Table 26-6 Classification of Major Primary Tumors Involving Bones

Category and fraction (%)	Behavior	Tumor type	Common locations	Age (yr)	Morphology
Hematopoietic (20)	Malignant	Myeloma Lymphoma	Vertebrae, pelvis	50-60	Malignant plasma cells or lymphocytes replacing marrow space
Cartilage forming (30)	Benign	Osteochondroma	Metaphysis of long bones	10-30	Bony excrescence with cartilage cap
		Chondroma	Small bones of hands and feet	30-50	Circumscribed hyaline cartilage nodule in medulla
		Chondroblastoma	Epiphysis of long bones	10-20	Circumscribed, pericellular calcification
		Chondromyxoid fibroma	Tibia, pelvis	20-30	Collagenous to myxoid matrix, stellate cells
	Malignant	Chondrosarcoma (conventional)	Pelvis, shoulder	40-60	Extends from medulla through cortex into soft tissue, chondrocytes with increased cellularity and atypia
Bone forming (26)	Benign	Osteoid osteoma	Metaphysis of long bones	10-20	Cortical, interlacing microtrabeculae of woven bone
		Osteoblastoma	Vertebral column	10-20	Posterior elements of vertebra, histology similar to osteoid osteoma
	Malignant	Osteosarcoma	Metaphysis of distal femur, proximal tibia	10-20	Extends from medulla to lift periosteum, malignant cells producing woven bone
Unknown origin (15)	Benign	Giant cell tumor	Epiphysis of long bones	20-40	Destroys medulla and cortex, sheets of osteoclasts
		Aneurysmal bone cyst	Proximal tibia, distal femur, vertebra	10-20	Vertebral body, hemorrhagic spaces separated by cellular, fibrous septae
	Malignant	Ewing sarcoma	Diaphysis of long bones	10-20	Sheets of primitive small round cells
		Adamantinoma	Tibia	30-40	Cortical, fibrous , bone matrix with epithelial islands
Notochordal (4)	Malignant	Chordoma	Clivus, sacrum	30-60	Destroys medulla and cortex, foamy cells in myxoid matrix

Adapted from Unni KK, Inwards CY: Dahlin's Bone Tumors, 6th ed. Philadelphia, Lippincott-Williams & Wilkins, 2010, p 5; by permission of Mayo Foundation.

body parts. Most bone neoplasms develop during the first several decades of life and have a propensity for the long bones of the extremities. The occurrence in certain age groups and predilection for particular anatomic sites provides important diagnostic clues about specific types of tumors. For example, osteosarcoma peaks during adolescence and most frequently involves the knee whereas chondrosarcoma affects older adults and involves the pelvis and proximal extremities.

Bone tumors may present in a number of ways. The more common benign lesions are often asymptomatic incidental findings. Many tumors, however, produce pain or a slow-growing mass. In some circumstances the first hint of a tumor's presence is a pathologic fracture. Radiographic imaging studies have an important role in diagnosing these lesions. In addition to providing the exact location and extent of the tumor, imaging studies can detect features that narrow the diagnostic possibilities. Ultimately, in almost all instances biopsy is necessary for definitive diagnosis.

When possible, bone tumors are classified according to the normal cell or matrix they produce. Lesions that do not have normal tissue counterparts are grouped according to their clinicopathologic features (Table 26-6). **Benign tumors greatly outnumber their malignant counterparts** and occur with greatest frequency within the first three decades of life, whereas in older adults, a bone tumor is likely to be malignant. Excluding neoplasms originating from hematopoietic cells (myeloma, lymphoma, and leukemia), osteosarcoma is the most common primary cancer of bone, followed by chondrosarcoma and Ewing sarcoma.

Insults that induce chronic injury and inflammation, such as bone infarcts, chronic osteomyelitis, Paget disease, radiation, and metal prostheses, increase the risk of bone neoplasia, possibly because proliferation associated with chronic inflammation and repair set the stage for acquisition of oncogenic mutations. As we will describe, some of the causative mutations involve classic oncogenes and tumor suppressors that are implicated in many other tumors, whereas others involve genes that are specifically involved in bone development and are mutated only in bone tumors.

Bone-Forming Tumors

Tumors in this category all produce unmineralized osteoid or mineralized woven bone.

Osteoid Osteoma and Osteoblastoma

Osteoid osteoma and osteoblastoma are benign bone-producing tumors that have identical histologic features but differ in size, sites of origin, and symptoms. Osteoid osteomas are, by definition less than 2 cm in diameter, and usually occur in young men in their teens and 20s. These tumors can arise in any bone but have a predilection for the appendicular skeleton. About 50% of cases involve the femur or tibia, wherein they typically arise in the cortex and less frequently within the medullary cavity. Usually, there is a thick rind of reactive cortical bone that may be the only clue radiographically. Despite the small size, they present with severe nocturnal pain that is relieved by aspirin and other non-steroidal anti-inflammatory agents. The pain is probably caused by prostaglandin E_2 (PGE_2) produced by the proliferating osteoblasts. Osteoblastoma is larger than 2 cm and involves the posterior spine (laminae and pedicles) more frequently; the pain is unresponsive to aspirin, and the tumor usually does not induce a marked bony reaction. Osteoid osteoma is frequently treated by radiofrequency ablation, whereas osteoblastoma is usually curetted or excised en bloc. Malignant transformation is rare.