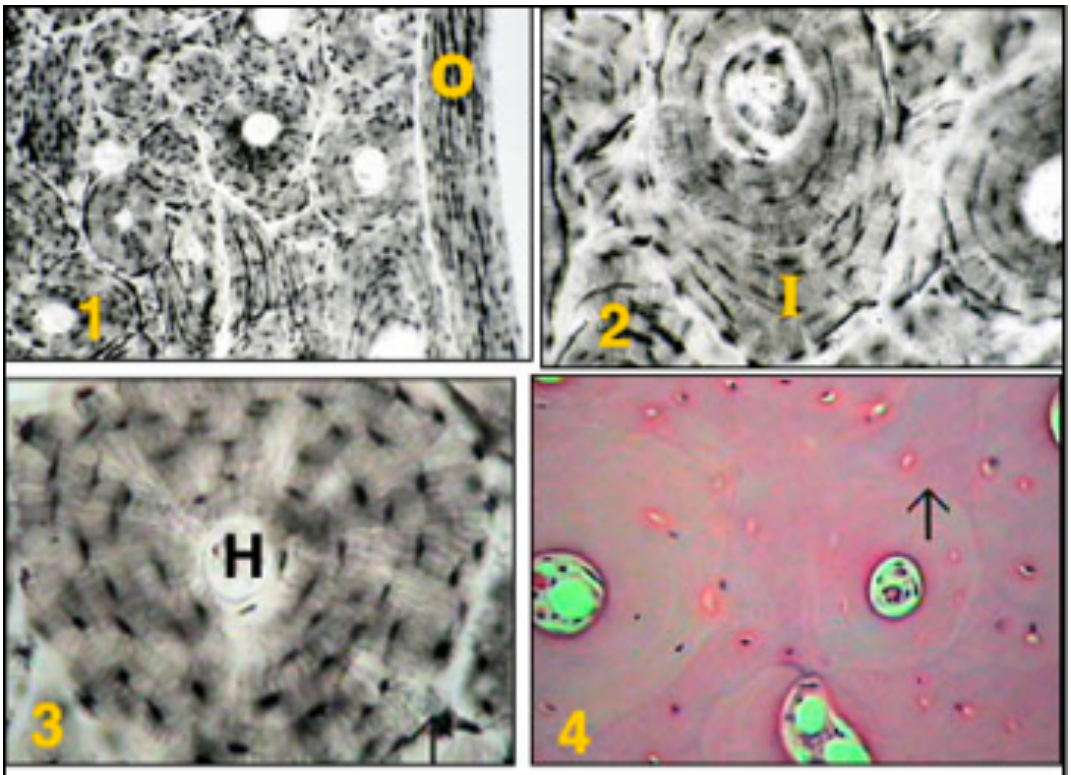
Bone



1. Ground bone. An outer circumferential lamella (O) is shown at the right.
2. Ground bone. An interstitial lamella (I) lies beneath an osteon unit located near the center.
3. Ground bone. An osteon unit fills the field of view. Note the centeral Haversian canal (H), numerous lacunae and interconnecting canaliculi.
4. A section of decalcified bone. The arrow points to the cement line which limits an osteon unit.

Bone also is a connective tissue specialized for support. However, in bone the matrix is mineralized and forms a dense, hard, unyielding substance with high tensile, weight-bearing, and compression strength. Despite its strength and rigidity, bone is a dynamic, living tissue constantly turning over, constantly being renewed and reformed throughout life.

Macroscopic Structure

Grossly, cancellous and compact forms of bone can be identified. *Cancellous (spongy) bone* consists of irregular bars or *trabeculae* of bone that branch and unites to form a three-dimensional, interlacing network of boney rods, delineating a vast system of small communicating spaces that in life are filled with bone marrow. Trabeculae of spongy bone from weight bearing lower limb bones do not form a random network but occur in a precisely organized pattern along compression and tension stress lines. This strut-like arrangement of the trabeculae contributes to the strength of these bones. *Compact (dense) bone* appears as a solid, continuous mass in which spaces cannot be seen with the naked eye. The two types of

bone are not sharply delineated and merge into one another. In a typical long bone the shaft or diaphysis appears as a hollow cylinder of compact bone enclosing a large central space called the marrow cavity. The ends of the long bones, the epiphyses, consist mainly of cancellous bone covered by a thin layer of compact bone. The small inter-communicating spaces in the spongy bone are continuous with the marrow cavity of the shaft. Except over articular surfaces and where tendons and ligaments insert, bone is covered by a dense irregular fibroelastic connective tissue called the periosteum. The marrow cavity of the diaphysis and the spaces within spongy bone are lined by endosteum, which is similar to periosteum but is thinner and not as fibrous. Both the periosteum and endosteum have the ability to form new bone under appropriate stimulation. Flat bones, such as those of the skull, also consist of compact and spongy bone. The inner and outer plates (often called tables) consist of thick layers of compact bone, while the space between the plates is bridged by spongy bone called the diploë.

Microscopic Structure

A fundamental characteristic of bone is the arrangement of its mineralized matrix into layers or plates called lamellae. Small, ovoid spaces, the lacunae, occur rather uniformly within and between the lamellae, each occupied by a single bone cell or osteocyte. Slender tubules called canaliculi radiate from each lacuna and penetrate the lamellae to link up with the canaliculi of adjacent lacunae. Thus, lacunae are interconnected by an extensive system of fine canals. In compact bone, the lamellae show three arrangements. Most are arranged concentrically around a longitudinal space to form cylindrical units that run parallel to the long axis of the bone. These are osteons or Haversian systems and make up the structural units of bone. Osteons vary in size and consist of 8 to 15 concentric lamellae that surround a wide space occupied by blood vessels. In longitudinal sections, an osteon appears as plates of boney matrix running parallel to the slitlike space of the vascular channel. Throughout its thickness, compact bone contains a number of osteons running side by side. Osteons take an irregular course through the length of the bone and may branch. Other lamellae appear as angular, irregular bundles of lamellar bone that fill the spaces between osteons. These are called interstitial lamellae. Osteons and interstitial lamellae are outlined by a refractile line, the cement line, which consists of modified matrix. Cement lines are not traversed by canaliculi. At the external surface of the bone, immediately beneath the periosteum, several lamellae run around the circumference of the entire bone. A similar but less well-developed system of lamellae is present on the inner surface, just beneath the endosteum. These two systems of lamellae are the outer and inner circumferential lamellae, respectively. The longitudinally oriented channels at the center of osteons are the Haversian canals. These communicate with one another by oblique branches and by transverse connections called Volkmann's canals that penetrate the bone from the endosteal and periosteal surfaces. Unlike Haversian canals, Volkmann's canals are not surrounded by concentric lamellae. Volkmann's canals unite the blood vessels within the Haversian canals with vessels of the marrow cavity and periosteum. Thus, the nutritional needs of compact bone are met by a vast, continuous network of vascular channels. Canaliculi adjacent to a Haversian canal open into the perivascular space, and the canalicular system brings all the lacunae within that osteon into communication with the canal. Spongy bone shows a lamellar structure also but differs from compact bone in that it is not usually traversed by blood vessels. Therefore, osteons are rare or lacking in the irregular rods of lamellar bone that comprise spongy bone. It is thought that a critical distance (number of lamellae) exists beyond which osteocytes cannot be maintained by the canalicular system. These nutritional needs are met in trabeculae only a few lamellae in width as the canalicular system is linked to the perivascular region of the marrow cavity that resides around all

trabeculae. Trabeculae that exceed this critical distance, like compact bone, must contain Haversian systems to meet their nutritional needs.

Periosteum and Endosteum

The outermost layer of the periosteum is a relatively acellular dense irregular connective tissue with abundant collagen fibers, a few elastic fibers, and a network of blood vessels, branches of which enter Volkmann's canals. The deeper layers of periosteum (those closest to the bone) are more cellular (with osteogenetic potential) and consist of more loosely arranged connective tissue. During development of bone, collagen fibers of the periosteum are trapped in the circumferential lamellae and form Sharpey's fibers, which anchor the periosteum to the underlying bone. Endosteum lines all the cavities of bone, including the marrow spaces of the diaphysis and epiphysis and the Haversian and Volkmann's canals. It consists of a single layer of squamous to cuboidal cells with a small and variable content of supporting reticular and collagen fibers. As do the cells of the inner layer of the periosteum, the cells of the endosteum retain osteogenic potential.

Cells of Bone

Osteocytes are the primary cells found in mature bone and take the shape of the lacunae in which they are housed. They differ from osteoblasts, which are bone-forming cells. Osteocytes are not isolated in their lacunae but maintain extensive communication with nearby osteocytes. Delicate cytoplasmic processes extend from the cell bodies and traverse the canaliculi to contact processes from neighboring cells. At the points of contact, apposed cells form nexus (communicating) junctions. A thin layer of unmineralized matrix separates the cell and its processes from the walls of the lacunae and canaliculi and provides the means for diffusion of materials throughout the bony matrix. Osteocytes contain the usual cell organelles, but the Golgi apparatus is relatively inconspicuous, and ribosomes, mitochondria, and endoplasmic reticulum are scarce. Although the osteocyte appears to be not actively elaborating protein, it is not metabolically inert. It is responsible for maintaining bone, plays an active role in regulating calcium concentration in the body fluids, and is implicated in the resorption of bone. In areas where bone is being resorbed, large multinucleate giant cells are present. These are osteoclasts that often lie within shallow depressions along the surface of the bone, most frequently on an endosteal surface. These cavities are called Howship's lacunae. Although the cell may contain as many as 30 nuclei, the individual nuclei show no unusual features and usually are located in the part of the cell farthest from the bone. The cytoplasm, usually weakly to moderately acidophilic, contains multiple Golgi complexes and centriole pairs and numerous mitochondria and lysosomes. The cell surface adjacent to the bone shows a ruffled border, a surface modification unique to osteoclasts; osteoclasts that lack a ruffled border do not participate in bone resorption. The ruffled border consists of elaborate folds and clefts that abut the surface of the bone; the plasmalemma of the ruffled border is covered by small, bristle-like projections. A clear zone containing many actin filaments lies adjacent to the ruffled border, and mitochondria tend to accumulate nearby. The cell surface farthest from the bone shows a smooth contour. The cytoplasm of active osteoclasts has a frothy appearance due to numerous vacuoles that contain fragments of collagen and crystals of matrix. The plasmalemma of the ruffled border is rich in sodium/potassium ATPase and carbonic anhydrase that produces hydrogen ions. The area beneath the ruffled border is sealed off by the osteoclast and an acidic environment created to aid in the digestion of the mineral component of the bone matrix. In addition, the osteoclasts secret lysosomal enzymes,

primarily β-glucuronidase and aryl sulfatase, to breakdown the proteoglycans of the bone matrix and collagenase to digest type 1 collagen. Osteoclasts arise by fusion of monocytes that have emigrated from the blood. Osteoclast activity is stimulated indirectly by parathyroid hormone and vitamin D (via osteoblasts stimulated to secrete Interleukin-1) to increase bone resorption and elevate blood calcium levels. Osteoclasts have calcitonin receptors and their activity is reduced by the presence of calcitonin thereby reducing blood calcium levels.

Matrix of Bone

Bone matrix forms the bulk of bone and consists of collagen fibers, ground substance, and inorganic components. The ground substance contains proteoglycans similar to those of cartilage but in a lesser concentration. Glycosaminoglycans of bone include chondroitin sulfate, keratin sulfate, and hyaluronic acid. Osteocalcin and osteopontin are glycoproteins of bone that play a role in binding calcium salts to the collagenous component of the matrix. An additional glycoprotein isolated from bone, osteonectin, aids in binding cells of bone to the matrix. Bone has a relatively low degree of hydration of about 7% water. The collagen of bone is about 90% type I and forms the bulk of the bone matrix. When long bones such as the fibula are demineralized, they retain their shape and size due the large amount of collagen, but now are extremely flexible. They can even be tied in a knot. The unit fibrils of the collagen form a sophisticated internal network on which bone mineral is deposited. The collagen of more mature bone is laid down in a highly organized fashion so that in any one lamella the unit fibrils are parallel to one other and run a helical course about the Haversian canal. The pitch of the helix differs in adjacent lamellae so that the collagen unit fibrils of adjacent lamellae lie at right angles to one another. It is this highly organized arrangement of the collagen unit fibrils of bone that gives bone its strength. The inorganic component is responsible for the rigidity of bone and consists of calcium phosphate, citrate ions, and bicarbonate ions with small amounts of calcium and magnesium fluoride. The minerals are deposited as crystals of calcium and phosphate hydroxides called hydroxyapatite ($Ca_{10}(PO_4)_6(OH)_2$) and are present on and within the osteoid collagen (type 1) at regular intervals along the fibers.

Bone forms the principal tissue of support and is capable of bearing great weight. It provides attachment for muscles of locomotion, carries the joints, serves as a covering to protect vital organs, and houses the hemopoietic tissue. Bone is the major storehouse of calcium and phosphorus in the body. Osteocytes are the dominant cells of mature bones and are responsible for maintaining the matrix. They also aid in regulating the calcium and phosphorus levels of the body and play a role in the resorption of bone. Osteoclasts are specifically implicated in bone resorption. They destroy the ground substance and collagen and release minerals from the matrix. These cells elaborate lysosomal enzymes and contain high concentrations of citrate, which is involved in mobilizing calcium from bone. The initial stage of bone resorption by osteoclasts is extracellular: glycosaminoglycans of the matrix are degraded, permitting fragmentation of the bone. The fragments are phagocytosed by osteoclasts and digested intracellularly. The ruffled border of the osteoclasts increases the surface area and seals off the area of resorption and allows a local environment conducive to the digestion of bone.