ELSEVIER
SAUNDERS

Dent Clin N Am 49 (2005) 463–484

THE DENTAL
CLINICS
OF NORTH AMERICA

Osteoporosis: Diagnostic Testing, Interpretation, and Correlations with Oral Health—Implications for Dentistry

Roseann Mulligan, DDS, MS[a,b,*], Stephen Sobel, DDS[a]

[a]*University of Southern California, School of Dentistry, 925 West 34th Street, Los Angeles, CA 90089-0641, USA*
[b]*University of Southern California, School of Geronotology, 3715 McClintock Avenue, Los Angeles, CA 90089-0191, USA*

Osteoporosis is a condition of the skeleton that is characterized by compromised bone strength and predisposition to an increased risk of fracture. It is the most prevalent metabolic bone disease in this country. Osteopenia describes a condition of bone mass that is lower than normal but not severe enough to be considered osteoporotic. In the third National Health and Nutrition Examination Survey (NHANES III, 1988 to 1994), bone mineral density tests of the femur were completed for the first time [1]. According to the World Health Organization's (WHO) recommended criteria for osteoporosis and reduced bone mineral density (BMD), 56% of women 50 years of age and older had a reduced level of bone density, with 16% of these meeting the criteria for osteoporosis, whereas 18% of men demonstrated reduced BMD (Fig. 1) [1]. Using these data, it is estimated that more than 10 million Americans over the age of 50 have osteoporosis, including 7.8 million women and 2.3 million men; another 33.6 million over the age of 50 have low bone mass and hence are at risk for osteoporosis [2].

Increasing age is clearly a factor in osteoporosis, with an age-related BMD loss of 1% to 2% per year. Women in their 80s have a 10 times greater risk of being osteoporotic than women in their 50s (Fig. 2) [1]. Some racial and ethnic groups are more vulnerable to this condition, with non-Hispanic whites and Asians being at higher risk than Mexican Americans or non-Hispanic blacks [2]. Osteoporosis also is more prevalent in individuals with

* Corresponding author. University of Southern California, School of Dentistry, 925 West 34th Street, Room 4338, Los Angeles, CA 90089-0641.
E-mail address: mulligan@usc.edu (R. Mulligan).

doi:10.1016/j.cden.2004.10.005

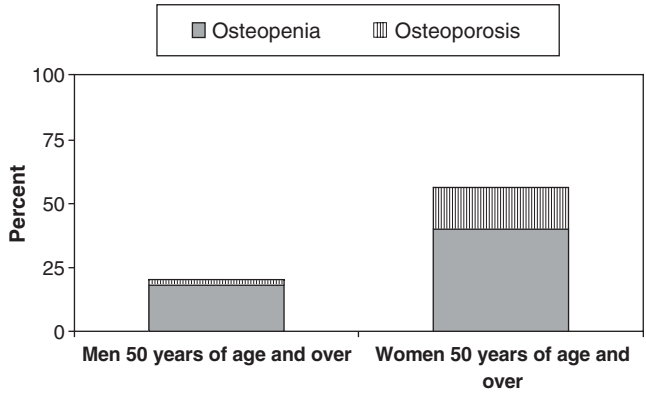

Fig. 1. Prevalence of low femur bone density in the United States as reflected in NHANES III, 1988–94. (*From* Department of Health and Human Services. Centers for Disease Control and Prevention. National Center for Health Statistics. Osteoporosis. National Health and Nutrition Survey (NHANES III). Available at: http://www.cdc.gov/nchs/data/nhanes/databriefs/osteoporosis.pdf. Accessed July 3, 2004.)

less than a 12th-grade education than it is in those who had a 12th-grade education or higher [3].

Overall, osteoporosis results in 1.5 million fractures per year: 700,000 are vertebral; 250,000 are wrist fractures; 300,000 are located in a variety of sites; and 300,000 are in the hip, resulting in a mortality of 25% [4]. One of every two women and one of every four men will have a fracture related to osteoporosis. By the year 2001, the direct medical costs of osteoporotic fractures came to $17 billion for the year [4], and the annual costs are expected to continue to rise.

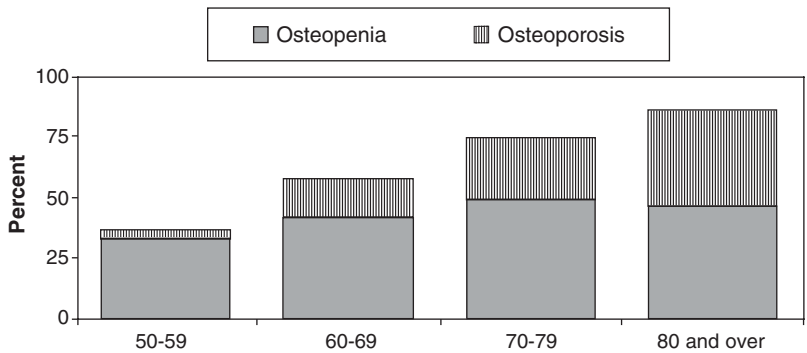

Fig. 2. Prevalence of low femur bone density in older women in the United States as reflected in NHANES III, 1988–94. (*From* Department of Health and Human Services. Centers for Disease Control and Prevention. National Center for Health Statistics. Osteoporosis. National Health and Nutrition Survey (NHANES III). Available at: http://www.cdc.gov/nchs/data/nhanes/databriefs/osteoporosis.pdf. Accessed July 3, 2004.)

Osteoporosis is likely to become an even larger contributor to morbidity and mortality as the population of the United States continues to gray. By the year 2000, 12.4% of the population was 65 years of age or older, amounting to 35 million people. It is projected that by the year 2020, 20% of the population, or 54 million people, will be over 65.

Data from the National Health Interview Surveys of 1983 and 1993 also demonstrate that more adults are retaining teeth, with disparities in the number of teeth remaining based on age and race or ethnicity [5]. More and more elderly people are seeking care from oral health providers to maintain oral health. What are the issues linking oral health and osteoporosis? We know that prevention is a key to avoiding osteoporosis. How might dentists be engaged in a preventive role? Is osteoporosis detectable with dental radiography techniques? Do the current medications for osteoporosis have an impact on oral health? Are they likely to cause adverse interactions with medications that are typically used in dental practices? Do these medications also play a positive role in maintaining the density of the mandible and maxilla? Should dentists be prescribing medications for osteoporosis to maintain the health of the oral facial complex? Should fluoride usage be prescribed for the elderly, not only to decrease caries but to strengthen bone? All these questions are addressed in this article.

The nature of osteoporosis

Osteoporosis is a result of low bone mass and weakening of the microarchitecture of the bone that results in an increased risk of fracture [6]. Different types of bone undergo different changes. For example, cortical bone loss occurs mainly from the endosteal surfaces, resulting in enlarged marrow cavities, whereas affected bone of the vertebrae shows disruption in the trabecular network as a result of weakening of the horizontal supporting struts [7]. Bone is in a continuous state of resorption and deposition [8]. During aging, the balance between these activities is disturbed, resulting in a negative bone mass change. Bone strength can be predicted by bone mass and bone quality changes. Bone mass frequently is measured by dual energy x-ray absorptiometry (DEXA). Bone quality, which is related to micro-architecture, mineralization, and mechanical properties, cannot be assessed by DEXA technology and hence is assessed using invasive techniques such as density fractionation, microradiography, and microhardness testing or noninvasive techniques such as back scattered electron imaging. Typically, screening protocols call for the use of DEXA measurements [9].

Measuring bone density using dual energy x-ray absorptiometry

DEXA is a noninvasive and painless way to measure bone mass or density. Although a number of sites can be measured (eg, spine, femur, radius, calcaneus), chosen primarily for their high incidence of osteoporotic

fractures, there is some debate as to the best site for predicting osteoporosis. The best way to assess BMD at a particular site is to measure that area directly, rather than having a measurement at another site serve as a proxy for the region of interest [10].

The purposes of BMD testing are multiple. This testing can detect low bone density before a fracture occurs, confirm a diagnosis of osteoporosis, predict the possibility of future fractures, determine the rate of bone loss, and monitor the effects of treatment [4].

DEXA results are reported as t-scores and z-scores. The t-scores are comparisons of the patient's BMD with a young population's peak reference value, whereas the z-scores are comparisons of the patient's BMD with a population's age-matched reference value, allowing a comparison with the patient's peer group [11]. Using WHO criteria, a patient with a BMD score greater than a 2.5 standard deviation (SD) below the young average peak bone mass (the t-score) is considered osteoporotic. If the BMD score is between 1 SD and 2.5 SD below the t-score, the patient is considered osteopenic [12]. Cautions should be applied to the use of these reference values for those who are not white women, such as Asian women and men of all ethnic and racial groups.

The goal for those with a diagnosis of osteopenia is to prevent the onset of osteoporosis by modifying behavior, increasing nutrient intake, or taking medications. Those with osteoporosis need to engage in treatments that provide active therapy to prevent further bone loss and foster bone deposition. The National Osteoporosis Foundation recommends treatment for those with a BMD t-score greater than a -2 when there are no risk factors or greater than -1.5 when there are coexisting risk factors or a prior vertebral or hip fracture has occurred [13].

Risk factors

Risk factors for osteoporosis include female gender, white or Asian ancestry, thinness or small frame (<127 lbs), advanced age, a family history of osteoporosis, postmenopausal condition, hyperthyroidism, certain medications (eg, corticosteroids, anticonvulsants), a diet low in calcium, an inactive life-style, cigarette smoking, excessive use of alcohol, and low testosterone. In addition to the risk factors for osteoporosis, fracture risk is increased by poor bone quality and higher rates of falling in the elderly [2,4,6,14].

Screening for risk

In an effort to predict reliably who is at risk for osteoporosis, so that diagnostic tests (typically DEXA studies) may be performed and warranted preventive or therapeutic measures initiated, there have been attempts to develop risk assessment protocols. Michaelsson et al [15] suggested using

body weight alone, whereas others have developed screening questionnaires. A three-item Osteoporosis Risk Assessment Instrument (ORAI) based on age, weight, and current estrogen usage demonstrated a sensitivity of 93.3% and a specificity of 46.4% for accurately assessing women who have low BMD [16]. The Simple Calculated Osteoporosis Risk Estimation (SCORE) uses age, race, history of rheumatoid arthritis, history of nontraumatic fracture after age 45, estrogen use, and weight [17]. It has similar sensitivity and specificity outcomes to the ORAI [18]. The goal of these instruments is to help identify women in the population who are at the greatest risk for osteoporosis and have them undergo DEXA examinations, without referring all women for such a diagnostic work-up.

Prevention of osteoporosis

Interventions to prevent osteoporosis should include physical conditioning that incorporates muscle strengthening and coordination activities, nutrients, reduction of behavioral risk factors, and pharmacotherapies [7]. Osteoporosis can be prevented by weight-bearing exercise (eg, walking, hiking, jogging, stair-climbing, weight training, tennis, dancing), a diet rich in calcium and vitamin D [19], healthy habits, with no smoking or excessive alcohol intake [20], bone density testing, the use of certain medications that promote bone health, and minimal use of medications such as glucocorticoids and anticonvulsants, which contribute to bone loss [21].

Diet and nutrients

The American diet is highly deficient in calcium, with elderly females consuming approximately one third of the daily recommended intake and males consuming about one half. The need for increased calcium intake with aging is recognized. Increases in the daily dose of calcium are recommended, in view of the less efficient absorption of this mineral from the intestinal tract of older individuals [8]. Decreases in 25-hydroxy vitamin D also occur with age [22]. Vitamin D is important because it facilitates intestinal calcium absorption and new bone formation. Vitamin D is made in the skin, but aging is accompanied by a decrease in skin composition and thickness [23] that affects vitamin D production. In some parts of the country, because of climate, the elderly are less likely to be outside where they have sun exposure; the same is true of those who are institutionalized [24]. Therefore, their diets must be supplemented. Patients on calcium supplements are less than half as likely to lose teeth as those who are not, according to work by Krall et al [25], although once a patient stops taking calcium and vitamin D the odds for tooth loss immediately increase. Even with a daily intake of 1000 mg of calcium alone, the odds of losing teeth are half those of people who do not take calcium—a result that does not obtain from taking vitamin D alone [25].

High sodium and animal protein intake increases urinary calcium loss and thus is a significant risk factor for osteoporotic fracture. However, when there is low protein intake, a condition referred to as protein-calorie malnutrition occurs. This deficiency stimulates bone resorption and impedes bone formation directly and indirectly through a reduction in serum insulin-like growth factor I [21]. Additionally, the malnourished are more likely to fall and, having less padding over their bones to absorb falls, have a greater risk for fracture. Deficiency of vitamin K and excessive intake of vitamin A also may contribute to osteoporotic fractures [21].

Caffeine and nicotine effects

Smoking has been recognized as a significant risk factor for osteoporosis [26]. Direct effects are due to nicotine's action on bone cells and possibly to the effects of cadmium. Indirect effects include decreased intestinal calcium absorption, changes to vitamin D or in the metabolism of multiple hormones in the body, and the decreased body weight and physical activity that are typically seen in smokers compared with nonsmokers [27]. Studies have shown smoking to have a negative effect on men and women, with some studies showing a greater effect in older men. Increased bone loss due to smoking may be slowed or reversed once smoking has stopped [27]. Hip fractures have been shown to be strongly associated with smoking [28], as have vertebral fractures [29] and fractures at other sites [30].

High caffeine consumption has been implicated as a cause of low BMD. Although some investigators have conjectured that this finding is due to a reduced consumption of milk by avid coffee drinkers [31], others have demonstrated that increased caffeine intake (greater than an equivalent of 18 ounces of brewed coffee per day) accelerates spinal bone loss in elderly women [32].

Although drinking alcohol is associated with lower bone density in premenopausal women, moderate amounts of alcohol seem to have a protective effect in postmenopausal woman [33,34]. Heavy alcohol consumption is, however, a strong risk factor for osteoporosis, being associated with impaired osteoblast function that results in suppression of bone turn-over and formation [35]. The inhibition of calcium absorption is another direct effect of heavy alcohol use with negative indirect effects related to the reduction of testosterone levels in men, deterioration of liver function, and protein-calorie malnutrition [36]. The threshold for adverse effects of alcohol is lower in women than in men. Of course, inebriation from alcohol overuse also greatly increases the risk of falling, with a fracture being the potential result.

The contribution of hormone replacement therapy

Bone loss in adults typically occurs in two distinct portions of the lifespan: one period of bone loss occurs around menopause (type I or high

turn-over osteoporosis) and another relates to advancing old age (type II or low bone turn-over osteoporosis) [37]. Although men are protected from the former, the osteoporosis of old age is of concern to them as well. Overall decreases in bone mass are greater in women than in men, because at the time of menopause substantial decreases in estrogen levels occur in women. These decreases in estrogen strongly correlate to increased bone loss. When estrogen levels are replaced through hormone replacement therapy (HRT), a protective effect on bone loss and a reduced fracture incidence are demonstrated [38]. Similar decreases do not occur in men. The positive effect of HRT in maintaining BMD only occurs while the hormone is being administered; as a result, no upper age limit has been established for stopping this therapy [38].

It has been conjectured that HRT might also protect bones in the maxilla or mandible. A 7-year longitudinal study by Krall et al [39] followed 189 women who had no HRT. A definite decrease in bone density related to tooth loss was found, even while controlling for menopause and smoking. August et al [40] performed a chart review of people who had received implants in the maxilla (n = 761) and in the mandible (n = 652) and then grouped the subjects by estrogen status: postmenopausal without HRT, postmenopausal with HRT, premenopausal, men younger than 50 years, and men aged 50 or older. No statistically significant differences between groups or sites were found; however, there were also no controls over variables (eg, smoking) that might have confounded the effect.

This study and others demonstrate the need to develop specific measurement protocols that control for confounding factors and to use a longitudinal approach to answer questions about the effect of osteoporosis on oral skeletal findings [41].

Pharmacotherapies for osteoporosis

Several pharmacologic agents, with various mechanisms of action, are used in the treatment of osteoporosis. Calcitonin and bisphosphonates inhibit bone resorption. Selective estrogen-receptor modulators (SERMs) have an estrogen-like effect on the skeleton. Whichever medication regimen is prescribed, the key to successful treatment and prevention is adequate concomitant intake of calcium and vitamin D.

Calcium and vitamin D

Supplemental calcium (in addition to that achieved in the diet) and vitamin D are safe and cost-effective measures to prevent bone loss resulting from osteoporosis [21]. These nutrients should be recommended in the dosages applicable for the age of the patient (Table 1). The recommended dosage for individuals aged 65 and over is 1500 mg of calcium and 600 to 800 IU of vitamin D per day [19].

Table 1
Optimal calcium requirements as recommended by the National Institutes of Health Consensus Development Conference, June 6–8, 1994

Group	Optimal daily intake (in mg of calcium)
Infant	
Birth–6 mo	400
6 mo–1 y	600
Children	
1–5 y	800
6–10 y	800–1200
Adolescents/Young adults	
11–24 y	1200–1500
Men	
25–65 y	1000
Over 65 y	1500
Women	
25–50 y	1000
Over 50 y (postmenopausal)	1500
On estrogens	1000
Not on estrogens	1500
Over 65 y	1500
Pregnant and nursing	1200–1500

From Optimal calcium intake. NIH Consensus Statement Online 1994 (June 6–8); 12(4): 1–31. Available at: http://consenus.nih.gov/cons/097/097_statement.htm. Accessed August 11, 2004.

Bisphosphonates

The bisphosphonates are so named because they have a phosphate-carbon-phosphate bond. This class of medication induces a shift in mineralization. Binding strongly to hydroxyapatite crystals, they inhibit bone resorption, thus reducing the rate of bone turn-over. They also are potent inhibitors of osteoclasts and reduce the rate at which new bone remodeling units are formed, thereby reducing the depth of resorption. Overall, the result is to produce a positive bone balance at individual remodeling units, which increases bone mass. Alendronate (Fosamax) and risedronate (Actonel) are the two bisphosphonates that are approved by the US Food and Drug Administration for use in the treatment of osteoporosis.

The recommended dose of alendronate (the first bisphosphonate to be approved for osteoporosis, in 1995) for the treatment of osteoporosis is 10 mg per day and may be taken as one weekly dose of 70 mg. The dose recommended for prevention of osteoporosis is half that amount [42]. Instructions for taking alendronate are very specific in terms of timing, posture, and use of water. Following these instructions is crucial for absorption of the medication and avoidance of side effects. This medication must be taken on an empty stomach on rising in the morning with 6 to 8 ounces of water. The patient must stay upright for 30 minutes after taking

the medication and not consume any food or other medications during that time. Alendronate is contraindicated in patients with esophageal emptying delays, such as stricture or achalasia, and it can cause esophagitis, a potentially serious side effect in a small percentage of patients. Alendronate may also cause taste alterations [42].

Risedronate differs from alendronate in its chemical structure, but the instructions for its use are similar to and as specific as those for alendronate. The recommended dose for risedronate is 5 mg per day, and it may be taken as a weekly dose of 35 mg [42]. The dose is the same for both treatment and prevention of osteoporosis. Risedronate may increase the gastrointestinal side effects of aspirin and nonsteroidal anti-inflammatory drugs. Patients taking either of these bisphosphonates should be taking supplemental calcium and vitamin D if their dietary intake is inadequate [42].

Etidronate was the first bisphosphonate studied for treatment of osteoporosis [43]. Although it is approved for use in Paget's disease and hypercalcemia of malignancy, it is not approved for treatment of osteoporosis in the United States. However, because it is inexpensive and well tolerated, it is sometimes used "off label" in the United States for osteoporotic patients who cannot tolerate other bisphosphonates [43]. Etidronate is available in tablet form and as an injectable. Parenteral administration may cause taste alterations [42].

Similarly, pamidronate is an injectable bisphosphonate approved for Paget's disease and hypercalcemia of malignancy but not approved for osteoporosis in the United States. It too is sometimes used "off label" for patients who cannot tolerate or absorb oral bisphosphonates [43].

Zoledronate, the most potent bisphosphonate, is available for intravenous administration only. It is approved for hypercalcemia of malignancy and metastatic bone disease and is only used in oncology units and hospitals [42]. Trials to evaluate the antifracture effect of intravenous zoledronate are under way. The potential side effect of significance to dentistry is oral candidiasis [42].

Ibandronate is another bisphosphonate that is in clinical trials for the treatment of osteoporosis.

Selective estrogen-receptor modulators

Tamoxifen, an effective agent in the treatment of breast cancer that has an antiestrogenic effect on breast tissue, has been observed to have an estrogen-like effect on the skeleton [44]. Although tamoxifen is not approved for the treatment of osteoporosis, this serves to demonstrate that an estrogen-like compound that binds with high affinity to the estrogen receptor could have either estrogen agonist or antagonist activity, according to the type of estrogen-responsive tissue. The clinical interest in SERMs is linked to the limitations of HRT. The potential risks of long-term HRT include uterine bleeding and breast cancer [44].

Raloxifene, the first of the second-generation SERMs to be available worldwide for the treatment of osteoporosis, prevents postmenopausal bone loss and reduces the incidence of vertebral fractures and new breast cancer cases in osteoporotic patients without stimulating the endometrium [44]. The observations that estrogens may play a crucial role in the bone metabolism of men and that SERMs prevent bone loss and produce prostatic atrophy in orchidectomized male rats [45] suggest that SERMs may be useful for the treatment of elderly men.

Tibolone, a synthetic steroid, acts on the estrogen, progesterone, and androgen receptors. It does this directly or indirectly through its metabolites, with different patterns depending on the target tissue. It prevents bone loss in early and late postmenopausal women [46,47], reduces menopausal symptoms, has a neutral effect on the endometrium [44], and does not induce breast tenderness. Tibolone has been used in the United Kingdom, Mexico, and South America for the last 20 years. It is still in trials in the United States, where there is some concern that the risk of breast cancer may be linked to its use [48].

Calcitonin

Calcitonin is a polypeptide hormone that regulates calcium and bone metabolism. It has direct renal effects and direct actions on the gastrointestinal tract and is associated with a decreased rate of bone resorption, resorptive activity, and number of osteoclasts [49]. Originally it was available only as an injectable. Now a nasal spray preparation of salmon calcitonin is available [50], with a dose of 200 IU administered intranasally in alternate nostrils daily. Side effects of the nasal spray are minimal, the most significant one being rhinitis. Potential side effects of dental significance are dry mouth and metallic taste, but these are infrequent. Administration of calcitonin should always be accompanied by optimum calcium and vitamin D intake. Calcitonin, when injected, has been found to have an analgesic effect on bone pain associated with acute vertebral fracture, Paget's disease, and bony metastasis. It may play a role in the management of acute vertebral fractures by decreasing analgesic dependence and immobilization. It does not appear to have a role in reduction of hip fracture risk [14].

Fluoride

Fluoride has been shown to have a high affinity for bone and has been used in the past to prevent skeletal fractures because of its ability to stimulate osteoblastic activity without increasing bone resorption [51]. Although the positive effects of drinking fluoridated water on rates of dental caries are well documented, the same cannot be said for water fluoridation and BMD. Early studies were in conflict, leading some scientists to conclude

that fluoride ingestion increases fractures, whereas others came to the opposite conclusions. These contradictions appear to be explained by the fact that fluoride's outcome on BMD is dose-dependent. A lower level of fluoride in water (eg, about 1 mg/L) has a positive effect on bone strength; however, higher levels of community water fluoridation correlate with an increased level of fractures [51].

Studies that examine the use of fluoride as a preventive or therapeutic treatment for osteoporosis on an individual basis have typically enrolled too few people to be conclusive, although trends for increased BMD of the lumbar spine when fluoride and HRT are given together have been found [51]. Intermittent fluoride dosing (ie, 15 mg/d, 3-month continuous dosing followed by a 1-month holiday) for a study duration of 3 years demonstrated a significant increase at all lumbar, femur, and radial sites measured [52].

A meta-analysis demonstrating no protective effects was recently completed on studies using fluoride treatment for osteoporosis [13]. However, such an analysis is difficult, because of the number of different fluoride compounds and other covariables (eg, HRT, calcium, vitamin D) that were part of the protocols of the various studies.

The low cost of fluoride compared with many of the other pharmacologic interventions available for prevention or treatment of osteoporosis and the narrow range of benefit versus detriment that fluoride appears capable of causing on the skeleton clearly point to the need for continuing study in this area.

Anabolic agents

It was observed as early as the 1930s that parathyroid hormone (PTH) could have an anabolic action on the skeleton [53]. Teriparatide (rhPTH[1–34]), an anabolic therapy for osteoporosis, has recently been approved by the US Food and Drug Administration. It stimulates new bone formation on trabecular and cortical (periosteal or endosteal) bone surfaces by preferential stimulation of osteoblastic activity over osteoclastic activity. Another anabolic agent, strontium ranelate, provides an alternative approach. The strontium ion appears to be incorporated into the hydroxyapatite crystalline structure and binds to its surface. This process prevents osteoclasts from resorbing bone efficiently, but it does not impede the ability of osteoblasts to make new bone [53].

Statins

Other approaches include the development of statins that reportedly increase bone formation in growing rodents [54] and could also modulate osteoclast function through their actions on the mevalonate pathway. The applicability of current statins is thought to be limited, because they are optimized for liver rather than bone uptake [53].

Oral effects of medications for the treatment of osteoporosis

A number of scientists are examining the bone-growth enhancing effects of the bisphosphonates in improving the outcomes of oral treatments. For example, in an experimental effort to improve bone deposition around dental implants, dogs [55] with hydroxyapatite-coated and titanium machine–polished (TMP) dental implants coated with alendronate were compared with controls. The findings indicated that locally applied alendronate increases the early bone formation rate around implants and results in greater bone-to-implant contact with TMP implants. These findings resemble those of Denissen et al [56], who performed similar experiments in goats and found alveolar bone deposition around bisphosphonate-complexed hydroxyapatite implants in the animals. In another study, rats who received systemic alendronate before and after surgery demonstrated less alveolar bone loss and better fibrosis and collagen bundle formation after mucoperiosteal flap surgery than those receiving saline [57].

Not all findings concerning the bisphosphonates and dental or oral health have been salutary. Bisphosphonates are known to cause mucosal erosions. In a case report published by Demerjian et al [58], a 54-year-old man being treated with alendronate for steroid-induced osteoporosis presented with severe oral ulcers. Instead of swallowing the alendronate, the patient was sucking on the tablets. It is important to instruct patients in the proper use of the bisphosphonate medications to reduce the potential for these harmful outcomes.

Another negative finding was published by Ruggiero et al [59], who reviewed 63 cases of osteonecrosis of the jaw. The common clinical feature was chronic bisphosphonate therapy of 56 patients who had received intravenous bisphosphonates for at least 1 year and 7 patients who were on long-term oral bisphosphonates. The typical lesions were exposed bone or nonhealing extraction sites. Most of the lesions did not respond to conservative debridement and antibiotics and had to be surgically corrected. The findings suggest that oral health care providers should monitor patients on chronic bisphosphonate therapy for this potential complication.

Positive findings emerged from a study of nonosteoporotic patients with periodontitis on a 6-month regimen of alendronate. These subjects demonstrated an increase in maxillary and mandibular bone density over controls, suggesting that alendronate could play the role of an adjunct to conventional periodontal therapy [60]. Reddy et al [61] reviewed the bisphosphonate literature and concluded that there is a potential role for these medications in periodontitis management.

Osteoporosis in men

Osteoporosis in men was scarcely recognized 20 years ago, and to this day it is not generally perceived as a significant problem among men. Although

the risk is one third of that for women, when osteoporosis occurs in men the mortality is greater. Fortunately, the health professions now recognize the scope of the problem, and osteoporosis in men is the subject of much active research. However, in view of the limited information available, recommendations come from assumptions based on the current understanding of bone biology and pathophysiology and from the much larger experience with osteoporotic women.

Several factors contribute to the etiology of osteoporosis in men. Over half of men with osteoporosis have secondary osteoporosis, which is associated with other medical conditions, medications, or life-style factors that result in bone loss and fragility. The most important of these are alcohol abuse, glucocorticoid excess, and hypogonadism. A significant portion of men with osteoporosis have idiopathic disease [62].

Several possible contributors have been identified in osteoporosis of unknown origin. Most prominent among them are genetic factors, given that bone density and fracture risk are heritable. Hypogonadism is associated with low BMD, and an important cause of severe hypogonadism is androgen deprivation therapy for prostate cancer.

Life-style factors that contribute to the risk of osteoporosis in men include inadequate nutrition, physical inactivity, and tobacco use.

The recommendations for prevention of osteoporosis in men are similar to those for women [62]. In early life, proper nutrition and exercise have positive effects on bone mass. These principles and avoidance of life-style factors known to be associated with bone loss remain important throughout life. It was previously recommended that men over age 50 have a daily intake of 1200 mg of calcium. That recommendation has been changed to 1500 mg per day of calcium [18], and the suggested intake of vitamin D ranges from 600 IU/d to 800 IU/d [19].

Treatment of osteoporosis in men, as in women, is an extension of prevention. Adequate intake of calcium and vitamin D and appropriate physical activity are essential. Secondary causes of osteoporosis should be identified and treated. The indications for pharmacologic therapies are similar for men and women. Alendronate and PTH are effective in idiopathic osteoporosis, regardless of age or gonadal function. Alendronate and risedronate are effective in glucocorticoid-induced osteoporosis [62]. Testosterone replacement therapy increases BMD in men with hypogonadism, but the effect on fracture risk is unknown. This therapy is appropriate for management of the hypogonadal syndrome, but men with osteoporosis and low testosterone levels should be treated with a bisphosphonate or PTH [62].

Estradiol levels in men better predict BMD than do testosterone levels. BMD for men cannot be extrapolated from that of women; gender-specific reference databases must be used. Androgen therapy may increase BMD in men with hypogonadism or low testosterone, but no data on BMD effects of testosterone therapy exist. As in women, bisphosphonate therapy has been shown to increase BMD in men with osteoporosis.

Evidence supports the beneficial effect of administration of a thiazide diuretic on bone mass, rates of bone loss, and hip fracture risk in men. Other diuretics do not seem to impart the same benefits. The mechanism for the positive effect is not clear, but it has been hypothesized to stem from the decreased excretion of calcium in the urine [63].

Osteoporosis and oral health

Because the lifetime osteoporotic fracture rate is so high for the elderly, investigators remain interested in the possibility of detecting osteoporosis in the maxilla or mandible during routine dental diagnostic procedures. These studies have been criticized for being preliminary and cross-sectional in nature and for not controlling for many variables, such as HRT and smoking, thus leaving unresolved the question of whether mandibular bone density was indicative of systemic bone density [64,65].

If osteoporosis does manifest in the mandible or maxilla, some investigators hypothesize that its presence should have a significant effect on oral findings. Initial work in this area using DEXA technology was accomplished by von Wowern et al [66,67]. Subsequently, others have studied edentulous mandibles using DEXA techniques [68–71]. In general, older women are at greater risk for bone mineral content (BMC) loss of the mandible than are older men. For edentulous individuals, the height of the residual ridge correlates with both the total body calcium and the mandibular BMD [72].

In an effort to continue this line of inquiry, some investigators have attempted to use as measurements of osteoporosis the diagnostic clinical data that are routinely collected in the dental office. For example, Jonasson et al [73] attempted to detect osteoporosis by using periapical radiographs of mandibular alveolar bone as well as dental cast measurements, which were then correlated with DEXA of the forearm. Significant correlations between the BMD of the forearm and alveolar bone (ratio = 0.46; $P < 0.001$) were found; however, interdental cast bone measurements did not correlate, possibly because they did not take into consideration the size of the patient. The authors also found that a gross impression of coarseness of trabeculation, as seen on dental periapical radiographs, significantly correlated to BMD of the forearm (ratio = 0.62), with dense trabeculation being a strong indicator of high BMD, sparse trabeculation a predictor of low BMD, and radiographs demonstrating intermediate trabeculation less obviously correlated.

Although recent literature reveals more interest in systemic disease as a factor in alveolar bone loss, functional factors also may be relevant, because it is well known that tension on bone caused by muscles is a positive force. Therefore, some theorize that it is important to replace missing dentition with implants to ensure function by duplicating loading and thus ensuring bone density [74,75].

Because residual ridge resorption is a common and incapacitating problem in edentulous mandibles, several studies suggest a correlation between ridge resorption and osteoporosis [72,76]. Some examinations through radiologic studies indicate that the mineral density of the cortex and the bone mass in the mandible may be correlated with skeletal bone density. However, in edentulous mandibles, most resorption occurs in the alveolar process without much change to the basal portion. It is here that the bone mass of the mandible is greatest and the functional stresses of mastication may positively impact bone density. These considerations lead some to conclude that routine radiologic measurements are unlikely to be able to assess the effect of osteoporosis on alveolar resorption [77].

Southard et al [78] pointed out that studies that measured BMD were in the posterior alveolar process and examined thick cortical bone, rather than in the anterior mandible and maxillary bone, which have more trabecular bone. Given that areas with trabecular bone are more sensitive to the measurement and detection of bone density decline and that this type of bone is subject to bone loss before cortical bone, these researchers hypothesized that the anterior mandible and maxilla are the regions of interest and that these sites should be the focus for further measurements and comparisons. They therefore designed a protocol specifically to determine whether there were correlations between the BMD of the anterior maxillary and mandibular alveolar processes and that of the spine, hip, or radius in healthy women and found significant correlations of maxillary bone density with all other sites. The lumbar spine, hip trochanter, and mandibular alveolar process correlated at a moderate level (ratio $>$ 0.50). Weaker correlations were found for the radius and total hip measurement (ratio $<$ 0.40), whereas the mandibular readings correlated with the maxilla and no other site [78]. The authors conjectured that the lack of mandibular BMD correlation with other skeletal sites may be due to the presence of mandibular tori or other unexplained causes and that, therefore, this area requires additional study with larger sample sizes.

Implants and osteoporosis

Because dental implants are viewed as viable therapies for our increasingly older population, a number of investigators have focused on their success and longevity in patients with diagnosed or undiagnosed osteoporosis. Becker et al [79] searched for a relationship between osteoporosis in other bones and the maxilla or mandible to predict implant success. Using a strong (case-controlled) study design, they assessed each patient using (1) peripheral DEXA (pDEXA) bone measurements at the distal and proximal radius and ulna, (2) classification of bone quality and quantity at the time of implant placement by visualization, and (3) a questionnaire collecting data variables that could potentially affect the outcome. They found no association between the pDEXA scores at the

radius and ulna and the risk for implant failure, yet the visual assessment of bone quality made at the time of placement showed a moderate relationship to implant failure [79]. Becker et al [79] also compared thin cortical bone sites with placements where the cortical bone was thicker or where there was compact bone; as expected, the latter had 2.3 times greater success. These findings demonstrate that the pDEXAs of the radius or ulna are not predictive of implant failure and do not perform better than visual assessments. They do not rule out the possibility that DEXAs of other bones of the skeleton may be better prognosticators of implant success than the pDEXAs and visual assessments.

Looking at the same issue, van Steenberghe et al [80] described a prospective study of 399 consecutive patients with a mean age of 50 and an age range of 15 to 80 years. They concluded that a diagnosis of systemic osteoporosis did not lead to early implant failure; however, poorer bone quality, as determined by radiographic or CT scans, and a preoperative tactile assessment did have a negative impact on survival. Friberg et al [81] followed 13 implant patients who were referred for a medical work-up subsequent to implant placement as a result of the detection of risk factors for osteoporosis. During the mean follow-up period of 3 years and 4 months, the overall success rate for implant placement in these patients with confirmed osteoporosis or osteopenia was 97.1% when an adapted bone site preparation technique and extended healing times were employed.

Future study directions

To determine whether there is an oral effect on all the systemic treatments for osteoporosis, special jaw bone scanners are needed. Likewise, gender-related normative scales for BMC and BMD need to be developed. But especially desirable is the development of a way to study the magnitude of the site-specific effect of treatment.

Von Wowern et al reviewed 115 papers on clinical findings concerning systemic and jaw osteoporosis [82]. The future directions they discuss include especially constructed jaw bone scanners and development of a corresponding gender-related set of normal BMC and BMD values for young adults, as in other sites of the skeleton. The authors suggest that site-specific measurement modalities need to be developed to determine whether treatments such as bisphosphonate medications have positive or negative effects on the BMC and BMD of the jaw bones and their various components in a variety of situations, such as edentulous patients, overdenture conditions, and peri-implant sites [82].

Preventive actions for dentists

The ground for the development of osteoporosis is laid early. Educating teenagers, girls in particular, about consuming enough calcium to achieve

their peak bone mass will do much to build bone mass and decrease risk for osteoporosis as aging occurs [83]. Dentists should know the recommended doses of calcium and vitamin D for each age group (see Table 1) and provide guidance about the optimal use of these products to their patients [19,84]. Because dentists see their patients on a regular basis throughout the life span, typically twice a year, they are in a unique position to promote healthy behaviors. The following are suggested strategies that dentists can easily pursue in their practices to promote systemic bone health, thus potentially promoting a healthier oral facial complex.

Osteoporosis-preventive strategies for the dental office

Diet analysis

Diet analysis is routinely done for caries risk assessment. At the same time, the dentist can evaluate whether a patient's diet is appropriate or needs modification for the prevention of osteoporosis.

Life-style considerations

Diets that are good for teeth are generally good for overall health. Dental professionals encourage smokers to quit and advise patients with undiagnosed but suspected systemic conditions to be evaluated by the appropriate health care provider. If a patient is perceived to be at risk (eg, postmenopausal women), it is appropriate to recommend evaluation. Exercise does not prevent or treat caries or periodontal disease, but exercise can always be recommended as part of the health promotion picture.

Medication misuse

Patients who take prescription or over-the-counter medications arbitrarily or inappropriately should be encouraged to reconsider and consult the physician if appropriate, and patients who have discontinued their medications without consulting the physician must be encouraged to reconsider.

Standard of care and risk assessment

Taking a medical history is standard. By being thorough and following up on positive findings, the dentist may find clues to potential problems that are not initially obvious. Using one of the short risk assessment questionnaires previously discussed in this paper, dentists can detect who is at risk for osteoporosis and refer these patients to the physician for DEXA screening and treatment strategies.

Common sense

The dental environment (eg, office, clinic) should be set up to minimize the risk of falls. Patient positioning must be done with patient safety and comfort in mind. Adequate head and neck support is essential.

Research and the future

If well-designed, controlled studies find indicators of osteoporosis in dental radiographs, dentists will be among the first health care providers with an opportunity to recognize disease activity and to recommend evaluation for osteoporosis. As a profession, we are already among the first to refer patients to rule out (or rule in) hypertension and other cardiovascular conditions, diabetes, allergic diseases, and neoplasms, among many other possible problems.

Summary

Osteoporosis, the most prevalent metabolic bone disease in the United States, affects over 10 million people, results in over 1.5 million fractures per year, and imposes medical costs of $17 billion per year. Impressive technological advances in the noninvasive evaluation of bone mass and bone density aid in the assessment and diagnosis of osteoporosis. Preventive strategies, although effective, often are initiated too late to offset damage. The medical approach to treatment remains predominantly pharmacologic, with various classes of medication regimens available. Regardless of the medication indicated for a particular patient, the key to prevention and treatment remains adequate intake of calcium and vitamin D throughout life.

Dentistry is in a position to aid in the prevention and evaluation of osteoporosis, primarily by doing what has always been appropriate practice: taking a thorough history, analyzing diet, and encouraging healthy life-style behaviors. If future research finds more evidence of the correlation between the bones of the orofacial complex and systemic osteoporosis, or if it confirms positive outcomes of bisphosphonate therapy for periodontitis treatment and the enhancement of osseointegration of implants, dentists may find themselves prescribing such drugs.

References

[1] Department of Health and Human Services. Centers for Disease Control and Prevention. National Center for Health Statistics. Osteoporosis. National Health and Nutrition Survey (NHANES III). Available at: http://www.cdc.gov/nchs/data/nhanes/databriefs/osteoporosis.pdf. Accessed July 3, 2004.

[2] Anonymous. Report of the Surgeon General's workshop on osteoporosis and bone health. Washington, DC, December 12–13, 2002. Department of Health and Human Services. Available at: http://www.surgeongeneral.gov/topics/bonehealth/workshop_report/pdf/Summary_Final.PDF. Accessed July 24, 2004.

[3] Centers for Disease Control. Osteoporosis among estrogen-deficient women—US. MMWR Morbid Mortal Wkly Rep 1998;47(45):969–72.

[4] National Osteoporosis Foundation. Disease statistics. Fast facts. June 2004. Available at: www.nof.org/osteoporosis/stats.htm. Accessed July 24, 2004.

[5] Vargas CM, Kramarow EA, Yellowitz JA. The oral health of older Americans. Aging trends, No. 3. Hyattsville (MD): National Center for Health Statistics; 2001.

[6] Anonymous. Consensus development conference: diagnosis, prophylaxis, and treatment of osteoporosis. Am J Med 1993;94(6):646–50.
[7] Rosen CJ. Anatomy, physiology and disease. In: Langton CM, Njeh CF, editors. The physical measurement of bone. Bristol (UK): Institute of Physics Publishing; 2004. p. 20–1.
[8] Timiras PS. Aging of the skeleton, joints and muscles. In: Timiras PS, editor. Physiological basis of aging and geriatrics. 2nd edition. Boca Raton (FL): CRC Press; 1994. p. 259–72.
[9] US Preventive Services Task Force. Screening for osteoporosis in postmenopausal women: recommendations and rationale. Rockville (MD): Agency for Healthcare Research and Quality; September 2002. Available at: http://www.ahrq.gov/clinic/3rduspstf/osteoporosis/osteorr.htm. Accessed July 3, 2004.
[10] Njeh CF, Shepherd JA. Absorptiometric measurement. In: Langton CM, Njeh CF, editors. The physical measurement of bone. Bristol (UK): Institute of Physics Publishing; 2004. p. 267–307.
[11] Njeh CF, Shepherd J, Genant HK. Human studies. In: Langton CM, Njeh CF, editors. The physical measurement of bone. Bristol (UK): Institute of Physics Publishing; 2004. p. 551–70.
[12] World Health Organization. Assessment of fracture risk and its application to screening for postmenopausal osteoporosis. Geneva (Switzerland): World Health Organization; 1994. Technical Report Series No. 843. Available at: www.radiology.ab.ca/rcalinksOD.htm. Accessed August 12, 2004.
[13] National Osteoporosis Foundation. Physician's guide to prevention and treatment of osteoporosis. Washington, DC: National Osteoporosis Foundation; 2003 Available at: http://www.nof.org/physguide/pharmacologic.htm. Accessed August 12, 2004.
[14] NIH Consensus Development Panel. Osteoporosis prevention, diagnosis and therapy. JAMA 2001;285(6):785–95.
[15] Michaelsson K, Bergstrom R, Mallmin H, et al. Screening for osteopenia and osteoporosis: selection by body composition. Osteoporos Int 1996;6(2):120–6.
[16] Cadarette SM, Jaglal SB, Kreiger N, et al. Development and validation of the Osteoporosis Risk Assessment Instrument to facilitate selection of women for bone densitometry. CMAJ 2000;162(9):1289–94.
[17] Lydick E, Cook K, Turpin J, et al. Development and validation of a simple questionnaire to facilitate identification of women likely to have low bone density. Am J Manag Care 1998; 4(1):37–48.
[18] Reginster J-Y. A simple clinical tool that included age, weight, and estrogen use helped to select women for bone densitometry. ACP J Club 2001;134(1):37.
[19] National Institutes of Health. Optimal calcium intake. NIH Consensus Statement Online 1994(June 6–8);12(4):1–31. Available at: http://consensus.nih.gov/cons/097_statement.htm. Accessed August 11, 2004.
[20] National Institutes of Health. Osteoporosis overview fact sheets. Bethesda (MD): NIH Osteoporosis and Related Bone Diseases National Resources Center; 2003 Available at: www.osteo.org/newfile.asp?doc=osteo&doctitle=Osteoporosis+Overview&doctype=HTML+Fact+Sheet. Accessed August 12, 2004.
[21] Rosen CJ. Nutrition and bone health in the elderly. In: Holick MF, Dawson-Hughes B, editors. Nutrition and bone health. Totowa (NJ): Humana Press; 2004. p. 211–26.
[22] Dawson-Hughes B. Calcium and vitamin D for bone health in adults. In: Holick MF, Dawson-Hughes B, editors. Nutrition and bone health. Totowa (NJ): Humana Press; 2004. p. 197–210.
[23] Timiras ML. The skin and connective tissue. In: Timiras PS, editor. Physiological basis of aging and geriatrics. Boca Raton (FL): CRC Press; 1994. p. 273–8.
[24] Lipschitz DA. Nutrition. In: Cassel CK, Leipzig RM, Cohen HJ, et al, editors. Geriatric medicine: an evidence based approach. 4th edition. New York: Springer-Verlag; 2003. p. 1009–21.

[25] Krall EA, Wehler C, Garcia RI, et al. Calcium and vitamin D supplements reduce tooth loss in the elderly. Am J Med 2001;111(6):452–6.
[26] Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health. The health consequences of smoking: a report of the Surgeon General [Atlanta, GA]. Washington, DC: 2004. Available at: http://www.cdc.gov/tobacco/sgr/sgr_2004/chapters.htm. Accessed August 13, 2004.
[27] Kiel DP. Smoking, alcohol and bone health. In: Holick MF, Dawson-Hughes B, editors. Nutrition and bone health. Totowa (NJ): Humana Press; 2004. p. 481–513.
[28] Law M. Smoking and osteoporosis. In: Wald N, Baron J, editors. Smoking and hormone related disorders. New York: Oxford University Press; 1990. p. 83–92.
[29] Scane AC, Francis RM, Sutcliffe AM, et al. Case-controlled study of the pathogenesis and sequelae of symptomatic vertebral fractures in men. Osteoporos Int 1999;9(1):91–7.
[30] Jacqmin-Gadda H, Fourrier A, Commenges D, et al. Risk factors for fractures in the elderly. Epidemiology 1998;9(4):417–23.
[31] Heaney RP. Effects of caffeine on bone and the calcium economy. Food Chem Toxicol 2002; 40(9):1263–70.
[32] Rapuri PB, Gallagher JC, Kinyamu HK, et al. Caffeine intake increases the rate of bone loss in elderly women and interacts with vitamin D receptor genotypes. Am J Clin Nutr 2001; 74(5):694–700.
[33] Macdonald HM, New SA, Golden MH, et al. Nutritional associations with bone loss during the menopausal transition: evidence of a beneficial effect of calcium, alcohol, and fruit and vegetable nutrients and of a detrimental effect of fatty acids. Am J Clin Nutr 2004;79(1): 155–65.
[34] Feskanich D, Korrick SA, Greenspan SL, et al. Moderate alcohol consumption and bone density among postmenopausal women. J Womens Health 1999;8:65–73.
[35] Gong Z, Wezeman FH. Inhibitory effect of alcohol on osteogenic differentiation in human bone marrow–derived mesenchymal stem cells. Alcohol Clin Exp Res 2004;28(3):468–79.
[36] Kim MJ, Shim MS, Kim MK, et al. Effect of chronic alcohol ingestion on bone mineral density in males without liver cirrhosis. Korean J Intern Med 2003;18(3):174–80.
[37] Inzerillo A, Iqbal J, Troen B, et al. Skeletal fragility in the elderly. In: Cassel CK, Leipzig RM, Cohen HJ, et al, editors. Geriatric medicine: an evidence based approach. 4th edition. New York: Springer-Verlag; 2003. p. 621–50.
[38] Bloom H. Prevention. In: Cassel CK, Leipzig RM, Cohen HJ, et al, editors. Geriatric medicine: an evidence based approach. 4th edition. New York: Springer-Verlag; 2003. p. 169–84.
[39] Krall EA, Garcia RI, Dawson-Hughes B. Increased risk of tooth loss is related to bone loss at the whole body, hip, and spine. Calcif Tissue Int 1996;59(6):433–7.
[40] August M, Chung K, Chang YC, et al. Influence of estrogen status and endosseous implant osseointegration. J Oral Maxillofac Surg 2001;59:1285–91.
[41] Jeffcoat M. Osteoporosis: a possible modifying factor in oral bone loss. Ann Periodontol 1998;3:312–21.
[42] Gage TW, Pickett FA. Dental drug reference. 6th edition. St Louis (MO): Mosby; 2003.
[43] Watts NB. Bisphosphonates for treatment of osteoporosis. In: Favus MJ, editor. Primer on the metabolic bone diseases and disorders of mineral metabolism. 5th edition. Washington, DC: American Society for Bone and Mineral Research; 2003. p. 338–9.
[44] Delmas PD. Clinical use of selective estrogen receptor modulators and other estrogen analogs. In: Favus MJ, editor. Primer on the metabolic bone diseases and disorders of mineral metabolism. 5th edition. Washington, DC: American Society for Bone and Mineral Research; 2003. p. 331–5.
[45] Ke HZ, Qi H, Chidsey-Frink KL, et al. Lasofoxifene (CP-336, 156) protects against the age-related changes in bone mass, bone strength, and total serum cholesterol in intact aged male rats. J Bone Miner Res 2001;16:765–73.

[46] Bjarnason NH, Bjarnason K, Haarbo J, et al. Tibolone: prevention of bone loss in late postmenopausal women. J Clin Endocrinol Metab 1996;81:2419–22.
[47] Berning B, Kuijk CV, Kuiper JW, et al. Effects of two doses of tibolone on trabecular and cortical bone loss in early postmenopausal women: a two-year randomized, placebo-controlled study. Bone 1996;19:395–9.
[48] Harvard Health Publications Newsletter. April 2004. Available at: http://www.health.harvard.edu/hhp/article/content.do?name=W1201c. Accessed August 8, 2004.
[49] Watts NB. Pharmacology of agents to treat osteoporosis. In: Favus MJ, editor. Primer on the metabolic bone diseases and disorders of mineral metabolism. 4th edition. Philadelphia: Lippincott Williams & Wilkins; 1999. p. 278–83.
[50] Dawson-Hughes B. Pharmacologic treatment of postmenopausal osteoporosis. In: Favus MJ, editor. Primer on the metabolic bone diseases and disorders of mineral metabolism. 4th edition. Philadelphia: Lippincott Williams & Wilkins; 1999. p. 283–8.
[51] Ringe JD. Fluoride and bone health. In: Holick MF, Dawson-Hughes B, editors. Nutrition and bone health. Totowa (NJ): Humana Press; 2004. p. 345–62.
[52] Ringe JD, Kipshoven C, Coster A, et al. Therapy of established postmenopausal osteoporosis and monofluorophosphate plus calcium: dose-related effects on bone density and fracture rate. Osteoporos Int 1999;9(2):171–8.
[53] Reeve J. Teriparatide (rhPTH[1–34]) and future anabolic treatments for osteoporosis. In: Favus MJ, editor. Primer on the metabolic bone diseases and disorders of mineral metabolism. 5th edition. Washington, DC: American Society for Bone and Mineral Research; 2003. p. 344–8.
[54] Mundy G, Garrett R, Harris S, et al. Stimulation of bone formation in vitro and in rodents by statins. Science 1999;286:1946–9.
[55] Meraw SJ, Reeve CM, Wollan PC. Use of alendronate in peri-implant defect regeneration. J Periodontol 1999;70(2):151–8.
[56] Denissen H, Montanari C, Martinetti R, et al. Alveolar bone response to submerged bisphosphonate-complexed hydroxyapatite implants. J Periodontol 2000;71(2):279–86.
[57] Kaynak D, Meffert R, Bostanci H, et al. A histopathological investigation on the effect of systemic administration of the bisphosphonate alendronate on resorptive phase following mucoperiosteal flap surgery in the rat mandible. J Periodontol 2003;74(9):1348–54.
[58] Demerjian N, Bolla G, Spreux A. Severe oral ulcerations induced by alendronate. Clin Rheumatol 1999;18(4):349–50.
[59] Ruggiero SL, Mehrotra B, Rosenberg TJ, et al. Osteonecrosis of the jaws associated with the use of bisphosphonates: a review of 63 cases. J Oral Maxillofac Surg 2004;62(5):527–34.
[60] El-Shinnawi UM, El-Tantawy SI. The effect of alendronate sodium on alveolar bone loss in periodontitis (clinical trial). J Int Acad Periodontol 2003;5(1):5–10.
[61] Reddy MS, Geurs NC, Gunsolley JC. Periodontal host modulation with antiproteinase, anti-inflammatory and bone-sparing agents. A systemic review. Ann Periodontol 2003;8(1):12–37.
[62] Orwoll ES. Osteoporosis in men. In: Favus MJ, editor. Primer on the metabolic bone diseases and disorders of mineral metabolism. 5th edition. Washington, DC: American Society for Bone and Mineral Research; 2003. p. 361–3.
[63] Orwoll ES. The prevention and therapy of osteoporosis in men. In: Orwoll ES, editor. Osteoporosis in men. San Diego (CA): Academic Press; 1999. p. 562–3.
[64] Wactawski-Wende J. Oral bone loss and osteoporosis. In: Favus MJ, editor. Primer on the metabolic bone diseases and disorders of mineral metabolism. 5th edition. Washington, DC: American Society for Bone and Mineral Research; 2003. p. 541–4.
[65] Zeeman GG, Veth EO, Dennison DK. Focus on primary care: periodontal disease: implications for women's health. Obstet Gynecol Surv 2001;56(1):43–9.
[66] Von Wowern N. In vivo measurement of bone mineral content of mandibles by dual-photon absorptiometry. Scand J Dent Res 1985;93:162–8.

[67] Von Wowern N, Storm TL, Olgaard K. Bone mineral content by photon absorptiometry of the mandible compared with that of the forearm and the lumbar spine. Calcif Tissue Int 1988; 42:157–61.
[68] Corten FG, van't Hof MA, Buijs WC, et al. Measurement of mandibular bone density ex vivo and in vivo by dual energy absorptiometry. Arch Oral Biol 1993;38(3):215–9.
[69] Horner K, Devlin H, Alsop CW, et al. Mandibular bone mineral density as a predictor of skeletal osteoporosis. Br J Radiol 1996;69(827):1019–25.
[70] Devlin H, Horner K, Ledgerton D. A comparison of maxillary and mandibular bone mineral densities. J Prosthet Dent 1998;79:323–7.
[71] Horner K, Devlin H. The relationship between two indices of mandibular bone quality and bone mineral density measured by dual energy x-ray absorptiometry. Dentomaxillofac Radiol 1998;27(1):17–21.
[72] Kribbs P, Chesnut C. Relationships between mandibular and skeletal bone in an osteoporotic population. J Prosthet Dent 1989;62:703–7.
[73] Jonasson G, Bankvall G, Kiliaridis S. Estimation of skeletal bone mineral density by means of the trabecular pattern of the alveolar bone, its interdental thickness, and the bone mass of the mandible. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2001;92:346–52.
[74] Sanfilippo F, Bianchi AE. Osteoporosis: the effect on maxillary bone resorption and therapeutic possibilities by means of implant prostheses—a literature review and clinical considerations. Int J Periodontics Restorative Dent 2003;23(5):447–57.
[75] Bianchi A, Sanfilippo F. Osteoporosis: the effect on mandibular bone resorption and therapeutic possibilities by means of implant prostheses. Int J Periodontics Restorative Dent 2002;22(3):230–9.
[76] Hirai T, Ishijima T, Hashikawa Y, et al. Osteoporosis and reduction of residual ridge in edentulous patients. J Prosthet Dent 1993;69:49–56.
[77] Klemetti E. A review of residual ridge resorption and bone density. J Prosthet Dent 1996; 75(5):512–4.
[78] Southard KA, Southard TE, Schlechte JA, et al. The relationship between the density of the alveolar processes and that of post-cranial bone. J Dent Res 2000;79(4):964–9.
[79] Becker W, Hujoel PP, Becker BE, et al. Osteoporosis and implant failure: an exploratory case-control study. J Periodontol 2000;71(4):625–31.
[80] van Steenberghe D, Jacobs R, Desnyder M, et al. The relative impact of local and endogenous patient-related factors on implant failure up to the abutment stage. Clin Oral Implants Res 2002;13(6):617–22.
[81] Friberg B, Ekestubbe A, Mellstrom D, et al. Branemark implants and osteoporosis: a clinical exploratory study. Clin Implant Dent Relat Res 2001;3(1):50–6.
[82] von Wowern N. General and oral aspects of osteoporosis: a review. Clin Oral Invest 2001; 5(2):71–82.
[83] National Osteoporosis Foundation. Advocacy news and updates. Available at: http://www.nof.org/advocacy/prevalence/index.htm. Accessed July 24, 2004.
[84] Boonen S, Rizzoli R, Meunier PJ, et al. The need for clinical guidance in the use of calcium and vitamin D in the management of osteoporosis: a consensus report. Osteoporos Int 2004; 15(7):511–9.