Imaging Findings of Metabolic Bone Disease

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Abbreviation: SD = standard deviation
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SA-CME LEARNING OBJECTIVES
After completing this journal-based SA-CME activity, participants will be able to:
■ Identify the most common metabolic bone diseases.
■ Describe the imaging findings related to the most common metabolic bone diseases.
■ Discuss the most common causes of these metabolic bone diseases.
See www.rsna.org/education/search/RG.

Introduction
Metabolic bone diseases are a diverse group of diseases that result in abnormalities of (a) bone mass, (b) structure mineral homeostasis, (c) bone turnover, or (d) growth. Osteoporosis, the most common metabolic bone disease, results in generalized loss of bone mass and deterioration in the bone microarchitecture. Impaired chondrocyte development and failure to mineralize growth plate cartilage in rickets lead to widened growth plates and frayed metaphyses at sites of greatest growth. Osteomalacia is the result of impaired mineralization of newly formed osteoid, which leads to characteristic Looser zones. Hypophosphatasia is a congenital condition of impaired bone mineralization with wide phenotypic variability. Findings of hyperparathyroidism are the result of bone resorption, most often manifesting as subperiosteal resorption in the hand. Renal osteodystrophy is the collection of skeletal findings observed in patients with chronic renal failure and associated secondary hyperparathyroidism and can include osteopenia, osteosclerosis, and “rugger jersey spine.” Hypoparathyroidism is most commonly due to iatrogenic injury, and radiographic findings of hypoparathyroidism reflect an overall increase in bone mass. Thyroid hormone regulates endochondral bone formation; and congenital hypothyroidism, when untreated, leads to delayed bone age and absent, irregular, or fragmented distal femoral and proximal tibial epiphyses. Soft-tissue proliferation of thyroid acropachy is most often observed in the hands and feet. The findings of acromegaly are due to excess growth hormone secretion and therefore proliferation of the bones and soft tissues. Vitamin C deficiency, or scurvy, impairs posttranslational collagen modification, leading to subperiosteal hemorrhage and fractures.
Osteoporosis

Osteoporosis is defined as a condition characterized by diminished but otherwise normal bone. An osteoporotic state may arise either when bone formation is inadequate or when bone resorption exceeds bone formation. Osteoporosis may be a local phenomenon (as in disuse osteoporosis) or a generalized condition. The imaging features depend to some degree on the rate at which osteoporosis develops.

Osteoporosis is the most common metabolic bone disease, affecting 13%–18% of women older than 50 years and 1%–4% of men older than 50 years (2–5). In the years prior to reliable quantification of bone mass, a patient was considered to have osteoporosis only when a nontraumatic fracture had occurred. With the development of quantitative computed tomography (CT), dual-energy photon absorptiometry, and, later, dual-energy x-ray absorptiometry, reliable measurement methods became available, leading to a change in the definition.

Osteoporosis results in substantial morbidity and mortality, primarily through fractures. Worldwide, one osteoporotic fracture occurs almost every 3 seconds, which results in 9 million fractures each year (6). One-third of women older than 50 years and one-fifth of men older than 50 years will have an osteoporotic fracture (7–9). The three most common fracture locations are the forearm, the hip, and the spine (Fig 1) (10). Severe osteoporosis may prevent detection of nondisplaced fractures, and CT or magnetic resonance (MR) imaging may be helpful for diagnosis if the patient has severe pain and a normal radiograph.

Clinically, osteoporosis is a state of low bone mass and microarchitectural deterioration leading to increased bone fragility. In 1994, the World Health Organization defined osteoporosis as a bone mineral density that is 2.5 or more standard deviations (SD) less than that of a young healthy adult (T-score of −2.5 or less) as measured with dual-energy x-ray absorptiometry for postmenopausal women and for men older than 50 years (11,12). This definition was a radical “rebranding” of several concepts. In science and medicine, an individual is usually considered to have an abnormal result if his or her result is 2 SD away from the mean of his or her age- and sex-matched norm, which is measured by the z score. However, for predicting fracture risk, it is more meaningful to compare an individual’s bone mineral density to that of a young healthy individual prior to the occurrence of bone loss than to that of an age- and sex-matched norm. The T-score therefore compares the patient’s bone mineral density to that of a young healthy reference population and is therefore an absolute quantity, not a relative one. This definition has led to some confusion because of the fact that an individual can have a normal T-score and yet may still have osteoporosis. The World Health Organization also defined osteopenia as a mild form of osteoporosis.

Primary osteoporosis takes slightly different forms in men and women. Traditionally, these forms were separated into types I and II, although these distinctions have not been used in the endocrine literature for many years. After menopause, estrogen deficiency results in a period of accelerated bone loss, chiefly manifest in cancellous (trabecular) bone, but cortical bone loss also plays an important role (13). Men experience a more linear pattern of bone loss. Typically, by about 80 years of age, the two sexes are equivalent (2,10,14).

Several disorders can interfere with bone formation or promote bone resorption, leading to secondary osteoporosis. Hypogonadism and the resultant acceleration of bone resorption are observed in conditions that include hyperprolactinemia; disorders of energy imbalance such as anorexia nervosa and the female athlete triad (disordered eating, osteoporosis, and amenorrhea); primary gonadal failure, as in Turner syndrome or Klinefelter syndrome; and hypothalamic or pituitary dysfunction. Hyperthyroidism and hyperparathyroidism are additional causes of accelerated bone resorption, whereas growth hormone deficiency interferes with bone formation. Hypercortisolism, whether iatrogenic from exogenous glucocorticoids or from Cushing syndrome, is another important cause of low bone mineral density (2,15). Regional osteoporosis can also occur because of inflammatory arthropathy, immobilization, transient osteoporosis of large joints, or complex regional pain syndrome (2,16,17).

In weight-bearing bones with little cortical bone, such as the vertebral bodies, which are composed of only about 5% cortical bone and 95% trabecular bone, the vertical weight-bearing

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**TEACHING POINTS**

- Osteoporosis is the most common metabolic bone disease.
- Rickets is the interruption of orderly development and mineralization of growth plates.
- Osteomalacia is inadequate or abnormal mineralization of osteoid in cortical and trabecular bone.
- In 95% of patients with hyperparathyroidism, skeletal findings are most readily recognized in the hand.
- Renal osteodystrophy refers to the complex of findings observed in the setting of chronic renal insufficiency. These include the findings of osteomalacia (and rickets in children) and secondary hyperparathyroidism.
Rickets and Osteomalacia

Rickets is the interruption of orderly development and mineralization of growth plates. Osteomalacia is inadequate or abnormal mineralization of osteoid in cortical and trabecular bone. Prior to growth plate fusion, rickets and osteomalacia coexist. Rickets occurs as a result of hypophosphatemia. Any problem in the bone mineralization pathway, including insufficient calcium or phosphate levels, abnormal pH, or the presence of inhibitors of mineralization, can result in osteomalacia (Fig 3). Causes of rickets and osteomalacia are listed in Table 1 (23–25).

The radiographic findings observed in rickets are listed in Table 2 and illustrated in Figure 4. Rachitic manifestations are most prominent at the sites of greatest growth, including the knee.
Figure 2. Patterns of trabecular bone loss in osteoporosis. (a) Radiograph and diagram show normal mineralization of the vertebra of a 17-year-old girl. Note the fine meshwork pattern of trabecular bone. (b) Radiograph and diagram show osteoporosis of the vertebra of a 57-year-old man. There is preferential loss of the horizontal trabecular bone, with increased prominence of the vertical trabeculae. (c) Radiograph and diagram show osteoporosis of the vertebra of an 82-year-old woman. Note the marked loss of vertical and horizontal trabecular bone, resulting in large gaps between the vertical trabeculae.

Figure 3. Diagram of the calcium homeostasis pathway. Ingested calcium is absorbed in the gastrointestinal tract, and vitamin D is either absorbed in the gastrointestinal tract or generated from 7-dehydrocholesterol through exposure to UV light (UVB). Vitamin D is further processed in the liver and kidney, where it is converted to its fully active form, which promotes calcium absorption in the gut. Parathyroid hormone acts on the bones and the kidneys to increase serum calcium levels, and high serum calcium levels in turn suppress parathyroid hormone secretion. Parathyroid hormone, calcium, and phosphorus also modulate vitamin D metabolism in the kidney (21). 25(OH)D = 25-hydroxy-vitamin D, 1,25-(OH)2D = 1,25-dihydroxy-vitamin D.

(distal femur and proximal tibia), distal tibia, proximal humerus, distal radius and ulna, and the anterior rib ends of the middle ribs. The findings are observed on the metaphyseal side of the growth plate because unmineralized osteoid is concentrated along the metaphyseal side of the growth plate. Failure of mineralization leads to disorganized chondrocyte growth, and hypophosphatemia leads to impaired apoptosis of hypertrophic chondrocytes, which results in excessively long cartilage cell columns and the radiographic findings of widening of the growth plate and cupping and fraying of the metaphyses (23–26).

Decreased bone mass is frequently observed in osteomalacia; however, it is not an essential feature in the diagnosis because an inability to mineralize newly synthesized osteoid does not imply that there is low bone mass of the skeleton. The presence of large quantities of unmineralized osteoid can sometimes be observed as indistinct ill-defined trabecular bone, because osteoid on the surface of the trabeculae is intermediate in density between that of bone and that of marrow, sometimes giving the impression of a “poor-quality” radiograph.

Looser zones are another distinctive feature of osteomalacia. They occur late in the overall course of the disease (Fig 5). Looser zones are the result of deposition of unmineralized osteoid at sites of stress or along nutrient vessels. These
zones can occur with no or minimal trauma, are often bilateral and symmetric, and appear as transverse lucent bands oriented at right angles to the cortex that only span a portion of the bone diameter. Although known as pseudofractures, Looser zones are a type of insufficiency fracture, with locations and appearances modified by abnormal repair mechanisms, and Looser zones are typically painful. Some of the common locations of Looser zones are similar to those of stress fractures, such as the inner margin of the femoral neck or the pubic rami. However, Looser zones also occur in non–weight-bearing bones, which are atypical locations for stress fractures, such as the lateral aspect of the femoral shaft at the level of the lesser trochanter, the ischium, the iliac wing, and the lateral scapula (23,24).

**Hypophosphatasia**

Hypophosphatasia is a rare genetic disorder caused by mutations in the gene that encodes tissue-nonspecific alkaline phosphatase, resulting in accumulation of pyrophosphate, an inhibitor of bone mineralization. The clinical spectrum of disease varies widely, and it can be roughly categorized into the following four clinical phenotypes of decreasing severity: perinatal (Fig 6), infantile, childhood (Fig 7), and adult (27). In the perinatal form, mineralization can be remarkably poor, with entire segments of the spine not depicted (absent) on radiographs. In the infantile and childhood forms, there can be craniosynostosis; and in the childhood form, characteristic “tongues” of lucency extend from the growth plate to the metaphysis. Skeletal findings can improve after enzyme replacement therapy with asfotase alfa, a recently developed recombinant tissue-nonspecific alkaline phosphatase (Fig 8) (23,24,28).

**Hyperparathyroidism**

Hyperparathyroidism is a pathologic state of elevated parathyroid hormone concentrations, which causes increased bone resorption. Primary hyperparathyroidism is a state of autonomous parathyroid hormone secretion by the parathyroid glands and lack of feedback inhibition by serum calcium. Primary hyperparathyroidism is usually caused by a parathyroid adenoma, but in approximately 10% of cases, it is a result of four-gland hyperplasia, and in extremely rare cases, primary hyperparathyroidism is due to parathyroid carcinoma (29). Secondary hyperparathyroidism is more common than primary hyperparathyroidism and is a response to low serum calcium levels. The most common cause is chronic renal failure, in which chronically elevated serum phosphate levels depress the serum calcium level, which leads to compensatory hyperplasia of the chief cells of

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**Table 1: Causes of Rickets and Osteomalacia (Partial List)**

<table>
<thead>
<tr>
<th>Category of Rickets and Osteomalacia</th>
<th>Causes</th>
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<tr>
<td>Inadequate vitamin D (synthesis or diet)</td>
<td>Poor nutrition, poor sunlight exposure</td>
</tr>
<tr>
<td>Malabsorption</td>
<td>Pancreatic insufficiency, small bowel disease, rapid intestinal transit</td>
</tr>
<tr>
<td>Abnormal vitamin D metabolism</td>
<td>Liver disease, chronic renal failure, nephrotic syndrome, vitamin D–dependent rickets type I, medications that accelerate degradation of vitamin D or metabolites</td>
</tr>
<tr>
<td>Vitamin D resistance</td>
<td>Vitamin D–dependent rickets type II</td>
</tr>
<tr>
<td>Other cases (rare)</td>
<td>Dietary calcium deficiency, X-linked phosphatemic rickets, tumor-induced osteomalacia (unregulated secretion of fibroblast growth factor 23)</td>
</tr>
</tbody>
</table>

**Table 2: Radiographic Findings of Rickets**

<table>
<thead>
<tr>
<th>Body Part</th>
<th>Active Rickets</th>
<th>Healing Rickets</th>
</tr>
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<tbody>
<tr>
<td>Extremity</td>
<td>Widened growth plate; irregularity and osteopenia along metaphyseal side of growth plate; flared, frayed, or fractured metaphysis; bowing; fracture</td>
<td>Widened growth plate (especially distal femoral), mild metaphyseal cupping, sclerosis along metaphyseal side of growth plate, bowing</td>
</tr>
<tr>
<td>Chest</td>
<td>Rachitic rosary, bell-shaped thorax</td>
<td>…</td>
</tr>
<tr>
<td>Skull</td>
<td>Flat occiput, widened sutures, squared appearance of skull, basilar invagination</td>
<td>…</td>
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Table 2: Radiographic Findings of Rickets
Figure 4. Nutritional rickets and femoral fracture in the setting of parental neglect of a 3-year-old girl. (a) Anteroposterior radiograph of the skull shows a partially patent frontal suture (arrow). (b) Posteroanterior radiograph of the chest shows wide and rounded anterior rib ends (circles). This finding is often called a “rachitic rosary” because the chain of rounded rib ends resembles rosary beads at physical examination. (c) Posteroanterior radiograph of both hands shows diffuse osteopenia, age-indeterminate fractures of several metacarpals (solid arrows), and cupped fragmented frayed metaphyses of the distal radii and ulnae (ovals). A peripheral rim of bone along the metaphysis (dashed arrow) occurs by membranous ossification. (d) Anteroposterior radiograph of both knees shows a fracture of the patient’s right distal femur (black arrow), as well as age-indeterminate fractures of her right tibia and both fibulae (dashed white arrows). The metaphyses are fragmented, frayed, and fractured (solid white arrows). (e) Anteroposterior radiograph of both lower extremities obtained 2 years later than a–d shows diffuse osteopenia, bowing of the tibiae and fibulae, flared metaphyses, and widening of the growth plates with sclerosis and irregularity on the metaphyseal side. Transverse sclerotic metaphyseal bands (arrows) parallel to the growth plate reflect periods of intermittent adequate mineralization followed by poor mineralization. (Images courtesy of Ok-Hwa Kim, MD, Ajou University, Seoul, Korea.)

the parathyroid gland. Renal insufficiency also affects parathyroid hormone metabolism, further increasing the serum parathyroid hormone levels. Secondary hyperparathyroidism can also be observed in vitamin D deficiency and dietary calcium deficiency (30). In 95% of patients with hyperparathyroidism, skeletal findings are most readily recognized in the hand (31). The pathognomonic subperiosteal bone resorption in hyperparathyroidism begins at the radial aspects of the middle phalanges of the middle and index fingers as lacelike irregularity and at the distal phalangeal tufts as acro-osteolysis (Fig 9). In later stages, the resorption can appear similar to scalloping or “periosteal reaction” (pseudoperiostitis) (30). Subperiosteal resorption can also be observed in the ribs, lamina dura (bone that surrounds the tooth sockets), humerus, femur, and upper medial tibia.

Trabecular, intracortical, endosteal, subchondral, and subligamentous or subtendinous bone resorption can also occur. In the skull, bone
Figure 5. Tumor-induced osteomalacia in a 41-year-old man presenting with acute left hip pain after a fall down stairs, who had a history of multiple fractures during the previous 10 years. Lateral radiograph of the thoracic spine (a) and anteroposterior radiographs of the left forearm (b) and pelvis (c) show generalized osteopenia, vertebral body fractures (arrows on a), and multiple Looser zones (arrows on b, c). The patient later underwent left total hip arthroplasty, and a fibroblast growth factor 23–secreting mesenchymal tumor was found in the specimen from resection, a finding that led to the diagnosis of tumor-induced osteomalacia.

Figure 6. Hypophosphatasia in a newborn boy who presented when his mother was transferred to the hospital after sudden onset of labor. No Apgar scores are available. Knowing the poor prognosis, the parents did not wish further resuscitation, and the newborn died 35 minutes after birth. The alkaline phosphatase level was less than 5 IU/L (normal range for age, 150–420 IU/L). Prenatal ultrasonography (US) disclosed short femoral length (–5 SD at 23 weeks; –7 SD at 33 weeks) (images not shown). (a) Anteroposterior skull radiograph shows severe calvarial ossification defects, with only small residual islands of bone in the frontal (dashed white arrows) and parietal (solid white arrows) regions. The skull base and the facial bones (black arrows) are only partially ossified. (b) Anteroposterior radiograph shows abnormal ossification in the axial and appendicular skeleton, including thin clavicles (white arrowheads) and ribs (solid white arrows); absent cervical, thoracic, and lumbar vertebral bodies (rectangles); small scapulae (dashed white arrows) and ilia (black arrowheads); absent ischia and pubic bones (oval); tonguelike metaphyseal ossification defects of the long bones (black arrows); and absent ossification of the short tubular bones in the hands and feet. (Images courtesy of Gen Nishimura, MD, St. Luke’s International Hospital, Tokyo, Japan.)
Resorption is described as a salt-and-pepper appearance and can lead to decreased differentiation between the inner and outer tables of the skull (Fig 10a). Trabecular resorption results in a smudgy appearance of the trabeculae. Intracortical resorption is also described as cortical tunneling (Fig 10b) and is often a prominent feature of hyperparathyroidism. Endosteal resorption may lead to cortical thinning and may obscure the corticomedullary junction.

Subchondral resorption can affect any joint, leading to a widened and irregular appearance. In the hands, subchondral resorption most often begins along the distal interphalangeal joints and progresses to the metacarpophalangeal and proximal interphalangeal joints. Subchondral resorption can also occur along the acromioclavicular joint, more pronounced along the clavicular side.

In the sacroiliac joint, subchondral resorption is more pronounced at the iliac side and may simulate an inflammatory or infectious arthritis (Fig 11a). Sternoclavicular joint resorption tends to affect both sides of the joint equally. Subligamentous or subtendinous resorption also can occur anywhere but most often occurs at the calcaneus, clavicle (Fig 11c), greater and lesser tuberosities of the humerus, greater and lesser trochanters of the femur, anterior inferior iliac spine, and ischial tuberosity (Fig 11b) (29–32).

Brown tumors, also known as osteoclastomas, are lytic lesions that result from the parathyroid hormone–driven activation of osteoclasts. Brown tumors are generally solitary but can be multifocal and are at risk for pathologic fracture. Brown tumors commonly involve the facial bones (Fig 12), ribs, pelvis, and femora and can have a large
Figure 8. Hypophosphatasia in a neonate with a low serum alkaline phosphatase level (5 IU/L) who had short femoral length at prenatal US (images not shown). (a) Anteroposterior radiograph shows abnormal ossification in the axial and appendicular skeleton, with a thin calvaria, thin clavicles and ribs, small vertebral bodies, small scapulae and ilia, stunted ends of the long bones, and poor ossification of the short tubular bones in the hands. (b) Posteroanterior chest radiograph obtained at the age of 6 months, after administration of recombinant enzyme replacement therapy, shows a remarkable increase in the ossification of the ribs, clavicles, scapulae, vertebrae, and long bones. The ends of the ribs and long bones are broader than normal because of the accumulation of osteoid in patients with hypophosphatasia. (Images courtesy of Gen Nishimura, MD, St. Luke’s International Hospital, Tokyo, Japan.)

Figure 9. Hyperparathyroidism in a 15-year-old boy presenting with minor trauma to his left hand. His calcium level was 12.2 mmol/L (normal range, 8.5–10.2 mmol/L). Radiograph of the left hand shows a mildly angulated fifth metacarpal fracture (circle). There is resorption of the distal phalangeal tufts (solid arrows), a finding consistent with acro-osteolysis. Subperiosteal resorption is depicted along the distal radial aspects of the middle phalanges of the index and long fingers (dashed arrows).

Renal Osteodystrophy
Renal osteodystrophy refers to the complex of findings observed in the setting of chronic renal insufficiency. These include the findings of osteomalacia (and rickets in children) and secondary hyperparathyroidism. In any given patient, the findings of one or the other may predominate.

In patients with chronic renal insufficiency, radiographs may show a diffuse increase in bone radiodensity, a finding that is seen more often in the axial skeleton, which has more trabecular bone than cortical bone (Fig 14). The etiology of this diffuse osteosclerosis is not well understood, although it probably reflects the anabolic effect of parathyroid hormone. Despite the increased radiodensity, the bone is structurally weak and prone to stress fractures (35). The spine often

associated soft-tissue component. Treatment of hyperparathyroidism may also lead to resolution of brown tumors. Brown tumors were originally described with primary hyperparathyroidism but are now more common in patients with chronic renal insufficiency and secondary hyperparathyroidism (Fig 13) (30,33,34).
Amyloid deposition can occur in patients undergoing long-term hemodialysis and is due to $\beta_2$-microglobulin deposition in bone and soft tissues, including cartilage, joint capsules, ligaments, tenosynovium, muscles, and intervertebral disks. This deposition can lead to carpal tunnel syndrome in as many as 31% of patients. Amyloid deposition in joints leads to a destructive
arthropathy (Fig 17). Renal transplantation can arrest progression but does not reverse dialysis-related amyloid arthropathy (30,38–43).

Hypoparathyroidism
Hypoparathyroidism is most commonly an acquired disorder caused by iatrogenic injury to the parathyroid glands during thyroid surgery or excision of the parathyroid glands or, more rarely, during wide excision of a head and neck cancer. Hypoparathyroidism may also result from autoimmune disease or genetic causes (eg, DiGeorge syndrome) (44,45). End-organ insensitivity to parathyroid hormone is called pseudohypoparathyroidism and has different radiographic findings. Hypoparathyroidism that is due to genetic causes usually manifests in childhood, but the clinical spectrum varies widely, and in some cases, hypoparathyroidism may not be detected until adulthood (46,47).
In rare cases, spinal ossification similar in appearance to the enthesitis observed in psoriatic arthritis can occur (47–51).

Figure 15. Renal osteodystrophy in a 28-year-old woman with nephrotic syndrome and end-stage renal disease who was undergoing treatment with dialysis. Lateral radiograph of the lumbar spine shows alternating bands of sclerosis along the endplates (dashed arrows) and areas of lucency centrally (solid arrows). This pattern is known as rugger jersey spine, a finding named for the pattern of the jerseys worn by rugby players (shown at right).

Figure 16. Secondary hyperparathyroidism in a 57-year-old woman with renal failure and a parathyroid hormone level of 1313 pg/mL. (a) Lateral radiograph of the left forearm shows soft-tissue calcification (arrows) in the dorsal soft tissues of the forearm. (b) Axial nonenhanced CT image through the level of the external auditory canal shows soft-tissue calcification (arrows) in both pinnae. (c) Anteroposterior radiograph of the right knee shows chondrocalcinosis (arrows) of the medial and lateral menisci. (d) Axial nonenhanced CT image through the level of the pubic symphysis shows calcification with fluid-fluid levels (arrows) in and around the pubic symphysis, as well as erosions of both pubic bones (circles).

Radiographic findings of hypoparathyroidism reflect an overall increase in bone mass, including generalized or localized osteosclerosis and thickening of the calvaria, with a narrowed diploic space. In rare cases, spinal ossification similar in appearance to the enthesitis observed in psoriatic arthritis can occur (47–51).
Figure 17. Amyloid arthropathy in an 83-year-old man with polycystic kidney disease who had undergone treatment with hemodialysis for 18 years. (a) Lateral frog-leg radiograph of the left hip shows a large erosion (arrows) along the superolateral femoral head. The joint space is only mildly narrowed, and there is minimal proliferative change of the bone. (b) Axial contrast material–enhanced CT image of the left hip shows the erosion (arrow) along the superolateral femoral head, with only mild joint space narrowing and minimal bone proliferative change. There is mineralized soft tissue within the erosion, consistent with amyloid deposition.

Hypothyroidism
Hypothyroidism may be congenital, which leads to severe skeletal abnormalities and delayed development, or it may be acquired, which results in relatively mild skeletal abnormalities, if any. Acquired hypothyroidism may occur after surgery or after treatment (radioactive iodine therapy) or may be due to glandular atrophy, acute or chronic (Hashimoto) thyroiditis, infiltrative diseases such as amyloidosis or lymphoma, therapy with certain medications, iodine deficiency, or a pituitary disorder resulting in a deficiency of thyroid-stimulating hormone (52).

In children, there is delayed skeletal development, often with absent, irregular, or fragmented distal femoral and proximal tibial epiphyses (Fig 18) resembling multiple epiphyseal dysplasia. Dental development may also be delayed (52–54).

Hyperthyroidism
Hyperthyroidism is most commonly due to oversecretion of thyroid hormone by the thyroid gland diffusely (Graves disease) or focally (single or multiple adenomas). The most common skeletal manifestation of hyperthyroidism is osteoporosis. As many as 1% of patients with Graves disease may have thyroid acropachy, which usually occurs after treatment, when the patient’s condition becomes euthyroid or hypothyroid.

Radiographic findings of thyroid acropachy are best observed in the hands and feet, in which clubbing, periostitis, and soft-tissue swelling may be seen. The periostitis is greatest along the radial margins of the metacarpal, metatarsal, and middle and proximal phalangeal diaphyses. Soft-tissue swelling may also be seen in the pretibial region. Exophthalmos, which is the result of thyroid-stimulating hormone receptor–stimulating antibodies of Graves disease stimulating proliferation of the retro-orbital fibroblasts, may be depicted on skull radiographs or head CT images (52).

Acromegaly
Acromegaly is due to excess growth hormone secretion from the anterior lobe of the pituitary. The radiographic findings of acromegaly are listed in Table 3 and shown in Figure 19 (47).

Table 3: Radiographic Findings of Acromegaly

<table>
<thead>
<tr>
<th>Body Part</th>
<th>Radiographic Findings</th>
</tr>
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<tbody>
<tr>
<td>Hands</td>
<td>Spade-shaped tufts, tubulation of phalangeal shafts, exostoses, widened joint spaces, sesamoid enlargement</td>
</tr>
<tr>
<td>Feet</td>
<td>Heel pad thickness &gt; 25 mm in men and &gt; 23 mm in women, skin thickening, tendon insertion ossification, sesamoid enlargement</td>
</tr>
<tr>
<td>Skull</td>
<td>Thick skull bones; enlarged sella; frontal bossing; prominence of frontal and maxillary sinuses, supra-orbital ridge, and zygomatic arch; prognathism (protrusion of jaw); enlargement of the mandible</td>
</tr>
</tbody>
</table>
Figure 18. Congenital hypothyroidism in a 12-year-old boy with short stature and developmental delay. (a) Oblique radiograph of the right hand shows ossification centers of only the capitate (arrowhead), hamate (arrow), and radius (circle). The bone age is estimated at 1.5 years. (b) Lateral radiograph of the lumbar spine shows hypoplastic vertebral bodies. L1 has a bullet-shaped vertebral body (arrow). (c) Anteroposterior radiograph of the pelvis shows mild flaring of the iliac bones with shallow acetabula (solid arrows). The femoral capital epiphyses (dashed arrows) are small and fragmented. (d) Anteroposterior radiograph of the right knee shows small and irregular distal femoral and proximal tibial epiphyses (arrows). (e) Posteroanterior radiograph of the left hand obtained after 2 years of thyroid hormone replacement therapy shows interval ossification of all of the carpal ossification centers. The bone age remains delayed but has progressed to approximately 9 years (patient age, 14 years). (f) Anteroposterior radiograph of the right knee obtained after 2 years of thyroid hormone replacement therapy shows maturation of the epiphyses but residual irregularity of the tibial and femoral epiphyses (arrows). (Images courtesy of Ok-Hwa Kim, MD, Ajou University, Seoul, South Korea.)

**Scurvy**

Scurvy is a nutritional deficiency of vitamin C, a required cofactor for hydroxylation of many proteins, including collagen. At one time the scourge of all ocean-going seamen, scurvy is now exceedingly rare. Vitamin C deficiency results in abnormal collagen production, leading to vascular fragility and abnormal bone matrix, especially in areas of greatest growth, such as the distal femur, proximal tibia and fibula (Fig 20), distal radius and ulna, proximal humerus, and distal rib ends. The bones are diffusely osteopenic, and there are thin cortices, especially in the epiphyses. Along the growth plates, there is decreased and disorganized cartilage proliferation, resulting in an irregular appearance of the growth plate along the metaphyseal side. A dense band along the metaphyseal side of the growth plate in the zone of provisional calcification (Frankel line) represents the sclerotic provisional zone of calcification. Peripheral extension of the zone of calcification results in a pointed contour of the metaphyses known as “beaking.”
Fragility of the trabeculae in this region results in subepiphyseal “corner” fractures (Fig 21a). A lucent line adjacent to the Frankel line called the Trummerfeld zone, or scurvy line, reflects accumulation of hemorrhage in this zone, which tends to fracture. Subperiosteal hemorrhage results in periosteal elevation and periosteal reaction. At MR imaging, bone marrow is heterogeneous on T1- and T2-weighted MR images, and subperiosteal hemorrhage can be seen as periosteal elevation with increased subperiosteal T1 and T2 signal intensity (Fig 21b) (55–57).
Conclusion

Metabolic bone diseases are a heterogeneous group of disorders that diffusely affect the bones. Understanding the underlying mechanism of the diseases helps the radiologist to also understand the radiographic findings and to make a correct diagnosis.

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References

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