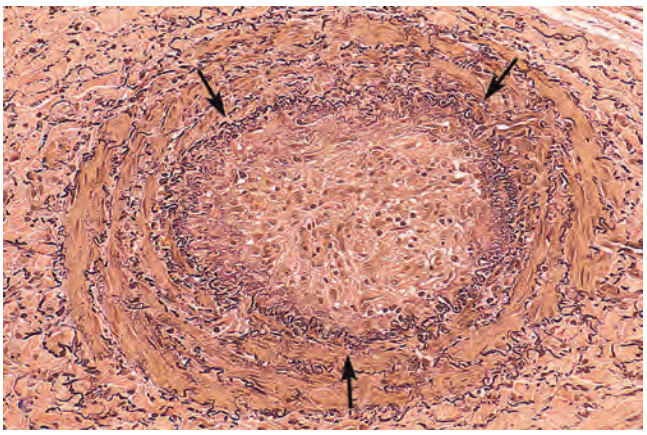

Figure 4-14 Low-power view of a thrombosed artery stained for elastic tissue. The original lumen is delineated by the internal elastic lamina *(arrows)* and is totally filled with organized thrombus, now punctuated by several recanalized endothelium-lined channels (white spaces).

agents such as t-PA (e.g., in the setting of acute coronary thrombosis) is generally effective only when given during the first few hours of a thrombotic event.

- *Organization and recanalization.* Older thrombi become organized by the ingrowth of endothelial cells, smooth muscle cells, and fibroblasts (Fig. 4-14). Capillary channels eventually form that reestablish the continuity of the original lumen, albeit to a variable degree. Continued recanalization may convert a thrombus into a smaller mass of connective tissue that becomes incorporated into the vessel wall. Eventually, with remodeling and contraction of the mesenchymal elements, only a fibrous lump may remain to mark the original thrombus.

Occasionally the centers of thrombi undergo enzymatic digestion, presumably as a result of the release of lysosomal enzymes from trapped leukocytes and platelets. In the setting of bacteremia, such thrombi may become infected, producing an inflammatory mass that erodes and weakens the vessel wall. If unchecked, this may result in a mycotic aneurysm (Chapter 11).

Clinical Features

Thrombi come to clinical attention when they obstruct arteries or veins, or give rise to emboli. The clinical presentation depends on the involved site. Venous thrombi can cause painful congestion and edema distal to an obstruction, but are mainly of concern due to their tendency to embolize to the lungs (see later). Conversely, although arterial thrombi can also embolize and cause downstream infarctions, the chief clinical problem is more often related to occlusion of a critical vessel (e.g., a coronary or cerebral artery), which can have serious or fatal consequences.

Venous Thrombosis (Phlebothrombosis). Most venous thrombi occur in the superficial or deep veins of the leg. Superficial venous thrombi typically occur in the saphenous veins in the setting of varicosities. Such thrombi can cause local congestion, swelling, pain, and tenderness, but rarely embolize. Nevertheless, the associated edema and impaired venous drainage predispose the overlying skin to the development of infections and ulcers (*varicose ulcers*). Deep venous thrombosis (DVT) involving one of the large leg veins—at or above the knee (e.g., the popliteal, femoral, and iliac veins)—is more serious because such thrombi more often embolize to the lungs and give rise to pulmonary infarction (see later and Chapter 15). Although DVTs may cause local pain and edema due to venous obstruction, these symptoms are often absent due the opening of venous collateral channels. Consequently, DVTs are asymptomatic in approximately 50% of affected individuals and are recognized only in retrospect after embolization.

Lower extremity DVTs are often associated with hypercoagulable states, as described earlier (Table 4-2). Common predisposing factors include bed rest and immobilization (because they reduce the milking action of the leg muscles, resulting in stasis), and congestive heart failure (also a cause of impaired venous return). Trauma, surgery, and burns not only immobilize a person but are also associated with vascular insults, procoagulant release from injured tissues, increased hepatic synthesis of coagulation factors, and decreased t-PA production. Many elements contribute to the thrombotic diathesis of pregnancy, including decreased venous return from leg veins and systemic hypercoagulability associated with the hormonal changes of late pregnancy and the postpartum period. Tumor-associated inflammation and coagulation factors (tissue factor, factor VIII), as well as procoagulants (e.g., mucin) released from tumor cells, all contribute to the increased risk of thromboembolism in disseminated cancers, so-called *migratory thrombophlebitis* or *Trousseau syndrome.* Regardless of the specific clinical setting, advanced age also increases the risk of DVT.

Arterial and Cardiac Thrombosis. *Atherosclerosis* is a major cause of arterial thromboses because it is associated with loss of endothelial integrity and with abnormal blood flow (Fig. 4-13*B*). Myocardial infarction can predispose to cardiac mural thrombi by causing dyskinetic myocardial contraction and endocardial injury (Fig. 4-13*A*), and rheumatic heart disease may engender atrial mural thrombi by causing atrial dilation and fibrillation. Both cardiac and aortic mural thrombi are prone to embolization. Although any tissue can be affected, the brain, kidneys, and spleen are particularly likely targets because of their rich blood supply.

KEY CONCEPTS

Thrombosis

- Thrombus development usually is related to one or more components of the Virchow triad:
  - Endothelial injury (e.g., by toxins, hypertension, inflammation, or metabolic products) associated with endothelial activation and changes in endothelial gene expression that favor coagulation
  - Abnormal blood flow—stasis or turbulence (e.g., due to aneurysms, atherosclerotic plaque)