

# Don't Write Off Low-Dose HT for Bone Health

*Low-dose HT should be considered to reduce fracture risk and menopausal symptoms in certain patients.*

BY COLIN NELSON  
Contributing Writer

DEDHAM, MASS. — Has the backlash against hormone therapy gone too far? Should doctors take yet another look at the evidence and find selective uses for HT that maximize its benefits and minimize its risks?

The answer to both questions is yes, according to Isaac Schiff, M.D., professor of gynecology at Harvard Medical School and chief of the ob.gyn. service at Massachusetts General Hospital. At a symposium on bone health sponsored by Boston University School of Medicine, Dr. Schiff recommended discussing HT with select patients as a double-duty medication for bone health and menopausal symptoms.

"Just as the pendulum went too far in the early 1990s—when all the retrospective studies suggested estrogens prevented heart disease, osteoporosis, Alzheimer's disease—after the Women's Health Initiative [WHI], the pendulum swung way too far to the other side, suggesting that estrogens are too risky," Dr. Schiff said.

News reports about the WHI trial tended to focus on the risks of HT and to overlook benefits. Estrogen therapy is "certainly one of the most potent agents we

have available" for preventing hip, vertebral, and wrist fractures, he said.

When the National Institutes of Health announced the landmark findings of the WHI trial, HT prescriptions declined precipitously. "Overall health risks [of HT] exceeded benefits," investigators concluded after they stopped the trial early (JAMA 2002;288:321-33).

According to the WHI findings, therapy with estrogen plus progestin was associated with a major increase in the relative risk of several serious health problems. For example, it was tied to a 29% increased risk of coronary heart disease (CHD), a 41% increased risk of stroke, a twofold increased risk of pulmonary embolism (PE), and a 26% increased risk of breast cancer.

Many observers found the absolute risks less alarming, however. According to the WHI data, if 10,000 women took estrogen plus progestin for 1 year, there would be an excess risk of seven more CHD events, eight more strokes, eight more PEs, and eight more invasive breast cancers. There would be no extra deaths. Among women with no uterus taking estrogen only, there would be 12 more strokes (JAMA 2004;291:1701-12).

HT would also confer some benefits among those 10,000 women. There would

be six fewer colorectal cancers and five fewer hip fractures. Among women with no uterus taking estrogen, there would be six fewer hip fractures. The WHI did not state whether HT would relieve menopausal symptoms.

Dr. Schiff termed the findings on fracture prevention "quite impressive." Citing the reductions in relative risk, he noted that women taking progestin plus estrogen had a 29% reduction in lower forearm fractures and a 33% reduction in hip fractures. In the estrogen-only arm of the study, there was a 39% decrease in hip fractures and a 38% decrease in vertebral fractures.

Studies of other drugs designed to prevent and treat osteoporosis have had difficulty showing a reduction in hip fractures. The effect of medium-dose HT on fractures "is equivalent to bisphosphonates," he said.

Hidden amid the WHI data is information on the impact of low-dose estrogens that might help clinicians balance benefits and risks of HT therapy, Dr. Schiff suggested.

At low doses, estrogens increased bone mineral density by 2.4% and 3.9% at the femoral neck and spine, respectively.

Dr. Schiff did not provide evidence from WHI to show that low-dose estrogens were associated with fewer fractures, however. As the NIH noted in a 2000 consensus statement on osteoporosis, improvements in bone density do not always

translate to a decrease in fractures. "The risks for osteoporosis, as reflected by low bone density, and the risks for fracture overlap, but are not identical" (NIH Consensus Statement 2000;17[1]:1-36).

Still, Dr. Schiff said that there is enough evidence to support prescribing low-dose estrogen for the prevention of devastating hip fractures.

Citing data on low-dose oral contraceptives in relatively young, healthy women, Dr. Schiff said that, in theory, lower doses of estrogen should yield fewer health risks in the middle-aged and elderly. And "even very-low-dose estrogen is quite effective at maintaining bone density."

That said, patients must be thoroughly informed about their individual risk profile regarding HT so they can make informed decisions. "A woman of age 50 is not worried about a hip fracture at age 80," he said. "She is worried about the potential for breast cancer at age 55."

And the data on estrogens and breast cancer are mixed. Some studies show an increased risk, some do not. "I tell my patients I personally have major concerns about the long-term risk" of breast cancer associated with estrogen therapy, he said.

In general, Dr. Schiff said that he prescribes estrogens for the minority of women with very severe hot flashes. For vaginal dryness topical estrogen therapy can help. Very-low-dose estrogen will also help with urogenital symptoms. ■

## Most Elderly Women Vitamin D Deficient

BY SHERRY BOSCHERT  
San Francisco Bureau

SAN FRANCISCO — A majority of 1,536 elderly women taking medication to prevent or treat osteoporosis were deficient in vitamin D, a study of community-dwelling patients found.

The findings echo a previous study that found 56% of medical inpatients had vitamin D deficiency. "This is a very common problem" that deserves more attention, Dolores M. Shoback, M.D., said at a meeting on osteoporosis sponsored by the University of California, San Francisco.

Physicians should look more carefully for vitamin D deficiency in inpatients and outpatients, even those who are ambulatory, on prescription therapy for osteoporosis, and lacking risk factors for vitamin D deficiency—"many of the patients, probably, in our own practices," said Dr. Shoback, professor of medicine at the university.

The recent outpatient study included postmenopausal women at 61 locations in North America who had been taking bisphosphonates, calcitonin, or a selective estrogen receptor modulator for at least 3 months under a physician's care to prevent or treat osteoporosis. They averaged 71 years in age, and were 92% white.

Investigators administered a questionnaire to assess risk factors for vitamin D deficiency and measured the women's serum concentrations of parathyroid hor-

mone (PTH) and 25-hydroxyvitamin D—known as 25(OH)D—the form of vitamin D stored in the body.

They found that 52% of the 1,536 women had levels of 25(OH)D lower than 30 ng/mL. Of these, 36% had levels below 25 ng/mL, and 18% were below 20 ng/mL, showing that most of the women with inadequate vitamin D were severely deficient (J. Clin. Endocrinol. Metab. 2005;90:3215-24).

"We aren't doing a good job with the people we're actively treating for osteoporosis," said Dr. Shoback. Vitamin D deficiency is one of the most common causes of secondary osteoporosis.

Although there's no consensus on how much vitamin D the human body needs, the idea that 15-25 ng/mL is adequate has been replaced in the last few years by general cutoffs closer to 30 ng/mL or higher, she said. Some experts say people need at least 20 ng/mL 25(OH)D or else PTH levels rise and frank hyperparathyroidism develops. Others say that elderly people need 32-36 ng/mL to maximize intestinal calcium transport.

In the study, patients tended to develop secondary hyperparathyroidism at 25(OH)D levels of 25 ng/mL and lower. Many physicians use PTH levels to help diagnose vitamin D deficiency, but the study found that high PTH is not 100% sensitive for low vitamin D. Only 75% of women with 25(OH)D levels of 0-9 ng/mL had secondary hyperparathyroidism. "This surprised me," Dr. Shoback said.

Women who had not discussed vitamin D and bone health with their doctors were more likely to have 25(OH)D levels below 30 ng/mL. "Sometimes we think we're talking to the wall or ourselves, but these discussions actually may be having some kind of an impact," she said.

Other risk factors for vitamin D deficiency included age older than 80, a body mass index over 30 kg/m<sup>2</sup>, taking medications that affect metabolism of vitamin D, and taking less than 400 IU per day of vitamin D supplements. Women also were more likely to be deficient in vitamin D if they rated themselves as having "poor general health," if they exercised less than six times per week, if they ate fewer servings of foods containing vitamin D, and if they completed less than 12 years in school. Among patients with none of these risk factors, 32% had inadequate levels of 25(OH)D. "There just seem to be people out there who have vitamin D deficiency," she said.

The 1998 inpatient study that detected vitamin D deficiency in 56% of 290 patients consecutively admitted to a hospital medical service also found that risk factors predicted the deficiency only about 60% of the time. The investigators recommended that medical inpatients be screened for vitamin D deficiency, she noted. Taking multivitamins did not prevent vitamin D deficiency in that study.

Dr. Shoback said that she has no affiliation with companies that make vitamin D supplements. ■

## Past Vertebral Fractures Predict Future Risk

WASHINGTON — The risk of vertebral fragility fractures is threefold higher among postmenopausal women with at least one prevalent radiographic fracture, compared with those without such a history, Ethel S. Siris, M.D., said at an international symposium sponsored by the National Osteoporosis Foundation.

Awareness of previous vertebral fractures can help physicians evaluate vertebral fragility and target osteoporosis therapy appropriately, Dr. Siris, a professor of clinical medicine at Columbia University, New York, and her colleagues, said in a poster presented at the meeting.

Their review of data on 2,651 postmenopausal women, mean age 67 years, included 1,181 women with prevalent vertebral fractures and assessed risk independent of lumbar spine bone mineral density.

Overall, the greater the number of prevalent vertebral fractures, the greater the risk of sustaining subsequent fractures.

Patients with three or more fractures had as much as an eightfold increased risk. Greater severity scores on the semi-quantitative deformity scale were associated with as much as an 11-fold increase in risk.

Dr. Siris is a consultant for and has received honoraria from Eli Lilly & Co., Merck & Co., Sanofi-Aventis, Procter & Gamble Pharmaceuticals, and Novartis.

—Heidi Splete