also called *calcitriol*. Increases in $1,25(OH)_2D$ enhance calcium absorption, and decreases in $1,25(OH)_2D$ reduce absorption of dietary calcium. Dietary calcium absorption can be increased over the short term by increasing calcium intake or increasing plasma $1,25(OH)_2D$ concentrations, or both. Pathologic increases in serum calcium (i.e., hypercalcemia) can be caused by increases in circulating $1,25(OH)_2D$ (e.g., in sarcoidosis) or by excessive calcium intake (i.e., milk-alkali syndrome). Conversely, hypocalcemia can result from a decline in $1,25(OH)_2D$ (e.g., chronic renal failure, hypoparathyroidism). If a normal individual consumes 1000 mg of calcium per day and the net absorption from the gastrointestinal (GI) tract is 150 mg per day, 850 mg of calcium will be excreted in the feces each day.

Renal Calcium Handling

The filtered load of calcium by the kidneys is about 10,000 mg per day. In terms of overall regulation of calcium homeostasis, this number is very large, making the point that the kidney is the most important moment-to-moment regulator of the serum calcium concentration. The amount also emphasizes that disorders of renal calcium handling (e.g., thiazide diuretic use, hypoparathyroidism) can be expected to produce significant abnormalities in serum calcium homeostasis.

Of the 10,000 mg filtered at the glomerulus each day, about 9000 mg (90%) is reabsorbed *proximally* by the proximal convoluted tubule, the pars recta, and the thick ascending limb of Henle loop. This 90% is absorbed in conjunction with sodium and chloride reabsorption and is not subject to regulation by parathyroid hormone (PTH). The remaining 10% (1000 mg) that arrives at the distal tubule on a daily basis is subject to regulation by PTH, which stimulates renal calcium reabsorption. The anticalciuric effect of PTH can be extremely efficient, and elevated PTH concentrations can essentially eliminate calcium excretion into the urine. This action is a potent mechanism for retaining calcium under conditions of calcium deprivation (e.g., a low-calcium diet, vitamin D deficiency, intestinal malabsorption) and can contribute to hypercalcemia under pathologic conditions, as in primary hyperparathyroidism.

About 150 mg of calcium is excreted by the kidney in the final urine on a daily basis in a healthy individual. If the kidney filters 10,000 mg of calcium each day, and if 150 mg is excreted in the final urine, 9850 mg (98.5%) is reabsorbed at proximal and distal sites. A healthy person is in zero calcium balance with respect to the outside world: intake (1000 mg/day) − output [(850 mg/day in feces) + (150 mg/day in urine)] = 0.

Skeletal Biology and Calcium Homeostasis

The skeletal compartment contains about 1.2 kg of calcium in a male adult and 1.0 kg in a female adult. Most of this calcium is in the form of crystal hydroxyapatite, a calcium phosphate salt. Although calcium contributes in an important way to the structural integrity of the skeleton, the skeleton also serves as a quantitatively large reservoir (i.e., a sink) for adding and removing calcium to and from the extracellular fluid (ECF) compartment at appropriate times.

The adult skeleton is composed of two types of bone: cortical (or lamellar) bone and trabecular (or cancellous) bone (Fig. 72-2). Cortical bone predominates in the skull and the shafts of long bones, and trabecular bone predominates at other sites, such as the distal radius, the vertebral bodies, and the trochanters of the hip.

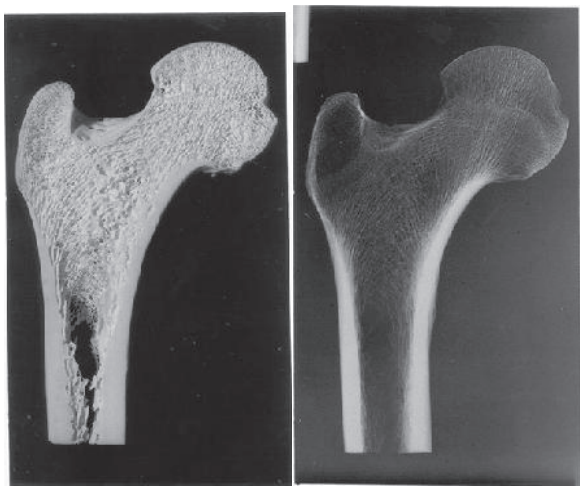

FIGURE 72-2 The structure of human bone. A human proximal femur examined using a gross pathologic specimen *(left panel)* and a radiograph of the same section *(right panel)*. Notice that two types of bone are represented. One type is cortical bone (i.e., lamellar bone), and the other is cancellous bone (i.e., trabecular bone). The proportion of trabecular and cortical bone differs by location. For example, the shaft of the femur contains mostly cortical bone, whereas the proximal end of the femoral neck and the greater trochanter contain little cortical bone and almost exclusively contain trabecular bone. This distinction is important, because most osteoporotic fractures occur at sites in which trabecular bone predominates, including the greater trochanter, the femoral neck, the vertebrae, and the distal radius. (Courtesy Webster S. S. Jee, MD, University of Utah, Salt Lake City, Utah.)

Bone is not an inert tissue, as might be imagined from visiting the dinosaur room at a natural history museum; instead, bone is a vital tissue that is continually turning over. The adult skeleton is completely remodeled every 3 to 10 years. Remodeling is perhaps best appreciated by recalling that orthopedic surgeons routinely and intentionally set fractures imperfectly, knowing that the normal processes of bone remodeling will restore the bone's original shape with the passage of time.

The cells that regulate bone turnover can be divided into those that remove old bone, those that provide new bone (Fig. 72-3) (see Chapter 74), and those that regulate these two processes. Cells that remove, or *resorb*, old bone are *osteoclasts*. These cells are large, metabolically active, multinucleated cells derived from the fusion of circulating macrophages. They deposit themselves on the surface of bone and form a *sealing zone* over the bone surface into which they secrete protons (i.e., acid), proteases (e.g., collagenase), and proteoglycan-digesting enzymes (e.g., hyaluronidase). The acid solubilizes hydroxyapatite crystals, releasing calcium, and the enzymes digest bone proteins and proteoglycans (e.g., collagen, osteocalcin, osteopontin), which constitute the nonmineral, or *osteoid*, component of bone. Osteoclasts move along the surface of trabecular bone plates and drill tunnels in cortical bone, periodically releasing the digested contents within their sealed zones into the bone marrow space and thereby creating resorption lacunae, called *Howship's lacunae*, on the trabecular bone surface. The released calcium contributes to the ECF calcium pool, and the released proteolytic products, such as