



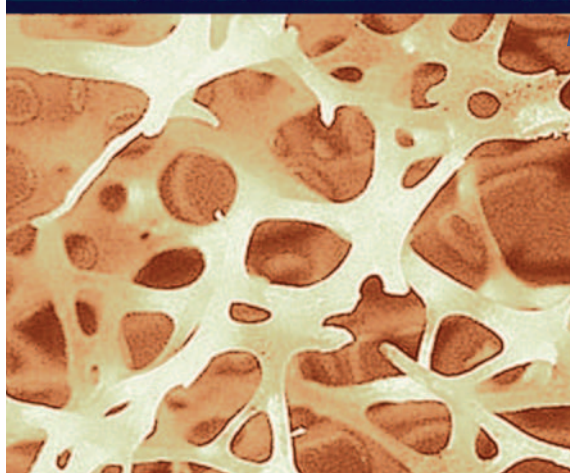
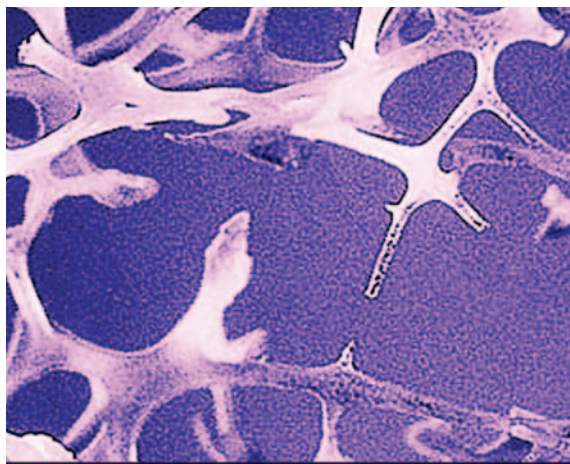
CURRENTS IN PRACTICE

Osteoporosis

PART 2

Investigating low bone density in men and premenopausal women

BY FAIZAN AMIN AND ALIYA KHAN, MD



in developed countries, osteoporosis is the most common form of metabolic bone disease. Although associated more frequently with postmenopausal women, the incidence of osteoporosis in younger women and men over age 50 is becoming an increasingly important health issue — one that shouldn't be overlooked.

On routine examination, it's estimated that 15% of premenopausal healthy women have a T score of less than -1 and about 0.5% have a T score of -2.5 or below. With men, the Osteoporosis Society of Canada (OSC) estimates that one in eight men over age 50 has osteoporosis. Approximately 30% of hip fractures occur in men; however, the mortality rate in this population is approximately two times higher than in

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women who experience a fracture. As such, evaluating bone mineral density (BMD) and making an early and accurate diagnosis in these two groups are essential components to combating this debilitating disease.

Is BMD useful for a diagnosis?

In premenopausal women, BMD follows a bell curve distribution, so those who have a low bone density may simply have low peak bone mass, which might not necessarily be pathologic. To accurately

diagnose osteoporosis in the premenopausal patient, the initial evaluation must consider an underlying cause. In the absence of a secondary cause, low bone density may represent low peak bone mass, which can be the result of genetic and environmental factors. Inadequate dietary calcium intake, smoking, heavy alcohol consumption and inadequate exercise can also prevent individuals from reaching their genetically determined peak bone densities. When evaluating premenopausal women with low bone density, it's necessary, therefore, to distinguish between low peak bone mass and osteoporosis, which is associated with an increased risk of fracture.

Who needs to be assessed?

In younger women, a diagnosis of osteoporosis isn't made by bone mineral density alone. Osteoporosis can only be diagnosed in the presence of a fragility fracture, and may also be confirmed by features

found on a bone biopsy. If there is no fragility fracture, a bone biopsy is necessary to confirm the diagnosis because a low BMD during the premenopausal years may reflect low peak bone mass.

Premenopausal women who experience low trauma fractures (i.e. those that occur from standing height) should undergo BMD testing. Patients who've been taking certain medications that can cause bone loss should also be tested, e.g. those on long-term prednisone therapy, some anticonvulsants and extended use of medroxyprogesterone acetate (see Table 1 for a more detailed list).

Women who experience irregular menses or prolonged periods of amenorrhea of more than six months should be further evaluated for

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low bone density, as should those who have diseases or conditions associated with bone loss (see Table 1 for a detailed list).

How should a low BMD be investigated?

In addition to a comprehensive history and physical examination, additional lab tests are recommended in premenopausal women to ensure no other factors are contributing to progressive bone loss.

It's also important to evaluate gonadal status in this population. Prolonged amenorrhea is associated with estrogen deficiency and accelerated bone loss. Research indicates that individuals who have follicle stimulating hormone (FSH) levels of more than 20 mIU/mL have increased rates of bone turnover and progressive bone loss during their perimenopausal years. Therefore, a detailed assessment of a woman's menstrual status is an important assessment tool as ovulatory disturbances are more frequently observed in premenopausal women with low BMD. Remember also that a low BMD in a premenopausal patient isn't necessarily associated with the same increase in fracture risk as the postmenopausal woman. Premenopausal women have a much lower risk of fracture, even with falls. Because they're younger and have normal neuromuscular function, they're less likely to fall, and their bone turnover rates aren't accelerated during this period (see the list on page 103 for the recommended workup for low BMD in this group).

How is a low premenopausal BMD managed?

In the absence of a fracture and secondary causes, treat low bone density in premenopausal women conservatively. Encourage all women to modify their lifestyle to ensure an adequate intake of calcium and vitamin D, in addition to a regular weight-bearing exercise program. It's important to emphasize

maintaining a normal body weight, giving up cigarette smoking and limiting the intake of caffeine and soft drinks. Alcohol should be consumed only in moderation.

Women who are estrogen-deficient — either clinically or sub-clinically — will benefit from estrogen supplementation, taken in the form

**WORKUP FOR LOW BMD IN
PREMENOPAUSAL WOMEN****Lab investigations**

- calcium (albumin corrected)
- complete blood count
- erythrocyte sedimentation rate
- phosphate
- magnesium
- thyroid stimulating hormone
- creatinine
- alkaline phosphatase
- follicle stimulating hormone
- estradiol

24-hour urine collection

- for calcium, creatinine

Additional investigations

- 25-hydroxy vitamin D
- parathyroid hormone
- antiigliadin antibodies
- antiendomysial antibodies

TABLE 1. SECONDARY CAUSES OF BONE LOSS IN WOMEN

Diseases/Conditions	Medications
hypogonadism (primary and secondary)	glucocorticoids
primary hyperparathyroidism	thyroxine (excessive)
thyrotoxicosis	anticonvulsants (phenytoin, phenobarbital)
growth hormone deficiency	lithium
osteomalacia	gonadotropin-releasing hormone agonists
hypophosphatasia	medroxyprogesterone acetate
connective tissue disorders	
hypercalciuria	
osteogenesis imperfecta	
celiac disease	
anorexia	

of oral contraceptives or 17 beta-estradiol combined with a progestin to prevent progressive bone loss. For patients who aren't estrogen-deficient, estrogen supplementation is controversial. Some evidence shows that oral contraceptives may provide a protective effect on bone density in both pre- and postmenopausal women. Other trials, however, demonstrate otherwise. Data from the Canadian Multi-Centre Osteoporosis Study, for example, indicates that oral contraceptive users have decreased bone density at the trochanter and spine compared to non-users. Further evaluation of this study population does show that women who use oral contraceptives have higher rates of smoking and alcohol use, which contribute to bone density loss. In addition, oral contraceptive users have a greater prevalence of menstrual irregularities than non-users. It's abundantly clear that prospective data is needed to further evaluate the effects of oral contraceptives on bone density in premenopausal women.

If a secondary cause for low bone density is identified, treat the underlying cause. Patients diagnosed with celiac disease, for example, show significant gains in bone density when they are placed on a gluten-free diet.

In premenopausal women who have a secondary cause for osteoporosis, such as long-term steroid use or hyperparathyroidism, anti-resorptive therapy has been shown to be valuable in improving bone density and reducing fracture risk. Bisphosphonates, a staple in the prevention and treatment of postmenopausal osteoporosis, shouldn't be used in these premenopausal women — these agents have only been

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studied and evaluated in younger women whose bone loss is attributed to a secondary cause. The value of a bisphosphonate in premenopausal women without secondary causes of bone loss, however, has been assessed. If bone turnover is normal, then any further suppression may not be beneficial in reducing fracture risk.

What about men? **Osteoporosis is** sadly under-

diagnosed and undertreated in men. Only when a fracture oc-

currs are men typically assessed for osteoporosis. The OSC identifies major and minor risk factors for osteoporosis in men. Those who have one major or two minor risk factors should have a BMD test if they're older than age 50 (see Table 2 for a more complete list of risk factors). The OSC recommends that BMD testing be completed in all men over age 65. Men who sustain a low trauma fracture should also be tested. In addition, men whose osteoporosis is due to a secondary cause and those who've been exposed to prolonged use of glucocorticoids (longer than three months and doses of 7.5 mg or greater) need to be evaluated as well.

How do we diagnose osteoporosis in men? **The relationship** between bone

density and fracture risk isn't as

well understood in men as it is in women. An explanation for this may be that there are skeletal differences in aging between men and women. In addition to these variations, other factors lower the risk of fracture in men. For one, they achieve a higher peak bone mass than women. Furthermore, they don't have a menopausal equivalent — androgen levels in men are relatively well maintained into the later stages of life. Also, men have a shorter life expectancy than women, which results in a lower incidence of osteoporosis and fragility fractures.

How are men treated? **Following the** diagnosis of oste-

oporosis, ensure that patients

adhere to appropriate lifestyle changes. Intake of alcohol, caffeine and soft drinks should be limited and smoking cessation must be advised. As well, a regular weight-bearing exercise program that increases muscle strength and coordination

TABLE 2. RISK FACTORS FOR OSTEOPOROSIS IN MEN

Major risk factors (one or more)	Minor risk factors (two or more)
vertebral deformity	low dietary calcium
non-traumatic loss of vertebral height/kyphosis	weight < 57 kg
radiographic evidence of osteopenia	cigarette smoking
older than age 65	excessive alcohol or caffeine intake
hyperparathyroidism	chronic use of anticonvulsants
hypogonadism	long-term heparin use
systemic glucocorticoids	rheumatoid arthritis
prior fragility fracture after age 40	history of clinical hyperthyroidism
family history of osteoporotic fracture	
malabsorption	
propensity to fall	

WORKUP FOR OSTEOPOROSIS IN MEN**Tests to exclude secondary causes**

- complete blood count
- serum calcium (total and ionized)
- serum creatinine
- liver function
- alkaline phosphatase
- thyroid stimulating hormone
- PTH and serum 25-hydroxy vitamin D (to exclude the possibility of parathyroid disease and/or vitamin D deficiency)

Where indicated:

- protein electrophoresis in patients over age 60 (to rule out multiple myeloma)
- 24-hour urine calcium (to exclude hypercalciuria in the presence of a history of nephrolithiasis or hypocalciuria in the presence of malabsorption)
- 24-hour urine-free cortisol
- total and free serum testosterone, bioavailable testosterone (to exclude hypogonadism)
- antibody testing for celiac disease in patients who have features of calcium malabsorption

has been shown to lower the risk of falls by 25%. Supplements, such as calcium and vitamin D, will help with normal bone mineralization. Men under age 50 are advised to take a daily calcium supplement of 1,000 mg, and those over 50 should receive 1,500 mg each day. Vitamin D is recommended in doses of 400 IU daily for men under age 50 and 800 IU for those older than 50.

For patients with glucocorticoid-induced osteoporosis, both alendronate and risedronate have been proven to be effective treatment options. In studies of men with idiopathic osteoporosis, alendronate was shown to significantly increase bone density and lower the risk of fracture. This was apparent in both eugonadal and hypogonadal men. The anabolic agent, teriparatide, has also been approved for osteoporosis in men. Additional clinical trial data on the effectiveness of antiresorptive therapy in treating male osteoporosis, though, is still required. **PE**

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