streaking follows the course of the lymphatic channels and is diagnostic of lymphangitis; it may be accompanied by painful enlargement of the draining lymph nodes, indicating lymphadenitis.

KEY CONCEPTS

Vascular Reactions in Acute Inflammation

- Vasodilation is induced by chemical mediators such as histamine (described later), and is the cause of erythema and stasis of blood flow.
- Increased vascular permeability is induced by histamine, kinins, and other mediators that produce gaps between endothelial cells, by direct or leukocyte-induced endothelial injury, and by increased passage of fluids through the endothelium.
- Increased vascular permeability allows plasma proteins and leukocytes, the mediators of host defense, to enter sites of infection or tissue damage. Fluid leak from blood vessels results in edema.
- Lymphatic vessels and lymph nodes are also involved in inflammation, and often show redness and swelling.

Leukocyte Recruitment to Sites of Inflammation

The changes in blood flow and vascular permeability are quickly followed by an influx of leukocytes into the tissue. These leukocytes perform the key function of eliminating the offending agents. The most important leukocytes in typical inflammatory reactions are the ones capable of phagocytosis, namely neutrophils and macrophages. These leukocytes ingest and destroy bacteria and other microbes, as well as necrotic tissue and foreign substances. Leukocytes also produce growth factors that aid in repair. A price that is paid for the defensive potency of leukocytes is that, when strongly activated, they may induce tissue damage and prolong inflammation, because the leukocyte products that destroy microbes and help "clean up" necrotic tissues can also injure normal bystander host tissues.

The journey of leukocytes from the vessel lumen to the tissue is a multistep process that is mediated and controlled by adhesion molecules and cytokines called chemokines. This process can be divided into sequential phases (Fig. 3-4):

1. In the lumen: *margination, rolling, and adhesion to endothelium.* Vascular endothelium in its normal, unactivated state does not bind circulating cells or impede their passage. In inflammation, the endothelium is activated and can bind leukocytes as a prelude to their exit from the blood vessels.
2. Migration across the endothelium and vessel wall
3. Migration in the tissues toward a chemotactic stimulus

Leukocyte Adhesion to Endothelium

In normally flowing blood in venules, red cells are confined to a central axial column, displacing the leukocytes toward the wall of the vessel. Because blood flow slows early in inflammation (stasis), hemodynamic conditions change (wall shear stress decreases), and more white cells assume a peripheral position along the endothelial surface. This process of leukocyte redistribution is called *margination*. Subsequently, leukocytes adhere transiently to the

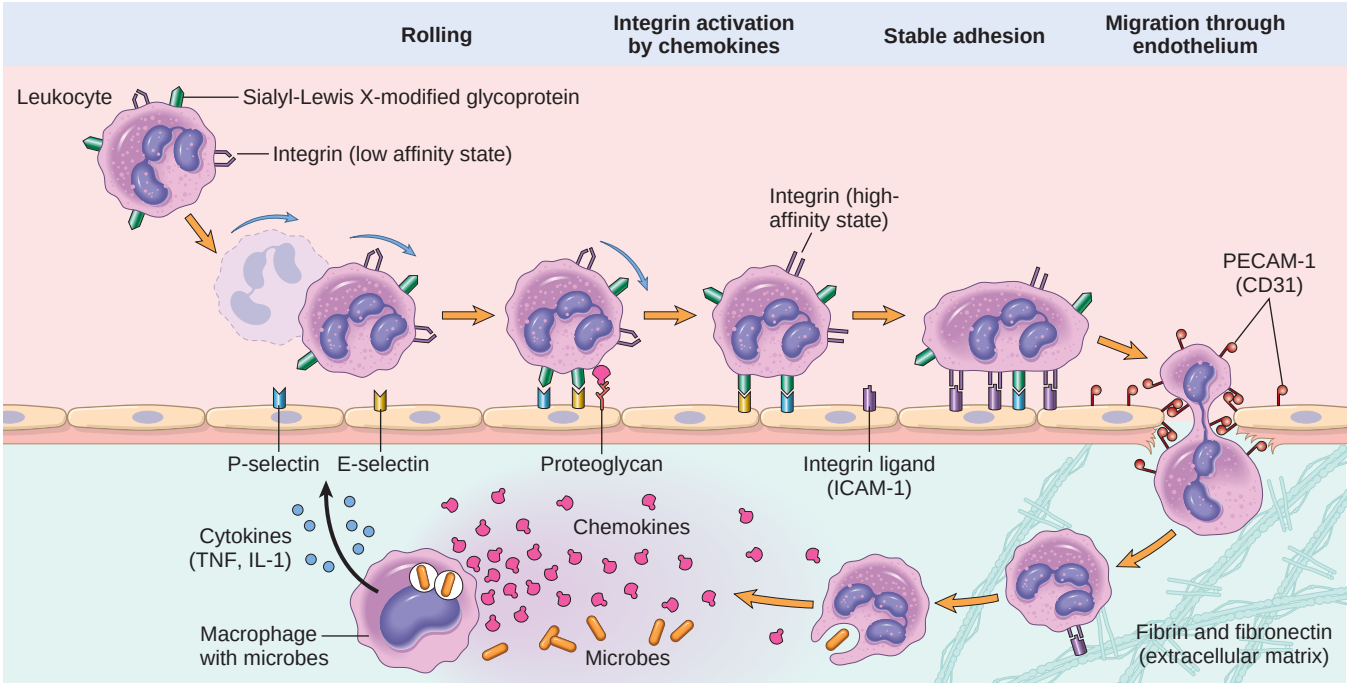

Figure 3-4 The multistep process of leukocyte migration through blood vessels, shown here for neutrophils. The leukocytes first roll, then become activated and adhere to endothelium, then transmigrate across the endothelium, pierce the basement membrane, and migrate toward chemoattractants emanating from the source of injury. Different molecules play predominant roles in different steps of this process: selectins in rolling; chemokines (usually displayed bound to proteoglycans) in activating the neutrophils to increase avidity of integrins; integrins in firm adhesion; and CD31 (PECAM-1) in transmigration. ICAM-1, Intercellular adhesion molecule 1; PECAM-1 (CD31), platelet endothelial cell adhesion molecule-1; TNF, tumor necrosis factor.