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Metabolic Bone Diseases

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INTRODUCTION

Metabolic bone disease is a general term used to describe a host of diffuse skeletal disorders. Many are associated with low bone mass, and some are not metabolic but have genetic, infectious, or other causes. However, metabolic bone disease remains a useful umbrella term. In its broadest sense, it includes common diseases such as osteoporosis (see Chapter 75), rare osteosclerotic disorders such as fluoride intoxication, genetic disorders, and focal skeletal diseases such as polyostotic fibrous dysplasia.

In this chapter, the focus is on the more common members of this family (Table 74-1) that may be encountered by an internist. Many additional rare metabolic bone diseases exist and, depending on the context, should be sought. Normal skeletal homeostasis and histopathology are reviewed in Chapter 72 and Figure 74-1.

Osteoclast and osteoblast activity and osteoid mineralization can be assessed by undecalcified bone biopsy of the anterior iliac crest, which is the standard for assessing bone histology. Undecalcified sections are essential because the acid-mediated decalcification performed on routine pathology specimens removes calcium and therefore cannot distinguish between mineralized mature bone and unmineralized osteoid that may be normal or pathologic. The examples shown in Figure 74-1 employ histologic sections of undecalcified bone and highlight osteoclasts, osteoblasts, and osteoid. Because tetracycline is fluorescent and incorporated into the hydroxyapatite crystals as osteoid mineralizes, administering tetracycline to patients before a bone biopsy allows assessment of the rates and efficacy of skeletal mineralization (see Fig. 74-1B and F).

TABLE 74-1 CONDITIONS, DISEASES, AND MEDICATIONS THAT CAUSE OR CONTRIBUTE TO METABOLIC BONE DISEASE

- Osteoporosis (see Chapter 75)
- Paget disease of bone
- Hyperparathyroid bone disease (i.e., osteitis fibrosa cystica)
- Osteomalacia and rickets
  - Hypophosphatemic syndromes
  - Vitamin D syndromes
  - Anticonvulsants
  - Aluminum
  - Metabolic acidosis
- Renal osteodystrophy
- Genetic diseases
  - Osteogenesis imperfecta
  - Hypophosphatasia
  - Osteoporosis-pseudoglioma syndrome
  - X-linked osteoporosis
  - Miscellaneous factors
- Infiltrative diseases
  - Multiple myeloma
  - Lymphoma, leukemia
  - Sarcoid
  - Malignant histiocytosis
  - Mastocytosis
  - Gaucher' disease
  - Hemolytic diseases (e.g., thalassemia, sickle cell anemia)
- Transplantation osteodystrophy

DIFFERENTIAL DIAGNOSIS

Paget's Disease of Bone

Paget's disease, also called *otitis deformans*, is the second most common bone disease after osteoporosis. It affects approximately 2% of the population older than 45 years of age in the United States, but the incidence varies geographically. It is most common in those of European descent and rare in those of African or Asian descent.

In contrast to most metabolic bone diseases, which are diffuse and involve the entire skeleton, Paget's disease is a focal bone disorder. It can be *monostotic* (involving a single bone) or *polyostotic* (involving multiple bones). Paget's disease may affect any skeletal site, but it most commonly involves the pelvis, vertebrae, skull, tibia, and femur. Although Paget's disease is a chronic condition and original lesions may expand, new lesions rarely develop.

The primary cellular abnormality of Paget's disease is increased osteoclastic bone resorption, which is followed by exuberant formation of new bone that is of poor quality (see Fig. 74-1C). This marked increase in osteoblast activity accounts for the typical sclerotic lesions seen on radiographic examination (Fig. 74-2A-C), for the increased uptake of radionuclide seen on a bone scan (see Fig. 74-2D), and for increases in serum levels of alkaline phosphatase, which is the biochemical hallmark of Paget's disease.

Most patients with Paget's disease are asymptomatic, and the disorder is most often detected unexpectedly by an increased serum alkaline phosphatase level on routine testing or on a routine radiograph obtained for other reasons. At clinical presentation, patients may have bone pain, skeletal deformities, fractures, related complications such as osteoarthritis, and nerve compression syndromes (e.g., deafness, spinal stenosis). Rare complications include hypercalcemia in immobilized patients and high-output cardiac failure. Because pagetic lesions tend to be highly vascular, the skin over affected bones may be warmer than in other areas. The most dreaded complication of Paget's disease is the rare (<1%) development of osteosarcoma in a pagetic lesion.

The cause of Paget's disease is unknown but may include a viral origin and a genetic predisposition. Paget's disease is most often diagnosed using a combination of biochemical markers for bone turnover and radiologic studies. For most