loss is greater in sites rich in trabecular bone (e.g., spine) than cortical bone (e.g., femoral neck) (Fig. 75-2). Women lose significantly more trabecular bone than men. Estrogen deficiency during menopause contributes significantly to bone loss in women, and they may lose 1% to 5% of bone mass per year in the first few years after menopause. Women continue to lose bone mass throughout the remainder of their lives, with another acceleration of bone loss occurring after age 75 years. The mechanism of this accelerated loss in old age is not clear.

Multiple causes of secondary bone loss contribute to osteoporosis and fractures. Medications that commonly cause bone loss include glucocorticoids, antiseizure medications, excess thyroid hormone, heparin, androgen deprivation therapy, aromatase inhibitors, and depo-medroxyprogesterone. Endocrine diseases resulting in female or male hypogonadism also lead to bone loss. Hyperparathyroidism, hyperthyroidism, and hypercortisolism commonly cause bone loss, as can vitamin D deficiency. Gastrointestinal problems can contribute to decreased absorption of calcium and vitamin D (Table 75-1). Risk factors for falls (e.g., age, poor vision, previous falls, immobility, orthostatic hypotension, cognitive impairment, vitamin D insufficiency, poor balance, gait problems, weak muscles) also contribute to fractures.

CLINICAL PRESENTATION

Unlike many other chronic diseases with multiple signs and symptoms, osteoporosis is considered a silent disease until fractures occur. Whereas 90% of hip fractures occur after a fall, two thirds of vertebral fractures are silent and occur with minimal stress, such as lifting, sneezing, and bending. An acute vertebral fracture may result in significant back pain that decreases gradually over several weeks with analgesics and physical therapy. Patients with significant vertebral osteoporosis may have height loss, kyphosis, and severe cervical lordosis, also known as a *dowager's hump*. Prolonged bisphosphonate use (>5 years) may result in an atypical femoral fracture, which may manifest as unilateral or bilateral thigh pain and result in a femoral shaft fracture with no or minimal trauma.

DIAGNOSIS AND DIFFERENTIAL DIAGNOSIS

The diagnosis of osteoporosis is made after an acute clinical vertebral or hip fracture or on assessment of bone mineral density.

Radiography

Radiographs can reveal a vertebral compression fracture (Fig. 75-3). However, low bone mass may not be evident on radiographs until 30% of the mass has been lost. When assessing bone mass, radiographs may be read inappropriately as a result of overpenetration or underpenetration of the film. Radiographs therefore are a poor indicator of osteoporosis (with the exception of vertebral fractures), and the diagnosis is instead often based on bone mineral densitometric results.

Bone Mineral Density and Other Bone Mass Assessments

In 1994, the World Health Organization (WHO) developed a classification system for osteoporosis and low bone mass based on data from white, postmenopausal women (Table 75-2). Osteoporosis is defined as a bone mineral density less than or equal to 2.5 standard deviations (SDs) below young adult peak bone mass (T-score ≤ −2.5 SD). Low bone mass (i.e., osteopenia) is defined as a bone mass measurement between 1.0 and 2.5 SDs below adult peak bone mass (T-score between −1.0 and −2.5 SD). Normal bone mineral density is defined as assessments above 1.0 SD below adult peak bone mass (T-score ≥ −1.0 SD).

The standard for assessing bone mineral density is dual-energy x-ray absorptiometry (DEXA), which has excellent precision and accuracy. Measurements are made at the hip and spine, and in about 30% of cases, discordance is found between these measurements (Fig. 75-4). Classification should be made only if two or more vertebrae are available for analysis because of the high error rate when a single vertebra is assessed. Classification is based on the lowest value (i.e., total spine, total hip, or femoral neck).

In patients with hyperparathyroidism, in which cortical bone loss is often seen, forearm DEXA using the one-third distal radius site should also be assessed. Forearm assessments may be helpful in older patients who often have falsely elevated bone mineral density measurements at the spine as a result of atypical calcifications from degenerative joint disease, sclerosis, or aortic calcifications or in obese patients whose weight exceeds the table limit.

Bone mineral density can be measured by hip or spine quantitative computed tomography (QCT). However, less normative data are available for hip QCT, vertebral precision is inferior to

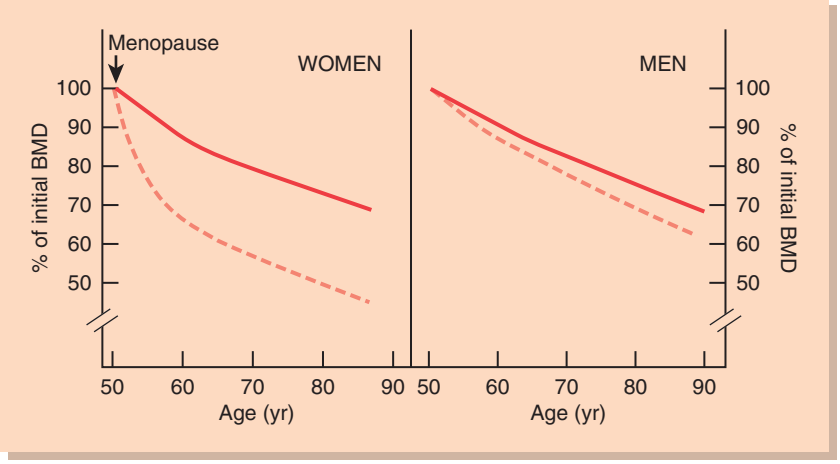

FIGURE 75-2 Patterns of age-related bone loss in women and in men. *Dashed lines* represent trabecular bone, and *solid lines* represent cortical bone. The figure is based on multiple cross-sectional and longitudinal studies using dual-energy x-ray absorptiometry. BMD, Bone mineral density. (From Khosla S, Riggs BL: Pathophysiology of age-related bone loss and osteoporosis, Endocrinol Metab Clin North Am 34:1015–1030, 2005.)