progressively more sharply defined, yellow-tan, and soft. By 10 days to 2 weeks, it is rimmed by a hyperemic zone of highly vascularized granulation tissue. Over the succeeding weeks, the injured region evolves to a fibrous scar.

The histopathologic changes also proceed in a fairly predictable sequence (Fig. 12-14). The typical changes of coagulative necrosis become detectable in the first 6 to 12 hours. "Wavy fibers" may be present at the periphery of the infarct; these changes probably result from the forceful systolic tugs of the viable fibers on immediately adjacent, noncontractile dead fibers, causing stretching and folding. An additional sublethal ischemic change may be seen in the margins of infarcts: so-called myocyte vacuolization or **myocytolysis**, which reflects intracellular accumulations of salt and water within the sarcoplasmic reticulum. The necrotic muscle elicits acute inflammation (most prominent between 1 and 3 days). Thereafter, macrophages remove the necrotic myocytes (most noticeable by 3 to 7 days), and the damaged zone is progressively replaced by the ingrowth of highly vascularized granulation tissue (most prominent at 1 to 2 weeks); as healing progresses, this is replaced by fibrous tissue. In most instances, scarring is well advanced by the end of the sixth week, but the efficiency of repair depends on the size of the original lesion, as well as the relative metabolic and inflammatory state of the host.

Since healing requires the participation of inflammatory cells, immune suppression (e.g., due to steroids) can impair the vigor of the healing response. Moreover, delivering inflammatory cells to the site of necrosis requires intact vasculature; since blood vessels often survive only at the edges of an infarct, MIs typically heal from the margins toward the center. Consequently, a large infarct may not heal as quickly or as completely as a small one. A healing infarct can also appear nonuniform, with the most advanced healing at the periphery. Once a lesion is completely healed, it is impossible to determine its age (i.e., the dense fibrous scar of 8-week-old and 10-year-old infarcts looks virtually identical).

The following discussion considers the changes that result from interventions that can limit infarct size by salvaging myocardium that is not yet necrotic.

Infarct Modification by Reperfusion. **Reperfusion is the restoration of blood flow to ischemic myocardium threatened by infarction; the goal is to salvage cardiac muscle at risk and limit infarct size.** The cardiology adage that *"time is myocardium"* succinctly captures the impetus to intervene promptly once ongoing infarction is diagnosed; patient outcome materially worsens with progressively larger infarcts. Not only does reperfusion improve short- and long-term survival, but it also impacts short- and long-term myocardial function. Thus, prompt reperfusion is the preeminent objective for treatment of patients with MI. This can be accomplished by a host of coronary interventions, that is, thrombolysis, angioplasty, stent placement, or coronary artery bypass graft [CABG] surgery. The goal is to dissolve, mechanically alter, or bypass the lesion that precipitated the acute infarction. The benefits of reperfusion correlate with (1) the rapidity of reestablishing

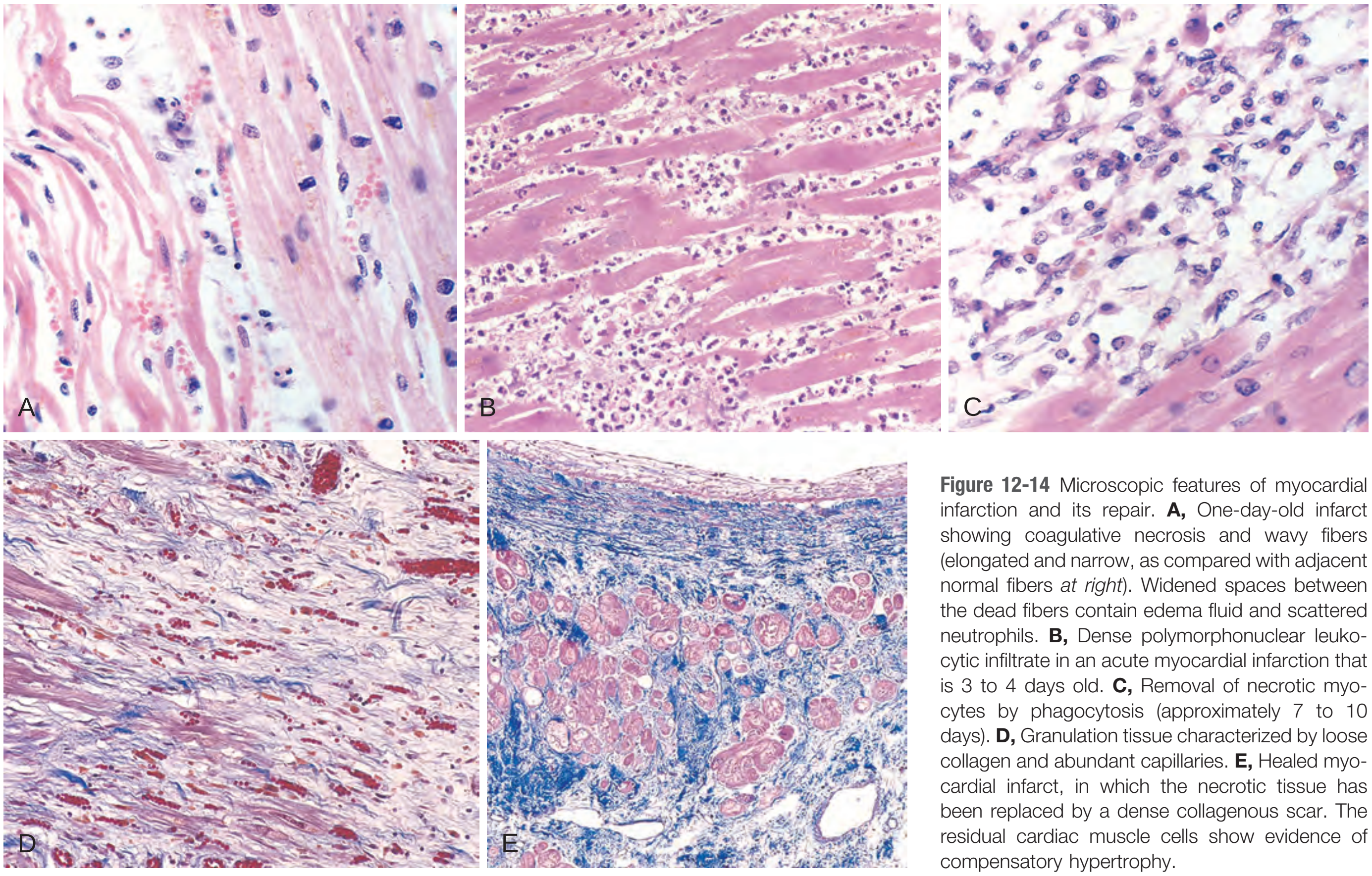

Figure 12-14 Microscopic features of myocardial infarction and its repair. **A,** One-day-old infarct showing coagulative necrosis and wavy fibers (elongated and narrow, as compared with adjacent normal fibers *at right*). Widened spaces between the dead fibers contain edema fluid and scattered neutrophils. **B,** Dense polymorphonuclear leukocytic infiltrate in an acute myocardial infarction that is 3 to 4 days old. **C,** Removal of necrotic myocytes by phagocytosis (approximately 7 to 10 days). **D,** Granulation tissue characterized by loose collagen and abundant capillaries. **E,** Healed myocardial infarct, in which the necrotic tissue has been replaced by a dense collagenous scar. The residual cardiac muscle cells show evidence of compensatory hypertrophy.