

## Repair of Cartilage and Bone

Because of its avascularity, *mammalian cartilage* has a very limited capacity to restore itself after injury. Damaged regions of cartilage become necrotic, and these areas then are filled in by connective tissue from the perichondrium. Some of the connective tissue may slowly differentiate into cartilage, but most remains as dense irregular connective tissue that may later calcify or even ossify.

### Bone

Repair of a broken bone is influenced by the size of the bone, the thickness of its compact bone, and the complexity of the fracture. However, the underlying process of repair remains the same and in general recalls the events of bone formation. A fracture ruptures blood vessels in the marrow, periosteum, and the bone itself, and bleeding may be extensive. As a result of the vascular damage, bone dies for some distance back from the fracture site, as do the periosteum and marrow. However, the latter have a greater blood supply than bone tissue itself, so the area of cell death in these tissues is not as great. The blood clot that forms is removed by lysis and phagocytosis. Fibrovascular invasion of the clot immediately around and within the fracture and its conversion to a fibroconnective tissue are not prominent phenomena in humans. Repair occurs by activation of osteogenic cells in the viable endosteum and periosteum near the fracture site. The cells proliferate and form new trabeculae of bone within the marrow cavity and beneath the periosteum.

Repair occurring within the marrow cavity can be very important in human fractures. Medullary healing begins as foci of vascular and fibroblastic proliferations in the viable tissue that borders the damaged marrow, followed by osteogenic activity and bone formation. Ultimately, a network of fine bony trabeculae extends across the marrow cavity from cortex to cortex on either side of the fracture and finally across the fracture line, providing an internal scaffold until union of the fractured ends can be effected. All this new bone arises by intramembranous bone formation and is woven bone. Medullary bone healing is particularly important for the union of fractures in cancellous bones such as the vertebral bodies and lower end of the radius and fractures through the metaphysis of long bones. On the periosteal surface, the repair process arises from the inner osteoblastic layer of the periosteum (osteogenetic layer) beginning a short distance from the fracture zone. Periosteal proliferation occurs on both sides of the fracture gap, resulting in collars of bony trabeculae that grow outward and toward each other, ultimately fusing to span the gap in a continuous arch. The new trabeculae are firmly attached to the old bone surface, including the dead bone. Growth of the osteogenic cells outstrips their vascular supply so that in the midzone of the fracture site the cells differentiate into chondroblasts rather than osteoblasts and lay down a callus of hyaline cartilage. This also bridges the fracture gap to form a stabilizing splint around the fracture. The cartilage is converted to bone by endochondral bone formation, but the process is self-limiting, and all the cartilage disappears without continuous formation of new cartilage as in an epiphyseal plate. Cartilage always appears during the repair of long bones, whereas flat bones heal without cartilage formation.

Union of the compact cortical bone occurs from sources arising in the medullary cavity or from the periosteum. Since the ends of the bone at the fracture line consist of dead bone, direct union of the fractured ends is very rare if it occurs at all. Occasionally the gap is filled by formation of hyaline cartilage, which then undergoes endochondral ossification to achieve cortical union. More frequently, the bone that initially unites the broken ends is a network of

woven bone formed by intramembranous bone formation. The last act in repair is the resorption of excess bone and the remodeling of newly formed and dead bone that is replaced by lamellar bone. Bone morphogenic proteins, which belong to the TGF- $\beta$  superfamily of proteins, are involved in regulating bone formation and repair. Bone morphogenic proteins act at all the important steps in the cascade of events that form new bone: chemotaxis of progenitor cells, mitosis, differentiation and proliferation of chondrocytes and osteoblasts, stimulation of extracellular matrix formation and binding to specific matrix molecules.

©William J. Krause