It is one of the earliest manifestations of acute inflammation. Vasodilation first involves the arterioles and then leads to opening of new capillary beds in the area. The result is *increased blood flow*, which is the cause of heat and redness *(erythema)* at the site of inflammation.

- Vasodilation is quickly followed by **increased permeability of the microvasculature**, with the outpouring of protein-rich fluid into the extravascular tissues; this process is described in detail below.
- The loss of fluid and increased vessel diameter lead to slower blood flow, concentration of red cells in small vessels, and increased viscosity of the blood. These changes result in **engorgement of small vessels with slowly moving red cells, a condition termed *stasis*,** which is seen as *vascular congestion* and localized redness of the involved tissue.
- As stasis develops, **blood leukocytes, principally neutrophils, accumulate along the vascular endothelium.** At the same time endothelial cells are activated by mediators produced at sites of infection and tissue damage, and express increased levels of adhesion molecules. Leukocytes then adhere to the endothelium, and soon afterward they migrate through the vascular wall into the interstitial tissue, in a sequence that is described later.

Increased Vascular Permeability (Vascular Leakage)

Several mechanisms are responsible for the increased permeability of postcapillary venules, a hallmark of acute inflammation (Fig. 3-3):

- **Contraction of endothelial cells resulting in increased interendothelial spaces is the most common mechanism of vascular leakage**. It is elicited by histamine, bradykinin, leukotrienes, and other chemical mediators. It is called the *immediate transient response* because it occurs rapidly after exposure to the mediator and is usually short-lived (15 to 30 minutes). In some forms of mild injury (e.g., after burns, irradiation or ultraviolet radiation, and exposure to certain bacterial toxins), vascular leakage begins after a delay of 2 to 12 hours and lasts for several hours or even days; this *delayed prolonged leakage* may be caused by contraction of endothelial cells or mild endothelial damage. Late-appearing sunburn is a good example of this type of leakage.
- **Endothelial injury, resulting in endothelial cell necrosis and detachment.** Direct damage to the endothelium is encountered in severe injuries, for example, in burns, or is induced by the actions of microbes and microbial toxins that target endothelial cells. Neutrophils that adhere to the endothelium during inflammation may also injure the endothelial cells and thus amplify the reaction. In most instances leakage starts immediately after injury and is sustained for several hours until the damaged vessels are thrombosed or repaired.
- Increased transport of fluids and proteins, called *transcytosis*, through the endothelial cell. This process may involve intracellular channels that may be stimulated by certain factors, such as vascular endothelial growth factor (VEGF), that promote vascular leakage. However, the contribution of this process to the vascular permeability of acute inflammation is uncertain.

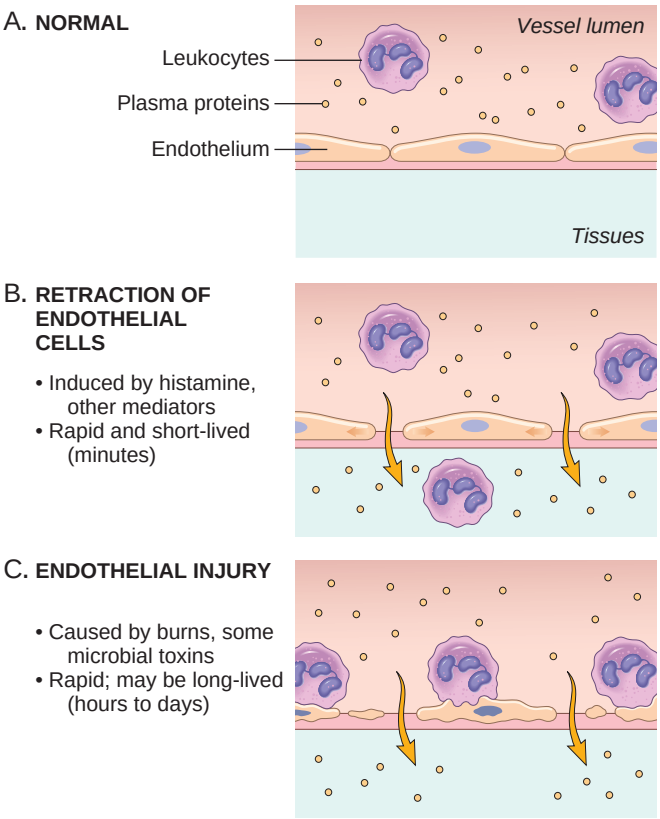

Figure 3-3 Principal mechanisms of increased vascular permeability in inflammation and their features and underlying causes.

Although these mechanisms of increased vascular permeability are described separately, all probably contribute in varying degrees in responses to most stimuli. For example, at different stages of a thermal burn, leakage results from chemically mediated endothelial contraction and direct and leukocyte-dependent endothelial injury. The vascular leakage induced by these mechanisms can cause life-threatening loss of fluid in severely burned patients.

Responses of Lymphatic Vessels and Lymph Nodes

In addition to blood vessels, lymphatic vessels also participate in acute inflammation. The system of lymphatics and lymph nodes filters and polices the extravascular fluids. Lymphatics normally drain the small amount of extravascular fluid that has seeped out of capillaries. In inflammation, lymph flow is increased and helps drain edema fluid that accumulates because of increased vascular permeability. In addition to fluid, leukocytes and cell debris, as well as microbes, may find their way into lymph. Lymphatic vessels, like blood vessels, proliferate during inflammatory reactions to handle the increased load. The lymphatics may become secondarily inflamed *(lymphangitis)*, as may the draining lymph nodes *(lymphadenitis)*. Inflamed lymph nodes are often enlarged because of hyperplasia of the lymphoid follicles and increased numbers of lymphocytes and macrophages. This constellation of pathologic changes is termed *reactive*, or *inflammatory*, *lymphadenitis* (Chapter 13). For clinicians the presence of red streaks near a skin wound is a telltale sign of an infection in the wound. This