display them for recognition by lymphocytes. The most efficient APCs are dendritic cells, which live in epithelia and most tissues.

- The cells of the immune system are organized in tissues, some of which are the sites of production of mature lymphocytes (the generative lymphoid organs, the bone marrow and thymus), and others are the sites of immune responses (the peripheral lymphoid organs, including lymph nodes, spleen, and mucosal lymphoid tissues).
- The early reaction to microbes is mediated by the mechanisms of innate immunity, which are ready to respond to microbes. These mechanisms include epithelial barriers, phagocytes, NK cells, and plasma proteins, for example, of the complement system. The reaction of innate immunity is often manifested as inflammation. Innate immunity, unlike adaptive immunity, does not have fine antigen specificity or memory.
- The defense reactions of adaptive immunity develop slowly, but are more potent and specialized.
- Microbes and other foreign antigens are captured by dendritic cells and transported to lymph nodes, where the antigens are recognized by naïve lymphocytes. The lymphocytes are activated to proliferate and differentiate into effector and memory cells.
- Cell-mediated immunity is the reaction of T lymphocytes, designed to combat cell-associated microbes (e.g., phagocytosed microbes and microbes in the cytoplasm of infected cells). Humoral immunity is mediated by antibodies and is effective against extracellular microbes (in the circulation and mucosal lumens).
- CD4+ helper T cells help B cells to make antibodies, activate macrophages to destroy ingested microbes, stimulate recruitment of leukocytes, and regulate all immune responses to protein antigens. The functions of CD4+ T cells are mediated by secreted proteins called cytokines. CD8+ cytotoxic T lymphocytes kill cells that express antigens in the cytoplasm that are seen as foreign (e.g., virus-infected and tumor cells) and can also produce cytokines.
- Antibodies secreted by plasma cells neutralize microbes and block their infectivity, and promote the phagocytosis and destruction of pathogens. Antibodies also confer passive immunity to neonates.

The brief outline of basic immunology presented here provides a foundation for considering the diseases of the immune system. We first discuss the immune reactions that cause injury, called *hypersensitivity* reactions, and then disorders caused by the failure of tolerance to self antigens, called *autoimmune disorders*, and the rejection of transplants. This is followed by diseases caused by a defective immune system, called *immunodeficiency diseases*. We close with a consideration of *amyloidosis*, a disorder that is often associated with immune and inflammatory diseases.

Hypersensitivity: Immunologically Mediated Tissue Injury

Injurious immune reactions, called *hypersensitivity*, are the basis of the pathology associated with immunologic diseases. This term arose from the idea that individuals who have been previously exposed to an antigen manifest detectable reactions to that antigen and are therefore said to be *sensitized*. Hypersensitivity implies an excessive or harmful reaction to antigen. There are several important general features of hypersensitivity disorders.

- **Hypersensitivity reactions can be elicited by exogenous environmental antigens (microbial and nonmicrobial) or endogenous self antigens.** Humans live in an environment teeming with substances capable of eliciting immune responses. Exogenous antigens include those in dust, pollens, foods, drugs, microbes, and various chemicals. The immune responses against such exogenous antigens may take a variety of forms, ranging from annoying but trivial discomforts, such as itching of the skin, to potentially fatal diseases, such as bronchial asthma and anaphylaxis. Some of the most common reactions to environmental antigens cause the group of diseases known as *allergy*. Immune responses against self, or autologous, antigens, result in *autoimmune diseases*.
- **Hypersensitivity usually results from an imbalance between the effector mechanisms of immune responses and the control mechanisms that serve to normally limit such responses.** In fact, in many hypersensitivity diseases, it is suspected that the underlying cause is a failure of normal regulation. We will return to this concept when we consider autoimmunity.
- **The development of hypersensitivity diseases (both allergic and autoimmune) is often associated with the inheritance of particular susceptibility genes.** HLA genes and many non-HLA genes have been implicated in different diseases; specific examples will be described in the context of the diseases.
- **The mechanisms of tissue injury in hypersensitivity reactions are the same as the effector mechanisms of defense against infectious pathogens.** The problem in hypersensitivity is that these reactions are poorly controlled, excessive, or misdirected (e.g., against normally harmless environmental and self antigens).

Classification of Hypersensitivity Diseases

Hypersensitivity diseases can be classified on the basis of the immunologic mechanism that mediates the disease (Table 6-1). This classification is of value in distinguishing the manner in which the immune response causes tissue injury and disease, and the accompanying pathologic and clinical manifestations. However, it is now increasingly recognized that multiple mechanisms may be operative in any one hypersensitivity disease. The main types of hypersensitivity reactions are the following:

- **In immediate hypersensitivity (type I hypersensitivity), the injury is caused by T_H2 cells, IgE antibodies, and mast cells and other leukocytes.** Mast cells release mediators that act on vessels and smooth muscle and proinflammatory cytokines that recruit inflammatory cells.
- **In antibody-mediated disorders (type II hypersensitivity), secreted IgG and IgM antibodies injure cells by promoting their phagocytosis or lysis and injure tissues by inducing inflammation.** Antibodies may also