chapter **42**

Physiology of the Hematopoietic and Immune Systems

Objectives

AFTER STUDYING THIS CHAPTER, THE STUDENT WILL BE ABLE TO:

1. Review hematopoiesis, body defense mechanisms, and immune mechanisms.
2. Differentiate between cellular and humoral types of immunity.
3. Describe the antigen–antibody reaction.
4. Discuss roles of various white blood cells in the immune response.
5. Describe the functions and roles of cytokines and hematopoietic growth factors.
6. Discuss therapeutic uses of selected cytokines.

OVERVIEW

All blood cells originate in bone marrow in stem cells that are capable of becoming different types of blood cells. As these pluripotential stem cells reproduce, some reproduced cells are exactly like the original pluripotential cells and are retained in bone marrow to maintain a continuing supply. However, most reproduced stem cells differentiate to form other types of cells. The early offspring are committed to become a particular type of cell, and a committed stem cell that will produce a cell type is called a colony-forming unit (CFU), such as CFU-erythrocyte or CFU-granulocyte. Hematopoietic growth factors or cytokines control the reproduction, growth, and differentiation of stem cells and CFUs. They also initiate the processes required to produce fully mature cells.

HEMATOPOIETIC CYTOKINES

Cytokines (Table 42–1) are substances produced by bone marrow stromal cells, activated helper T cells, activated macrophages, and other cells. They regulate many cellular activities by acting as chemical messengers among cells. Some cytokines are growth factors that induce proliferation and differentiation of blood cells. These cytokines comprise a large group of proteins that are structurally and functionally diverse. They were initially named and defined by their action on one type of blood cell, but some of them act on multiple types of blood cells. The term *cytokine* includes lymphokines secreted by lymphocytes and monokines secreted by monocytes and macrophages. The terms *lymphokines* and *monokines* are still used, but they are misleading because secretion of many lymphokines and monokines is not limited to lymphocytes and monocytes as these terms imply. In general, secretion of cytokines occurs after activation of a particular cell and lasts a few hours to a few days. Although several cells can secrete cytokines, helper T cells and macrophages are the main producers.

Cytokines act by binding to receptors on the membranes of numerous types of target cells. A cytokine may bind to receptors on the membrane of the same cell that secreted it (autocrine action), it may bind to receptors on a target cell near the cell that produced it (paracrine action), and, occasionally, it may bind to target cells in distant parts of the body (endocrine or hormonal action). After binding, the cytokine-receptor complex triggers signal-transduction pathways that alter gene expression in the target cells. Overall, cytokines are involved in numerous physiologic responses, including hematopoiesis, cellular proliferation and differentiation, inflammation, wound healing, and cellular and humoral immunity.

Cytokine actions and functions are affected by several factors. First, although the immune response to an antigen may include the production of cytokines, cytokines do not act in response to specific antigens. Instead, they affect whatever cells they encounter that have cytokine receptors and are able to respond. Cytokine receptors are often expressed on a cell only after that cell has interacted with an antigen, so that cytokine activation is limited to antigen-activated lymphocytes. Second, the actions of most cytokines have been determined in laboratories by analysis of the effects of recombinant cytokines, often at nonphysiologic concentrations, and added individually to in vitro systems. Within the human body,