BONE

Basic Structure and Function of Bone

The adult human skeleton is composed of 206 bones and accounts for approximately 12% of body weight. The functions of bone include mechanical support, transmission of forces generated by muscles, protection of viscera, mineral homeostasis, and providing a niche for production of blood cells. The constituents of bone include an extracellular matrix and specialized cells responsible for production and maintenance of the matrix.

Matrix

Bone matrix is the extracellular component of bone. It is composed of an organic component known as osteoid (35%) and a mineral component (65%). Osteoid is made up of predominantly type I collagen with smaller amounts of glycosaminoglycans and other proteins, which are grouped according to function in Table 26-1. Of these, only osteopontin (also called osteocalcin) is unique to bone. It is produced by osteoblasts and plays a role in bone formation and mineralization and in calcium homeostasis. It is measurable in the serum and serves as a sensitive and specific marker for osteoblast activity. Several cytokines and growth factors also control bone cell proliferation, maturation, and metabolism, thereby playing a crucial role in translating mechanical and metabolic signals into local bone cell activity and eventual skeletal adaptation.

The unique feature of bone matrix, its hardness, is imparted by the inorganic moiety hydroxyapatite [$Ca_{10}(PO_4)_6(OH)_2$], which also serves as a repository for 99% of the body's calcium and 85% of its phosphorus. The bone matrix is synthesized in one of two histologic forms, woven or lamellar (Fig. 26-1). Woven bone is produced rapidly, such as during fetal development or fracture repair, but the haphazard arrangement of collagen fibers imparts less structural integrity than the parallel collagen fibers in slowly produced lamellar bone. In an adult, the presence of woven bone is always abnormal, but it is not specific for any particular bone disease since it can be found in a variety of pathologic settings (discussed later). A cross-section of a typical long bone shows a dense outer cortex and a central medulla composed of bony trabeculae separated by marrow.

Table 26-1 Proteins of Bone Matrix

Osteoblast-Derived Proteins
Type I collagen
Calcium-binding proteins
Osteonectin, bone sialoprotein
Cell adhesion proteins
Osteopontin, fibronectin, thrombospondin
Cytokines
IL-1, IL-6, RANKL
Enzymes
Collagenase, alkaline phosphatase
Growth factors
IGF-1, TGF-β, PDGF
Proteins involved in mineralization
Osteocalcin
Proteins Concentrated from Serum
Albumin
β_2-microglobulin

IGF, linsulin-like growth factor; *TGF*, transforming growth factor; *PDGF*, platelet-derived growth factor; *IL*, interleukin; *RANKL*, receptor activator of nuclear factor-κB ligand.

Cells

The cellular component of mature bone consists of bone synthesizing osteoblasts, osteocytes, and bone-resorbing osteoclasts.

- **Osteoblasts,** located on the surface of the matrix, synthesize, transport and assemble the matrix and regulate its mineralization (Fig. 26-2*A*). The synthesis of matrix is tightly regulated by hormonal and local mediators as described in detail later. Over time, osteoblasts may become inactive, indicated by a decrease in cytoplasm. Some inactive cells remain on the surface of

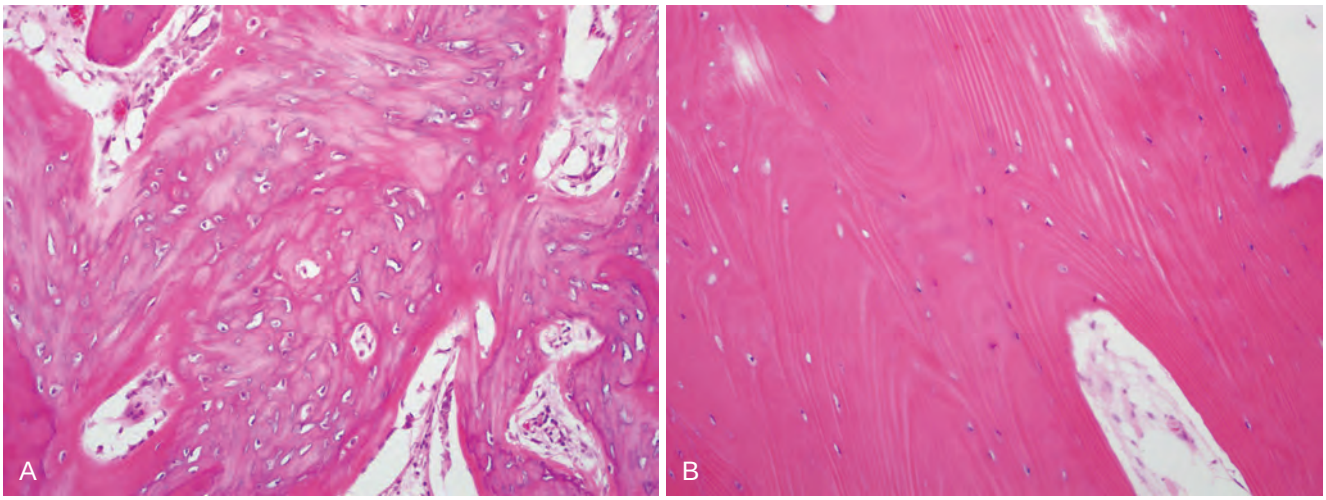

Figure 26-1 Woven bone (**A**) is more cellular and disorganized than lamellar bone (**B**).