Osteonecrosis is common and represents loss of blood supply to a region of bone. Common sites affected include the femoral head, humeral head, knee, femoral/tibial metaphysis, scaphoid, lunate, and talus. Symptomatic femoral head osteonecrosis accounts for 10,000–20,000 new cases annually in the United States. In contradistinction, metadiaphyseal osteonecrosis is often occult and asymptomatic. There are numerous causes of osteonecrosis most commonly related to trauma, corticosteroids, and idiopathic. Imaging of osteonecrosis is frequently diagnostic with a serpentine rim of sclerosis on radiographs, photopenia in early disease at bone scintigraphy, and maintained yellow marrow at MR imaging with a serpentine rim of high signal intensity (double-line sign) on images obtained with long repetition time sequences. These radiologic features correspond to the underlying pathology of osseous response to wall off the osteonecrotic process and attempts at repair with vascularized granulation tissue at the reactive interface. The long-term clinical importance of epiphyseal osteonecrosis is almost exclusively based on the likelihood of overlying articular collapse. MR imaging is generally considered the most sensitive and specific imaging modality both for early diagnosis and identifying features that increase the possibility of this complication. Treatment subsequent to articular collapse and development of secondary osteoarthritis typically requires reconstructive surgery. Malignant transformation of osteonecrosis is rare and almost exclusively associated with metadiaphyseal lesions. Imaging features of this dire sequela include aggressive bone destruction about the lesion margin, cortical involvement, and an associated soft-tissue mass. Recognizing the appearance of osteonecrosis, which reflects the underlying pathology, improves radiologic assessment and is important to guide optimal patient management.

Introduction and Clinical Characteristics

Osteonecrosis (ON), similar to ischemia in other organ systems, results from a reduction or complete loss of blood supply to bone. The term ischemic necrosis or avascular necrosis (or aseptic necrosis), by convention, has been applied to epiphyseal or subarticular bone involvement and bone infarction to metadiaphyseal sites. In this article, we will use the more all-inclusive term osteonecrosis to describe all these locations of devitalized bone.

ON is a common condition. It is estimated that the rate of symptomatic femoral head ON is 2–4.5 cases per patient year, resulting in 10,000–20,000 new cases annually in the United States (1–3). However, this incidence markedly underestimates the true prevalence of ON, as the majority of patients are asymptomatic, particularly with
metadiaphyseal involvement. This is further emphasized by the estimates that between 3% and 38% of patients with cardiac transplantation and acute lymphoblastic leukemia (ALL) reveal areas of ON at magnetic resonance (MR) imaging, presumably related to corticosteroid treatment (4,5).

The etiology of ON is varied with many associated diseases (Table 1). However, the most common causes are idiopathic, trauma, corticosteroids, and alcoholism. In the study by Ito and colleagues (6) from Japan of femoral head ON, 35% of cases were due to steroids, 22% were due to alcoholism, and 37% were idiopathic. Trauma is also a frequent cause of ON in the femoral head (owing to femoral neck fractures or hip dislocations), scaphoid (proximal pole related to scaphoid waist fractures), and talus (associated with talar neck fractures) with disruption of end-artery blood supply. Traumatic ON is typically unilateral, in contradistinction to nontraumatic ON, which is commonly bilateral in up to 70%-80% of cases (6,7).

The pathogenesis of corticosteroid-induced ON is uncertain. Primary considerations include adipose infiltration of the liver with subsequent fatty embolization, osteoporotic induced microfractures and subsequent collapse, vasculitis, vascular coagulation with increased blood viscosity, and increased bone marrow fatty deposition (7,8). The likelihood of secondary ON is increased with higher steroid dose and longer duration of therapy (>6 months) as well as divided doses (8).

Common sites to be affected with ON include the femoral head (Figs 1–3), humeral head, about the knee (distal femur and proximal tibia), femoral metadiaphysis (Fig 4), tibial metadiaphysis (Figs 4, 5), scaphoid, lunate, and talus. Idiopathic ON is more common in males (4–8:1 ratio) in the 4th to 6th decades of life (6,7). The clinical diagnosis of ON is often difficult owing to lack of specific symptoms and the multiplicity of locations that can be affected. Symptomatic patients typically reveal pain and reduced range of motion. Initially, pain is associated with an increase in intramedullary pressure resulting from medullary bone marrow edema. Subsequent symptoms and the long-term clinical importance of ON are largely predicated on the likelihood of overlying articular collapse. This is the explanation why metadiaphyseal areas of ON have limited to no long-term sequelae, as bone collapse does not occur and dead bone is as strong as viable bone but lacks the ability to remodel. Similarly, identification of imaging features associated with an increased incidence of

<table>
<thead>
<tr>
<th>Table 1: Causes of ON</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Common</strong></td>
</tr>
<tr>
<td>Trauma</td>
</tr>
<tr>
<td>Corticosteroids (exogenous and endogenous)</td>
</tr>
<tr>
<td>Idiopathic</td>
</tr>
<tr>
<td>Sickle cell anemia</td>
</tr>
<tr>
<td>Collagen vascular disease</td>
</tr>
<tr>
<td>Alcoholism</td>
</tr>
<tr>
<td><strong>Uncommon</strong></td>
</tr>
<tr>
<td>Pancreatitis</td>
</tr>
<tr>
<td>Renal transplantation</td>
</tr>
<tr>
<td>Drug therapy (immunosuppressive, cytotoxic therapy, bisphosphonates [jaw])</td>
</tr>
<tr>
<td>Pregnancy</td>
</tr>
<tr>
<td>Radiation therapy</td>
</tr>
<tr>
<td>Occlusive vascular disease (thromboembolic disease and arteriosclerosis)</td>
</tr>
<tr>
<td>Infection (including human immunodeficiency virus)</td>
</tr>
<tr>
<td>Leukemia/lymphoma</td>
</tr>
<tr>
<td>Vasculitis</td>
</tr>
<tr>
<td>Diabetes</td>
</tr>
<tr>
<td><strong>Rare</strong></td>
</tr>
<tr>
<td>Dysbaric conditions (caisson disease)</td>
</tr>
<tr>
<td>Hemophilia</td>
</tr>
<tr>
<td>Gout</td>
</tr>
<tr>
<td>Thermal injury (burn, frostbite)</td>
</tr>
<tr>
<td>Gaucher disease</td>
</tr>
<tr>
<td>Langerhans cell histiocytosis</td>
</tr>
<tr>
<td>Neuropathic arthropathy</td>
</tr>
<tr>
<td>Polycythemia vera</td>
</tr>
<tr>
<td>Multiple epiphyseal dysplasia</td>
</tr>
</tbody>
</table>

Figure 1. Radiologic manifestations of ON in the adult femoral head in several different patients. (a) Static bone scintigram of the pelvis shows photopenia in the left femoral head (circle), representing early ON. (b–d) Frontal radiograph of the pelvis (b), frog-leg lateral radiograph of the left hip (c), and coronal computed tomographic (CT) image (d) reveal typical features of ON, with an area of abnormality in the superolateral femoral heads (Δ) and a rim of sclerosis (arrows), but no evidence of articular collapse on the pelvic radiograph. There is a small focus of femoral head flattening and collapse on the left (arrowheads in e and d), where the rim of sclerosis extends to the articular surface. (e–g) Coronally sectioned gross specimen (e), whole-mount specimen (f) (hematoxylin-eosin [H-E] stain), and pictorial representation (g) demonstrate similar features as seen at imaging and typical appearances of ON, with the zone of cell death (*), reactive interface or creeping zone of substitution (area between straight arrows), zone of reinforcing trabecular bone (arrowheads in f), zone of reactive marrow (RM), and zone of normal marrow (NM). There is a focal area of femoral head flattening and collapse where the lateral rim of sclerosis extends to the articular surface (curved arrow) with disruption of the overlying cartilage (G). (Fig 1g courtesy of Aletta Ann Frazier, MD, American Institute for Radiologic Pathology, Silver Spring, Md, and University of Maryland School of Medicine, Baltimore, Md.)
Figure 2. Radiologic manifestations of the crescent sign indicative of articular collapse in ON of the adult femoral head in several different patients. (a) Static bone scintigram of the right hip demonstrates increased uptake of radionuclide (circle) with photopenia centrally (*). (b) Frontal radiograph of the right femoral head shows typical features of ON with patchy sclerosis in the femoral head (arrowheads) and a lucent crescent in the subarticular bone representing early articular collapse (arrowheads). (c–e) Sagittal T1-weighted (500/9 [repetition time msec/echo time msec]) (c), sagittal T2-weighted with fat suppression (3350/37) (d), and coronal T2-weighted with fat suppression (3116/40) (e) MR images reveal typical features of ON and collapse with a subarticular fracture (crescent sign). The area of ON demonstrates maintained yellow marrow (*) with the double-line sign, represented by the inner high-signal-intensity area (black arrowheads in d and e), the reactive interface or zone of creeping substitution, and the outer low-signal-intensity sclerotic rim (white arrowheads). The crescent of high signal on the water-sensitive images (d and e) and low signal on the T1-weighted image (c) represents the subarticular fracture (arrows), and there is surrounding marrow edema (M) and joint effusion (E). (f–h) Coronal sectioned gross specimen (f), whole-mount specimen (H-E stain) (g), and pictorial representation (h) demonstrate ON with the zone of cell death (*), active interface or creeping zone of substitution (area between straight arrows), zone of reinforcing trabecular bone (arrowheads in g), zone of reactive marrow (RM), and zone of normal marrow (NM). The curvilinear crescent of a subchondral fracture (curved arrows) and separation between the ON and overlying cartilage and attached cortex (C) is also apparent (crescent sign). (Fig 2h courtesy of Aletta Ann Frazier, MD, American Institute for Radiologic Pathology, Silver Spring, Md, and University of Maryland School of Medicine, Baltimore, Md.)

Figure 3. ON in a 50-year-old man with failed core decompression 2 years earlier for treatment of avascular necrosis and development of femoral head collapse. (a) Conventional tomogram shows core decompression tracts (arrows) and changes of ON (arrowheads) with articular collapse (arrowheads). (b) Specimen CT image reveals ON (black *), with marginal sclerosis (arrows) and a core decompression tract (white *) that does not extend prominently into the area of ON. Articular collapse with the crescent sign (CR) is also seen, with separation between the overlying cartilage (C) and attached cortex and subchondral bone (SB) creating this radiologic appearance. (c) Coronally sectioned gross specimen shows similar features of a core decompression tract (arrows), areas of ON (*), a rim of sclerosis (arrowheads), and collapse with the crescent of a subchondral fracture (CR) separating cartilage and attached cortex (C) and subchondral bone (SB) from the underlying area of necrosis.
Figure 4. Femoral and tibial metadiaphysseal areas of ON in several different patients. (a) Lateral radiograph of the knee shows typical features of ON, with a serpentine rim of sclerosis (arrowheads) in the distal femoral and proximal tibial metadiaphyses. (b) Axial CT image reveals a typical serpentine rim of sclerosis (arrows) surrounding the area of ON. (c, d) Coronal T1-weighted (500/20) (c) and T2-weighted fat-suppressed (4000/100) (d) MR images demonstrate an area of ON with maintained adipose signal intensity (*) and the double-line sign, representing a rim of sclerosis (arrows) (outer border with low signal intensity with all pulse sequences) and an inner rim of high signal intensity on the long repetition time image (circles in d), corresponding to the reactive interface or zone of creeping substitution. (e, f) Coronal sectioned gross specimen (e) and whole-mount specimen (H-E stain) (f) demonstrate a serpentine rim of sclerosis (arrowheads), central infarcted adipose tissue (A), and fibrosis (F) surrounding viable yellow marrow (M) and a small reactive interface or creeping zone of substitution (circles).

Pathology of Osteonecrosis

The initial phase of ON is cell death, interruption of cell enzymes, and loss of cell metabolic activity. However, the cells that make up bone vary in their ability to withstand ischemic injury. Hematopoietic cells are most sensitive and die within 6–12 hours (9). Bone cells (osteoclasts, osteoblasts, and osteocytes) may survive from 12 to 48 hours (9,10). Uniformly empty lacunae (lacking osteocytes) in localized areas indicate ON if artifactual loss due to tissue processing overlying articular collapse is important to guide appropriate therapy.
and decalcification can be excluded. A few empty lacunae are not diagnostic of ON because there is normal loss of osteocytes with aging. Conversely, observation of osteocytes within lacunae is not definite evidence of viability because these may be present for some time after cell death.

The marrow fat is most resistant to ischemic insult, and these cells may survive for 2–5 days of anoxia (9,11). Marrow fat necrosis is characterized by loss of adipocyte nuclei, opacification of adipocyte cytoplasm, formation of foam cells or lipid-filled cysts, and occasional dystrophic calcification (9–12). Finally, chondrocytes are normally adapted to relatively low oxygen tension and do not become devitalized, with the exception of the cartilage cells below the tidemark, seen as absence of chondrocytes. This initial phase of ON typically reveals no gross or macroscopic pathologic manifestations and is limited to microscopic alterations (12).

The next pathologic phases represent a continuum of development of a reactive interface in an attempt to wall off and repair the area of ON. Initially, the tissue adjacent to the area of ON reveals increased vascularity and marrow reaction with increased inflammatory fibrovascular infiltration. This can result in trabecular resorption resulting from hyperemia as opposed to the area of ON, with increased density and trabeculation relative to the adjacent hyperemic areas. At gross pathologic evaluation, this can appear as a wedge-shaped, dull, chalky, and opaque area within the trabecular bone and a thin red border representing the developing reactive interface (12–14).

Over time, the reactive interface continues to develop and mature as a discrete zone at the margin of the area of ON. This reactive interface zone is essentially vascularized granulation tissue attempting to repair the area of ON and has been termed the creeping zone of substitution (Figs 1, 2, 4, 5). Because of vascularity in this area, osteoblasts and osteoclasts are supported, in contradistinction to the area of ON. The process of osteoblast deposition of appositional bone, often upon dead trabeculae, and osteoclastic resorption of devitalized bone occurs in and about the reactive interface. At the margin of the creeping zone of substitution with viable vascularized bone, osseous reinforcement occurs in compensatory response to bone weakening caused by the reactive interface (Figs 1, 2, 4, 5). This progresses to a rim of sclerosis that is frequently prominently undulating or serpentine in morphology. The reactive interface undergoes progressive remodeling and repair at the junction with the area of ON. Unfortunately, this creeping zone of substitution neither creeps nor substitutes or repairs the areas of ON extensively in the vast majority of cases (15).

In epiphyseal ON, the junction of the reactive zone with the articular subchondral bone plate also undergoes increased bone resorption. Forces are often maximized at the site with weight-bearing and impaction along the soft reactive zone tissue, particularly in the femoral head. This can initiate early fracture of the overlying cartilage at these locations (Fig 1). The impaction associated with the reactive zone soft tissue may cause
cleavage of the subchondral bone from the overlying cartilage and cortex, creating a subchondral fracture plane (16) (Fig 2). This is often the earliest manifestation of articular collapse and has a crescentic appearance in the femoral or humeral heads both pathologically and radiologically (crescent sign) (Figs 2, 3). Progressive fragmentation of the articular surface and secondary osteoarthrosis are almost inevitable subsequent to these initial changes of cortical flattening and collapse (17) (Fig 3).

**Imaging of Adult Osteonecrosis**

Imaging evaluation of ON should begin with radiography, as it is the least expensive and most widely available method of radiologic assessment. While radiography is insensitive for early changes of ON, which require several months to occur, the imaging features are often characteristic and may obviate the need for additional radiologic evaluation. Initially, bone sclerosis may be present and related to the surrounding bone osteopenia, as opposed to the avascular regions. However, the typical radiographic appearance is of patchy areas of lucency and sclerosis. Importantly, the sclerosis is characteristically about the lesion rim with a serpentine (more common in metadiaphyseal lesions) or undulating morphology (Figs 1–5). The sclerotic margin corresponds to the host bone response to wall off the areas of necrosis. Radiography may also demonstrate early areas of articular collapse in epiphyseal ON, particularly involving the anterolateral and anterior femoral head, and both frontal and frog-leg lateral projections should be obtained (Figs 2, 3). Early changes of articular collapse typically occur at the junction of the serpentine sclerotic rim and the articular surface, where stress is maximally exerted (Fig 1). Continued subsidence may create a crescentic subchondral lucency (crescent sign), representing collapse of the subchondral bone and separation from the overlying cartilage and attached subchondral bone plate (Figs 2, 3). Subsequently, articular fragmentation, progressive articular collapse, and secondary osteoarthrosis often occur.

The relative insensitivity of radiography for early changes of ON has led to use of additional imaging modalities including nuclear medicine. In early stages of ON, bone scintigraphy (including blood flow, blood pool, and static phases) and bone marrow scans may reveal photopenia and may require high-resolution (pinhole collimation) techniques (Fig 1). Lesions typically reveal increased radionuclide during the more chronic reparative process, which is frequently peripheral with central photopenia at bone scintigraphy (Fig 2). More diffuse increased radionuclide activity is usually present in epiphyseal involvement with articular collapse and secondary osteoarthrosis. The addition of single-photon-emission computed tomography (SPECT) may improve the accuracy of radionuclide imaging for diagnosis of ON (18,19). In a study by Ryu and colleagues (19), SPECT was determined to be more sensitive than MR imaging (100% vs 66%) in detecting early ON following renal transplantation.

Multidetector CT has not been extensively studied in evaluation of ON. CT of early femoral head ON may reveal alteration of the normal “asterisk” that is formed by condensation of the compressive and tensile trabeculae. However, CT is not advocated for early detection of ON and is less sensitive than scintigraphy or MR imaging (20). Later stages of ON are well depicted with CT, and similar to radiography, show a serpentine or undulating sclerotic margin (Figs 1, 3, 4). Multidetector CT is useful for detecting articular collapse location and extent in epiphyseal ON and was superior to both radiography and MR imaging in several studies (21,22). This information is particularly important in surgical planning for rotational arthroplasty (23).

MR imaging is generally regarded as the most sensitive and specific image modality for identification of ON, with some series reporting 97%–100% accuracy (4,8,24–27). Two MR imaging features that increase the risk of development of femoral head ON are a thick physeal scar and early conversion to yellow marrow (28). MR imaging findings of ON have been reported to be present as early as 1 week subsequent to induced vascular injury in an animal study by Brody et al (29). There are only rare reports of ON with a normal MR imaging examination (30).

The most common MR imaging pattern seen in ON is an area of yellow marrow surrounded by a low-signal-intensity rim with all pulse sequences (Figs 2, 4). This imaging appearance corresponds to the underlying pathology and walling off of the areas of ON by a rim of sclerosis. The yellow marrow signal intensity is maintained because viable and devitalized adipose tissues have an identical intrinsic MR imaging appearance. The rim of sclerosis is often crescentic/band-like/ring-like or wedge shaped with epiphyseal ON or serpentine with metadiaphyseal ON. A “double-line” sign has been described in 65%–85% of cases of ON (31,32) (Figs 2, 4). The outer low-signal-intensity rim of sclerosis and a second inner zone of high signal intensity on long repetition time MR images represent the reparative granulation tissue of the reactive interface. This inner zone corresponds to the pathologic “creeping zone of substitu-
tion” (Figs 2, 4). Unfortunately, identical to the pathology literature, this reparative tissue neither creeps nor substitutes significantly radiologically, resulting in limited true healing in the vast majority of patients with ON. Kopecky and co-workers (33) have reported healing of small lesions in the femoral head in a limited number of asymptomatic patients, but this is the exception and rare, in our experience, in epiphyseal or metadiaphyseal areas of ON. The double-line sign may also partially result from chemical-shift misregistration artifact (34).

The MR signal intensity in the area of ON may also show intrinsic characteristics other than adipose tissue in a minority of patients. These were originally described by Mitchell and colleagues (35) and include hemorrhage (high signal intensity on T1- and T2-weighted images), cystic areas (low signal intensity on T1-weighted images and high signal intensity on T2-weighted images), and fibrous tissue (low signal intensity with all pulse sequences). In our experience, this variability is much more common in epiphyseal areas of ON and does not have prognostic significance as originally suggested. Additional variations in the MR imaging appearance of ON are also described, including nonspecific diffuse marrow signal abnormality (decreased signal intensity on T1-weighted images and variable signal intensity on T2-weighted images) (32,36,37). This more nonspecific MR imaging pattern is unusual, in our experience, and is often associated in patients with diffuse marrow disease or red marrow reconversion (sickle cell anemia, Gaucher disease, and chronic renal failure patients treated with erythropoietin).

The use of contrast-enhanced MR imaging in adult ON is typically not necessary for diagnosis or assessment in the vast majority of cases. However, in animal studies, Nadal and colleagues (38) showed that dynamic contrast-enhanced MR imaging was most sensitive to detect ON in early surgically induced femoral head disease. The typical appearance of ON on postcontrast MR imaging is lack of enhancement of the devitalized tissue. There is often a peripheral rim of enhancement corresponding to the zone of creeping substitution granulation tissue. Dynamic contrast-enhanced studies reveal increased peak enhancement and delayed time to peak enhancement (39,40). More variable patterns of enhancement, perhaps corresponding to mixtures of ischemia and fibrosis, have been reported by Li and Hiette (41) and Hauzeur and colleagues (42). Several investigations have described use of contrast enhancement to assess risk of development of femoral head ON after femoral neck fracture (43,44). Foci of ON as a result of femoral neck fractures are common and have been reported in up to 75% of cases at histologic evaluation (45). MR imaging with a diffusion sequence, T2 mapping, and apparent diffusion coefficient (ADC) mapping has also been advocated more recently to evaluate epiphyseal ON, although these techniques remain investigational (2,46–48).

### Staging of Adult Femoral Head Osteonecrosis

Various staging systems have been developed for assessment of adult femoral head ON. These include the Ficat and Arlet, Steinberg, and Association Research Circulation Osseous (ARCO) classifications (Tables 2–4). All of these staging systems have in common progression from radiologically occult disease to positive imaging alterations of ON to femoral head collapse and finally development of secondary osteoarthritis. As previously emphasized, the clinical significance of epiphyseal ON is almost entirely dependent on the likelihood of articular collapse. Imaging predictors of this sequela are therefore important to identify and guide appropriate treatment. The volume of the femoral head involved by ON appears to be the most important imaging predictor of subsequent articular

<table>
<thead>
<tr>
<th>Stage</th>
<th>Clinical Features</th>
<th>Radiologic Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>No pain</td>
<td>Normal radiographs</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Decreased or increased uptake on bone scan</td>
</tr>
<tr>
<td>II</td>
<td>Variable pain</td>
<td>Variable change in trabecular bone appearance with sclerosis and cyst formation with preserved femoral head shape</td>
</tr>
<tr>
<td>III</td>
<td>Pain</td>
<td>Collapse of subchondral bone/crescent sign secondary to subchondral bone fracture</td>
</tr>
<tr>
<td>IV</td>
<td>Pain</td>
<td>Marked collapse of subchondral bone with preservation of joint space</td>
</tr>
<tr>
<td>V</td>
<td>Pain</td>
<td>Secondary osteoarthritis</td>
</tr>
</tbody>
</table>

Source.—Reference 118.
collapse. This is optimally assessed with MR imaging. ON affecting more than 25%–50% of the femoral head volume is much more likely to progress to articular collapse (43%–87% of patients) (Fig 2) (49–51). In contradistinction, femoral head ON involving less than 25%–30% of the femoral head is unlikely to lead to articular collapse (0%–5% of patients) (49–51). While all MR imaging planes should be assessed for volume involved by ON of the femoral head, Ha and co-workers (52) have emphasized the importance of the sagittal plane. We also postulate that increased thickness of the reparative zone may predispose to articular collapse, because impaction of this soft-tissue region with weight-bearing accentuates forces at the sclerotic rim articular surface junction. Additional MR imaging features associated with increased stage and likelihood of femoral head collapse include older patient age (>40 years), increasing volume of joint effusion, presence of prominent surrounding edema, and larger body mass index (≥24 kg/m²) (52–54).

There are two conditions involving the femoral head that can simulate ON leading to misdiagnosis and require imaging distinction. These two diseases are transient osteoporosis of the hip (bone marrow edema syndrome) and subchondral insufficiency fracture. Transient osteoporosis of the hip reveals femoral head osteopenia at radiography, diffuse marked increased radionuclide uptake in the femoral head (without central photopenia as in ON), and narrow replacement of the femoral head marrow on T1-weighted MR images that demonstrates marked diffuse

<table>
<thead>
<tr>
<th>Stage</th>
<th>Imaging Characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Normal radiographs, bone scan, and MR images</td>
</tr>
<tr>
<td>I*</td>
<td>Normal radiograph</td>
</tr>
<tr>
<td></td>
<td>Abnormal bone scan and/or MR images</td>
</tr>
<tr>
<td>II*</td>
<td>Abnormal radiograph with cystic and sclerotic changes in femoral head</td>
</tr>
<tr>
<td>III*</td>
<td>Subchondral collapse producing crescent sign</td>
</tr>
<tr>
<td>IV*</td>
<td>Flattening of the femoral head</td>
</tr>
<tr>
<td>V*</td>
<td>Joint space narrowing with or without acetabular involvement</td>
</tr>
<tr>
<td>VI*</td>
<td>Advanced secondary degenerative changes</td>
</tr>
</tbody>
</table>

Source.—Reference 119.
*Extent or grade of involvement should be indicated as A = mild, B = moderate, C = severe.

<table>
<thead>
<tr>
<th>Stage</th>
<th>Clinical Features</th>
<th>Radiologic Findings</th>
<th>Histologic Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>No symptoms</td>
<td>Normal radiographs and MR images</td>
<td>ON present</td>
</tr>
<tr>
<td>I</td>
<td>Presence or absence of symptoms</td>
<td>Normal radiographs Abnormal MR images</td>
<td>ON present</td>
</tr>
<tr>
<td>II</td>
<td>Symptoms present</td>
<td>Radiographs with trabecular bone changes without subchondral bone changes and preserved joint space Diagnostic MR images</td>
<td>ON present</td>
</tr>
<tr>
<td>III*</td>
<td>Symptoms present</td>
<td>Variable trabecular bone changes with subchondral bone fracture (crescent sign and/or subchondral bone collapse) Preserved femoral head shape and hip joint space</td>
<td>ON present</td>
</tr>
<tr>
<td>IV†</td>
<td>Symptoms present</td>
<td>Altered shape of femoral head with variable joint space</td>
<td>ON present</td>
</tr>
</tbody>
</table>

Source.—Reference 120.
Note.—ARCO = Association Research Circulation Osseous.
*Stage III subclassification (based on extent of crescent): IIIa = crescent <15% of articular surface, IIIb = crescent 15%–30% of articular surface, IIIc = crescent >30% of articular surface.
†Stage IV subclassification (based on extent of collapsed articular surface): IVa = <15% of surface collapsed, IVb = 15%–30% of surface collapsed, IVc = >30% of surface collapsed.
increased signal intensity on long repetition time images and diffuse enhancement after contrast (without crescentic areas of signal variation or nonenhancement in the superolateral femoral head as in ON) (32,55). In subchondral insufficiency fracture, the low-signal-intensity bandlike region in the superolateral femoral head is convex toward the articular surface (as opposed to concave in ON) and contrast enhancement is frequently apparent proximal to this region (90% of cases) (56).

**Legg-Calvé-Perthes Disease**

Legg-Calvé-Perthes disease (LCP) is idiopathic ON of the immature femoral head epiphysis, which affects approximately 1 in 10,000 children (57). There is a 3–5:1 male-to-female predominance and Caucasians are more commonly affected (57,58). There is an increased incidence in children with lower socioeconomic status, low birth weight, and delayed skeletal maturation. The peak age of incidence is 5–6 years, although LCP tends to occur in girls at a younger age (57). The disease is bilateral in 10%–15% of patients but almost always metachronous (59,60).

Children with LCP typically present clinically with several weeks to months of limping gait. Knee pain may be the only presenting symptom. Evaluation of the hip should be pursued in a patient in the proper age group who complains of knee pain. Physical examination reveals decreased range of motion of the hip, particularly in abduction and internal rotation (60).

The etiology of LCP remains unclear a century after it was initially described, but ischemia due to disruption of the delicate subsynovial vascular supply to the developing femoral head epiphysis, transient disorder of epiphyseal cartilage maturation, microtrauma, and hypercoagulability have been implicated (61,62). Several relatively unique features of ON in the immature skeleton deserve recognition. During the initial avascular phase, the child is usually asymptomatic. The ossific nucleus of the affected femoral head fails to grow due to absence of blood flow necessary for enchondral ossification. The articular cartilage is supplied with nutrients from the synovium and continues to grow (62). In the revascularization stage, the child becomes symptomatic. Granulation tissue invades the necrotic femoral head with a variable degree of repair continuing into the healing phase, and there is susceptibility to collapse. Accompanying epiphysal cartilage thickening, synovial hypertrophy, and joint effusion as well as lateral collapse of the ossific nucleus may lead to lateral subluxation and loss of containment of the femoral head. Changes may also develop in the metaphysis, which appear radiolucent on radiographs. These may pathologically represent extension of physeal cartilage into the metaphysis due to impaired enchondral ossification (63,64). The more the femoral head is contained by the acetabulum in the healing phase, the greater the sphericity of the remodeled head. Eventually, the osseous fragments (if present) coalesce and the femoral head epiphysis is replaced by mature trabecular bone. The residual deformity may be mild or may be severe if there is femoral head collapse and loss of sphericity resulting in incongruity of the hip joint.

Several clinical and pathophysiologic features have prognostic implications and help to guide therapeutic decisions. Girls tend to have a worse outcome compared with boys. Children affected before age 6 years generally have a benign course usually requiring only conservative therapy, whereas those afflicted after age 8 years have a more complicated course. Under the age of 6 years, there is more plasticity in the developing acetabulum so that it is able to remodel in response to changes in the shape of the femoral head, thereby maintaining joint congruity. Furthermore, greater extent of necrosis of the femoral head is associated with a worsened prognosis (65). The degree of preservation of the lateral one-third or lateral pillar has particular prognostic importance because this is the site of weight bearing and early revascularization. Preservation of the height of the lateral pillar portends a good outcome, while collapse of the lateral pillar is associated with increased complications (66–68). Finally, the development of metaphyseal “cystic” changes is also associated with physeal growth disturbance and greater degree of deformity (Fig 6) (63,64,69).

Similar to adults, radiography is considered the best initial examination for suspected LCP (59,70,71), with frontal and frog-leg lateral projections mandatory for complete evaluation. Radiographic features of LCP may be apparent only on frog-leg lateral views (Fig 6). Many of the radiographic manifestations of LCP are similar to those seen in adults including normal, heterogeneous increased density and fragmentation in the femoral head ossific nucleus, osteopenia of the adjacent bone and development of a sclerotic margin, and femoral head collapse (leading to the crescent sign) (35). The revascularization phase is also characterized by synovial proliferation and joint effusion, which may cause mild lateral subluxation of the femoral head (35). Residual deformities may develop including a flattened (coxa plana), widened (coxa magna) femoral head with or without joint incongruity, lateral subluxation or loss of containment.
of the femoral head, acetabular remodeling and growth disturbances of the femoral neck (coxa breva, coxa valga or vara), and a superiorly located (“high-standing”) greater trochanter (Fig 6). CT may be useful to evaluate the extent of these deformities before surgical intervention but involves exposure to ionizing radiation. Many staging systems have been developed based on radiographic findings, but no consensus has been reached as to which is the most useful for guiding therapy (Tables 5, 6) (65,66,71–73).

Ultrasonography (US) of the hip can provide information about associated joint effusion and synovitis, although these are nonspecific findings. US with power Doppler has been used to evaluate the blood flow to the femoral head in cases of suspected ischemia and during the revascularization phase of LCP, but it is user-dependent and not as well evaluated as other modalities (74).

Three-phase bone scintigraphy with pinhole imaging shows similar findings as described in adults, with initial absence of uptake of radiopharmaceutical noted on early dynamic images. In the revascularization phase, recanalization of vessels is demonstrated by increased activity in the lateral pillar; whereas transphyseal neovascularization is represented by increased activity at the base of the epiphysis near the physis.

MR imaging is considered the gold standard in evaluation of LCP throughout its course. MR imaging is particularly useful in early evaluation of patients with hip pain but normal radiographs. Later in the disease course, MR imaging is useful in the evaluation of prognostic indicators to guide therapy and assess the effects of residual deformity on articular cartilage and the acetabular labrum.

Early in the course of the disease, marrow edema is seen at conventional MR sequences, appearing as low to intermediate signal on T1-weighted images and increased signal on T2-weighted images (70,75,76). Later, the necrotic portion of the superior epiphysis is seen as low signal intensity on T1- and T2-weighted images. Several MR imaging features of LCP are similar to those seen in adults, including the double-line sign with internal fat signal, subchondral fracture (MR crescent sign), more prominent involvement...
in the anterosuperior and lateral femoral head (often best seen on sagittal images), and larger volume of involvement associated with increased likelihood of deformity and collapse (70,76).

Contrast-enhanced MR imaging including dynamic subtraction (DS) evaluation has been more extensively used in evaluation of LCP compared with adult ON and is sensitive for the avascular phase, showing absent enhancement of the femoral head epiphysis (Fig 7) (67,75). Proximal femoral epiphyseal enhancement peaks at 2 minutes, so imaging should begin immediately after injection of contrast material (67,68,77). In the revascularization phase, DS MR imaging is comparable to scintigraphy for demonstrating the presence and characterizing the mode of revascularization (67,68,75). Recanalization of existing vessels appears as increased enhancement (compared with normal) of the lateral pillar of the epiphysis (better prognosis), whereas transphyseal neovascularization (worsened prognosis) is represented by increased enhancement at the base of the epiphysis and in the physis. Revascularized areas appear hyperintense on T2-weighted images (67,76). Metaphyseal “cystic” lucencies seen at radiography are also demonstrated at MR imaging (63,69). These follow the signal characteristics of physeal cartilage and enhance avidly after intravenous gadolinium. Physeal disruption (poorer prognosis) is well demonstrated at MR imaging and may be depicted as irregularity or the formation of a physeal bar, both of which are more common with transphyseal neovascularization (63,69). Physeal abnormalities are best seen with spoiled gradient refocused echo with fat saturation and proton density with fat saturation MR sequences. Epiphyseal fragmentation and collapse as well as epiphyseal cartilage thickening, enhancing synovial hypertrophy, and joint effusion may also be noted (63,78,79). These findings contribute to lateral subluxation of the femoral head, loss of containment, and poorer outcome. Lateral subluxation of the femoral head may cause hypertrophy and abnormal angle of the acetabular labrum, which may lead to femoracetabular impingement and secondary osteoarthritis (70,78,80).

Diffusion-weighted imaging (DWI) in LCP has recently been compared with DS MR imaging (77,81). DWI showed early increased diffusivity in the affected femoral epiphysis compared with the normal hip. This increased diffusivity remained throughout the healing stage (81). Furthermore, increased diffusivity in the metaphysis is associated with DS MR evidence of transphyseal revascularization and a worse prognosis (77,81). DWI offers different and complementary information compared with enhanced MR imaging. Enhanced MR imaging findings reflect perfusion changes, whereas increased diffusivity likely reflects cell damage (81).

### Scaphoid Osteonecrosis

Osteonecrosis of the scaphoid is most commonly encountered following scaphoid fracture and nonunion. The mid to proximal 70% of the
scaphoid is supplied by branches of the radial artery that usually enter the bone near the midportion (waist) of the scaphoid, and no vessels directly enter the proximal pole (end-artery supply). Thus, a fracture through the waist or proximal pole of the scaphoid can significantly impair the blood flow to the more proximal scaphoid with resulting ON (82). Proximal pole ON has been reported to occur in over 60% of the fracture nonunions that involve the proximal third of the scaphoid and approximately 20% of the fractures that occur in the midscaphoid (83). Rarely, ON can involve the entire scaphoid and occur without a specific traumatic event; this condition is known as Preiser disease.

Patients with ON of the proximal pole of the scaphoid typically present with wrist pain and an antecedent history of trauma. Radiography is often the initial imaging modality, and ON can be suggested when the proximal scaphoid fracture fragment shows relatively increased density compared with the distal scaphoid or adjacent carpal bones (Figs 8, 9). Fracture margins are often sclerotic and rounded (nonunion), and surrounding lucencies representing cysts are also frequently seen (Fig 8). Unfortunately, radiographs are insensitive for detecting ON and a delay in diagnosis can result in scaphoid nonunion advanced collapse (SNAC), a condition characterized by a persistent fracture nonunion, radioscpahoid joint space narrowing, sclerosis, osteophytes, and potentially proximal pole collapse (8). ON may present as an area of decreased uptake in the proximal pole at bone scintigraphy, although scintigraphy is rarely used to determine the vascular status of the proximal pole (84). CT is commonly used to determine the presence or degree of osseous union following scaphoid fractures. In addition, CT can suggest the presence of ON when increased sclerosis and a lack of normal trabeculae are present in the proximal third of the scaphoid (Fig 8).

MR is considered the most useful imaging modality to determine the presence of ON of the proximal pole of the scaphoid (Figs 8, 9). However, there is no consensus in the literature as to the optimal criteria to use for diagnosing ON. The initial literature using a combination of T1- and T2-weighted images reported 75%–86% sensitivity and 100% specificity for detecting ON (85,86). The higher sensitivity was achieved using the criterion of abnormally decreased signal intensity

**Figure 7.** Early LCP in a 6-year-old boy with 1 month of right hip pain and normal radiographs (not shown). Coronal T1-weighted (500/25) (a), short inversion time inversion-recovery (STIR) (4000/100/90 [inversion time msec]) (b), and postcontrast fat-suppressed T1-weighted (500/25) (c) MR images show normal signal intensity in the capital femoral epiphysis but a large joint effusion on the noncontrast images (asterisk in a and b). The postcontrast MR image reveals markedly diffuse decreased contrast enhancement of the right capital femoral epiphysis (asterisk in c) as a result of ON. (Case courtesy of Dr Kyung Jin Suh.)
Figure 8. Scaphoid waist fracture with proximal pole ON in several different patients. (a) Frontal wrist radiograph shows chronic fracture through the scaphoid waist with sclerosis (arrow) of the margin and lucency representing cyst formation (*). The proximal pole is sclerotic. (b) Coronal CT also reveals scaphoid waist fracture, increased attenuation of the proximal pole (*), and cyst formation (arrowhead). (c) Coronal T1-weighted MR image (500/20) of the wrist demonstrates diffusely low signal intensity throughout the proximal pole of the scaphoid (*). (d) Coronal STIR MR image (400/1000) shows marrow edema throughout the scaphoid on both sides of the fracture line (arrows). (e, f) Two intraoperative photographs reveal scaphoid waist fracture (arrows). There is widening of the fracture plane with the probe in place (arrows) and lack of bleeding of the proximal pole with intraoperative puncture (circle in f). (Fig 8e and 8f courtesy of Patricia L. McKay, MD.)
in more than 50% of the proximal pole (Fig 8) (85,86). More recent studies have found that the sensitivity when requiring decreased signal with all pulse sequences in the proximal pole to diagnose ON was only 6%–18%, and use of this criterion is not recommended (83,87). This is primarily a result of frequently increased signal intensity on images obtained with water-sensitive sequences (83,87–91). The criterion of using homogeneously decreased (≤ the signal of skeletal muscle) T1-weighted signal intensity in the proximal pole of the scaphoid on unenhanced images to diagnose ON was recently reported to be 55% sensitive, 94% specific, and 79% accurate (Fig 8) (83).

Variable success in diagnosing ON of the proximal pole of the scaphoid in the setting of fracture nonunion has been reported using contrast-enhanced MR (Fig 9). Using the criterion for diagnosing ON in the proximal pole if there is less than 20% enhancement, Cerezal and coworkers (89) reported a sensitivity of 86% and specificity of 96% compared with a sensitivity of 71% and specificity of 74% when using the criterion of homogeneously decreased signal intensity on nonenhanced T1-weighted images in the proximal pole (Fig 9). Other researchers have reported a sensitivity of between 54% and 76% when using the criterion of complete absence of enhancement in the proximal pole (87,88).

Dynamic gadolinium-enhanced MR imaging of the scaphoid may improve the sensitivity for detecting ON of the proximal pole. Using the criterion of less than 20% enhancement in the proximal pole for diagnosing ON, Donati and colleagues (90) reported that dynamic contrast-enhanced MR imaging did not improve the 54%–62% sensitivity and 93% specificity as compared with standard contrast-enhanced MR imaging.
They also reported that unenhanced T1-weighted MR images were 85%–100% sensitive but only 13%–47% specific for detecting proximal pole ON. Ng and co-workers (91) also evaluated the usefulness of dynamic contrast-enhanced MR imaging for diagnosing ON in the proximal pole of the scaphoid by comparing proximal pole enhancement to distal pole enhancement. They were unable to categorize 15% of the patients using dynamic enhancement. However, in the patients categorized as having poor vascularity, which is the group most similar to those in the Donati et al (90) study, a similar sensitivity, specificity, and accuracy were reported using either standard or dynamic contrast-enhanced MR imaging (91). Using the criterion of decreased T1-weighted signal intensity involving greater than 50% of the proximal pole to represent poor vascularity, a similar sensitivity to both standard and dynamic contrast-enhanced MR imaging was reported, although the specificity was approximately 15% less with unenhanced imaging (91).

Accurate determination of the vascular status of the proximal pole is important for preoperative planning and for more detailed informed patient consent. Patients with chronic fracture nonunion and absence of fragmentation of the necrotic proximal pole are often treated surgically with a vascularized bone graft, usually from the 1,2 supratrochlear artery, as nonvascularized bone grafts are less effective at achieving osseous union (92). Following vascularized bone graft placement, MR imaging is effective in both documenting healing and demonstrating restoration of the normal bone marrow signal in a majority of the patients (88).

Many challenges exist for using MR imaging to detect ON of the proximal pole of the scaphoid in the setting of chronic fracture nonunion. At unenhanced imaging, mummified fat may have normal T1-weighted signal intensity in the presence of ON (89). The frequency of this occurring is uncertain, but is thought to be low in the scaphoid. Also complicating image interpretation is the fact that avascular bone at surgery can “enhance” after contrast material administration (83,87,90). The ingrowth of viable fibrous mesenchymal tissue (93) and the diffusion of contrast material into the proximal pole (68) likely account for some of the apparent “enhancement” in avascular bone. In addition, viable bone may appear to lack enhancement secondary to the high content of fat in bone marrow (94). It is also important to note the variable criteria used for diagnosing ON when comparing the literature, as some authors require absence of enhancement or complete replacement of the proximal pole bone marrow on T1-weighted images for diagnosis while others are less stringent.

**Kienböck Disease (Lunatomalacia)**

ON involving the lunate was described in 1910 by Robert Kienböck, who postulated that the condition was caused by traumatic disruption of the blood supply and ligaments to the lunate (95). The condition, also referred to as lunatomalacia, often presents as unilateral wrist pain in males aged 20–40 years, and there is usually a history of antecedent trauma months or years before presentation, although the exact etiology of Kienböck disease is unknown (96). The blood supply to the lunate is variable, with over 30% of patients reported to have either a single blood supply on the palmar or dorsal surface or dual blood supply but no intraosseous anastomoses between the palmar and dorsal vessels (96). Others have reported that patients with Kienböck disease may have impaired venous outflow (96). Kienböck disease may also be associated with ulnar minus variance, which causes greater and uneven force transmitted to the lunate.

Radiographs are usually the initial imaging modality used to diagnose Kienböck disease (Fig 10). The Lichtman classification for Kienböck disease is considered the most reliable and reproducible (97). The classification has four stages: I = normal radiographs but abnormal MR images, II = increased radiographic density in the lunate with preservation of the normal lunate shape, IIIA = lunate sclerosis and collapse on radiographs, IIIB = lunate sclerosis and collapse plus diminished carpal height and flexion of the scaphoid, and IV = stage IIIB plus extensive carpal degenerative changes (97). CT can demonstrate a coronal fracture through the lunate (creating a dorsal and volar half) or multiple lunate fragments (96). Complications of Kienböck disease include scapholunate dissociation, degenerative changes at the radiocarpal and midcarpal compartments, and ulnar deviation of the triquetrum (8).

MR imaging is often used to access the cause of wrist pain in patients with normal radiographs but a persistent clinical concern for Kienböck disease. On MR images, Kienböck disease can be diagnosed with certainty when diffusely decreased T1-weighted signal intensity involves the entire lunate, particularly in the setting of ulnar minus variance and otherwise normal-appearing carpal bones. Kienböck disease can be suggested with less specificity when only a portion of the lunate (typically the proximal aspect) demonstrates abnormal T1-weighted signal intensity (Fig 10). Variable T2-weighted or STIR signal intensity is often present in patients with Kienböck disease.

Treatment of patients with Kienböck disease depends on the stage at presentation. In patients with stage I or II disease, immobilization is typically the initial management (98). If symptoms
persist, a vascularized bone graft usually using the 4,5 extensor compartmental artery may be performed (96). This is often coupled with a radial-shortening procedure in patients with ulnar minus variance to reduce the load transmitted to the lunate at the wrist (96). In patients with stage III disease, in addition to radial shortening and placement of a vascularized bone graft, scaphocapitate pinning or arthrodesis is often performed. In patients with stage IV disease, proximal row carpectomy or carpal fusion may be performed (96).

**Malignant Transformation of Osteonecrosis**

Malignancy arising in association with ON is exceedingly rare but well-documented (99,100). Sarcoma associated with ON is almost exclusively seen with metadiaphyseal lesions (101–108). In contradistinction, sarcomas are essentially unknown in relation to epiphyseal ON (100). One can only speculate as to the reason for this, but if one hypothesizes that malignant transformation is time dependent, then the fact that metadiaphyseal ON is typically “clinically silent” may be an important factor, as this complications requires a long latent period (100). It has been postulated that ON undergoes malignant transformation in the reactive interface, representing the reparative tissue at the periphery of the lesion (109,110). These borders show evidence of a high degree of reparative and regenerative change, and it is possible that this excessive proliferative activity is the basis for the development of malignant transformation (110,111). Although malignant transformation with metadiaphyseal ON is well-described, it is generally not considered a pre-malignant lesion (100).

In 2009, Domson and colleagues (107) reported 15 cases of ON-associated sarcoma and reviewed the previous literature, identifying a total of 67 reported cases. They noted that the most common sarcoma was malignant fibrous histiocytoma, accounting for 69% of cases, followed by osteosarcoma (17%) and angiosarcoma (9%), with these three lesions accounting for 95% of reported histologies (107). The average age of patients having ON-associated sarcomas was 53 years, with men twice as commonly affected as women (107).
Figure 11. Malignant transformation of a long-standing area of distal femoral metaphyseal ON in a 55-year-old man. (a) Specimen frontal knee radiograph shows a radiodense area of ON with a sclerotic rim (*) and aggressive bone destruction (D) surrounding the region, including a focal area of cortical involvement (arrow). Old screw tracts are noted from previously removed fixation (arrowheads). (b) Axial CT image reveals the focal areas of ON with a sclerotic rim (N) and surrounding aggressive bone destruction (*) and an associated posterolateral soft-tissue mass. (c) Static frontal image of the knees from a whole-body bone scan demonstrates marked diffuse increased radionuclide uptake in the left distal femoral lesion. (d, e) Coronally sectioned gross specimen (d) and whole-mount specimen (H-E stain) (e) show the areas of ON (*) and surrounding malignant transformation (M) to malignant fibrous histiocytoma. The malignant transformation causes cortical destruction and soft-tissue extension laterally (arrows).

The majority of lesions (60%) arise around the knee, with the distal femur (Figs 11, 12) involved more frequently than the proximal tibia, followed by the proximal femur, femoral shaft, distal tibia, and proximal humerus (107). While 75% of patients with ON-associated sarcomas have multiple areas of bone infarctions, only approximately 30% have an identifiable etiology (most commonly caisson and sickle cell diseases) (101,107). To our knowledge, only a single case report of multifocal malignant transformation has been reported, with a second sarcoma presenting metachronously more than 3 years after the initial presentation (112). Despite aggressive treatment with limb salvage surgery or amputation and adjacent chemotherapy and radiation therapy, the prognosis of ON-associated sarcoma is poor. Disease-free survival is slightly less than 33% at 2 years following diagnosis, and the disease leads to patient demise in almost 60% of cases at an average of 19 months (107). This poor prognosis is related to the high-grade poorly differentiated histology, as with most secondary sarcomatous transformation, with metastases most frequent to the lungs.
Lesions are most commonly in the metaphysis or metadiaphysis of long bones (101). Radiographs demonstrate the previously described imaging features of ON, with an associated focal area of aggressive osteolysis involving the reactive interface and the adjacent cancellous bone, typically extending through the osseous cortex (Fig 11). Matrix mineralization may be present, depending on the histogenetic differentiation of the tumor (osteosarcoma). Bone scintigraphy demonstrates marked focal radiotracer accumulation in the region of the sarcomatous transformation (Figs 11, 12). As would be expected, fluordeoxyglucose positron emission tomography (PET)/CT demonstrates the hypermetabolic activity of the sarcoma at PET, with CT demonstrating the morphologic features of the underlying ON and marginal area of aggressive bone destruction and associated soft-tissue mass (Fig 11) (106). While the diagnosis of malignancy is readily appreciated on radiographs, MR imaging also shows the characteristic changes of multifocal ON. In addition, MR imaging depicts the area of malignant transformation, with focal masslike replacement of the marrow about the areas of ON with associated cortical destruction, and a soft-tissue mass is almost invariably present (Fig 12). Intrinsic MR imaging characteristics are nonspecific, with intermediate signal intensity on T1-weighted images, intermediate to high signal intensity on T2-weighted images, and diffuse heterogeneous enhancement. MR imaging also remains the modality of choice for accurate local staging of the tumor (Fig 12).

**Treatment of Osteonecrosis**

Treatment of ON with significant potential for articular collapse or symptomatic lesions encompasses both surgical and nonoperative management. Noninvasive options include pharmacologic agents, extracorporeal shock wave therapy, and hyperbaric oxygen treatment (113). In patients with LCP who are younger than 6 years of age at onset, reduction of mechanical stress, physical therapy, and follow-up are usually successful (60). Various pharmacologic agents have been used in an attempt to halt the progression of the disease, including lipid-lowering drugs, anticoagulants, vasodilators, and bisphosphonates (1,2,113–115). These medications are thought to target specific points in the pathophysiology of the disease such as lipid emboli, adipocyte hypertrophy, venous thrombosis, increased intrasosseous pressure, and resorption of bone (113). Statins have been used, with some success reported in the literature (113,114). The mechanism behind their efficacy is thought to be reduction of corticosteroid-induced adipogenesis, which is believed to be a major factor in the development of ON. The anticoagulant enoxaparin has been used to treat patients with thrombophilic or hypofibrinolytic disorders and early-stage ON (113,114). Prostacyclin, a vasodilator, has also been utilized in patients with ON and bone marrow edema syndrome. Lastly, bisphosphonates (osteoclast inhibitors) are the most studied and supported medication used for treatment of early-stage ON (113,114). The rationale for their use is that it is osteoclast-driven bone resorption that increases the likelihood of femoral head collapse (115). Unfortunately, multiple clinical trials have not yielded consistent, definitive results to further substantiate the routine use of bisphosphonates in treatment of ON. In a recent randomized, double-blind, placebo-controlled study, Chen and colleagues (1) found no obvious effect on preventing the necessity for total hip arthroplasty, reducing disease progression, or improving quality of life. Extracorporeal shock wave therapy has been used, predominantly in Europe,
for patients with early-stage disease (113). There are few peer-reviewed articles in the literature evaluating the efficacy of this therapy. Hyperbaric oxygen therapy has been performed in patients with early-stage/precollapse ON with some promising results in the literature (2). The treatment is thought to improve oxygenation, reduce bone marrow edema, and induce angiogenesis, thus causing a reduction in intraosseous pressure and improvement in the local microcirculation (113). In a recent double-blind, randomized, controlled, prospective study of 20 patients with unilateral Ficat stage 0–II ON of the femoral head, Campo- resi and co-workers (2) showed that at 7-year follow-up, all their patients reported being pain free and no patients required hip arthroplasty.

The surgical management of ON can be broadly categorized into prophylactic or reconstructive measures (114). Prophylactic measures are defined as surgical procedures in which the aim of treatment is to prevent or retard the progression of articular collapse (114). In contrast, reconstructive procedures are performed after articular collapse with the aim of recreating femoral head sphericity and reestablishing the normal contour of the femoral head.

The most commonly performed prophylactic operation for ON of the femoral head is core de- compression, the efficacy of which is highly controversial (114). In this procedure, one or more cores of necrotic bone are removed from the femoral head. The theory behind this procedure is that increased intramedullary pressure is involved in the pathogenesis of ON. Thus, proponents of this procedure theorize that removing this dead bone decreases intramedullary pressure and arrests or reverses the disease process (113). This procedure is indicated in patients with early-stage disease (Ficat stage 0–II), with minimal or no benefit in patients with advanced-stage disease or evidence of articular collapse (Ficat stage III) (Fig 3) (50). Core decompression can be supplemented with multiple accessory treatments, including bone grafting, biologic augmentation, electric stimulation, and vascularized fibular grafts (114). MR imaging allows earlier diagnosis of ON, and Radke and colleagues (3) showed improved success rates for core decompression from 30% (radiographic criteria for diagnosis) to 60% (MR imaging diagnosis). In a study of 24 patients (34 hips) who underwent core decompression of the femoral head for ON, Beltran and colleagues (50) showed results that indicated that a significant number of femoral heads collapse following core decompression (Fig 3). Their results also revealed that there was a direct relationship between the volume of femoral head involvement preoperatively and the probability of collapse, often seen as the crescent sign at imaging, subsequent to core decompression (Fig 3) (50). Furthermore, these authors demonstrated that patients with a large area of avascular necrosis (>50% femoral head volume) preoperatively would progress to collapse even if core decompression was performed prior to subchondral fracture at radiography (Fig 3) (50). Core decompression may be supplemented with placement of vascularized bone grafts, which allow union with the recipient bone (usually the femoral head) and serve as a source for revascularization of the surrounding avascular bone (116). The vascularized fibular bone grafting procedure has shown more clinically positive results, with one series reporting a 68% survival rate for hips followed for 2 years and 65% for hips followed for 5 years (117). However, this is a longer and more technically demanding surgery.

Various osteotomies have also been used to treat ON of the femoral head, with the idea that the necrotic, or collapsing, segment of the femoral head can be rotated out of the weight-bearing portion of the femoral head and the defect filled with a segment of articular cartilage supported by normal, viable bone (113). In LCP, the main goal of treatment is femoral head containment and surgical treatment may include femoral (varus or valgus) or pelvic osteotomies. Overall, the general belief is that osteotomies are procedures that are best performed on patients in whom ON of the femoral head is present but who are not undergoing long-term/chronic corticosteroid treatment and have minimal osteoarthritic changes in the joint, with no loss of joint space and no evidence of acetabular involvement.

Despite aggressive management, many pa- tients with ON progress to subchondral collapse and secondary osteoarthritis and require a reconstructive procedure. At this stage in the pathophysiology of the disease, treatment options include femoral resurfacing arthroplasty, bipolar arthroplasty, or total joint replacement. In fact, femoral head ON accounts for more than 10% of total hip replacement surgeries performed in the United States (114). The choice of joint arthroplasty is beyond the scope of this article and is largely based on patient age, surgeon preference, extent of articular involvement, and underlying comorbidities (114).

**Summary**

ON is a common musculoskeletal abnormality confronting radiologists for diagnosis and assessment. Frequently affected sites include the femoral head, humeral head, about the knee, femoral/tibial metadiaphysis, scaphoid, and lunate. Symptomatic femoral head ON accounts
for 10,000–20,000 new cases annually in the United States. While epiphyseal lesions are often symptomatic, metadiaphyseal lesions are usually discovered incidentally in asymptomatic patients and only rarely have clinical importance. Common causes of ON include trauma, corticosteroids, and idiopathic.

The pathologic appearance of ON reflects the initial vascular ischemia leading to infarction followed by the bone response to wall off the necrotic tissue with a rim of sclerosis and a reparative attempt with granulation tissue at the reactive interface. Unfortunately, this reparative process is typically of only limited success.

The imaging appearance of ON is frequently diagnostic and is a reflection of the underlying pathology. On radiographs, the lesion shows an often serpentine or undulating sclerotic rim. Bone scintigraphy may initially reveal photopenia with subsequent development of increased radioisotope uptake peripherally. MR imaging is generally considered the most sensitive and specific imaging modality for diagnosis and assessment of ON. The most common pattern of ON is a serpentine or undulating rim of low signal intensity surrounding a region of maintained fat signal intensity. On MR images obtained with water-sensitive sequences, there is frequently a high-signal-intensity zone representing the reactive interface on the inner aspect of the low-signal-intensity rim. ON in pediatric patients most often affects the capital femoral epiphysis and is referred to as Legg-Calvé-Perthes disease. LCP has similar features to its adult counterpart, although early disease may be best identified as decreased enhancement on postcontrast MR images. In addition, metaphyseal lucencies adjacent to the epiphyseal plate and growth sequelae are frequent.

The long-term clinical significance of epiphyseal ON is almost exclusively predicated on the likelihood of collapse of the overlying articular surface. This is optimally assessed with MR imaging, and involvement of greater than 25%–50% of the femoral head volume is significantly more likely to lead to articular collapse. Articular collapse can be seen as femoral head flattening or the crescent sign (representing a subarticular fracture) at radiography, CT, or MR imaging and almost invariably progresses to fragmentation and secondary osteoarthrosis. Malignant transformation is exceedingly rare, has a poor prognosis, and is almost exclusively associated with metadiaphyseal ON. Imaging features of this dire sequela include aggressive bone destruction about the lesion margin with associated cortical involvement and a soft-tissue mass.

Treatment of ON is based on lesion location, symptoms, and likelihood of articular collapse and encompasses both noninvasive and surgical management. The progression of ON to secondary osteoarthrosis almost invariably requires surgical intervention with joint arthroplasty. Understanding and recognizing the spectrum of radiologic appearances of ON and their pathologic basis allows improved patient assessment and is important to optimize clinical management.

Acknowledgments.—The authors gratefully acknowledge the support of Janice Dangin Liu for manuscript preparation and the residents, without whom this project would not have been possible, who attend the AIRP radiologic pathology courses (past, present, and future) for their contribution to our series of patients.

References


Subsequent symptoms and the long-term clinical importance of ON are largely predicated on the likelihood of overlying articular collapse.

The impaction associated with the reactive zone soft tissue may cause cleavage of the subchondral bone from the overlying cartilage and cortex, creating a subchondral fracture plane.

The most common MR imaging pattern seen in ON is an area of yellow marrow surrounded by a low-signal-intensity rim with all pulse sequences.

The degree of preservation of the lateral one-third or lateral pillar has particular prognostic importance because this is the site of weight bearing and early revascularization.

In addition, MR imaging depicts the area of malignant transformation, with focal masslike replacement of the marrow about the areas of ON with associated cortical destruction, and a soft-tissue mass is almost invariably present.