Table 3-1 Diseases Caused by Inflammatory Reactions

Disorders	Cells and Molecules Involved in Injury
Acute	
Acute respiratory distress syndrome	Neutrophils
Asthma	Eosinophils; IgE antibodies
Glomerulonephritis	Antibodies and complement; neutrophils, monocytes
Septic shock	Cytokines
Chronic	
Arthritis	Lymphocytes, macrophages; antibodies?
Asthma	Eosinophils; IgE antibodies
Atherosclerosis	Macrophages; lymphocytes
Pulmonary fibrosis	Macrophages; fibroblasts

Listed are selected examples of diseases in which the inflammatory response plays a significant role in tissue injury. Some, such as asthma, can present with acute inflammation or a chronic illness with repeated bouts of acute exacerbation. These diseases and their pathogenesis are discussed in relevant chapters.

in response to the inflammatory stimulus. Microbes, necrotic cells (whatever the cause of cell death), and even hypoxia can trigger the elaboration of inflammatory mediators and thus elicit inflammation. Such mediators initiate and amplify the inflammatory response and determine its pattern, severity, and clinical and pathologic manifestations.

- **Acute and chronic inflammation** (Table 3-2). The initial, rapid response to infections and tissue damage is called *acute inflammation*. It typically develops within minutes or hours and is of short duration, lasting for several hours or a few days; its main characteristics are the exudation of fluid and plasma proteins (edema) and the emigration of leukocytes, predominantly neutrophils (also called polymorphonuclear leukocytes). When acute inflammation achieves its desired goal of eliminating the offenders, the reaction subsides, but if the response fails to clear the stimulus, the reaction can progress to a protracted phase that is called *chronic inflammation*. Chronic inflammation is of longer duration and is associated with more tissue destruction, the presence of lymphocytes and macrophages, the proliferation of blood vessels, and the deposition of connective tissue. Chronic inflammation is discussed later in this chapter. Acute inflammation is one of the reactions of the type of host defense known as *innate immunity*, and chronic inflammation is more prominent in the reactions of *adaptive immunity* (Chapter 6).
- **Termination of inflammation and initiation of tissue repair.** Inflammation is terminated when the offending agent is eliminated. The reaction resolves because mediators are broken down and dissipated, and leukocytes have short life spans in tissues. In addition, antiinflammatory mechanisms are activated, serving to control the response and prevent it from causing excessive damage to the host. Once inflammation has achieved its goal of eliminating the offending agents, it also sets into motion the process of *tissue repair*. Repair consists of a series of events that heal damaged tissue. In this process, the injured tissue is replaced through *regeneration* of surviving cells and filling of residual defects with connective tissue *(scarring)*.

Table 3-2 Features of Acute and Chronic Inflammation

Feature	Acute	Chronic
Onset	Fast: minutes or hours	Slow: days
Cellular infiltrate	Mainly neutrophils	Monocytes/macrophages and lymphocytes
Tissue injury, fibrosis	Usually mild and self-limited	Often severe and progressive
Local and systemic signs	Prominent	Less

This chapter describes the causes (etiology) of and stimuli for inflammation, and then the sequence of events, mediators, and morphologic patterns of acute inflammation. This is followed by a discussion of chronic inflammation, and then the process of tissue repair. The study of inflammation has a rich history, and we first touch on past work that paved the way for our current understanding of this fascinating process.

Historical Highlights

Although clinical features of inflammation were described in an Egyptian papyrus dated around 3000 BC, Celsus, a Roman writer of the first century AD, first listed the four cardinal signs of inflammation: *rubor* (redness), *tumor* (swelling), *calor* (heat), and *dolor* (pain). These signs are hallmarks of acute inflammation. A fifth clinical sign, loss of function *(functio laesa)*, was added by Rudolf Virchow in the 19th century. In 1793, the Scottish surgeon John Hunter noted what is now considered an obvious fact: inflammation is not a disease but a stereotypic response that has a salutary effect on its host. In the 1880s, Russian biologist Elie Metchnikoff discovered the process of *phagocytosis* by observing the ingestion of rose thorns by amebocytes of starfish larvae and of bacteria by mammalian leukocytes. He concluded that the purpose of inflammation was to bring phagocytic cells to the injured area to engulf invading bacteria. This concept was satirized by George Bernard Shaw in his play "The Doctor's Dilemma," in which one physician's cure-all is to "stimulate the phagocytes!" Sir Thomas Lewis, studying the inflammatory response in skin, established the concept that *chemical substances, such as histamine (produced locally in response to injury), mediate the vascular changes of inflammation.* This fundamental concept underlies the important discoveries of chemical mediators of inflammation and the use of antiinflammatory drugs in clinical medicine.

Causes of Inflammation

Inflammatory reactions may be triggered by a variety of stimuli:

- **Infections** (bacterial, viral, fungal, parasitic) and microbial toxins are among the most common and medically important causes of inflammation. Different infectious pathogens elicit varied inflammatory responses, from mild acute inflammation that causes little or no lasting damage and successfully eradicates the infection, to severe systemic reactions that can be fatal, to prolonged