TABLE 48-1 DIFFERENTIAL DIAGNOSIS OF EOSINOPHILIA

CAUSES	COMMENTS
Infection*	Especially parasites; less commonly mycobacteria
Allergic diseases*	Drugs, asthma, allergic rhinitis, atopy, urticaria
Pulmonary diseases*	Churg-Strauss disease, Löffler's pneumonia, pulmonary infiltrates with eosinophilia
Drug reactions*	Usually disappears when drug discontinued
Malignancy*	Paraneoplastic, angioimmunoblastic T-cell lymphoma, Hodgkin's and non-Hodgkin's lymphoma
Connective tissue diseases*	Rheumatoid arthritis, eosinophilic fasciitis, vasculitis
Primary hypereosinophilic syndrome	More than 6 months of >1500 eosinophils/μL with no other apparent cause

*Reactive forms.

Basophils appear to play a role in immediate hypersensitivity reactions and chronic inflammatory conditions. Their levels are increased in chronic myeloid leukemias.

Monocytes

Monocytes arise from a common myeloid precursor along with granulocytes under the influence of granulocyte-macrophage colony-stimulating factor (GM-CSF) and macrophage colony-stimulating factor (M-CSF). Most circulating monocytes are marginated along the walls of blood vessels. They migrate from the vessels into tissues, where they develop into macrophages.

The monocyte-macrophage lineage has many diverse functions. These phagocytic cells perform chemotaxis, phagocytosis, and intracellular killing in much the same manner as neutrophils. They are especially important in killing infectious mycobacterial, fungal, and protozoal species.

Monocytes interact with other components of the immune system. They are antigen-presenting cells for T lymphocytes, they are capable of cellular cytotoxicity, and they secrete certain cytokines. The macrophages (i.e., differentiated monocytes) that process antigens and present them to T lymphocytes take on different forms in different tissues: Langerhans cells in the skin, interdigitating cells in the thymus, and dendritic cells in the lymph nodes. Antigen-presenting cells are nonphagocytic, and the process by which they internalize antigen is not fully understood. Protein antigens are partially digested and expressed on the cell surface in association with major histocompatibility complex class II (Ia) antigens. This feature permits interaction with and activation of helper T cells. Other macrophages, such as Kupffer cells of the liver and alveolar macrophages of the lung, play an important role in removing particulate and cellular debris and senescent erythrocytes from the circulation.

Monocytes are capable of antibody-dependent and antibody-independent cytotoxicity against tumor cells. Cytotoxicity is increased by tumor necrosis factor, interleukin-1, and interferon, which are secreted by monocytes. Monocytes secrete large numbers of immunomodulatory proteins (e.g., tumor necrosis factor, interleukin-1, interferon), cytokines (e.g., granulocyte colony-stimulating factor [G-CSF], GM-CSF), coagulation proteins, cell adhesion proteins, and proteases.

DETERMINANTS OF PERIPHERAL NEUTROPHIL NUMBERS

Most granulocyte precursors are in the bone marrow, where maturation occurs over 6 to 10 days. Marrow precursors represent 20% of the granulocyte mass, and the storage pool represents 75% of the granulocyte mass. Peripheral neutrophils represent only 5% of the total granulocyte mass.

Neutrophils circulate in transit between the marrow and peripheral tissues. More than one half of the circulating neutrophils adhere to the vascular endothelium (margination). The half-life of a neutrophil in the circulation was thought to be 6 to 12 hours, but in vivo studies suggest it may be as long as 3 to 4 days. After neutrophils migrate into tissues, they survive another 1 to 4 days. The peripheral neutrophil count therefore represents a sampling of less than 5% of the total granulocyte pool and is taken during a very short interval of the total neutrophil lifespan.

The peripheral white cell count is a poor reflection of granulocyte kinetics. Abnormalities in neutrophil number can occur rapidly and may reflect a change in marrow granulocyte production or a shift among various cellular compartments. An elevated peripheral white cell count may result from increased marrow production, or it may reflect mobilization of neutrophils from the marginated pool or release from the marrow storage pool. Similarly, a low granulocyte count may reflect decreased marrow production, increased margination or sequestration in the spleen, or increased destruction of peripheral cells.

The *total peripheral white cell count* represents the sum of lymphocytes and granulocytes. The significance of an elevated or depressed leukocyte count depends on the nature of the cellular elements that are increased or decreased. *Leukocytosis* is a nonspecific term that may denote an increase in lymphocytes (i.e., lymphocytosis) or neutrophils (i.e., granulocytosis). In rare cases, increases may reflect excessive numbers of monocytes or eosinophils. Leukocytosis related to an elevation in the neutrophil count is called *neutrophil leukocytosis* or *neutrophilia.*

Extreme elevation of the white blood cell count to more than 50,000 cells/μL of blood with the premature release of early myeloid precursors is called a *leukemoid reaction,* which may be associated with inflammation and infection. It requires consideration of a diagnosis of myeloproliferative disease, especially chronic myelogenous leukemia (CML). Evaluation of the peripheral blood smear may reveal characteristic changes that provide clues to the underlying disorder. A leukoerythroblastic smear shows immature granulocytes, teardrop-shaped erythrocytes, nucleated erythrocytes, and increased platelets. These changes reflect marrow infiltration (i.e., myelophthisis) by fibrous tissue, granulomas, or neoplasm. As with leukocytosis, leukopenia may reflect lymphopenia or neutropenia. Neutropenia is defined by an absolute neutrophil count of less than 1500 cells/μL.

NEUTROPHILIA

Neutrophilia (i.e., leukocytosis) usually results from other processes, and it rarely indicates a primary hematologic disorder