Diffuse Lymphatic Tissue

1. Diffuse lymphatic tissue (arrow) located between and around simple intestinal glands of the jejunum.
2. A lymphatic nodule with a light staining germinal center (arrow) within the lamina propria of the ileum.
3. A region of a lymphatic nodule illustrating a germinal center (left) and a cuff of small lymphocytes to the right. Note the large lymphocytes (lymphoblasts) at the arrows.
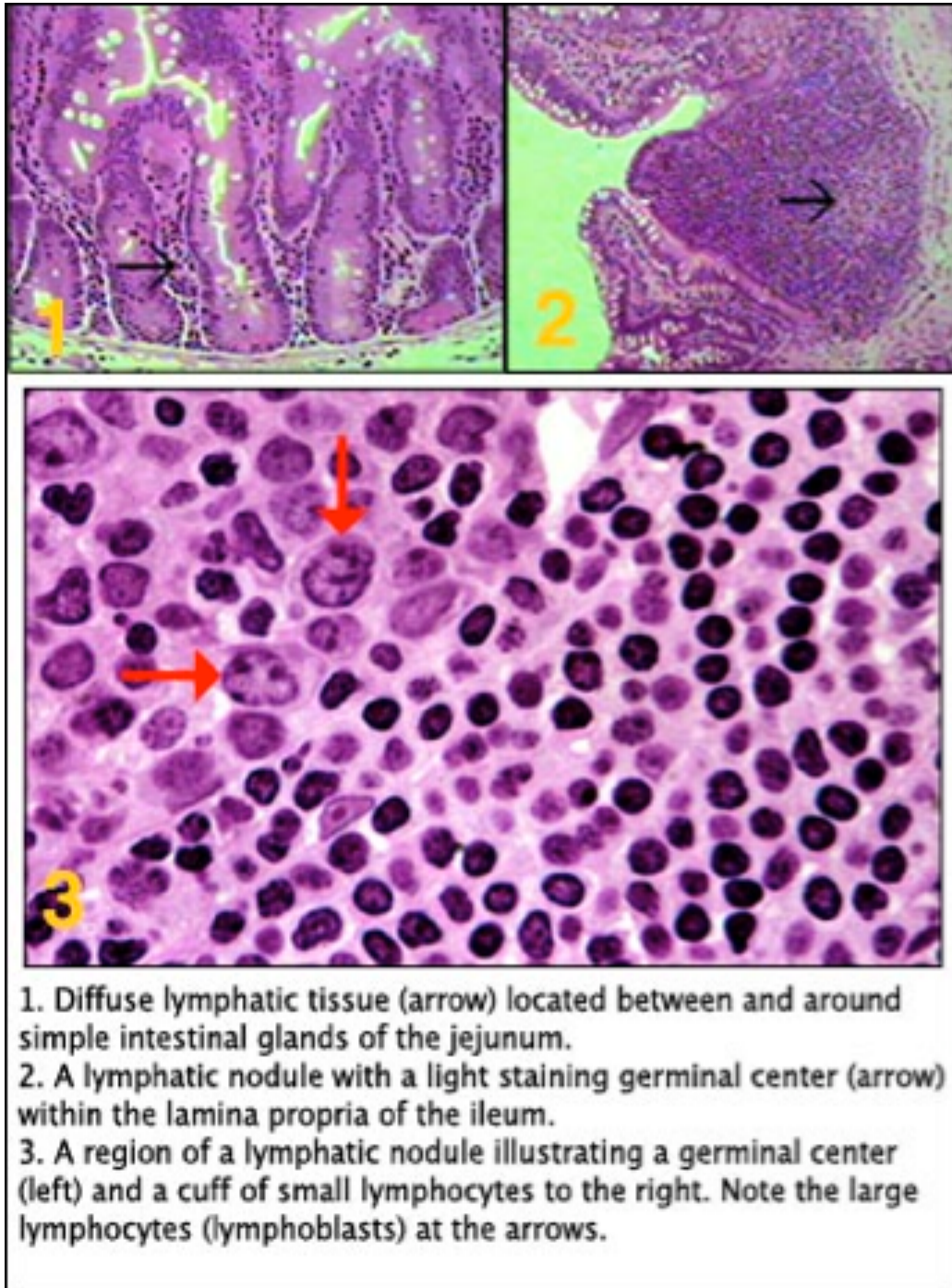
Scattered throughout the body are various lymphatic elements that form part of the body's defense system. Generally distributed so that noxious agents entering the body soon encounter them, lymphatic tissues are prominent in the connective tissue coats of the gastrointestinal, respiratory, and urogenital tracts. Here it is generally referred to as mucosa-associated lymphoid tissue (MALT); if specifically associated with the gastrointestinal tract it is termed gut-associated lymphoid tissue (GALT); if associated with intrapulmonary bronchi it is referred to as bronchi-associated lymphatic tissue (BALT). Lymphatic structures also are

inserted into the lymph drainage and blood circulation, where they serve to filter lymph and blood. Eventually, all the body fluids are filtered through some form of lymphatic structure. Lymphatic cells may be concentrated within the connective tissue and form the lymphatic tissues, or they may be organized into discrete structures, the lymphatic organs.

Classification

Lymphatic tissue represents a specialization within the connective tissue compartment and, as for all connective tissues, can be classified according to the type of fiber that is present. On this basis, lymphatic tissue can be defined as a reticular tissue. It also contributes cells (lymphocytes) to the blood, so it is a hemopoietic tissue. In common with bone marrow, the cellular content exceeds the intercellular material. Subdivision of lymphatic tissue into diffuse and nodular depends on the arrangement and concentration of the cells, not on differences in fiber types.

Cells of Lymphatic Tissues

The cells of lymphatic tissue are present as fixed and free cells. Fixed cells are the reticular cells responsible for the formation and maintenance of reticular fibers. The fixed cells of lymphatic tissue and reticular fibers, the two elements of the reticular network, are intimately related, and the fibers often reside in deep grooves in the cytoplasm of the reticular cells. By light microscopy, reticular cells appear as elongated or stellate elements with round or oval, palely stained nuclei and scant, lightly basophilic cytoplasm. The cytoplasm is more voluminous than is apparent under the light microscope, since the bulk of it is spread thinly along the reticular fibers. Electron microscopy reveals a variable amount of endoplasmic reticulum and a moderately well developed Golgi apparatus; other organelles are relatively inconspicuous. As in bone marrow, lymphatic reticular cells are incapable of giving rise to other cell types and show no special capacity for phagocytosis. The remaining cells of lymphatic tissue are contained within the spaces of the reticular network and constitute the free cells. The bulk of these are lymphocytes, but macrophages and plasma cells also are present in variable numbers. The term lymphocyte encompasses a spectrum of cells that possess some general common features. As a class they show a rounded, centrally placed nucleus; their cytoplasm shows variable degrees of basophilia and lacks specific granules. The lymphocyte population customarily is divided into small, medium, and large lymphocytes on the basis of their size, nuclear morphology, and intensity of cytoplasmic staining. Although useful for purposes of description, such a subdivision is somewhat artificial because between the small and large types there is a continuum of cell sizes and morphologies. Small lymphocytes are the most numerous. As seen in lymphatic tissues, these cells are 4 to 8 μm in diameter and contain a deeply stained nucleus surrounded by a thin rim of cytoplasm that may be expanded slightly at one side of the cell. Although rounded in shape in the blood or lymph, in tissues the cells are crowded together and assume various polyhedral shapes due to compression. The rounded or slightly indented nucleus contains a nucleolus that is barely discernible unless thin sections are examined. The chromatin is present as scattered masses of heterochromatin with some small patches of euchromatin. Electron microscopy shows a small Golgi complex, a few mitochondria and centrioles located in the region of the nuclear indentation, a moderate number of ribosomes, and a few lysosomes scattered throughout the cytoplasm. Granular endoplasmic reticulum is sparse. Medium lymphocytes (prolymphocytes) range from 8 to 12 μm in diameter. Their nuclei are somewhat larger and more palely stained because of greater

dispersion of the chromatin, and the nucleoli are larger and better defined. The cytoplasm is more voluminous and shows a greater basophilia because of an increased number of ribosomes. Large lymphocytes (lymphoblasts) range in size from 15 to 20 μm. Occasionally even larger forms (25 to 30 μm) may be found, and some authors reserve the term lymphoblast for these cells. The nucleus is rounded, palely stained, and contains one or two prominent nucleoli, and the fine chromatin is more uniformly dispersed. The basophilic cytoplasm is abundant and contains free ribosomes and polysomes. The centrosomal region and Golgi complex are more highly developed and mitochondria are abundant, but granular endoplasmic reticulum remains scanty. In the development of lymphocytes, it generally is accepted that the direction of maturation is from large (lymphoblast) to small. However, this progression is complicated by the ability of small lymphocytes to respond to antigenic agents, reassume a blast like appearance and character, and reproduce additional small lymphocytes and plasma cells. Plasma cells (plasmocytes) vary in size from 6 to 20 μm in diameter. By light microscopy, the cell presents a rounded, somewhat elongated or polyhedral form, depending on its location. The nucleus is round to oval and usually is eccentrically placed. This is most obvious in elongated cells, but in rounded cells the nucleus may be only slightly eccentric in its placement. The chromatin is dispersed in coarse heterochromatic blocks along the inside of the nuclear envelope, giving the nucleus a clock face or spoke wheel appearance. Binucleate cells may be seen. The cytoplasm is deeply basophilic except for a prominent pale area adjacent to the nucleus. This area represents a negative image of the Golgi apparatus. Occasionally, plasma cells contain globular or crystalline inclusions in their cytoplasm, the best known of which are Russell's bodies. These are round or ovoid acidophilic inclusions of variable size that represent incomplete antibody. In electron micrographs the characteristic feature of plasma cells is the extensive development of the granular endoplasmic reticulum, which almost completely fills the cytoplasm. The cisternae may be flat and parallel or distended with flocculent material. Free ribosomes are numerous, and a well-developed Golgi apparatus and centrioles are present in the paranuclear area. Russell's bodies, when present, are contained within distended cisternae of the granular endoplasmic reticulum. Plasma cells are sessile and ultimately degenerate. Despite the massive amounts of endoplasmic reticulum, most antibody production is carried out by forms that are intermediate between lymphocytes and plasma cells. The precursors of plasma cells are B-lymphocytes. The macrophages of lymphatic tissue are part of a system of mononuclear phagocytes widely spread throughout tissues and organs. The cells vary from 10 to 20 μm in diameter and have oval-, kidney-, or horseshoe-shaped nuclei in which one or more nucleoli are present. The cytoplasm is abundant and lightly basophilic and may be vacuolated or contain ingested material. Unless the cytoplasm does contain phagocytosed matter, the macrophage is difficult to distinguish from other large mononuclear cells including active fibroblasts. In electron micrographs, the cytoplasm shows numerous folds, processes, and invaginations of the surface and contains the usual assembly of organelles. The Golgi apparatus is conspicuous, lysosomes are numerous, and residual bodies may be prominent. As are macrophages elsewhere, those in lymphatic tissue are derived from blood monocytes.

Diffuse Lymphatic Tissue

Diffuse lymphatic tissue is a constituent of lymphatic organs and also is widely dispersed along mucous membranes. It appears as a rather loose aggregate of cells and shows no distinct demarcation from surrounding tissue with which it gradually merges. Basically, diffuse lymphatic tissue consists of a three-dimensional array of reticular fibers and their associated

reticular cells. The two form a sponge like framework pervaded by large numbers of cells, chief of which are lymphocytes. Diffuse lymphatic tissue is particularly prominent in the connective tissue that underlies the epithelium of the intestine. Here the lymphatic tissue, in association with the lining epithelium, produces antibody that bathes the luminal surface. Any antigen that does penetrate the epithelial lining induces an immune response in the lymphatic tissue, the cellularity of which is related to the bacterial content of the intestines.

Nodular Lymphatic Tissue

Nodular lymphatic tissue contains the same structural elements as diffuse lymphatic tissue, differing only in that the components are organized into compact, somewhat circumscribed structures. It may occur anywhere in connective tissue but is prominent along the digestive and respiratory tracts. Lymphatic nodules (also called follicles) may be present as solitary nodules or in masses forming confluent nodules, as occur in the appendix and the Peyer's patches of the ileum. Lymphatic nodules are prominent in organs such as the tonsils, lymph nodes, and spleen but are absent from the thymus. In ordinary histologic sections, some lymphatic nodules appear as rounded collections of densely packed small lymphocytes; this type of nodule is called a primary nodule. Other lymphatic nodules contain a lightly staining central area surrounded by a deeply stained cuff or cap of closely packed small lymphocytes. The pale region has been called a germinal center and the whole structure a secondary nodule. There are few reticular fibers within the germinal center, and the free cells are supported by a cellular framework consisting of stellate reticular cells. The numerous processes of the reticular cells are joined by desmosomes. Reticular fibers are present in the cuff of cells at the periphery of the center, where they form concentric layers around the structure. Germinal centers have dark and light poles. The light pole is sparsely populated by scattered small lymphocytes and reticular cells, whereas the dark pole is densely packed with large and medium lymphocytes, cells in transition to plasma cells, macrophages, mitotic cells, and the pyknotic nuclei of degenerating lymphocytes. Surrounding the center is a zone of small lymphocytes that usually is thicker at the light pole, where it forms the cap. A thinner layer of lymphocytes covers the dark pole. The structure shows definite polarity: The light pole always is directed toward a surface - the capsule in lymph nodes, red pulp in the spleen, and the epithelium of a tonsil. Germinal centers appear to be sites where lymphocytes are formed, but many of the newly formed cells die there. They also are the sites of antibody formation, and each germinal center appears to represent a clone of cells derived from an antigen-stimulated lymphocyte and active in the production of one specific antibody. Germinal centers produce B-cells that can migrate through the cap to leave the center and eventually pass to other lymphatic tissues. Areas where germinal centers develop contain follicular dendritic cells, which show numerous complex cytoplasmic processes that interdigitate with follicular lymphocytes. The cytoplasm contains many mitochondria, but ribosomes, lysosomes, and secretory granules are scarce. The nucleus is irregular and shows peripherally placed bars of heterochromatin and a distinct nucleolus. These cells are considered to be antigen-presenting cells that retain antigen on their surface for the stimulation of T-helper cells (lymphocytes). Germinal centers develop only after birth and in response to antigenic stimuli. They are absent in animals born and raised in a germ-free environment. Following a first exposure to antigen, germinal centers form de novo and then regress in the absence of antigen and eventually disappear. Upon a second stimulation by the same antigen, there is a rapid and marked production of germinal centers, which precedes a rise in circulating antibody. However, germinal centers are not essential for antibody formation, and it has been suggested that germinal centers arise only after repeated

contact with antigen and may be involved in long-term (memory) antibody responses. Aggregate or confluent lymphatic nodules occur in the appendix and are exemplified by Peyer's patches found in the lower half of the small intestine. Peyer's patches consist of many solitary nodules massed together to form grossly visible structures that underlie the intestinal epithelium. The light poles of their germinal centers are directed toward the epithelium. Individual nodules may be quite discrete and well defined, but usually they coalesce and can be distinguished only at their apices and by their germinal centers. Peyer's patches are prominent in children but undergo gradual regression with aging.