Prevention and Treatment of Osteoporosis

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Osteoporosis develops in older adults when the normal processes of bone formation and resorption become uncoupled or unbalanced, resulting in bone loss. Fractures are the result of decreased bone mass and strength and, in the case of wrist and hip fractures, usually involve a fall. Osteoporosis prevention and treatment programs should then focus on strategies that minimize bone resorption and maximize bone formation as well as on strategies that reduce falls. Optimal treatment and prevention of osteoporosis require modification of risk factors, particularly smoking cessation, adequate physical activity, and attention to diet, in addition to pharmacologic intervention. A number of pharmacologic options are now available to health care providers. This article focuses on US Food and Drug Administration–approved medications for osteoporosis and emphasizes the importance of using these agents as part of a comprehensive program that includes nonpharmacologic measures, complete diagnostic evaluation, and adequate follow-up with bone mineral density measurement.

THE ROLE OF EXERCISE

Exercise is an important component of osteoporosis treatment and prevention programs, although exercise alone is not adequate to prevent the rapid bone loss associated with estrogen deficiency in early menopause. Among exercisers in the Rancho Bernardo cohort, those who reported strenuous or moderate exercise had higher bone mineral density (BMD) at the hip than did those who reported mild or less-than-mild exercise. Similar associations were seen for lifelong regular exercisers and hip BMD. In a randomized study of women ≥10 years postmenopause, the group receiving calcium supplementation plus exercise had less bone loss at the hip than did those assigned to calcium alone. Further, Nelson et al demonstrated the effectiveness of high-intensity strength training in maintaining femoral neck BMD as well as in improving muscle mass, strength, and balance in postmenopausal women compared with controls who did not exercise, suggesting that resistance training would be useful to help maintain BMD and to reduce the risk of falls in older adults.

Marked decrease in physical activity or immobilization results in a decline in bone mass; accordingly, it is important to encourage older adults to be as active as possible. Weight-bearing exercise, such as walking, can be recommended for all adults, and they should be encouraged to start slowly and gradually increase both the number of days as well as the time spent walking each day.

CALCIUM AND VITAMIN D

Calcium and vitamin D are required for bone health at all ages. A 1994 consensus conference recommended 1500 mg/d of elemental calcium for postmenopausal women and men >65 years of age to maintain a positive calcium balance. The amount of vitamin D required is between 400 and 800 IU/d. In older adults (>65 years), regardless of climate or exposure to sunlight, a daily supplement of ≥400 IU/d vitamin D is recommended because skin changes that occur with aging result in less efficient use of UV light by the skin to synthesize vitamin D precursors. Younger adults who live in northern climates with little sun exposure may also require vitamin D supplementation, although this has not been well studied. One study suggested that hospitalized young people had low vitamin D levels during winter months. Calcium plus vitamin D at different doses have been shown to increase or maintain bone density in pre- and postmenopausal women and to prevent hip as well as all nonvertebral fractures in older adults. The dietary intake of calcium for women in the United States averages 500 to 700 mg/d, thus most women will require calcium supplementation to ensure adequate intake.

KEY POINT

Marked decrease in physical activity or immobilization results in a decline in bone mass; accordingly, it is important to encourage older adults to be as active as possible.

PHARMACOLOGIC OPTIONS

Estrogen Replacement Therapy

Estrogen replacement therapy (ERT) remains an important choice for the treatment and prevention of osteoporosis. In addition to the beneficial effect on bone, epidemiologic observations suggest that estrogen prevents cardiovascular disease and may also reduce the incidence of Alzheimer's disease. In case control and cohort studies, ERT is associated with a 30% to 70% reduction in hip fracture incidence. Multiple studies have demonstrated that postmenopausal estrogen use will prevent bone loss at the hip and spine when initiated within 10 years of menopause. Schneider et al, in a cross-sectional study, demonstrated that BMD in women who initiated hormone replacement therapy (HRT) after age 60 years was not significantly different from women who initiated HRT within 2 years of menopause. Postmenopausal women randomized to HRT in the Postmenopausal Estrogen/Progestin Intervention (PEPI) trial had increases in hip and spine BMD over 3 years compared with women in the placebo group. Older women, women with low initial BMD, and women who had not previously used HRT gained more bone than did young women, women with higher baseline BMD, and those who had previously used HRT. In a study of early postmenopausal women (mean age 53 years), 75% of women randomized to HRT had >2% increase in spine BMD, and 60% had an increase in hip BMD. Less than 10% of women on HRT demonstrated significant bone loss at either site. In the only prospective study of fracture prevention with estrogen, Lufkin et al reported decreased incidence of vertebral fractures in postmenopausal women using a transdermal preparation. Bone of older women (>70 years) continues to be responsive to ERT and data suggest that lower-than-usual doses of estrogen, when given with adequate calcium and vitamin D, are effective in reducing bone turnover and bone loss in older women. Recker et al, in a randomized controlled study, demonstrated that women treated with 0.3 mg/d conjugated

KEY POINT

The dietary intake of calcium for women in the United States averages 500 to 700 mg/d, thus most women will require calcium supplementation to ensure adequate intake.

TABLE 1. MEDICATIONS USED FOR THE PREVENTION AND TREATMENT OF OSTEOPOROSIS

Medication	*Dosage*	*Special Considerations*
Conjugated equine estrogen 17β-estradiol Transdermal estrogen	0.3–0.625 mg/d* 0.5–1.0 mg/d 0.05–0.1 mg biweekly	(1) In older (>70 y) women, continuous administration usually preferred (2) Lower doses may be effective in older women
Raloxifene	60 mg/d	May prevent breast cancer
Alendronate	10 mg/d 5 mg/d for prevention	Adherence to dosing instructions required (**Table II**)
Risedronate	5 mg/d	Adherence to dosing instructions required (**Table II**)
Calcitonin, nasal spray Calcitonin, injection (SC or IM)	200 IU/d 50–100 IU 3 to 5 times per week	(1) Metered spray; 1 spray gives daily dose (2) Alternate nostrils each day to reduce side effects (3) Injectable still useful depending on patient
Etidronate	400 mg/d for 2 weeks every 3 months	Not approved by FDA for osteoporosis; used only if all other treatments are not tolerated/effective

*For cyclical therapy, estrogen is given days 1 to 25 and then stopped. In women with a uterus, progesterone must be given with the estrogen to prevent endometrial hyperplasia. Medroxyprogesterone is given 2.5 to 5.0 mg/d continuously or 5 or 10 mg/d days 16 to 25 for cyclical treatment. Micronized progesterone is also available (200 mg/d days 16 to 25; or 100 mg/d as continuous dose). SC = subcutaneous; IM = intramuscular.
Adapted with permission from Prestwood KM, Kenny AM. Osteoporosis: Pathogenesis, diagnosis and treatment in older adults. *Clin Geriatr Med.* 1998;14:577–600.

equine estrogen (CEE) plus 2.5 mg/d medroxyprogesterone acetate gained spine and hip BMD compared with placebo. From the Study of Osteoporotic Fractures, separate analyses identified current estrogen use as a protective factor against hip fracture and demonstrated increased risk of hip and vertebral fractures in women with undetectable serum estradiol levels.

In osteoporosis management, patients who do not respond to treatment may be identified either by BMD (>4%/y loss at any site) or by fracture that occurs ≥3 months after initiation of treatment. If this situation arises in women who are taking ERT, then combination therapy with alendronate and ERT is indicated unless the patient is not tolerating ERT. In 2 studies, ERT and alendronate have been shown to have an additive effect on BMD compared with either agent alone, although fracture data for combination therapy are not available.

Although estrogen can benefit several organ systems, its use by postmenopausal women has been limited by side effects and concerns about increased cancer risk. Unopposed ERT in women with a uterus has been associated with endometrial hyperplasia at a rate of about 30% per year, with endometrial cancer at a lower rate. Concurrent progesterone therapy, however, greatly reduces the incidence of both conditions. HRT also has been associated, in some studies, with an increased incidence of breast cancer. Case control and cohort studies have suggested both increased and decreased breast cancer risk with ERT. In a recent study, the combination of estrogen and progesterone markedly increased the risk of breast cancer compared with estrogen alone. Prospective data regarding the relationship between HRT and the incidence of breast cancer are not currently available; however, the Women's Health Initiative is addressing this issue. In epidemiologic studies,

ERT use is associated with decreased incidence of cardiovascular disease and death. Further, numerous studies have demonstrated that ERT has a beneficial effect on lipids and arterial compliance. However, in the Heart and Estrogen/Progestin Replacement Study, HRT did not reduce cardiovascular events in women with symptomatic cardiovascular disease at baseline. In fact, in a subset of women, the risk of cardiovascular death was increased in the first year of treatment with HRT. The use of ERT for treatment and prevention of osteoporosis must be evaluated in the context of a woman's risk for heart disease and breast cancer. The various preparations of estrogen are listed, along with dosing regimens, in **Table I**. Progestins may be given in either continuous or cyclical fashion, depending on the preference of the woman. Given the Recker data, one can use lower doses in older women and follow bone turnover and bone density to ensure adequate response to treatment.

KEY POINT

Bone of older women (>70 years) continues to be responsive to ERT and data suggest that lower-than-usual doses of estrogen, when given with adequate calcium and vitamin D, are effective in reducing bone turnover and bone loss in older women.

Bisphosphonates

Alendronate was approved for osteoporosis treatment several years ago. The initial study demonstrated increased bone density of the spine and hip, as well as decreased vertebral fracture rate in women with osteoporosis who were randomly assigned to alendronate or placebo. The Fracture Intervention Trial examined the effect of alendronate on postmenopausal women with low bone density at the hip, with or without vertebral fracture at baseline. In women with low hip bone density and prevalent vertebral fractures at entry, a decrease in both vertebral and hip fractures was seen with alendronate compared with placebo. Women with ≥2 vertebral fractures at baseline had the best response to alendronate therapy, suggesting that alendronate is effective in preventing fractures in women at highest risk. In women with low hip bone mass without previous vertebral fracture, bone density of the spine and hip also increased, and vertebral fracture rate decreased by 51% with alendronate compared with placebo. A recent study in women 60 to 85 years of age indicated that an even lower dose of alendronate may be effective in older women. Alendronate has also been approved for prevention of osteoporosis in early postmenopausal women. The dose for prevention is a lower dose—5 mg/d—than that given for the treatment of osteoporosis—10 mg/d (**Table I**). In the prevention study, approximately 70% of women assigned to alendronate (5 mg/d) had >2% increase in spine BMD, and 50% had the same response in hip BMD. As mentioned earlier, if treatment with alendronate alone is not effective, the data support the addition of ERT to the regimen. To date, bone biopsy data indicate that alendronate does not cause mineralization defects or other abnormalities of bone, despite its long half-life in bone. Alendronate also prevents bone loss in men and women on glucocorticoids when initiated at the same time as the glucocorticoids. Alendronate should be considered in women with osteoporosis, as confirmed by BMD testing or by the presence of a fragility fracture, who are unwilling or unable to take HRT. Because of other health benefits, HRT remains a primary consideration in women in whom estrogen is not contraindicated.

The major side effects of alendronate are gastrointestinal, including abdominal pain, dyspepsia, esophagitis, nausea, vomiting, and diarrhea. Musculoskeletal pain may also occur. Esophagitis, particularly erosive esophagitis, may be seen most frequently in patients who do not take the medication properly. For this reason, it is extremely important to provide specific and detailed instructions for patients receiving any bisphosphonate therapy (**Table II**). Patients may report abdominal pain early in treatment; if medication is continued, the abdominal pain frequently goes away. If a patient is unable to tolerate alendronate initially, it may be discontinued until symptoms abate and then reinitiated; often the patient is able to tolerate alendronate the second time.

TABLE II. INSTRUCTIONS FOR ADMINISTRATION OF BISPHOSPHONATES

- Take first thing in the morning before anything else to eat or drink
- Take with ≥8 oz of **plain tap water (not juice, coffee, sparkling water)**
- Take while upright in a chair or standing and remain upright after ingestion
- Do not eat or drink anything for one half-hour after taking the medication

Adapted with permission from Prestwood KM, Kenny AM. Osteoporosis: Pathogenesis, diagnosis and treatment in older adults. *Clin Geriatr Med.* 1998;14:577–600.

Risedronate, a newer bisphosphonate, was recently approved for treatment of osteoporosis. In a 3-year study of postmenopausal women with ≥1 vertebral fracture at baseline, risedronate (5 mg/d) reduced the cumulative incidence of new vertebral fractures by 41% (95% CI, 18%–58%) compared with placebo. In addition, the incidence of nonvertebral fractures also decreased by 39% (95% CI, 6%–61%) in the group receiving risedronate. BMD of the hip and spine increased significantly in the risedronate group compared with placebo. In the same study, 2.5 mg/d of risedronate was found to be ineffective and was discontinued after the first year of the study. Withdrawals due to side effects and any upper gastrointestinal adverse events were similar in the risedronate and placebo groups.

Etidronate was shown to increase spinal bone mass and decrease vertebral fractures in 2 studies in the early 1990s, and a 5-year follow-up study demonstrated continued benefit. Etidronate was given intermittently—400 mg/d orally for 14 days, and then stopped for 2.5 months—in these studies because continuous high doses can impair mineralization and produce osteomalacia. However, etidronate is not approved for use in osteoporosis because the data supporting fracture reduction were not sufficient. A separate study indicated a role for etidronate in preventing bone loss in patients who required long-term glucocorticoids.

Selective Estrogen Receptor Modulators

The selective estrogen receptor modulators (SERMs) are agents that act as estrogen agonists in bone and heart, but act as estrogen antagonists in breast and uterine tissue. These medications have the potential to prevent osteoporosis or cardiovascular disease without the increased risk of breast or uterine cancer. Tamoxifen, an agent used in breast cancer treatment, has beneficial effects on bone as reported in several studies, but also has stimulatory effects on the uterus. Thus, tamoxifen is not indicated for osteoporosis treatment or prevention.

Raloxifene, a newer SERM, has been approved for treatment and prevention of osteoporosis in postmenopausal women. Raloxifene decreased bone turnover and maintained hip and total body bone density in postmenopausal women with osteoporosis compared with women who received placebo. There were no differences among groups in breast abnormalities or endometrial thickness. In a short-term study, raloxifene had effects on bone histomorphometry and bone turnover that were similar in direction to CEE, but were lower in magnitude than those achieved with CEE. Most importantly, recent data demonstrate that raloxifene (60 mg/d) reduces incident vertebral fractures by about 60%, compared with placebo, despite only modest increases in bone density. The substantial decrease in vertebral fractures with only modest changes in BMD suggests that antiresorptive therapies may affect some parameter in bone that we cannot yet measure sensitively (one possibility is bone quality). Similar discrepancies have also been seen with alendronate and risedronate. Raloxifene did not significantly reduce nonvertebral, hip, or wrist fractures in this study. Reported side effects with raloxifene include flulike symptoms, hot flashes, leg cramps, and peripheral edema.

Another important finding with raloxifene was a reduction in breast cancer in women who participated in the Multiple Outcomes of Raloxifene Trial. In women who received raloxifene, the relative risk of developing breast cancer was 0.24

(95% CI, 0.13–0.44) compared with the placebo group. In the same study, raloxifene did not increase the risk of endometrial cancer but did increase the risk of venous thromboembolic disease. In other studies, raloxifene decreased total and low-density lipoprotein cholesterol and lipoprotein(a) without affecting high-density lipoprotein cholesterol or triglycerides. Thus, in clinical trials to date, raloxifene appears beneficial to several organ systems, although further study is required with regard to cardiovascular disease and breast cancer prevention.

Calcitonin

Calcitonin is a hormonal inhibitor of bone resorption used to treat osteoporosis. It has been given as a subcutaneous injection for many years; however, it is also available as a nasal spray. The advantages of a nasal spray are fewer reported side effects and greater patient acceptance, but it may be less effective. Calcitonin has been shown to increase bone density in the spine and reduce vertebral fractures. In epidemiologic studies, calcitonin has been shown to reduce hip fractures, although in most clinical trials, hip bone density does not increase. Preliminary analysis of a 5-year study demonstrated a decrease in vertebral fracture in women receiving 200 IU/d compared with those on placebo. The reduction in hip fracture incidence was not statistically significant in the group receiving calcitonin compared with placebo. Doses of 100 and 400 IU/d were studied as well but they did not have the same effect on new fracture rate as did the 200 IU/d dose. In the same study, BMD changes at 3 years and changes in markers of bone turnover were not significantly different from placebo. Although there are no direct comparisons, calcitonin appears to be less effective than other antiresorptive drugs. Once calcitonin is discontinued, any gains in BMD are lost fairly quickly.

Parenteral calcitonin therapy has been associated with an analgesic effect in acute compression fractures, Paget's disease of bone, and bone pain due to metastatic disease. Suggested mechanisms for pain relief include increases in circulating beta endorphins, inhibition of prostaglandins, interference with calcium flux, involvement of the cholinergic or serotoninergic systems, direct effect on the central nervous system receptor, or neuromodulating effect.

INVESTIGATIONAL AGENTS FOR TREATMENT OF OSTEOPOROSIS

Other Antiresorptives

Other bisphosphonates currently under investigation for the treatment and prevention of osteoporosis include pamidronate, ibandronate, and tiludronate. New SERMs are also being tested for use in osteoporosis treatment.

Anabolic Agents

Parathyroid hormone (PTH), although leading to increased bone resorption when continuously elevated, can increase bone mass, trabecular connectivity, and mechanical strength when administered intermittently. PTH has been shown to increase spinal BMD in osteoporotic men and women. In a 3-year randomized study of postmenopausal women with osteoporosis, the group receiving estrogen plus intermittent PTH had continuous increase in spinal bone mass over the study period, as well as decreased vertebral fracture rate. Bone mass of the hip and total body also increased significantly in the estrogen-plus-PTH group, compared with estrogen alone.

Use of fluoride to treat osteoporosis is appealing, because fluoride results in a large increase in spine bone density; however, the increase in BMD was not consistently associated with a decrease in vertebral fractures. In fact, in the study by Riggs et al, the group receiving fluoride had a higher rate of appendicular fractures. Recently, slow-release fluoride therapy has been associated with an increase in spine BMD, as well as decreased incidence of vertebral fractures. Further studies are required before slow-release fluoride can be recommended for treatment of osteoporosis.

The use of testosterone for treatment of osteoporosis in women has been limited by side effects. In early menopause, combination treatment with ERT and low-dose testosterone results in decreased bone resorption and increased bone formation, as estimated by serum and urine biochemical markers. 3-hydroxy-3-methylglutaryl coenzyme A reductase inhibitors (statins), commonly

used for management of hypercholesterolemia, were recently shown to stimulate bone formation in animals and preliminary epidemiologic data suggest that the use of statins is associated with decreased incidence of fracture.

KEY POINT

One way of improving compliance and follow-up is to measure markers of bone resorption to assess the initial response to therapy.

WORKING WITH THE PATIENT

The information in this article is useful only if it is communicated effectively to patients, resulting in compliance with the recommended regimen.

Establishing an optimal regimen may require considerable discussion and will be aided greatly by having an informed patient. Physicians often do not have adequate time to carry out this task. The use of educational materials, particularly those provided by the National Osteoporosis Foundation, can be quite helpful as well as the efforts of a nurse or other office personnel. Effective prevention and treatment of osteoporosis is possible, but this is successful only if the patient and health caregivers work together in a sustained fashion.

As discussed previously, baseline and follow-up BMD measurements (every 1 to 2 years) are important to assess response to therapy, and these measurements may also improve compliance by encouraging the patient to maintain the regimen. Another way to inform patients of their response to therapy is to measure markers of bone resorption. In particular, adequate estrogen and bisphosphonate therapy will almost certainly decrease the levels of urine or serum markers of bone resorption within 3 to 6 months.

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New references added to original article.

Dialogue Box

ADVISORY BOARD

In what percentage of patients is alendronate effective in reducing bone loss?

PRESTWOOD

In a randomized trial, approximately 70% of patients treated with alendronate responded with an increase in bone density.

ADVISORY BOARD

If 30% of patients treated with alendronate and as many as 20% of patients treated with estro-

Dialogue Box

gen replacement fail to respond to therapy, shouldn't a greater effort be made to detect the nonresponders?

PRESTWOOD

Yes. We have to really monitor the patient response to treatment by measuring bone density before and after therapy. If the patient is not responding, we need to make sure that an additional agent is prescribed.

ADVISORY BOARD

You mentioned that the incidence of gastrointestinal (GI) side effects in patients treated with risedronate is no greater than that in patients treated with placebo. Do patients taking risedronate have to follow the same rigid pill-taking directions as they do for alendronate?

PRESTWOOD

Yes, that holds true for all the bisphosphonates. Like alendronate and etidronate, risedronate must be taken on an empty stomach because of poor absorption. Although the trials with risedronate demonstrated a low incidence of GI side effects, it is important to recognize that in those trials, patients were instructed to follow the same dosing instructions as they did with alendronate. GI upset was also uncommon in the initial alendronate trials, and as we get more experience with risedronate, we may find more GI side effects than reported in the early randomized clinical trials.

ADVISORY BOARD

Do you have any concerns about the use of alendronate in a young person?

PRESTWOOD

That is a really important question. Although there are short-term (2 years) data in early postmenopausal women that show that alendronate is safe in bone, I am not as confident with its use in very young adults, especially for long periods of time. On one hand, we now have about 10 years' experience with it, and we have not seen any problems with bone remodeling. On the other hand, we know that it possesses a 10-year half-life in bone. Primarily because of the latter fact, I must say that I still have some reservations with its long-term use in younger patients.

ADVISORY BOARD

What bone-sparing agent do you favor in a young patient who needs long-term therapy?

PRESTWOOD

I have used calcitonin in very young people. If a young person has severe osteoporosis or multiple fractures, I probably would use a bisphosphonate such as alendronate or etidronate. Which agent is most optimal is a question that still needs to be answered.

ADVISORY BOARD

In the patient who continues to show bone loss despite receiving estrogen replacement, is there any evidence that would support adding a SERM such as raloxifene to the regimen?

PRESTWOOD

Although there is evidence that a combination of alendronate and estrogen may be of value in such a patient, I know of no studies that have combined estrogen with an agent like raloxifene. Such a combination might theoretically have an additive effect because the 2 agents act on bone by slightly different mechanisms, but I would be concerned that side effects would pose a problem. For example, both of these agents are thrombogenic; thus, I would expect an increase in problems with deep venous thrombosis.

Dialogue Box

ADVISORY BOARD

Are the modes of action on bone of estrogen and raloxifene different enough that it is rational to consider a switch to the latter agent in a postmenopausal patient who continues to lose bone density while on estrogen therapy?

PRESTWOOD

Yes, but I would still favor a switch to alendronate before a switch to raloxifene. Patients who fail to respond to estrogen, however, might very well respond to raloxifene because the 2 agents have slightly different mechanisms of action. In addition, one of the reasons patients fail to respond to estrogen is that they fail to take it properly because of side effects. Raloxifene in such a patient might be effective simply because it may be better tolerated and the patient more compliant with taking it.

ADVISORY BOARD

You seem to favor hormone replacement as your first-line agent primarily because of its potential benefits in areas other than bone. If these other benefits did not exist, what would your view be then?

PRESTWOOD

Solely on the basis of fracture data, I might then shift to alendronate. I favor estrogen on one level because it is in a sense more physiologic, but if you told me it had no benefit at all on the heart or brain, I would probably lean toward alendronate. Although in terms of bone density, the 2 are very similar, there are just not the same beneficial fracture data with estrogen that there are with the bisphosphonates.

ADVISORY BOARD

The fracture data with raloxifene show benefit for vertebral fractures but not for fractures of the hip. Do you think this is due to a type 2 error, or do you think it really acts differently at different bones?

PRESTWOOD

Well, the bone in the vertebral body is primarily trabecular bone, which remodels more quickly than cortical bone. Therefore, the postmenopausal patient loses vertebral bone much more quickly than bone at other sites. The hip, on the other hand, is composed of both trabecular and cortical bone—the cortical bone provides additional strength to the hip and is much slower than trabecular bone in its remodeling rate. As a result, hip fractures occur later in life than do vertebral fractures. Therefore, for a study to detect an impact on hip fracture, it must be large or have a lengthy follow-up. Although the lack of benefit on hip fracture may very well be due to a type 2 error, one might also argue that it is due to raloxifene not working as well on cortical bone.

ADVISORY BOARD

Using BMD as a surrogate marker, are estrogen and raloxifene comparable to the bisphosphonates with respect to preservation of BMD at the hip as well as the spine?

PRESTWOOD

Yes, estrogen and alendronate are pretty similar in both sites. They may differ by a percentage point or 2 but their impact is fairly similar over the studies. Raloxifene has less of an effect on bone density than alendronate—although the 2 have not been directly compared.

ADVISORY BOARD

Were you surprised by the findings of the Rancho Bernardo study?

PRESTWOOD

No, I wasn't really surprised. Contrary to what

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many people believe, postmenopausal women are really a fairly heterogeneous group with regard to the BMD at which menopause is started as well as the rate at which bone is lost. Although we tend to treat all patients as if they were the same and advocate for everyone the use of an antiresorptive agent like estrogen at the onset of menopause, there is likely a very large group that we could wait to treat. Measuring BMD in a woman 70 to 75 years of age can provide helpful information because it is not necessarily going to be low. In fact, approximately 30% of women aged >70 years will still have normal bone density. These patients should not be managed with antiresorptive therapy; they should be followed to ensure an adequate calcium intake and simply watched.

ADVISORY BOARD

Are there any data suggesting that many obese postmenopausal patients who are not taking medications but whose Papanicolaou's smears show an endogenous estrogen effect may not be at risk for osteoporosis?

PRESTWOOD

Well, many studies have shown that high body mass index or high weight is associated with high bone density, but it is not a perfect correlation. For example, I have had very thin women with low estradiol levels whose Papanicolaou's smears have shown an estrogen effect. As a result, in the patient whose Papanicolaou's smear suggests an estrogen effect, the safe route would be to check the BMD and, if normal, repeat the measurement in 2 years.

ADVISORY BOARD

It seems counterintuitive that parathyroid hormone reduces bone loss. What is the mechanism of action?

PRESTWOOD

We don't know exactly how it works. It may have something to do with local factors acting in bone in response to parathyroid hormone. Regardless, if you give an intermittent bolus of parathyroid hormone, it may stimulate local growth factors and produce an increase in bone formation.

ADVISORY BOARD

Has parathyroid hormone been used to treat osteoporosis?

PRESTWOOD

No, parathyroid hormone is not available outside a clinical trial. There are ongoing studies trying to find a clinical preparation that will likely have to be either inhaled or injected.

ADVISORY BOARD

What is the evidence that 3-hydroxy-3-methylglutaryl coenzyme A reductase inhibitors, or statins, have a beneficial impact on preserving BMD?

PRESTWOOD

The evidence at this point is fairly limited. Benefit has been demonstrated in mice. In addition, there are some preliminary epidemiologic data that suggest that statin use is associated with reduced risk for osteoporotic fracture.

ADVISORY BOARD

What is the status of long-acting sodium fluoride?

PRESTWOOD

It is still being studied. The FDA is not yet convinced of its fracture efficacy despite a study by Pak and colleagues that showed both an increase in BMD and a reduction in spine fractures after treatment with sodium fluoride.