hyperparathyroidism caused by a parathyroid adenoma, or it may be *mixed*, occurring in patients with vitamin D–deficient osteomalacia, immunosuppressant-induced transplant bone disease, or renal osteodystrophy.

Osteomalacia and Rickets

Although common in the United States and throughout the world, osteomalacia and rickets are often overlooked. Osteomalacia and rickets are essentially the same disorders, but by definition, rickets occurs in children with open growth plates (i.e., epiphyses), and osteomalacia occurs in adults with closed epiphyses.

The fundamental abnormality in these disorders is an inability to mineralize (i.e., form hydroxylapatite crystals) osteoid seams (see Fig. 74-1). These patients have osteoblasts and can synthesize osteoid, but it is mineralized inefficiently or not at all. This fundamental inability to mineralize osteoid results in accumulation of the characteristic thick osteoid seams seen on bone biopsy (see Fig. 74-1E and F) and a reduction in the mineral content of bone so that it is mechanically deficient. These events lead to bone pain, pseudofractures, fractures, bowing of the long bones, and other skeletal deformities (Fig. 74-4). In children with rickets, the inability to mineralize the growth plate leads to bulbous, knobby deformities of the knees, ankles, and costochondral junctions (i.e., rachitic rosary) and to dental abnormalities. The characteristic radiologic signs of osteomalacia are Looser's zones or Milkman's pseudofractures.

Mineralization disorders result from an inability to form hydroxyapatite (calcium phosphate) crystals in osteoid, the nonmineralized phase of bone. This inability may result from hypophosphatemia (common), calcium deficiency (rare), or vitamin D deficiency (common). Toxins that interfere with mineralization include aluminum, incompletely defined inhibitors of mineralization in uremic plasma, and long-term, high-dose anticonvulsants. Because calcium salts are acid soluble, chronic metabolic acidoses can result in osteomalacia or rickets. Disordered mineralization can be caused by vitamin D deficiency (e.g., malabsorption, liver disease), hypophosphatemic disorders (e.g., X-linked hypophosphatemic rickets, autosomal dominant hypophosphatemia, oncogenic osteomalacia), metabolic acidoses, drug-related disorders, and genetic conditions (e.g., vitamin D–dependent rickets types I and II, hypophosphatasia) (see Chapter 73).

The diagnosis is suggested in the setting of low bone mass, the characteristic radiologic signs described previously, hypocalcemia, elevated PTH and alkaline phosphatase levels, and unexplained bone pain or weakness. However, these are late signs, and the disorder is optimally identified and treated early. The diagnosis is supported by demonstrating reductions of plasma 25-hydroxyvitamin D or its active form, 1,25-dihydroxyvitamin D_3 ($1,25[OH]_2D_3$); hypophosphatemia; or increased alkaline phosphatase levels in an appropriate clinical setting. Hypocalciuria is typical of vitamin D deficiency. Inappropriate phosphaturia with a low tubular maximum for

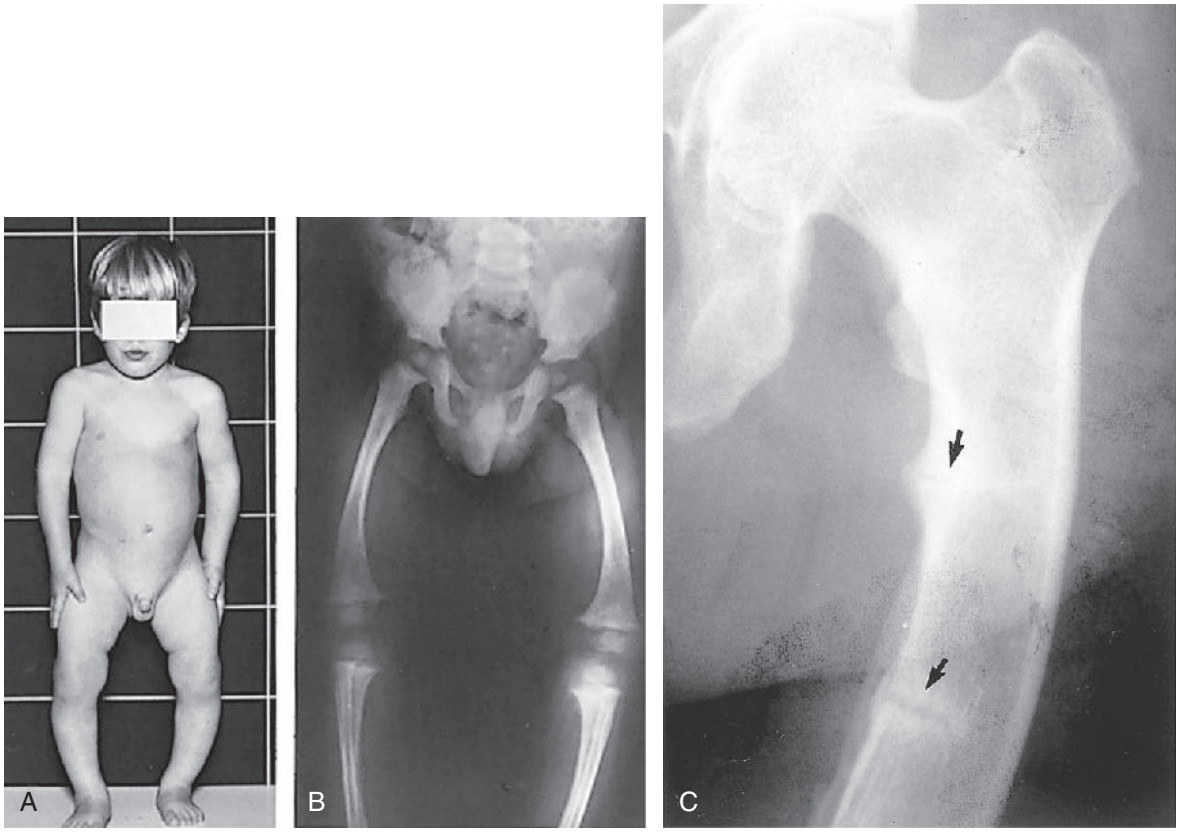

FIGURE 74-4 **A,** A typical example of rickets, with bowing of the femurs and tibias. **B,** A skeletal radiograph of a child with rickets. The weight-bearing bones of the lower extremities are bowed, and the epiphyses are open, mottled, and overgrown. **C,** Looser's zones or pseudofractures *(arrows)* are characteristic of osteomalacia or rickets. The closed epiphyses indicate the patient is an adult. This radiograph is diagnostic of osteomalacia.