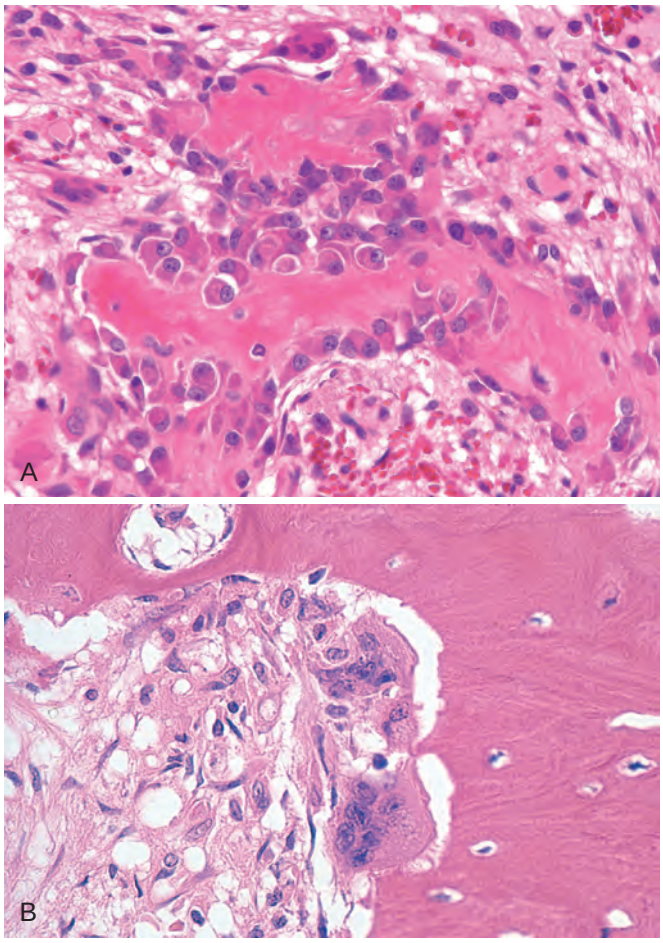

Figure 26-2 **A,** Active osteoblasts synthesizing bone matrix. The surrounding spindle cells represent osteoprogenitor cells. **B,** Two osteoclasts resorbing bone.

trabecula. Alternatively, they may become embedded within the matrix (osteocytes).

- **Osteocytes** are interconnected by an intricate network of dendritic cytoplasmic processes through tunnels known as canaliculi. Osteocytes help to control calcium and phosphate levels in the microenvironment, and detect mechanical forces and translate them into biologic activity—a process called mechanotransduction.
- **Osteoclasts** are specialized multinucleated macrophages derived from circulating monocytes that are responsible for bone resorption (Fig. 26-2*B*). By means of cell surface integrins, osteoclasts attach to bone matrix and create a sealed extracellular trench (resorption pit). Secretion of acid and neutral proteases (predominantly matrix metalloproteases, [MMPs]) into the pit results in dissolution of the inorganic and organic components of bone.

Development

During embryogenesis, most bones develop from a cartilage mold by the process of endochondral ossification. The cartilage mold *(anlagen)* is synthesized by mesenchymal precursor cells. At approximately 8 weeks' gestation, a putative mononuclear cell known as the chondroclast removes the central portion of the mold creating the medullary canal. Simultaneously, at midshaft *(diaphysis),* osteoblasts begin to deposit the cortex beneath the nascent periosteum. The resulting *primary center of ossification* produces radial growth of bone. At each longitudinal end *(epiphysis),* endochondral ossification proceeds in a centrifugal fashion *(secondary center of ossification).* Eventually, a plate of the cartilage anlage becomes entrapped between the two expanding centers of ossification forming the *physis* or *growth plate* (Fig. 26-3). The chondrocytes within the growth plate undergo sequential proliferation, hypertrophy and apoptosis. In the region of apoptosis the matrix mineralizes and is invaded by capillaries, providing the nutrients for osteoblasts to be activated and synthesize osteoid. Although the calcified cartilage matrix is resorbed, remnant struts persist and act as scaffolding for the deposition of bone on their surfaces. These structures are known as *primary spongiosa* and are the first bony trabeculae (Fig. 26-3). The above process progressively deposits new bone at the bottom of the growth plate resulting in longitudinal bone growth.

Intramembranous ossification, by contrast, is responsible for the development of flat bones. Bones of the cranium, for example, are formed by osteoblasts directly from a fibrous layer of tissue that is derived from mesenchyme, without a cartilage anlagen. Because bone is made only by osteoblasts, the enlargement of bones is achieved by the deposition of new bone on a preexisting surface. This mechanism of appositional growth is instrumental in bone development and modeling.

The development of bone is controlled by a number of local and systemic factors:

- Growth hormone (GH) is secreted by the anterior pituitary. It acts on resting chondrocytes to induce and maintain proliferation.

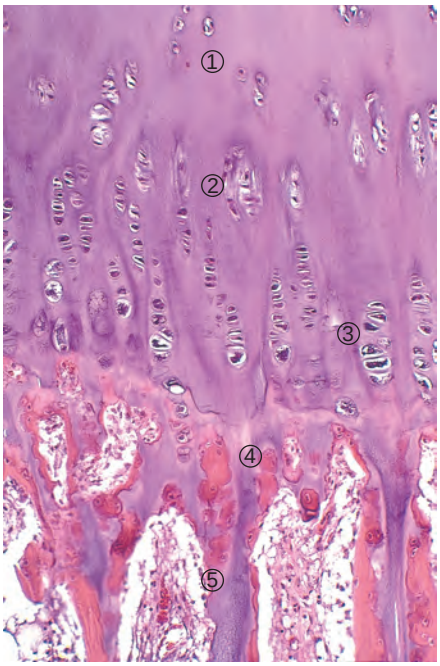

Figure 26-3 Active growth plate with ongoing enchondral ossification. 1, Reserve zone. 2, Zone of proliferation. 3, Zone of hypertrophy. 4, Zone of mineralization. 5, Primary spongiosa.