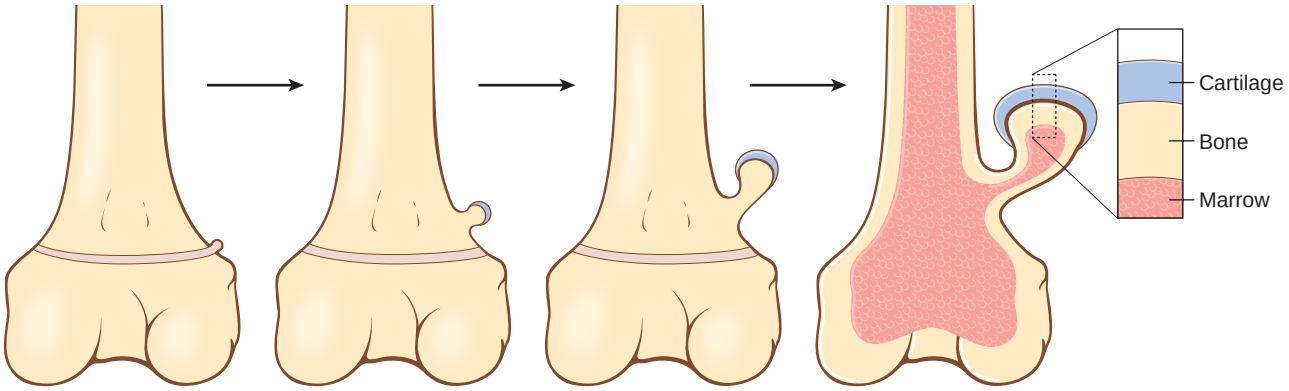

Figure 26-27 The development of an osteochondroma, beginning with an outgrowth from the epiphyseal cartilage.

Chondromas

Chondromas are benign tumors of hyaline cartilage that usually occur in bones of enchondral origin. They can arise within the medullary cavity, where they are known as *enchondromas*, or on the surface of bone, where they are called *juxtacortical chondromas*. Enchondromas are the most common of the intraosseous cartilage tumors and are usually diagnosed in individuals 20 to 50 years of age. Typically, they appear as solitary metaphyseal lesions of tubular bones of the hands and feet. The radiographic features consist of circumscribed lucencies with central irregular calcifications, a sclerotic rim and an intact cortex (Fig. 26-28). *Ollier disease* and *Maffucci syndrome* are nonhereditary disorders characterized by multiple enchondromas. *Maffucci syndrome* is, in addition, distinguished by presence of spindle cell hemangiomas.

Most enchondromas of large bones are asymptomatic and are detected incidentally. Occasionally, they are painful and cause pathologic fracture. The tumors in enchondromatosis may be numerous and large, producing severe deformities.

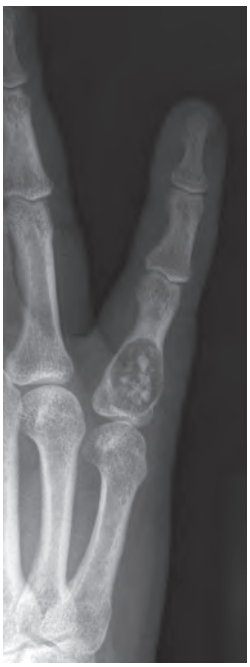

Figure 26-28 Enchondroma of the proximal phalanx. The radiolucent nodule of cartilage with central calcification thins but does not penetrate the cortex.

Pathogenesis. Heterozygous mutations in the *IDH1* and *IDH2* genes have been identified in the chondrocytes of syndromic and solitary enchondromas. Patients with enchondroma syndromes are mosaics, harboring IDH mutations in only a subset of otherwise normal cells throughout their bodies. Similarly, IDH mutations are found in only a subset of tumor cells in both syndromic and sporadic enchondromas. This unusual situation may be explained by the functional consequences of the IDH1 and IDH2 mutations. Both cause the encoded proteins, two isoforms of the enzyme isocitrate dehydrogenase, to acquire a new enzymatic activity that leads to the synthesis of 2-hydroxyglutarate. You will recall from Chapter 7 that this so-called "oncometabolite" interferes with regulation of DNA methylation. It is hypothesized that the 2-hydroxyglutarate produced by the subset of IDH-mutated cells in enchondromas diffuses into neighboring cells with normal IDH genes, thereby causing oncogenic epigenetic changes in genetically normal neighbors (transformation by association).

MORPHOLOGY

Enchondromas are usually smaller than 3 cm and are gray-blue and translucent. They are composed of well-circumscribed nodules of hyaline cartilage containing cytomorphologically benign chondrocytes (Fig. 26-29). The peripheral portion of the nodules may undergo enchondral ossification, and the center can calcify and infarct. The enchondromas in Ollier disease and Maffucci syndrome are sometimes more cellular than sporadic enchondromas and exhibit cytologic atypia, making them more difficult to distinguish from chondrosarcomas.

Clinical Course. The growth potential of chondromas is limited. Treatment depends on the clinical situation and is usually observation or curettage. Solitary chondromas rarely undergo sarcomatous transformation, but those associated with enchondromatosis do so more frequently. Individuals with Maffucci syndrome are also at risk of developing other types of malignancies, including ovarian carcinomas and brain gliomas.