migrate from the bone marrow to lymphoid tissue throughout the body and are readily identified by cell surface immunoglobulin and antigens that are B cell specific, including CD19, CD20, and CD21.

In response to antigen binding to cell surface immunoglobulin, mature B cells are activated to proliferate and undergo differentiation to end-stage plasma cells, which lose most of their B-cell surface markers and produce large quantities of soluble antibodies. Neoplastic disorders of B cells arise from B cells at different stages of development, and B-cell lymphomas can have highly varied morphology and cell surface expression of B-cell antigens (i.e., immunophenotype).

T Cells

T cells perform an array of functions in the immune response, including those that are regarded as classic cellular immune responses. T-cell precursors migrate from the bone marrow to the thymus, where they differentiate into mature T-cell subsets and undergo selection to eliminate autoreactive T cells that respond to self-peptides. In the thymus, T-cell precursors undergo a coordinated process of differentiation that involves rearrangement and expression of the T-cell receptor (TCR) genes and acquisition of cell surface proteins that are unique to T cells, including CD3, CD4, and CD8.

As T cells mature in the thymus, they ultimately lose the CD4 or CD8 protein. Mature T cells are composed of two major groups: $CD4^+$ and $CD8^+$ cells. After T-cell maturation and selection in the thymus, mature $CD4^+$ and $CD8^+$ T cells migrate to lymph nodes, spleen, and other sites in the peripheral immune system. Mature T cells constitute about 80% of peripheral blood lymphocytes, 40% of lymph node cells, and 25% of splenic lymphoid cells.

Mature $CD4^+$ and $CD8^+$ T-cell subsets mediate distinct immune functions. $CD8^+$ cells kill virus-infected or foreign cells and suppress immune functions; $CD8^+$ cells are called *cytotoxic T cells*. $CD4^+$ cells activate other immune response cells such as B cells and macrophages by producing cytokines and through direct cell contact; $CD4^+$ cells are caled *helper T cells*.

Similar to B cells, T cells express unique TCR molecules that recognize specific peptide antigens. In contrast to B cells, T cells respond only to peptides that are processed intracellularly and bound to (or presented by) specialized cell surface antigen-presenting proteins, designated major histocompatibility complex (MHC) molecules. $CD4^+$ and $CD8^+$ T cells are MHC class restricted in their response to peptide-MHC complexes. $CD4^+$ cells recognize antigenic peptide fragments only when they are presented by MHC class II molecules, and $CD8^+$ cells recognize antigenic peptide fragments only when they are presented by MHC class I molecules. Binding of the TCR by a specific peptide-MHC complex triggers activation signals that lead to the expression of gene products that mediate the wide diversity of helper functions of $CD4^+$ cells or cytotoxic effector functions of $CD8^+$ cells. A detailed discussion is provided in Chapter 45.

Lymphoid System

Lymphocytes localize to the peripheral lymphoid tissue, which is the site of antigen-lymphocyte interaction and lymphocyte activation. The peripheral lymphoid tissue is composed of lymph nodes, the spleen, and mucosal lymphoid tissue. Lymphocytes circulate continuously through these tissues through the vascular and lymphatic systems.

The lymph nodes are highly organized lymphoid tissues that are sites of convergence of the lymphatic drainage system, which carries antigens from draining lymph to the nodes, where they are trapped. A lymph node consists of an outer cortex and an inner medulla (Fig. 49-2). The cortex is organized into lymphoid follicles composed predominantly of B cells. Some of the follicles contain central areas or germinal centers, where activated B cells undergo proliferation after encountering a specific antigen, that are surrounded by a mantle zone. The T cells are distributed more diffusely in paracortical areas surrounding the follicles.

The spleen traps antigens from blood rather than from the lymphatic system and is the site of disposal of senescent red cells. The lymphocytes in the spleen reside in the areas described as the white pulp, which surround the arterioles entering the organ. As in lymph nodes, the B and T cells are segregated into a periarteriolar lymphoid sheath that is composed of T cells and flanking follicles composed of B cells. The mucosa-associated lymphoid tissues (MALTs) collect antigen from epithelial surfaces and include the gut-associated lymphoid tissue (i.e., tonsils, adenoids, appendix, and Peyer's patches of the small intestine) and more diffusely organized aggregates of lymphocytes at other mucosal sites.

Lymphocytes circulate in the peripheral blood and represent 20% to 40% of peripheral blood leukocytes in adults; the proportion is higher in newborns and children. Between 80% and 90% of peripheral blood lymphocytes are T cells, and the remaining lymphocytes are largely B cells. A small percentage of peripheral blood lymphoid cells represents a third category of lymphoid cells that are referred to as natural killer (NK) cells. These cells

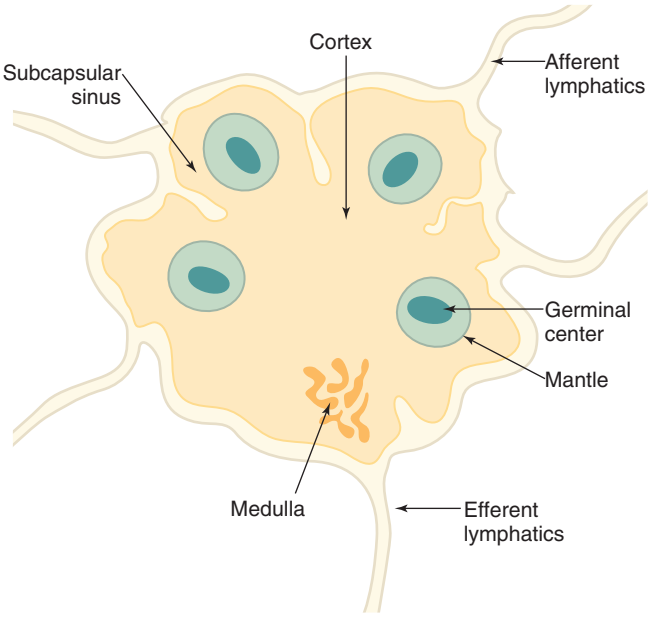

FIGURE 49-2 Structure of the normal lymph node. The cortical area contains the follicles, which consist of a germinal center and a mantle zone. The medulla contains a complex of channels that lead to the efferent lymphatics.