Chapter 5
Anatomy of the Lymphatic System and Its Disorders

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Definition of the Lymphatic System

Anatomical

The lymphatic system is a bodily complex composed of interstitial space, body cavities, and lymphatics (all of which form the lymphatic space), containing tissue fluid and lymph, migrating immune cells, and organized lymphoid tissue (Fig. 5.1). The total mass comprising extracellular fluid, lymph and lymphoid cells is estimated to be 13 kg. The cell mass alone approximates 1 kg,[1] Lymph nodes and lymphoid cell aggregates, identified as lamina propria and Peyer's patches in the intestine, contain the main aggregates of the recirculating lymphocytes.The lymphoid organs (thymus, spleen and bone marrow) are contained within the blood system and have no lymphatic drainage; however, their cells circulate in the loop of blood–tissue–space–lymphatics–lymphoid tissue–blood. In this sense, they belong to the lymphatic system.[2–4]

Functional

The lymphatic system (a) secures the chemical environment of the tissues, regulating water volume and stabilizing tissue fluid proteins at physiological concentrations; (b) maintains a normal supply of nutrients and removal of waste products from parenchymatous cells; (c) serves as a reservoir that accumulates surplus tissue fluid under conditions of lymph flow obstruction or excessive lymph production; (d) regulates

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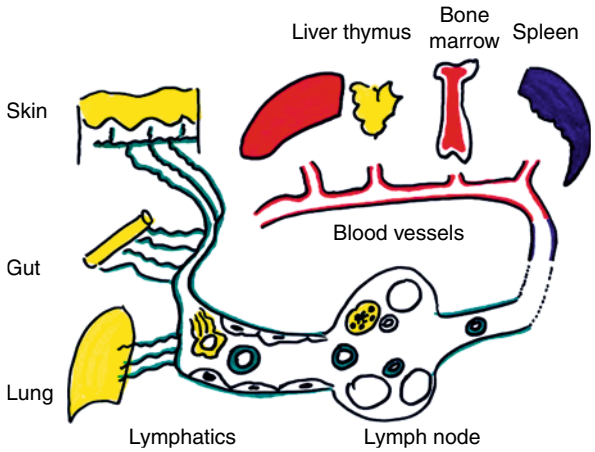

Fig. 5.1 Schematic presentation of the lymphatic system. Skin, gut, and lungs are naturally exposed to the environment and have the highest density of lymphatics draining to the regional lymph nodes. Any environmental antigen that penetrates the epithelial layer of these organs is immediately recognized by local dendritic cells and transported with tissue fluid and the lymph stream to the nodes. Organs such as the thymus, spleen, bone marrow, and even the liver supply the lymph nodes with immune cells. Some of these cells re-circulate among blood–tissues–lymphatics–lymph nodes in the process of immune surveillance. The antigen-laden Langerhans' (veiled) cells and lymphocytes are seen in afferent lymphatics. In the nodes, the antigens stimulate a complex cellular response based on cooperation between various cellular subsets. Moreover, a continuous process of filtration (extravasation) of plasma nutritive and immune proteins takes place in the interstitium. They flow toward the lymphatics. Some proteins are synthesized and secreted by local parenchymatous and migrating cells. In skin, these are keratinocytes and resident immune cells, in the gut, epithelial cells and lymphocytes, and in the lamina propria and in the lung, epithelial cells, and macrophages

the process of recirculation of lymphocytes that survey the integrity of tissue; (e) recognizes microbial antigens through pathogen-associated molecular pattern by immune (dendritic cells, tissue macrophages) and endothelial cells that migrate through the lymph; (f) participates in tumor antigen recognition, active transport of tumor cells to lymph nodes, either eliminating tumor cells or assisting them to proliferate, creating tolerance to tumors; (g) eliminates the host senescent disintegrated cells and cellular debris as well as cellular chemical components from traumatized tissues. Recognition of auto-antigens is achieved through the debris-associated molecular pattern by immune cells contained in lymph.

Lymph Flow Pathways

Lymphatics are found throughout the body, with the exception of the central nervous system (Fig. 5.2). The interstitial space and lymph vessel space form a common "lymph space." The initial lymph spaces are mere intercellular expanses within the

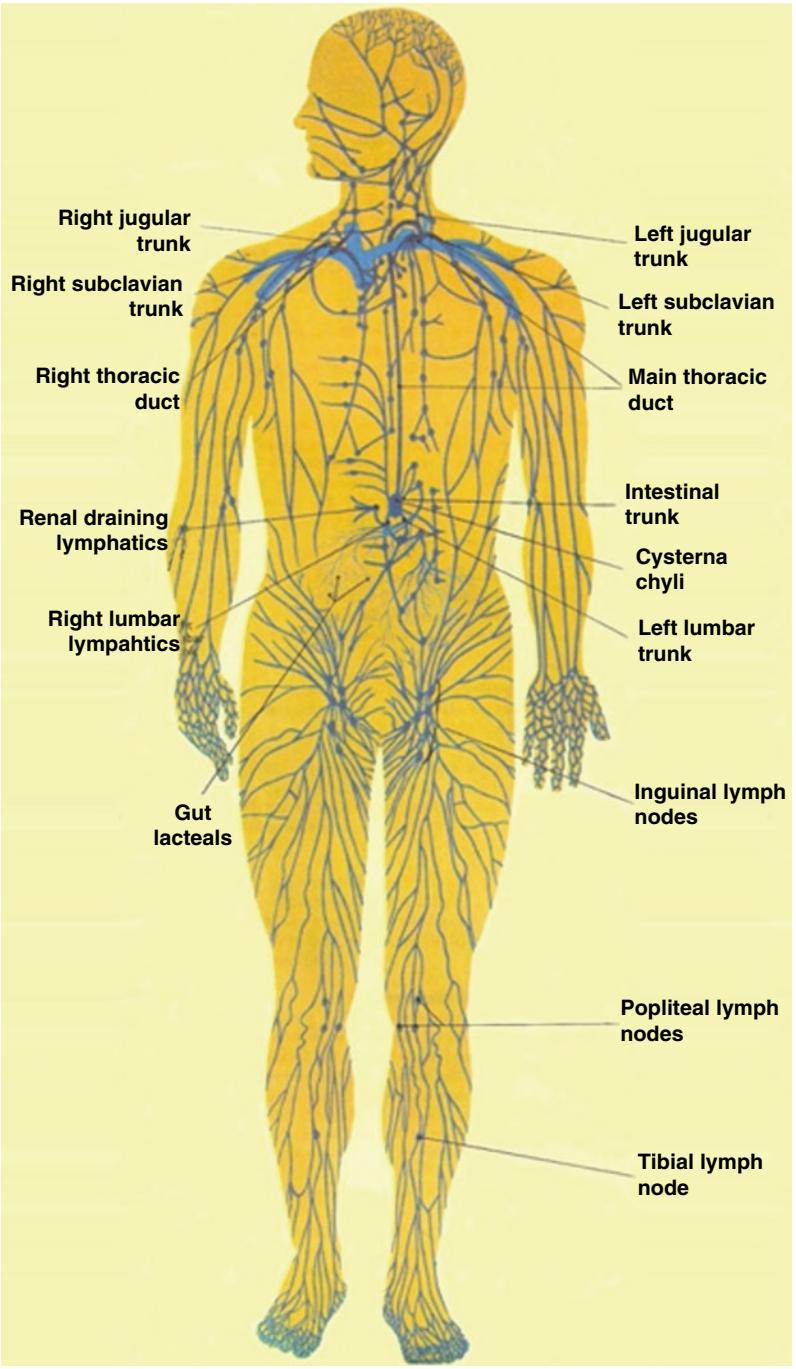

Fig. 5.2 General view of the distribution of lymphatic collecting vessels and nodes in man

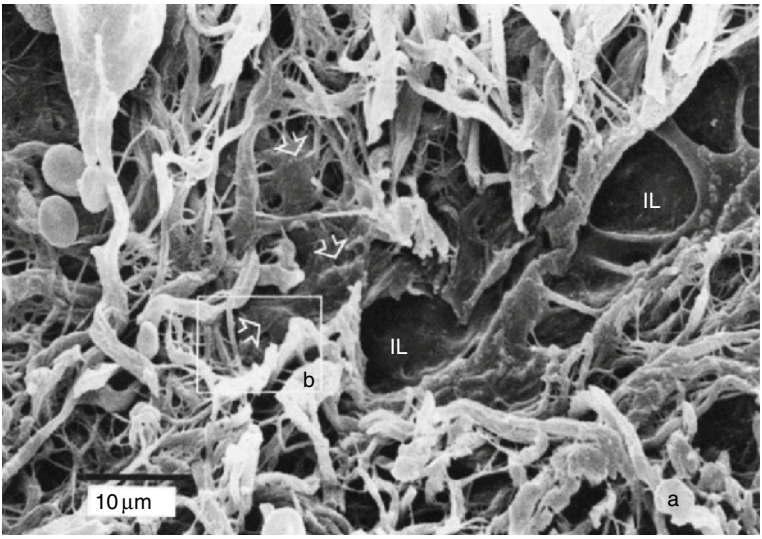

Fig. 5.3 Electron micrograph of the skin interstitial space. There is a network of matrix fibers, and among them, openings of the initial lymphatics (IL). The interstitial space, with millions of small inter-fiber spaces, is freely connected with the initial lymphatics. This allows a free plasma filtrate–tissue fluid flow to the lymphatic vessel system. Endothelial cells in the initial lymphatics possess chemoattractant properties directing immune cell traffic to their lumina

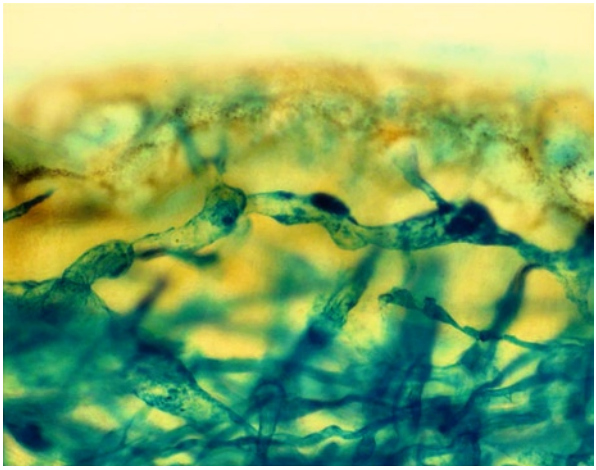

Fig. 5.4 The subepidermal lymphatic plexus in normal lower limb skin stained in tissue blocks with Paris Blue. Note horizontally- and vertically-oriented lymphatics with competent valves. The network is rather irregular. This depends on the site from which the specimen is harvested. Interestingly, the subepidemal plexus is preserved even in the most advanced stages of obstructive lymphedema

connective tissue. They have no endothelial lining (Fig. 5.3). They converge to the lymphatic vessels. These resemble veins, as they possess an internal layer of endothelium and a middle layer composed of intermingled muscular and collagen fibers. The external coat is built of scattered fibroblasts. There is no border between small (100–500 μ) lymphatics and the surrounding connective tissue. Lymphatics have numerous endothelial unidirectional valves (Fig. 5.4). They divide and anastomose very

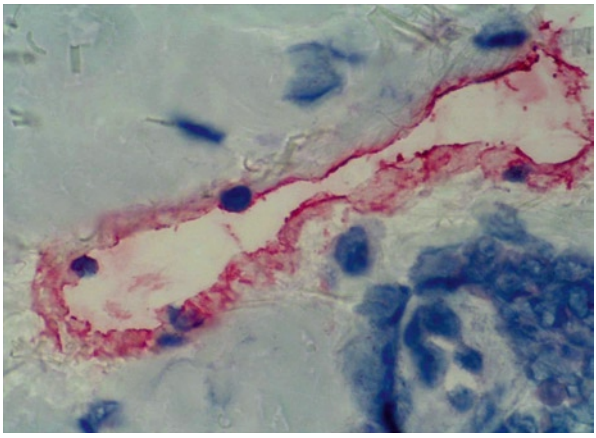

Fig. 5.5 Histological specimen of calf skin with a lymphatic vessel located in the dermis, stained for LYVE1 antigen, specific for lymphatic endothelial cells. This vessel is intermediate between the subepidermal plexus and collecting trunks. Close to the lymphatic is a blood capillary, which is LYVE1-negative, x 600

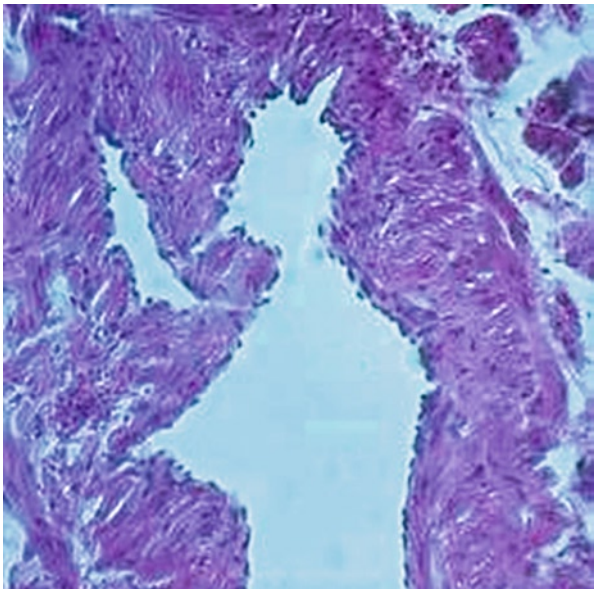

Fig. 5.6 Histological picture of a normal calf lymphatic collecting trunk. Note lining with endothelial cells and multiple irregularly distributed muscle cells and collagen fibers. The irregular shape of the lumen occurs because empty lymphatics collapse under in vivo conditions. Collecting lymphatics of the lower leg usually contain more muscle fibers than those of the upper limbs. They contract rhythmically and propel lymph centripetally. H&E stain, x 200

freely, and form a network depending on the local density of connective tissue. The initial-to-interconnecting dermal lymphatics have LYVE1-positive endothelial cells (Fig. 5.5). Lymph vessels that are approaching a lymph node are called afferent, while those leaving are the efferent lymphatics (Fig. 5.6). They are LYVE1-negative. Each lymph node is supplied with afferent lymph that flows through its vast sinuses toward the hilum and the efferent vessels (Fig. 5.7). In the intestine, lymphatics are called lacteals. They begin in the lymphatic spaces in the villi and end up in mesenteric nodes. The efferent vessels merge with the retroperitoneal cysterna chyli. This is an irregular structure that receives lymph not only from the gut but also from the liver, the pancreas and the stomach. Its continuation is the main thoracic duct, joining

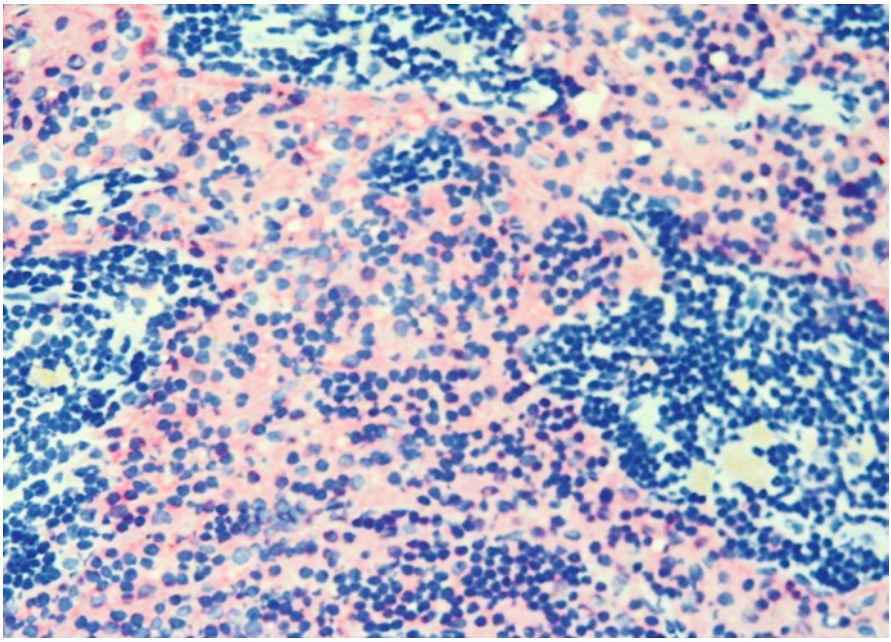

Fig. 5.7 Histological appearance of an inguinal lymph node. Lymphatic endothelial cells in paracortical sinuses stain red. The sinuses are filled with migrating lymphocyte and large cells, such as Langerhans' and macrophage-like cells. Lymph delivered to the node through afferent lymphatics flows along sinuses to the efferent lymphatics. Note that sinuses cover a large area of the node cross-section. In pathological conditions of long duration, the lymph nodes become fibrotic and sinuses become obstructed. LYVE1 antigen stain, x200

the venous angle where lymph flows to the blood circulation. Lung lymphatics drain into bronchial nodes and further to the right thoracic duct. Lower limb lymphatics are divided into the superficial and deep lymph vasculature. The superficial vessels lead to the inguinal nodes, whereas the deep vessels run along large blood vessels to the deep inguinal nodes. In their transit, they traverse one or two popliteal nodes. Moving cephalad, there are iliac lymphatics that join the distal part of cysterna chyli. Upper limb lymphatics run to the axillary lymph nodes. The exact position of the various groups of nodes is very important from a medical point of view. Damage to the lymphatics and nodes with subsequent obstruction of lymph flow brings about dysfunction of the organ distal to the obstruction. With the passage of time, bacterial colonization, immune cell infiltration and, ultimately, fibrosis develop.

Functional Classification of the Lymphatic Pathways

The lymphatics most commonly affected by noxious factors are those of skin, gut, and lung. These vessels become damaged by infections, trauma, and surgery. The

effect is tissue fluid stasis in the interstitial space and stasis of lymph in afferent lymphatics. The levels at which the lymphatic pathways are damaged by noxious factors are: (a) the subepidermal plexus, (b) dermal lymphatics, (c) collecting trunks, and (d) lymph node sinuses. The histological appearance at these sites is depicted in Figs. 5.3, 5.4, 5.5, and 5.6. This classification is important for rational therapy.

Skin and Subcutaneous Tissue

The subepidermal and dermal lymphatics directly participate in soft tissue infections and mechanical injury. (a) The most resistant to the impact of pathological factors are the subepidermal vessels. High plasma filtration rate and lymph formation in the dermal papillae presumably keep these minute vessels open, sometimes forming epidermal vesicles. (b) The collecting trunks become dilated during the acute and chronic phases of skin inflammation and after trauma of soft tissues and bones. With the passage of time, they lose spontaneous contractility and their lumina become obliterated by fibrous elements. (c) Chronic inflammation of soft tissues is reflected by a reaction in lymph nodes. They become depleted of lymphoid cells and replaced by fibrous tissue. Radiotherapy is another factor that damages lymph node structure. The fibrotic lymph nodes are an obstacle to lymph flow (see the chapter on excisional surgery). (d) Following surgical removal of lymph nodes and irradiation (upper and lower limb), the afferent lymphatics gradually become obliterated through their entire length (the die-back phenomenon).

Gut Lymphatics

Inflammatory processes in the gut bring about: (a) Dilatation of vessels and enlargement of mesenteric lymph nodes in the early stages, and (b) Fibrosis of vessels and nodes in the late stages. Intestinal lymph exudes through gut serosa to the peritoneal cavity (chyloperitoneum) (c) Inflammation and mechanical injury may damage the cysterna chili and the thoracic duct. Lack of outflow of the gut lymph to the venous system leads to dilatation of retroperitoneal lymphatics and backflow to the genitals and lower limbs.

Lung Lymphatics

The lung lymphatic system is difficult to evaluate clinically. Histopathologically, fibrosis of lymphatics and bronchial nodes is reported in chronic inflammatory conditions.

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