

Lab Tests, History Catch Secondary Osteoporosis

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WASHINGTON — A careful evaluation and thorough history can identify a large portion of patients with secondary osteoporosis, Dr. Meryl LeBoff, director of the skeletal health and osteoporosis center and bone density unit at Brigham and Women's Hospital in Boston, said at an international symposium sponsored by the National Osteoporosis Foundation.

The true prevalence of secondary osteoporosis is not known. However, about 50% of patients can be detected with a good medical history, Dr. LeBoff said. Although laboratory evaluations vary, such tests can be used to identify 25%-65% of patients with secondary osteoporosis.

Identifying secondary osteoporosis is important, because skeletal changes may

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be reversible and decreased acquisition of peak bone mass is a determinant of osteoporosis later in life.

In a 2004 report on bone health and osteoporosis, the surgeon general recommended that all patients who are diagnosed with

osteoporosis get at least a limited evaluation for secondary causes of bone loss. However, patients with a low z score are most in need of in-depth evaluation for secondary osteoporosis.

In particular, premenopausal women or men with unexplained fractures and those who are adherent but have a poor response to therapy should be evaluated for secondary osteoporosis.

A low z score—which compares a patient's bone mineral density (BMD) to the mean for a healthy age- and gender-matched population—may suggest an increased likelihood of secondary osteoporosis. A z score of -1.0 is associated with a twofold greater lifetime risk of fracture and a z score of -2.0 is associated with a fourfold greater lifetime risk of fracture.

"However, z scores do not consistently predict which patient has an underlying disorder, so it's important to use clinical judgment in the evaluation of a particular patient," Dr. LeBoff said.

There are no evidence-based guides for evaluating a patient for secondary osteoporosis. Dr. LeBoff recommends taking a detailed personal and family history. Be sure to ask about calcium intake. In addition to a thorough physical exam, do bone density testing and laboratory tests.

Laboratory tests for serum calcium, 25-hydroxy vitamin D, 24-hour urinary calcium, and parathyroid hormone—plus serum thyroid-stimulating hormone among women on thyroid replacement—can identify an estimated 98% of patients with secondary osteoporosis (J. Clin. Endocrinol. Metab. 2002;87:4431-7).

At the Brigham and Women's osteo-

porosis center, guidelines for evaluation of secondary osteoporosis include a z score less than -1.5 . Laboratory tests include serum calcium and phosphorus, renal function, 25-hydroxy vitamin D levels, thyroid-stimulating hormone, parathyroid hormone, and urinary calcium. In select patients, markers of bone turnover may be tested.

Dr. LeBoff also discussed some of the common causes of secondary osteoporosis:

► **Glucocorticoids.** "Use of glucocorticoids is the most common cause of sec-

ondary osteoporosis," said Dr. LeBoff. A number of other endocrine abnormalities—thyroid hormone excess, hypogonadism, anorexia, hyperparathyroidism, hypercalciuria, vitamin D deficiency, and androgen insensitivity—can also cause secondary osteoporosis.

Glucocorticoids increase fracture risk progressively. "Even extremely low doses of inhaled glucocorticoids can lead to bone loss," Dr. LeBoff said.

The pathophysiology of glucocorticoid-

induced osteoporosis is multifactorial, involving decreased osteoblast function, increased osteoblast apoptosis, increased gastrointestinal absorption of calcium, increased urinary calcium excretion, and an increase in osteoclast bone resorption.

► **Anorexia.** This disorder affects an estimated 4% of U.S. college students. Anorexia leads to a 25% lower spine BMD and a sevenfold increased fracture risk. Peak bone mass is decreased, and there may be a permanent deficit of bone mass

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in these young women. Anorexic women have subnormal levels of dehydroepiandrosterone, testosterone, estrogen, and cortisol. "Estrogen does not correct the low bone mass [in these women]," Dr. LeBoff said. A number of trials are underway looking at ways to reverse decreased bone mass in anorexic women.

► **Vitamin D deficiency.** Vitamin D deficiency is common and has been implicated in impaired muscle function, increased falls, increased muscle pain, multiple sclerosis, and some malignancies. There is seasonal variation in vitamin D levels and notably, vitamin D activation decreases with age, darker skin pigment, and increased

sunblock use. Gastrointestinal disorders also can lead to vitamin D deficiency, as it is absorbed in the small intestine.

Levels of vitamin D sufficiency and deficiency have been a matter of some debate. "Vitamin D deficiency is currently defined as 25-hydroxy vitamin D level of less than 20 ng/mL ... sufficiency for bone is [25-hydroxy vitamin D level] greater than 30-32 ng/mL," Dr. LeBoff said.

Inadequate levels of vitamin D have been documented in 52% of women who participated in osteoporosis trials. Women in these studies had an average T score of -1.8.

In a study based at Brigham and Women's, 90% of women admitted with

hip fractures had vitamin D insufficiency and 57% had vitamin D deficiency. Because of this, when women are admitted now with hip fragility fracture they are given 50,000 units of vitamin D. They are also evaluated for secondary osteoporosis.

► **Aromatase inhibitors.** "Bone loss is clearly associated with breast cancer therapies," Dr. LeBoff said. Aromatase inhibitors can lead to bone loss of about 2.6% per year, though long-term data are not yet available. Gonadotropin-releasing hormones can lead to bone loss of 4%-6% per year. Ovarian failure can lead to bone loss of about 8% per year. Oophorectomy is associated with bone loss of 11% per year. ■

VERBATIM

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—Dr. Pauline W. Chen, p. 38

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