CHAPTER 3  Hematopathology

FIGURE 3–1  Normal lymph node, microscopic
This benign reactive lymph node has a well-defined connective tissue capsule (●), and beneath that a subcapsular sinus (+) where afferent lymphatics drain lymph fluid from tissues peripheral to the node. The lymph may contain macrophages and dendritic cells, both forms of antigen-presenting cells, carrying antigens to the node. Beneath the subcapsular sinus is the paracortical zone (▲) with lymphoid follicles having pale germinal centers with a predominance of B lymphocytes. In the germinal centers (●), immune responses to antigens are generated, assisted by a ker mantle zone of mainly T lymphocytes. Central to the follicles are sinusoids extending to the hilum (●). Efferent lymphatics drain out the hilum (■).

FIGURE 3–2  Normal lymph node, microscopic
At high magnification, a lymph node follicle with a germinal center (●) contains larger lymphocytes undergoing cytokine activation. At the lower right is the subcapsular sinus (+). The center of the lymphoid follicle—the germinal center—is where CD4 helper lymphocytes and antigen-presenting cells (macrophages and follicular dendritic cells) interact with B lymphocytes, leading to an antibody-mediated immune response.

FIGURE 3–3  Normal lymph node, microscopic
The nature of the cell population and function of a lymph node are shown in the left panel with an immunohistochemical stain for CD20, a B-cell marker. Note the larger number of B cells staining with the red-brown reaction product within the germinal center of a lymph node follicle, with additional B cells scattered in the interfollicular zone. The node in the right panel has been stained for CD3, a T-cell marker. Note the larger number of T cells around the germinal center of a follicle, with additional T cells extending into the paracortex.
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FIGURE 3–4 Normal white blood cells, microscopic

The normal types of leukocytes that are routinely observed on the peripheral blood smear are shown here, including a segmented neutrophil, band neutrophil, eosinophil, basophil, lymphocyte, and monocyte. The red blood cells (RBCs) appear normal, and there is a normal platelet present. A complete blood count includes a total white blood cell (WBC) count. The types of leukocytes may be enumerated by a machine that measures size and chemical characteristics. A manual WBC differential count is performed by observing the peripheral blood smear with Wright-Giemsa stain by light microscopy.

FIGURE 3–5 Leukocytosis, microscopic

Many granulocytes, both segmented neutrophils and band neutrophils, are present in this peripheral blood smear. An elevated WBC count with neutrophilia suggests inflammation or infection. A very high WBC count (>50,000) that is not a leukemia is known as a “leukemoid reaction.” This leukemoid reaction is more pronounced than just the “left shift” with bandemia and the occasional metamyelocyte with acute inflammation. An acute inflammatory reaction is also accompanied by an increase in “acute-phase reactants” in the plasma, such as C-reactive protein (CRP). Inflammatory cytokines, such as tumor necrosis factor (TNF) and interleukin-1 (IL-1), stimulate proliferation and differentiation of marrow granulocytic cells.

FIGURE 3–6 Leukocyte alkaline phosphatase test, microscopic

Distinguishing a leukemoid reaction from chronic myelogenous leukemia (CML) may be done with the leukocyte alkaline phosphatase (LAP) stain. Seen here are neutrophils with red granular cytoplasmic staining for LAP. Counting granulocytic cells that are staining with LAP yields a score. A high LAP score is seen with a leukemoid reaction, whereas a low LAP score suggests CML. The myeloid cells in CML are not as differentiated as the normal myeloid cells. A leukemoid reaction is typically a transient but exaggerated bone marrow response to inflammatory cytokines, such as IL-1 and TNF, which stimulate bone marrow progenitor cells.
FIGURE 3–7 Pelger-Huët anomaly, microscopic
If most of the neutrophils appear bilobed on a peripheral blood smear, this is indicative of an uncommon condition known as Pelger-Huët anomaly, an inherited condition. This is the heterozygous form. The homozygous form, marked by neutrophils displaying just a single round nucleus without lobation, may be associated with abnormal neutrophil function. The clinician should be aware of this condition when a manual WBC differential count shows mostly “bands,” but the WBC count is normal, or the patient shows no signs of infection or inflammation. In the setting of myelodysplasia, these bilobed neutrophils represent pseudo-Pelger-Huët cells.

FIGURE 3–8 Chronic granulomatous disease, microscopic
The nitroblue tetrazolium (NBT) slide test is used for screening defects in NADPH oxidase. Patient neutrophils are exposed to a stimulus, incubated with NBT, and made into a smear on a slide. The number of neutrophils with dark cytoplasmic granules of reaction product are counted. Normally, more than 95% of the granulocytes are positive as shown in the left panel. In chronic granulomatous disease (CGD), there is an absent or reduced function of the respiratory burst, which is the intracellular process in neutrophils that is dependent on the enzyme NADPH oxidase, which produces oxygen free radicals used to kill phagocytized organisms. In the abnormal NBT test in CGD in the right panel, less than 5% of neutrophils stain.

FIGURE 3–9 Myelodysplasia, microscopic
Myelodysplastic syndromes (MDS) are clonal stem cell disorders leading to impaired cell proliferation and differentiation. MDS may be primary (idiopathic) or secondary to chemotherapy. Precursor erythroid, myeloid, and megakaryocytic cells appear abnormal. Morphologic bone marrow findings include dyserythropoietic changes with nuclear abnormalities, ringed sideroblasts (■) in erythroid precursors (seen here with iron stain), hypogranulation and hyposegmentation in myeloid precursors, increased myeloblasts, and reduced numbers of disorganized nuclei in megakaryocytes. There are peripheral blood cytopenias, and most patients initially present with anemia. There is a risk for transformation of an MDS to acute myelogenous leukemia.