immunity include other cells, such as natural killer cells, dendritic cells, and epithelial cells, as well as soluble factors such as the proteins of the complement system. Together, these components of innate immunity serve as the first responders to infection. They also function to eliminate damaged cells and foreign bodies.

The typical inflammatory reaction develops through a series of sequential steps:

- The offending agent, which is located in extravascular tissues, is recognized by host cells and molecules.
- Leukocytes and plasma proteins are recruited from the circulation to the site where the offending agent is located.
- The leukocytes and proteins are activated and work together to destroy and eliminate the offending substance.
- The reaction is controlled and terminated.
- The damaged tissue is repaired.

Before discussing the mechanisms, functions, and pathology of the inflammatory response, it is useful to review some of its fundamental properties.

- **Components of the inflammatory response.** The major participants in the inflammatory reaction in tissues are blood vessels and leukocytes (Fig. 3-1). As will be discussed in more detail later, blood vessels dilate to slow down blood flow, and by increasing their permeability, they enable selected circulating proteins to enter the site of infection or tissue damage. Characteristics of the endothelium lining blood vessels also change, such that circulating leukocytes first come to a halt and then migrate into the tissues. Leukocytes, once recruited, are activated and acquire the ability to ingest and destroy microbes and dead cells, as well as foreign bodies and other unwanted materials in the tissues.
- **Harmful consequences of inflammation.** Protective inflammatory reactions to infections are often accompanied by local tissue damage and its associated signs and symptoms (e.g., pain and functional impairment). Typically, however, these harmful consequences are self-limited and resolve as the inflammation abates, leaving little or no permanent damage. In contrast, there are many diseases in which the inflammatory reaction is misdirected (e.g., against self tissues in autoimmune diseases), occurs against normally harmless environmental substances (e.g., in allergies), or is inadequately controlled. In these cases, the normally protective inflammatory reaction becomes the cause of the disease, and the damage it causes is the dominant feature. In clinical medicine, great attention is given to the injurious consequences of inflammation (Table 3-1). Inflammatory reactions underlie common chronic diseases, such as rheumatoid arthritis, atherosclerosis, and lung fibrosis, as well as life-threatening hypersensitivity reactions to insect bites, drugs, and toxins. For this reason our pharmacies abound with antiinflammatory drugs, which ideally would control the harmful sequelae of inflammation yet not interfere with its beneficial effects. In fact, inflammation may contribute to a variety of diseases that are thought to be primarily metabolic, degenerative, or genetic disorders, such as type 2 diabetes, Alzheimer disease, and cancer. In recognition of the wide-ranging harmful consequences of inflammation, the lay press has rather melodramatically referred to it as "the silent killer."
- **Local and systemic inflammation.** Much of this discussion of inflammation focuses on the tissue reaction that is a local response to an infection or to localized damage. Although even such local reactions can have some systemic manifestations (e.g., fever in the setting of bacterial or viral pharyngitis), the reaction is largely confined to the site of infection or damage. In rare situations, such as some disseminated bacterial infections, the inflammatory reaction is systemic and causes widespread pathologic abnormalities. This reaction has been called *sepsis*, which is one form of the *systemic inflammatory response syndrome*. This serious disorder is discussed in Chapter 4.
- **Mediators of inflammation.** The vascular and cellular reactions of inflammation are triggered by soluble factors that are produced by various cells or derived from plasma proteins and are generated or activated

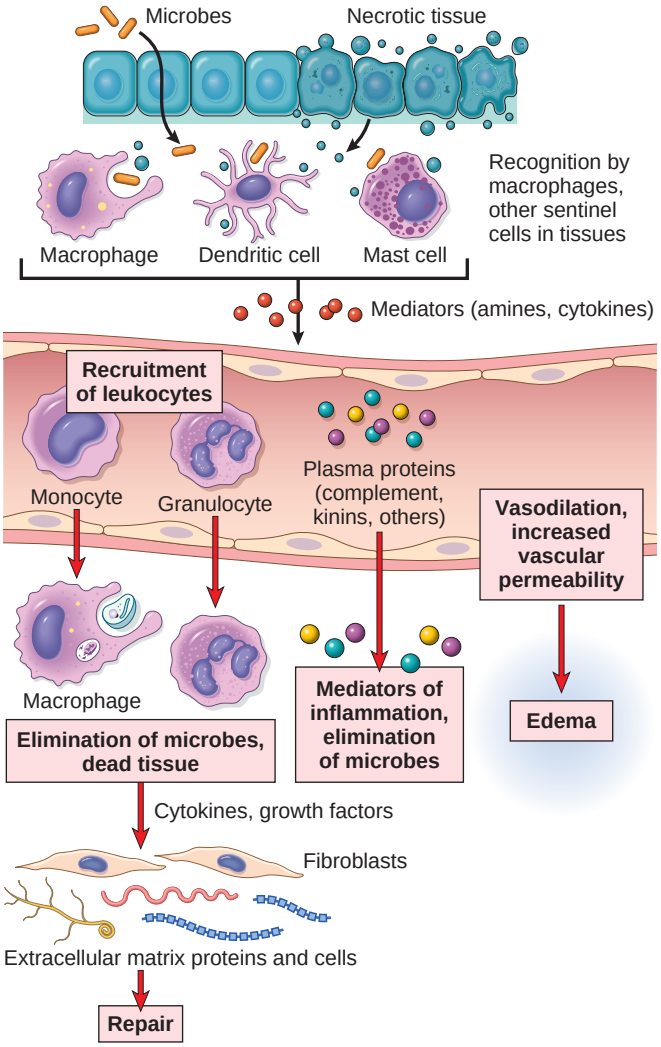

Figure 3-1 Sequence of events in an inflammatory reaction. Macrophages and other cells in tissues recognize microbes and damaged cells and liberate mediators, which trigger the vascular and cellular reactions of inflammation.