that activate resting stem cells to produce more granulocytes and monocyte–macrophages. Newly formed granulocytes and monocytes leave the bone marrow and enter the circulating blood in approximately 3 days.

Cytokine binding to target cells elicits wide-ranging effects, including increased expression of cytokine receptors and increased production of other cytokines. In general, the cytokines secreted by antigen-activated lymphocytes can affect the activity of most cells involved in the immune response. For example, cytokines produced by activated helper T cells influence the activity of B cells, cytotoxic T cells, natural killer cells, macrophages, granulocytes, and hematopoietic stem cells. As a result, a network of interacting cells is activated.

Some cytokines enhance macrophage activity by two main mechanisms. First, they cause macrophages to accumulate in damaged tissues by delaying or stopping macrophage migration from the area. Second, they increase the capacity and effectiveness of phagocytosis. Some cytokines, especially IL-2, directly stimulate helper T cells and enhance their antiantigenic activity. They also enhance the antiantigenic activity of the entire immune system. Interleukins 4, 5, and 6 are especially important in B-cell activities.

*Tumor necrosis factors* (TNF) are produced by activated macrophages and other cells and act on many immune and nonimmune target cells. They participate in the inflammatory response and cause hemorrhagic necrosis in several types of tumor cells. TNF-alpha is structurally the same as cachectin, a substance associated with debilitation and weight loss in patients with cancer. TNF-beta is also called lymphotoxin.

## PATIENT-RELATED FACTORS THAT INFLUENCE IMMUNE FUNCTION

### Age

#### *Immune Function During Fetal and Neonatal Periods*

During the first few months of gestation, the fetal immune system is deficient in antibody production and phagocytic activity. During the last trimester, the fetal immune system may be able to respond to infectious antigens, such as cytomegalovirus, rubella virus, and *Toxoplasma*. However, most fetal protection against infectious microorganisms is by maternal antibodies that reach the fetal circulation through the placenta. In the placenta, maternal blood and fetal blood are separated only by a layer of specialized cells called trophoblasts. Because antibodies are too large to diffuse across the trophoblastic layer, they are actively transported from the maternal to the fetal circulation by the trophoblastic cells.

At birth, the neonatal immune system is still immature, but IgG levels (from maternal blood) are near adult levels in umbilical cord blood. However, the source of maternal antibodies is severed at birth. Antibody titers in infants decrease over approximately 6 months as maternal antibodies are catabolized. Although the infant does start producing IgG, the rate of production is lower than the rate of breakdown of maternal antibodies. Cell-mediated immunity is probably completely functional at birth.

#### *Immune Function in Older Adults*

Both humoral and cell-mediated immune functions decline with aging, and this decline is probably a major factor in the older adult's increased susceptibility to infections and tumors. The regulation of immunologic functions also declines with age, which may account for the greater frequency of autoimmune diseases in this age group. Lymphocytes are less able to proliferate in response to antigenic stimulation, and a relative state of immunodeficiency prevails. With T lymphocytes, function is impaired, and the numbers in peripheral blood may be decreased. The functional impairment includes decreased activity of helper T cells. With B lymphocytes, the numbers probably do not decrease, but the cells are less able to form antibodies in response to antigens. Abnormal antibody production results from impaired function of B cells and helper T cells. In addition, older adults have increased blood levels of antibodies against their own tissues (autoantibodies).

Impaired immune mechanisms have several implications for clinicians who care for elderly patients, including the following:

- Older adults are more likely to contract infections and less able to recover from them. Therefore, older adults need protective measures, such as rigorous personal hygiene; good nutrition; adequate exercise, rest, and sleep; minimal exposure to potential pathogens, when possible; and appropriate immunizations (eg, influenza, pneumonia, tetanus). When an infection develops in older adults, signs and symptoms (eg, fever and drainage) may be absent or less pronounced than in younger adults.
- Older adults have impaired immune responses to antigens. Thus, achieving protective antibody titers may require higher doses of immunizing antigens in older adults than in younger adults.
- Older adults often exhibit a less intense positive reaction in skin tests for tuberculosis (indicating a decreased delayed hypersensitivity response).

### Nutritional Status

Nutritional status can have profound effects on immune function. Adequate nutrient intake contributes to immunocompetence (ability of the immune system to function effectively). Malnutrition contributes to immunodeficiency. A severe lack of calories or protein decreases numbers and functions of T cells, complement activity, neutrophil chemotaxis, and phagocytosis. An inadequate zinc intake can depress the functions of T and B cells. Zinc is a cofactor for many enzymes,