

if the tissue injury is severe or chronic and results in damage to parenchymal cells and epithelia as well as to the connective tissue framework, or if nondividing cells are injured. In contrast to regeneration, which involves the restitution of tissue components, scar formation is a response that “patches” rather than restores the tissue. The term *scar* is most often used in connection to *wound healing* in the skin, but may also be used to describe the replacement of parenchymal cells in any tissue by collagen, as in the heart after myocardial infarction.

Steps in Scar Formation

Repair by connective tissue deposition consists of sequential processes that follow tissue injury and the inflammatory response (Fig. 3-26):

- **Angiogenesis** is the formation of new blood vessels, which supply nutrients and oxygen needed to support the repair process. Newly formed vessels are leaky because of incomplete interendothelial junctions and because VEGF, the growth factor that drives angiogenesis, increases vascular permeability. This leakiness accounts in part for the edema that may persist in healing wounds long after the acute inflammatory response has resolved.
- **Formation of granulation tissue.** Migration and proliferation of fibroblasts and deposition of loose connective tissue, together with the vessels and interspersed leukocytes, form *granulation tissue*. The term *granulation tissue* derives from its pink, soft, granular gross appearance, such as that seen beneath the scab of a skin wound. Its histologic appearance is characterized by proliferation of fibroblasts and new thin-walled, delicate capillaries (angiogenesis), in a loose extracellular matrix, often with admixed inflammatory cells, mainly macrophages (Fig. 3-27A). Granulation tissue progressively invades the site of injury; the amount of granulation tissue that is formed depends on the size of the tissue deficit created by the wound and the intensity of inflammation.
- **Remodeling of connective tissue.** Maturation and reorganization of the connective tissue (remodeling) produce the stable fibrous *scar*. The amount of connective tissue increases in the granulation tissue, eventually resulting

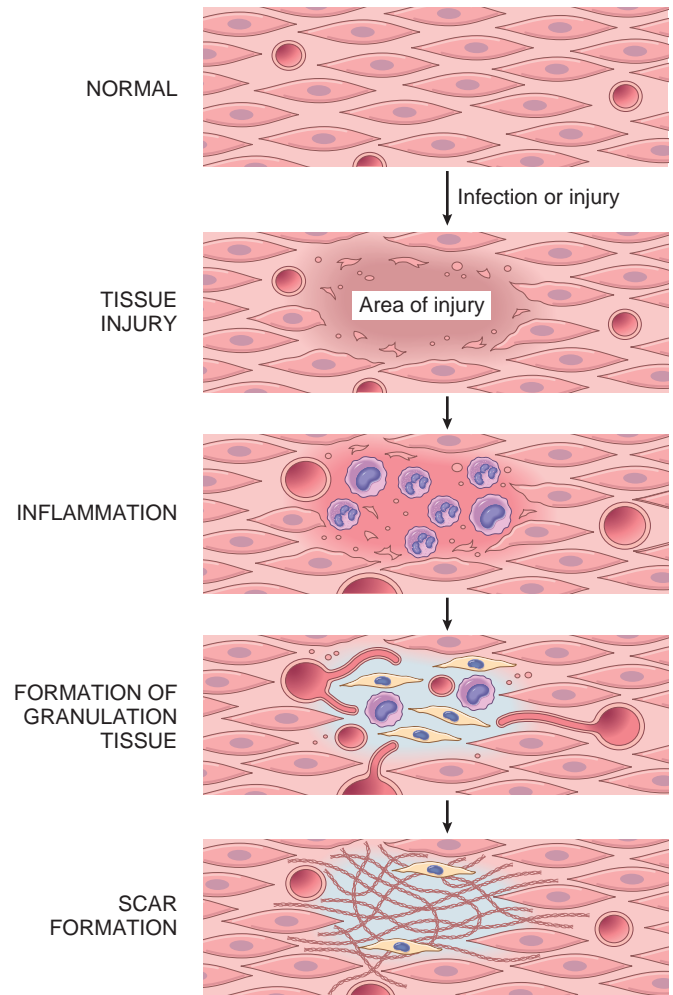


Figure 3-26 Steps in repair by scar formation. Injury to a tissue, such as muscle (which has limited regenerative capacity), first induces inflammation, which clears dead cells and microbes, if any. This is followed by the formation of vascularized granulation tissue and then the deposition of extracellular matrix to form the scar.

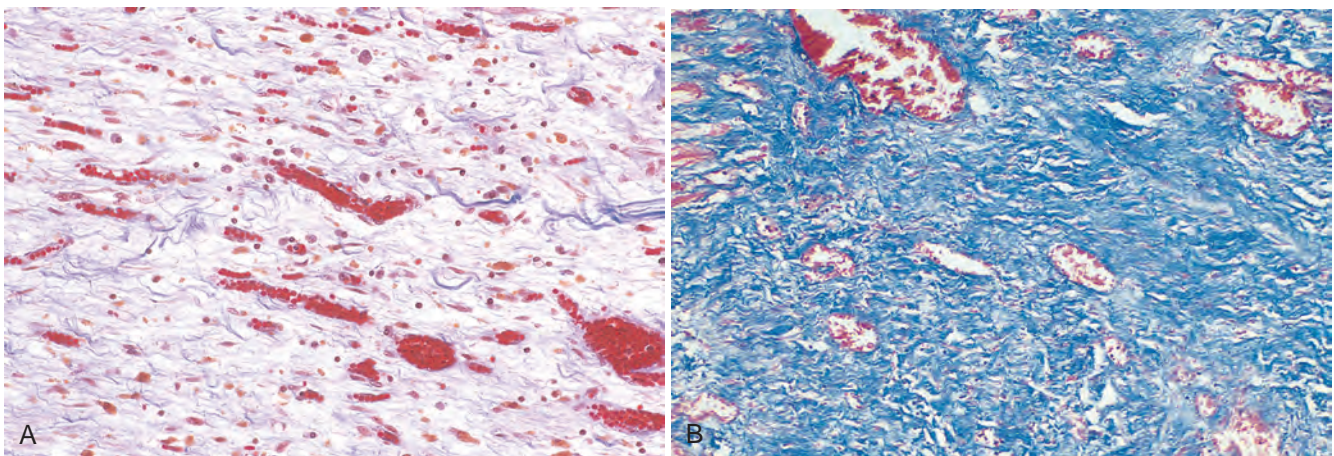


Figure 3-27 **A**, Granulation tissue showing numerous blood vessels, edema, and a loose extracellular matrix containing occasional inflammatory cells. Collagen is stained blue by the trichrome stain; minimal mature collagen can be seen at this point. **B**, Trichrome stain of mature scar, showing dense collagen, with only scattered vascular channels.