

HPO_4^{2-} , amino acids) are transported into the osteoclasts by endocytosis. The vesicles are then transported to the opposite side of the cell, where their contents are released into the interstitial fluid, from where the end products of the degradation can enter the blood.

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- 5 What are osteoblasts, and how are they formed?
- 6 What is osteoid, and how is it converted to bone substance?
- 7 What are osteocytes, and what is their main function?
- 8 What are osteoclasts, and how are they formed?
- 9 How do osteoclasts break down bone tissue

Formation of Bone Tissue

Bone can be formed by conversion of cartilage into bone tissue, *endochondral ossification*, (kondros = cartilage), or by ossification of fibrous connective tissue, *intramembranous ossification*. Most bones are formed by endochondral ossification. In endochondral ossification, cartilage that already has the shape of the bone is gradually replaced by bone tissue. The flat bones of the cranium and parts of the jaw (mandible and maxilla) are formed by intramembranous ossification. Intramembranous ossification also

occurs when bones increase in diameter as an animal grows.

Endochondral ossification

In the early stages of fetal life, the skeleton consists of cartilage. Although the rate of bone mineralization increases rapidly during the last third of pregnancy, the skeleton still contains significant amounts of cartilage at birth. Ossification of cartilage, and the subsequent growth in bone length, continues until some time after puberty.

Bones formed by endochondral ossification develop in the fetus from structures of hyaline cartilage, shaped as miniature models of the corresponding bones in adults. These cartilaginous bones continue to grow through the first part of fetal life, before ossification begins in the middle region of the long bones (Fig. 7.3a). With the exception of articular cartilage, all cartilage is lined with a connective tissue sheath, *perichondrium*. Ossification starts with growth of blood vessels into the perichondrium, which is then converted to a vascularized periosteum. The outer layer of periosteum consists of dense, fibrous connective tissue, whereas the innermost layer, which borders the bone, is made up of cells. At this stage, osteoprogenitor cells constitute the predominant cell type in the inner layer. Vascularization of the periosteum improves nourishment of osteoprogenitor cells and stimulates them to increased mitotic activity and differentiation to osteoblasts. In the newly formed periosteum,

Endochondral ossification is replacement of cartilage with bone tissue

Intramembranous ossification is ossification of fibrous connective tissue

In the fetus, bones are initially made of hyaline cartilage

Figure 7.2 Resorption of bone substance. Osteoclasts are multinuclear gigantic cells that attach to the bone surfaces. Bone resorption takes place in resorption cavities formed beneath the osteoclasts. Organic acids and proteolytic enzymes are secreted into the fluid in the resorption cavity (1, 2). Crystals of calcium phosphate then dissolve and proteins in the bone matrix are hydrolyzed. The end products of the degradation, i.e., Ca^{2+} , phosphate, and amino acids, are taken up into osteoclasts by endocytosis (3). The endosomes are transported through the osteoclast and release their contents into the tissue fluid by exocytosis (4). Subsequently, the end products enter the blood by diffusion (5).

