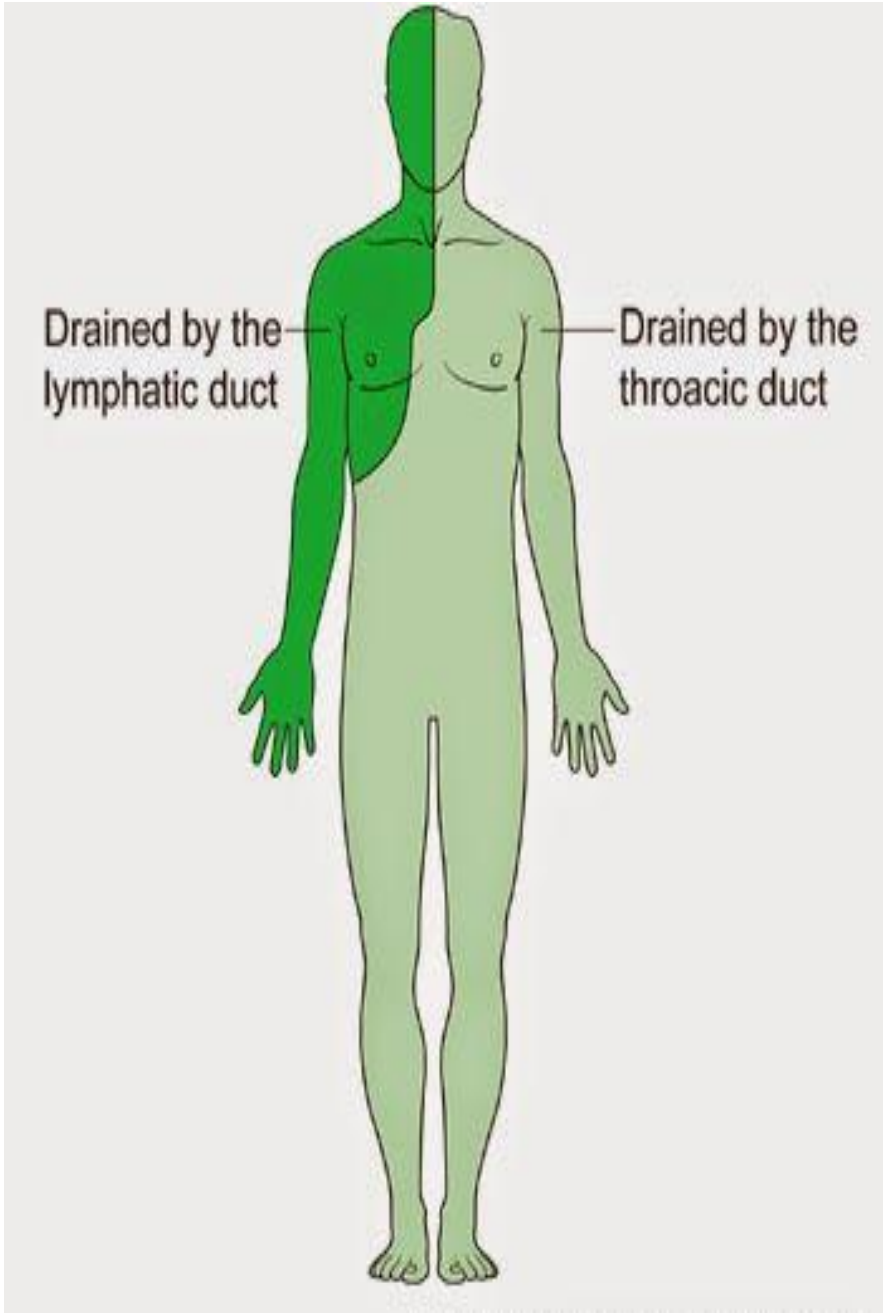
The largest lymphatic vessel, the thoracic duct, empties into the left subclavian vein near the heart.

The lymphatic system captures fluid lost from the blood and returns it to the blood, thus ensuring steady-state levels of fluid within the circulatory system.

The heart does not pump the lymph through the lymphatic system; instead the flow of lymph is achieved as the lymph vessels are squeezed by movements of the body's muscles.

A series of one-way valves along the lymphatic vessels ensures that lymph flows only in one direction.


Adenoids
Tonsil
Thoracic duct
Left subclavian vein
Lymph nodes
Right lymphatic duct
Thymus
Spleen
Peyer's patches
Small intestine
Large intestine
Appendix
Bone marrow
Tissue lymphatics


Drained by the lymphatic duct
Drained by the throacic duct

When a foreign antigen gains entrance to the tissues, it is picked up by the lymphatic system (which drains all the tissues of the body) and is carried to various organized lymphoid tissues such as lymph nodes, which trap the foreign antigen.

As lymph passes from the tissues to lymphatic vessels, it becomes progressively enriched in lymphocytes.

Thus, the lymphatic system also serves as a means of transporting lymphocytes and antigen from the connective tissues to organized lymphoid tissues where the lymphocytes may interact with the trapped antigen and undergo activation.

Secondary Lymphoid Organs

Various types of organized lymphoid tissues are located along the vessels of the lymphatic system. Some lymphoid tissue in the lung and lamina propria of the intestinal wall consists of diffuse collections of lymphocytes and macrophages.

Other lymphoid tissue is organized into structures called lymphoid follicles, which consist of aggregates of lymphoid and nonlymphoid cells surrounded by a network of draining lymphatic capillaries.

Lymph nodes and the spleen are the most highly organized secondary lymphoid organs; they comprise not only lymphoid follicles, but additional distinct regions of T-cell and B-cell activity, and they are surrounded by a fibrous capsule.

Less-organized lymphoid tissue, collectively called mucosal-associated lymphoid tissue (MALT), is found in various body sites.

MALT includes Peyer's patches (in the small intestine), the tonsils, and the appendix, as well as numerous lymphoid follicles within the lamina propria of the intestines and in the mucus membranes lining the upper airways, bronchi, and genital tract.

Lymph nodes are the sites where immune responses are mounted to antigens in lymph.

The spleen plays a major role in mounting immune responses to antigens in the blood stream.

It is a large, ovoid secondary lymphoid organ situated high in the left abdominal cavity.

While lymph nodes are specialized for trapping antigen from local tissues, the spleen specializes in filtering blood and trapping blood-borne antigens; thus, it can respond to systemic infections.

Unlike the lymph nodes, the spleen is not supplied by lymphatic vessels. Instead, bloodborne antigens and lymphocytes are carried into the spleen through the splenic artery.

The effects of splenectomy on the immune response depends on the age at which the spleen is removed. In children, splenectomy often leads to an increased incidence of bacterial sepsis caused primarily by *Streptococcus pneumoniae, Neisseria meningitidis, and Haemophilus influenzae.*

***Splenectomy in* adults has less adverse effects, although it leads to some increase in blood-borne bacterial infections (bacteremia).**

MUCOSAL-ASSOCIATED LYMPHOID TISSUE (MALT)

The mucous membranes lining the digestive, respiratory, and urogenital systems are the major sites of entry for most pathogens.

These vulnerable membrane surfaces are defended by a group of organized lymphoid tissues known collectively as **mucosal-associated lymphoid tissue (MALT).**

Structurally, these tissues range from loose, barely organized clusters of lymphoid cells in the lamina propria of intestinal villi to well-organized structures such as the familiar tonsils and appendix, as well as Peyer's patches, which are found within the submucosal layer of the intestinal lining.

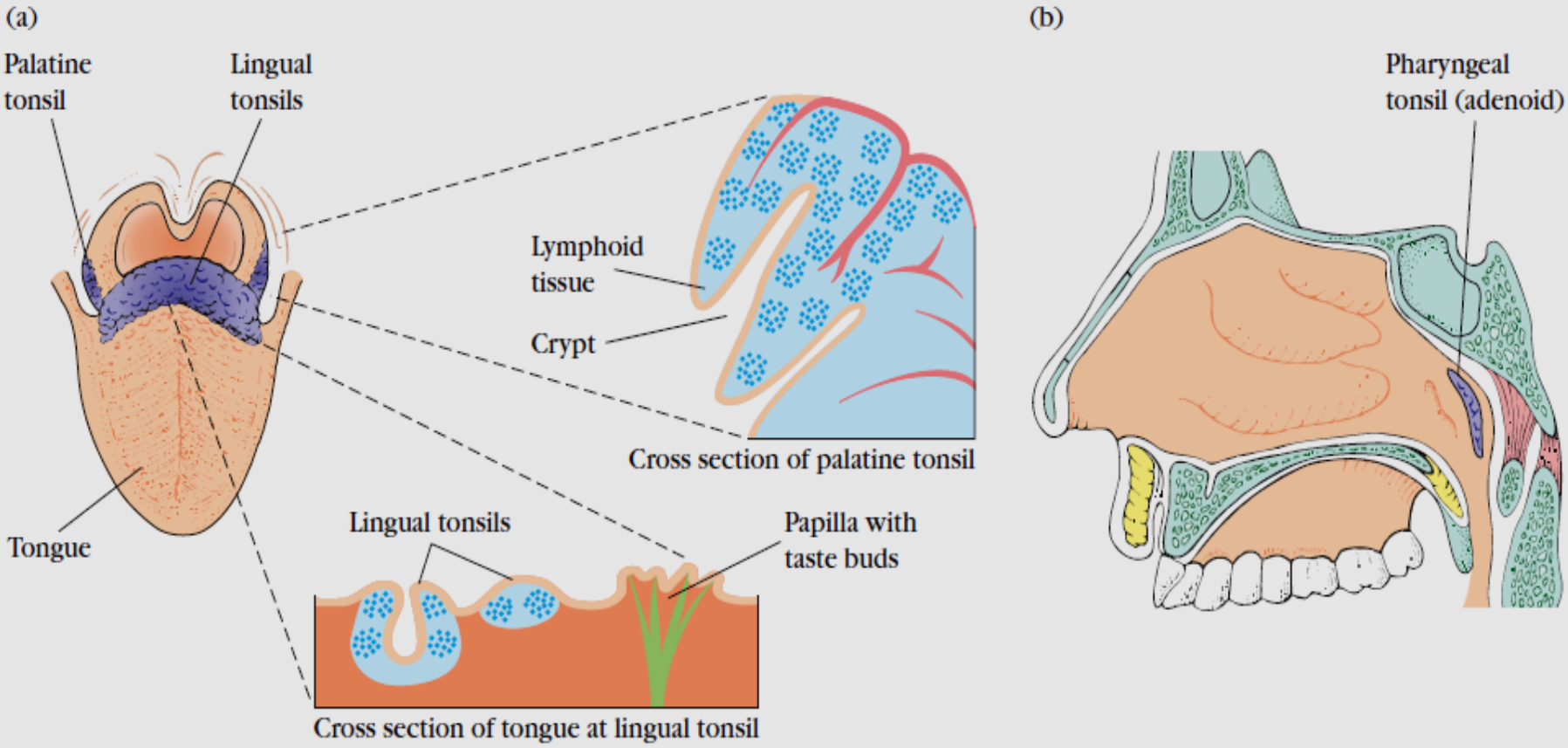
The functional importance of MALT in the body's defense is attested to by its large population of antibody-producing plasma cells, whose number far exceeds that of plasma cells in the spleen, lymph nodes, and bone marrow combined.

TONSILS

The tonsils are found in three locations: lingual at the base of the tongue; palatine at the sides of the back of the mouth; and pharyngeal (adenoids) in the roof of the nasopharynx .

All three tonsil groups are nodular structures consisting of a meshwork of reticular cells and fibers interspersed with lymphocytes, macrophages, granulocytes, and mast cells.

The tonsils defend against antigens entering through the nasal and oral epithelial routes.


(a)
Palatine tonsil
Lingual tonsils
Lymphoid tissue
Crypt
Cross section of palatine tonsil
Tongue
Lingual tonsils
Papilla with taste buds
Cross section of tongue at lingual tonsil
(b)
Pharyngeal tonsil (adenoid)