OSTEOPOROSIS: THE INCREASING ROLE OF THE ORTHOPAEDIST

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INTRODUCTION

Osteoporosis contributes to many of the fractures of the spine, proximal femur, distal radius as well as some diaphyseal fractures seen by orthopaedic surgeons. The number of patients with fractures associated with osteoporosis will increase dramatically in the next decade. Patients with decreased bone density with one fracture are at increased risk for another fracture and thus it is critical that these patients be identified and treated for their decreased bone density. For these reasons, orthopaedic surgeons will have an increasing role in the diagnosis of osteoporosis, prevention of fractures in patients with osteoporosis and in at least some instances treatment of osteoporosis. This article will address the current therapeutic options available to the orthopaedist for the prevention and treatment of osteoporosis. The field is progressing so rapidly that the physician now has a vast array of efficacious therapies.

Osteoporosis, a disorder characterized by low bone mass, and associated with pathologic fractures is the most common metabolic bone diseases in the developed countries. It effects more than 25 million Americans and leads to more than 1.5 million fractures each year[6]. Osteoporotic fractures may affect any part of the skeleton except the skull. Most commonly fractures occur in the distal forearm, thoracic and lumbar vertebrae, and proximal femur. The incidence of osteoporotic fractures increases with age, is higher in whites than in blacks, and higher in women than in men[18]. It has been estimated that after menopause a woman's lifetime risk of sustaining an osteoporotic fracture is one in two[18]. One in every three men over the age of 75 will be affected by the disease. A single hip fracture is estimated to cost $30,000, and the overall cost of acute and long-term care associated with osteoporosis exceeds 10 billion dollars annually. Because of the increased life expectancy of the aging population, the economic burden of osteoporosis is projected to reach $240 billion by the year 2040[6].

CLASSIFICATION

Two categories of osteoporosis have been identified: primary and secondary. Primary osteoporosis is the most common form of the disease and includes postmenopausal osteoporosis (type I), and senile osteoporosis (type II). Secondary osteoporosis is characterized as having a clearly definable etiologic mechanism. Type I is associated with a loss of estrogen and androgen resulting in increased bone turnover, with bone resorption exceeding bone formation, and a predominant loss of trabecular bone compared with cortical bone. Type II, which represents the gradual age-related bone loss found in both sexes caused by systemic senescence, is induced by the loss of stem-cell precursors, with a predominant loss of cortical bone[28].

After attaining peak bone mass at age 30, men and women lose bone at a rate of approximately 0.3% and 0.5% per year, respectively. Bone loss in women is accelerated further by a deficiency in estrogen at a rate of 2% year during menopause and continues for 6 years thereafter. Because age-related bone loss is a universal phenomenon in humans, any circumstance that limits an individual's ability to maximize peak adult bone mass increases the likelihood of developing osteoporosis later in life. In addition, since there are no safe and effective ways to rebuild the osteoporotic skeleton, prevention emerges as the crucial strategy[29]. Consequently, a knowledge of preventive approaches is essential, including the efficacy and safety of estrogen and progestin therapy, intake of calcium and vitamin D, exercise, bisphosphonates. Prevention also requires an understanding of the indications for estimating bone density and the methods of obtaining this data.

Some of the most important risk factors for osteoporosis are advanced age, white or Asian race, low body mass index, and family incidence of the disease. Other risks include low calcium intake, premature ovarian failure, smoking, alcohol use, and low level of physical activity (see Table 1).

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Table 1
Osteoporosis risk factors

Age-Related	
	Each decade beyond the fourth decade is 1.5-fold risk
	Reduction in absorption of calcium
	Rise in parathyroid hormone levels
	Decline in calcitonin
Genetic	
	White, Asian, Latino, and black (in order of risk potential)
	Women more than men
	Familial prevalence
	High concordance in monozygotic twins
Nutritional	
	Low calcium intake
	High alcohol
	High caffeine
	High sodium
	High animal protein
Lifestyle	
	Cigarette use
	Low physical activity
Endocrine	
	Menopausal age
	Obesity
	Exercise-induced amenorrhea

Table 2
Drugs associated with osteoporotic syndromes

Thyroid replacement therapy
Glucocorticoid drugs
Anticoagulants
Chronic lithium therapy
Chemotherapy (breast cancer or lymphoma)
Gonadotropin-releasing hormone
Anticonvulsants
Chronic phosphate binding antacid use
Extended tetracycline use
Diuretics producing calciuria
Phenothiazine derivatives
Cyclosporin A

Table 3
Laboratory Tests

Routine	
	Complete blood cell count
	Sedimentation rate
	Electrolytes
	Creatinine
	Blood urea nitrogen
	Calcium
	Phosphorus
	Protein
	Albumin
	Alkaline phosphatase
	Liver enzymes
	24-hour urine calcium
	Serum protein electrophoresis

DIAGNOSIS

The insidious removal of mineral from bone is asymptomatic until the bone fails under physiologic stress. Any patient over the age of 50 who presents to an orthopaedist with a hip, distal radius, or vertebral compression fracture should be evaluated for the presence of osteoporosis. The same diagnostic approach should be taken to patients suspected of having osteoporosis whether or not they have sustained a fracture. A thorough medical evaluation should seek potential causes of secondary osteoporosis, such as hyperthyroidism, Cushing's disease, or the use of drugs known to be associated with osteoporosis (Table 2). Although postmenopausal and senile osteoporosis are the most prevalent forms of the disease, it must be remembered that as many as 20% of women who otherwise appear to have postmenopausal osteoporosis can be shown to have additional etiologic factors above and beyond their age, gender, and ethnic background.

Therefore, it is appropriate to perform simple screening studies looking for secondary causes in each patient (Table 3). A simple biochemical profile will provide information about renal and hepatic function, primary hyperparathyroidism, and possible malnutrition. Hematologic profile might also provide clues for the presence of myeloma or malnutrition. Thyroid function should also be assessed. Serum protein electrophoresis should be performed on all potentially osteoporotic patients at initial evaluation. A normal pattern excludes the presence of multiple myeloma in 90% of patients.

Metabolic bone markers, such as urinary hydroxyproline, pyridinoline, deoxypyridinoline, and N-telopeptides (Table 4), are useful for determining which patients have high bone resorption. They also provide a convenient index of whether a chosen therapy is successfully curtailing bone loss; however, they are not sensitive for diagnosing osteoporosis or identifying associated fracture risk[6]. In addition, there are markers of new bone formation, such as osteocalcin and bone-specific alkaline phosphatase, that may be increased in patients with high bone turnover but are unreliable for

Table 4
Biochemical Markers of Bone Formation and Resorption

Bone Formation
Osteocalcin
Bone-specific alkaline phosphatase
Procollagen extension peptides
Bone Resorption
Tartrate-resistant acid phosphatase
Urinary calcium
Urinary hydroxyproline
Urinary hdroxyproline/creatinine ratio
Urinary pyridinoline/deoxypyridinoline
Urinary N-telopeptide

detecting osteoporosis. Large studies in older postmenopausal women show an association between elevated levels of free urinary deoxy-pyridinoline, low bone mass, and increased fracture risk, independent of low bone mineral density (BMD)[37,10]. One study showed that the combination of these markers and measurement of BMD could identify women who had a four-times-higher risk for hip fracture than women who had only a single risk factor[10].

RADIOGRAPHY

The most characteristic feature of osteoporosis is decreased radiodensity. However, conventional radiographs are neither sensitive nor accurate for the diagnosis of early bone loss. It has been reported, for example, that a reduction in bone-calcium content must exceed 30 percent to be observed with certainty on conventional radiographs. In addition, factors such as differences in film development, patient weight, and the amount of x-ray exposure can lead to variability in radiodensity and affect the accuracy of conventional radiographs.

BONE DENSITOMETRY

The most effective way of screening for osteoporosis and then following the results of treatment is by the measurement of bone density. Current methods include radiographic absorptiometry, single-energy x-ray absorptiometry, dual-energy x-ray absorptiometry, quantitive computed tomography, and quantitive ultrasound. Of these, dual-energy x-ray absorptiometry, is the most widely used modality for the clinical measurement of bone-mineral content. This technique is rapid, taking only 3 to 7 minutes, and delivers a radiation dose that is so low as to be equivalent to approximately 5% of the radiation dose of one chest radiograph. DEXA scanners simultaneously use a high- and a low-energy x-ray beam to measure BMD. The difference in soft-tissue and bone penetration of these two beams is used to calculate BMD. The relationship of decreased BMD seen on DEXA and increased fracture risk is exponential-for each standard deviation decrease of BMD, fracture risk increases twofold[32].

The World Health Organization defines osteoporosis as BMD or bone mineral content of more than 2.5 standard deviations (SD) below the young adult mean normal value[1]. Patients with a BMD of 1 to 2.5 SD below the young adult mean value are defined as osteopenic. BMD is important to measure because it correlates so strongly with the risk of osteoporotic fractures. For every SD of decrease in BMD, the relative risk of osteoporotic fracture in the elderly population increases by a factor of 1.5 to 1.8[32]. Therefore, a relatively small increase in BMD can significantly reduce fracture risk.

There are numerous potential indications for bone densitometry. However, there are insufficient data to justify routine screening with use of this technique. Recently, the Health Care Financing Administration defined five diagnostic categories that it considers to be indications for the use of bone densitometry.[12] These categories are listed in Table 5.

Perhaps the major value of bone densitometry in current orthopaedic practice is the identification of patients with osteoporosis who are at increased risk for fracture. Fracture of the proximal aspect of the femur is the most serious consequence of osteoporosis. Approximately 250,000 such fractures occur in the United States each year, resulting in annual expenditure exceeding 8 billion dollars. It has been estimated that after menopause a woman's lifetime risk of sustaining an osteoporotic fracture is one in three. There is an associated 20% mortality following an osteoporotic hip fracture. Perhaps more importantly, following such fractures less than one-third of the patients are restored to their prefracture functional state within 12 months of the fracture. Most patients require some form of ambulatory support and many require institutional care.

PREVENTION

Prevention of osteoporosis is of primary importance, since there are no safe and effective methods for restoring healthy bone tissue and normal bone architecture once they have been lost. Bone loss is an asymptomatic process and in some ways can be considered clinically to be equivalent to hypertension. In each case patients present to the health care system when a complication arises, either fracture, in the case of osteoporosis, or stroke in hypertension. The key in each case is

Table 5
Current recommended indications for DEXA

Group	*Comments*
Women who are estrogen-deficient as a result of premature ovarian failure or menopause	Many of these women are reluctant to take ERT because of a slightly increased risk of breast cancer. They will be more likely to take estrogen if there is objective evidence of pending or existing bone loss. DEXA scanning will also identify the significant subset of women who are not at risk for osteoporosis and do not require ERT for this indication.
Patients with established osteopenia or compression fractures	Patients with compression fractures are at extremely high risk for future osteoporotic fractures; most require urgent therapy. DEXA will establish a baseline for BMD that can be used to measure the effectiveness of future therapy. Patients with established osteopenia require follow-up DEXA within 6-12 months, depending on their risk factors for fracture.
Patients taking long-term corticosteroid therapy	Most of these patients are at risk for rapid and significant bone loss. Patients need to be studied at initiation of therapy, with follow-up in 6-12 months.
Patients with asymptomatic primary hyperparathyroidism or hyperthyroidism	Unlike type II osteoporosis, primary hyperparathyroidism usually leads to thinning of cortical bone.
Patients on drug therapy for treatment of osteoporosis	This allows monitoring of the effectiveness of various treatment modalities.

early identification of the patients at greatest risk, targeting those for intervention; the orthopaedist should be a key player in this process. For osteoporosis, these clues are divided into risk factors and estimates of skeletal status (Table 1).

In general, for each patient, the more risk factors present, and the longer the duration of their presence, the greater the risk of future problems[29]. Physicians can use the presence of these factors in two ways. First, they can be used to sensitize the patient, and physician, to the likelihood of osteoporosis. Second, those risk factors that are amenable to elimination or alteration should be discussed with the patient. Practically, menopause is the usual time when evaluation of the patient for osteoporosis begins, although nutritional and lifestyle habits should be changed as early in life as possible. Because most orthopaedists are exposed to a cross section of patients with respect to age, playing a proactive role in osteoporosis prevention is possible.

ADOLESCENCE AND YOUNG ADULTHOOD

Adequate calcium nutrition during growth and maturation are key determinants of adult bone mass. In addition, weight-bearing exercise, such as walking or jogging for 3 to 4 hours per week is beneficial. Exercise is highly effective in favorably affecting the skeleton and preventing falls[36,23]. The mechanism by which exercise signals the cell is still to be determined. Low levels of exercise are critical for maintenance of bone mass. Higher levels will lead to modeling of the bone to adapt to its new environment, and even higher levels will lead to failure.

The optimal type and duration of exercise have not been established, although several investigators have demonstrated that minimal amount of exercise of appropriate type may be sufficient to stimulate the osteoblasts for 24 to 48 hours. Bone mass is very closely correlated with the muscle mass acting on that bone. Thus, programs that are aimed at developing increased muscle strength will be translated into increased bone mass in the affected limb. The strength of a bone has been demonstrated to be related to the mass of the bone and the distribution of the mass. The latter is affected by exercise.

It is recommended that individuals adopt all three components of an ideal exercise program-impact exercises, strengthening exercises, and balance training. The impact exercises are utilized to directly stimulate

osteoblast formation and to ward off resorption. Exercises that meet these criteria include jogging, brisk walking, and stair climbing. Strengthening exercises will affect the bones underlying the exercised muscle. It is recommended that patients utilize light weights in a comprehensive program that strengthens the major axial and appendicular muscle groups. All exercises should be developed in terms of the potential of the individual and should progress from minimal loads to greater loads, giving sufficient time for the patient to accommodate to the program. Exercise to the point of caloric drain or development of amenorrhea is associated with stress fractures and osteoporosis.

It is also important to recognize risks in the young patient such as anorexia, bulimia, excessive athleticism, and prolactinoma which all can be associated with estrogen deficiency and resultant loss in skeletal mass. Certain medications can also impair skeletal metabolism such as glucocorticoids and antiepileptic drugs.

PERIMENOPAUSE AND POSTMENOPAUSE

At the time of menopause, each patient should be evaluated for the presence of risk factors, ascertained as part of a complete medical history. It is then important to assist in the modification of the patient's behavior to reduce the impact of the factors that are amenable to intervention. A strong family history of osteoporosis or a medical and social history that suggests an increased risk of osteoporosis should lead to the performance of a bone-density examination. If low bone mass is detected, a high calcium intake alone will not significantly mitigate the accelerated spinal loss of the postmenopausal period. Estrogen is the therapy of choice and will be discussed under the treatment section.

Changing the pattern of physical activity may be difficult, especially for patients who are less positively motivated. This is especially true when discussing prevention with patients, who are, by definition, asymptomatic. A number of studies have evaluated exercise in the prevention of bone loss after menopause[2]. A moderate level of exercise by an individual who receives an appropriate diet, with adequate calcium and vitamin D, can diminish the rate of bone loss. Load-bearing exercise is most effective in preserving or increasing skeletal mass. To be effective in altering bone density, the exercise must directly strain the skeletal sites. In the absence of proven benefit for any exercise for prevention of osteoporosis, any weight-bearing activity suffices[7].

TREATMENT

The treatment of patients who have sustained osteoporotic fractures includes maintaining their quality of life, encouraging mobilization, controlling pain, and promoting social interaction. Prolonged bed rest, poor nutrition, and social isolation are avoidable pitfalls.

For all patients with low bone mass or an osteoporotic fracture, a complete history and physical examination are necessary, and a thorough laboratory workup should be ordered to exclude common medical disorders known to cause bone loss. Treatment mainstays include adequate calcium intake, weight-bearing exercise, and the use of appropriate medications, which will be discussed below (Table 6).

CALCIUM

Adequate calcium is required during growth because the body does not make calcium. It continues to be an essential nutrient throughout life because the body loses calcium every day through shedding of skin and nails, as well as in sweat, urine, and feces. There is evidence of an increasing prevalence of calcium and/or vitamin D deficiency in the general population[13,31]. Sixty-five percent of women past the age of menopause have varying degrees of lactose intolerance and by preference avoid lactose-containing dairy products. Consequently, whether by choice, habit, or design most Americans have calcium intakes below the recommenced level, particularly in elder years. Therefore, addition of calcium-containing supplements is required if age-corrected physiologic calcium intake is to be achieved. The effect of calcium supplementation on bone mass and vertebral fracture rate in established osteoporotic syndromes is not well studied. Studies that are available suggest that calcium supplementation in perimenopausal females does decrease the rate of bone loss when administered in doses of 1,000-1,500 mg per day, especially in individuals with histories of marginally low calcium intakes[9]. A combination of calcium supplements and exercise has also proven effective in stabilizing skeletal bone loss rates in postmenopausal female populations. The current recommended dietary allowance in the United States is 1,200 mg/day in adolescence through age 24 and 800 mg/day for older adults. It is recommended that men and postmenopausal women ingest 1,000 mg/day and that postmenopausal women not receiving estrogen ingest 1,500 mg/day. When individuals taking calcium are compared with a placebo historical group who are not taking calcium, there is clear evidence that calcium supplementation is associated with a lower rate of bone loss[25]. However, high calcium intake alone will not significantly mitigate the accelerated spinal loss of the postmenopausal period.

Table 6
Options for prevention and treatment of osteoporosis

Therapy	*Appropriate population*	*Comments*
Exercise	All persons	Increases bone density; improves strength and coordination; reduces risk of falls
Calcium, 1,000-1,500 mg/day	Persons older than 4 years of age	In childhood, increases peak bone mass; in adulthood, prevents bone loss
Vitamin D, 400-800 IU/day	Persons older than 65 years of age	Dose of 800 IU/day may be preferred
Oral conjugated estrogen, 0.625 mg/day, or transdermal estradiol, 0.05 mg/day	All estrogen-deficient women, except those at high risk for an estrogen-sensitive tumor	Only agents for osteoporosis shown to reduce mortality; given with progesterone in women with an intact uterus
Alendronate sodium (Fosamax)	Postmenopausal women not taking estrogen whose bone-mineral density is 2.5 SD below mean peak levels POTENTIAL POPULATIONS Postmenopausal women not taking estrogen who: —Are less than 60 years of age and have a bone-mineral density of 1 to 2.5 SD below mean peak levels —Have had an osteoporotic fracture	Studies of use in potential populations have not been reported
Calcitonin, nasal, 200 IU/day	Same as for alendronate	Shown to have analgesic qualities; studies of use in potential populations have not been reported
Slow-release sodium fluoride, 25 mg bid for 12 mo, in 14-mo cycles	Postmenopausal women with an osteoporotic vertebral fracture	Not yet approved by FDA; only agent that stimulates bone formation; has neutral effect on appendicular bone mass and nonvertebral fractures

Calcium carbonate contains 40% elemental calcium and requires acidity to be solubilized. Therefore, it should be taken with foods. Achlorhydric individuals will not absorb calcium carbonate. The side effects of calcium carbonate intake include a sensation of gas and constipation.

Calcium citrate is 21% elemental calcium and will dissolve even in the absence of acidity. It does not form gas and tends to ameliorate constipation. Calcium citrate is chosen for those individuals who are achlorhydric, and it decreases the risk of kidney stones[15].

VITAMIN D

Vitamin D, a secosteroid that increases the functional absorption of calcium, usually is given in conjunction with calcium therapy. Most multivitamin supplements contain 400 IU of vitamin D. More than 800 IU of vitamin D per day is not recommended because of its potential toxic side effects. While vitamin D supplementation might offer some benefit, particularly among those with marginal or deficient intake or production of vitamin D, it is generally believed that it does not offset the rapid bone loss associated with estrogen deficiency due to menopause[35]. In those patients with subclinical vitamin-D deficiency, low doses of vitamin D (800IU

daily) are effective in maintaining bone mass and reducing the rate of fractures by 30%[3]. Consequently, it was the recommendation of the National Institutes of Health consensus conference (NIH) that individuals should take between 400 and 800 units of vitamin D daily, particularly if they have poor dietary intake or increased risk factors for osteoporosis. At this dosage there is no essentially no major risk. However, individuals who take 50,000 units of vitamin D per week have an increase risk of the development of kidney stones, nausea, and other manifestations of hypercalcemia.

ESTROGENS AND HORMONE REPLACEMENT

The most potent intervention for preventing osteoporosis in women with low levels of estrogen or men with low levels of androgen is sex hormone replacement therapy. Loss of estrogen at any age results in increased bone remodeling, which is associated with loss of bone mass. Estrogen replacement therapy returns bone remodeling to the level seen in premenopausal women and therefore reduces fracture risk. Estrogen is an "antiresorptive" agent in that it inhibits bone resorption by decreasing the frequency of activation of the bone remodeling cycle. Estrogen would be expected to be most efficient if bone remodeling or bone turnover was increased. This is why it is so effective in the early stages of menopause. If initiated at the time of menopause, estrogen replacement may prevent many cases of osteoporosis and reduce the incidence of fractures of the hip by 50%. Estrogen also acts to reduce the risk of coronary artery disease; maintain sexual characteristics; and minimize hot flushes, dysuria, and dyspareunia. Some studies have shown that estrogen may protect against osteoarthritis of the hip and Alzheimer's disease[20,34].

A definitive role for estrogen in established osteoporosis is much less well established. There is little evidence that estrogen reduces the rate of occurrence of new vertebral fractures in patients with established osteoporosis. Short-term complications of estrogen therapy in women with established osteoporosis include breast tenderness and vaginal bleeding[24]. If estrogens are given without progesterone there is increased risk of endometrial cancer. The relationship between estrogen therapy and breast cancer is not well established, but most studies suggest that there is little increased risk of breast cancer during the first 10-15 years of therapy[33]. Estrogen replacement therapy, if recommended by an orthopaedist, should be used in conjunction with the consultation of an obstetrician-gynecologist or endocrinologist.

BISPHOSPHONATES

Etidronate disodium (Didronel) and alendronated sodium (Fosamax) are analogues of pyrophosphate that are absorbed onto the hydroxyapatite of bone, thereby inhibiting bone resorption. Bisphosphonates have a long duration of skeletal retention, which raises concern about potential long-term side effects. In phase three clinical trials, alendronate was given daily for up to three years with no toxicity; it produced continued increases in bone density and resulted in a significant reduction in the rate of fractures[16]. Continuous dosing eventually results in impaired bone mineralization. Intermittent use of bisphosphonates prevents bone resorption and permits synthesis of new bone.

Cyclical treatment with etidronate has been shown to significantly increase spinal bone-mineral density and decrease the rate of vertebral fractures over the short term in severely osteoporotic older women. At high doses, however, impaired mineralization of bone occurs, potentially leading to osteomalacia. Thus, etidronate is used only in intermittent regimens for women with severe osteoporosis who are unable or unwilling to take estrogen. The use of this agent has been largely replaced by alendronate.

Alendronate is a selective inhibitor of bone resorption that is 400 times more potent than etidronate, without being detrimental to bone mineralization. There have been two fairly recent prospective, randomized, double-blind, placebo-controlled trials or oral alendronate in post-menopausal women with established osteoporosis[5,16]. Chestnut found that 5 to 10 mg daily of oral alendronate increased bone-mineral density in the spine and hip by 4% to 7% after 2 years. Liberman confirmed these results in a similar study, which also showed significant reduction in vertebral fractures. The 10 mg daily dose was considered optimal and was well tolerated; abdominal symptoms were the primary adverse effect.

An important aspect of the Liberman study is that the subjects were asymptomatic postmenopausal women with osteoporosis. Most previous trials have been limited to patients with symptomatic preexisting vertebral fractures. Therefore, this represents an advance in primary prevention of osteoporotic fractures.

Alendronate has been approved by the FDA for treatment of osteoporosis in postmenopausal women who are not receiving estrogen replacement therapy. Of postmenopausal women who do not take estrogen, three patient populations are reasonable candidates for therapy with alendronate:

— Women with osteoporosis (bone-mineral density of at least 2.5 SD below mean peak levels, as measured in young, healthy women)

— Women less than 60 years of age who have osteopenia (bone-mineral density of 1 to 2.5 SD below mean peak levels).
— Women who have already sustained an osteoporotic fracture.

It is uncertain how long alendronate should be continued. There is now evidence that bone mass continues to improve for at least 4 years. Cessation of alendronate does not lead to the rapid bone loss that occurs after cessation of estrogen. Besides the complications of dyspepsia and esophagitis, alendronate has been associated with occasional episodes of diarrhea and bone pain, the latter particularly in those individuals who did not receive calcium supplementation before treatment. Therefore, it is recommended that calcium be given in addition to alendronate.

Alendronate does not provide the analgesic benefit of calcitonin and does not offer the nonskeletal benefits that are associated with estrogen. There is some suggestion, currently being tested in clinical trials, that alendronate and estrogen may be synergistic, as they have different sites of action[11]. If a patient has not responded to one of the agents, the addition of the other may result in a positive bone-accretion stage.

CALCITONIN

Calcitonin is a non-sex, non-steroid hormone that specifically binds to osteoclasts and decreases their activity. Since the introduction of nasal formulations of calcitonin, interest in this agent has been renewed. Early studies of parenteral calcitonin therapy showed bone effects similar to those with estrogen replacement therapy; however, there have been many reported complications with use of parenteral forms[17].

There is one prospective study showing that nasal calcitonin, 50 IU daily for 5 consecutive days a week, significantly prevented postmenopausal bone loss over 5 years. In addition, small increases in bone-mineral density also were noted with the 200 IU dose[26]. Two other prospective studies showed that in women with established osteoporosis nasal calcitonin reduced the incidence of recurrent vertebral fracture by 60% compared with calcium alone[27,22].

The FDA has approved nasal calcitonin for treatment of osteoporosis in postmenopausal women not receiving estrogen replacement therapy. The recommended dose is 200 IU sprayed into alternating nostrils once a day. The most common side effects include facial flushing, gastrointestinal upset, and rash. Unlike the other osteoporotic agents, calcitonin appears to have an analgesic effect. Because of this analgesic effect, calcitonin is frequently used in patients with symptomatic acute vertebral fractures.

SODIUM FLUORIDE

The only therapeutic agent for osteoporosis that stimulates osteoblastic activity and bone formation is sodium fluoride. An early study involving a high-dose, immediate-release formulation[30] showed a marked increase in vertebral bone-mineral density but no decrease in spinal fracture rate. The rate of nonvertebral fractures actually increased, presumably owing to abnormal bone formation caused by excessive exposure to fluoride.

Slow-release formulations are now available and are able to maintain serum fluoride concentrations within the narrow therapeutic window. Pak recently published a prospective, randomized, controlled trial of cyclic slow-release sodium fluoride in post-menopausal women with vertebral fractures. Spinal bone-mineral density increased 4% to 5% a year, and the rate of new vertebral fractures in previously unaffected vertebrae was markedly decreased, particularly in patients with mild to moderate disease. The new fracture rate in patients with severe disease was not significantly reduced, and the rate of fractures in previously fractured vertebrae was unaffected by therapy. Therefore, the least benefit was seen in patients with the most severe disease (the opposite of that seen with bisphosphonates). Appendicular bone-mineral density and non-vertebral fracture rates were not significantly affected. Thus, slow-release sodium fluoride seems best used in patients with mild to moderate disease that have sustained a vertebral fracture.

In addition, the long-term safety of fluoride therapy remains to be established, but few side effects have been published (mainly gastrointestinal upset). This drug is currently awaiting approval by the FDA and thus is not available

SUMMARY

Osteoporosis is an ever-increasing problem as our population ages. However, it is also to a large extent a preventable problem. The orthopaedist now has the ability to determine bone mass, the rate of turnover, and the fracture risk. Skeletal bone mass can be evaluated with DXA; the rate of bone resorption can be determined by assessment of collagen-degradation urinary products; and the weight status, fracture history, and history of smoking can be used to predict the fracture risk in individual patients. The orthopaedic physician also needs to take an active role in advising their younger patients about achieving peak bone mass. All individuals should follow a program that includes adequate calcium replacement, 400 to 800 units of vitamin D, appropriate exercise, avoidance of significant weight loss, and cessation of smoking.

At menopause, women should evaluate their risk factors and consider the use of estrogen not only for its skeletal benefits but also for its nonosseous effects. In patients with contraindications or an aversion to hormone therapy, bone densitometry should be performed to determine risks before expensive nonhormonal treatment is initiated. Additional studies such as measurement of collagen degradation products will help establish whether the patient's resorptive rate is high or stable. If the bone mass is 2.5 SDs below normal peak or if there is an increase in resorption, use of either estrogen, bisphosphontes, or calcitonin may be appropriate. If there is evidence of low-turnover osteoporosis with decreased osteoblast formation, sodium fluoride should be considered.

Two thirds of the cost of osteoporosis in the United States is due to hip fractures. The orthopaedist is the primary physician who comes in contact with these fracture patients. It is therefore his or her responsibility to become knowledgeable about the treatment and prevention of osteoporosis. The bisphosphonates, hormones, and calcitonin provide predictable restoration of bone mass and significantly decrease the rate of osteoporotic fractures.

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