Recommendation: Test All HIV-Positive Men 50 and Older and All Post-Menopausal Women for Bone Loss

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All post-menopausal women living with HIV and all HIV-positive men 50 or older should be screened for low bone mineral density (BMD), according to new guidelines published in the October 15 issue of *Clinical Infectious Diseases (CID)*. The guidelines, authored by experts in the field of HIV medicine and metabolic issues, also highlight the need for aggressive workups to determine underlying causes of reduced BMD, while also providing guidance on treatment and preventive care.

Low BMD has been documented in people living with HIV, regardless of age. In one study, the prevalence of severe BMD loss, or osteoporosis, was three times higher among HIV-positive people than among HIV-negative controls, especially among those receiving antiretroviral (ARV) therapy. Studies have shown that BMD decreases by 2 to 6 percent within the first two years after starting ARV treatment, a rate of bone loss mirroring that seen in women during the first two years of menopause.

Importantly, studies are beginning to report an increased risk among HIV-positive people of fragility fractures—when a bone breaks as a result of a fall from standing height or less, usually involving the vertebrae, hip or wrist—with rates 30 to 70 percent higher than those among age-matched HIV-negative controls.

Research also indicates that low BMD in people living with HIV can be attributed to a number of causes, representing a complex interaction between HIV infection, high rates of tobacco and alcohol use, low vitamin D levels, ARV-related factors and traditional osteoporosis risk factors exacerbated by consequences of chronic HIV infection.

Testing Recommendations

Published guidelines for the general U.S. population recommend DEXA scanning—the gold standard for measuring BMD—for any person who experiences a fragility fracture, women 65 or older and men 70 or older. For those with an additional risk factor, the recommendation is to perform DEXA scanning in younger post-menopausal women and men 50 or older. Although HIV infection is not listed as a condition associated with low BMD in the recommendation for the

general U.S. population, the authors of the October 15 *CID* article state that current evidence support including HIV infection among the additional risk factors that warrant earlier screening.

The *CID* authors recommend a DEXA scan for all HIV-positive men 50 or older and all post-menopausal women. They note that their position is more aggressive than the guidelines from the Infectious Diseases Society of America, published last year, which recommend DEXA scanning for all people living with HIV 50 or older—but only if they have additional risk factors for osteopenia (less severe BMD depletion) or osteoporosis.

"If the results of [DEXA testing] do not warrant medical treatment," the *CID* authors write, "the test should be repeated every two to five years, depending on the results of initial testing."

Looking for Secondary Causes

Though HIV infection and ARVs are widely considered to be independent risk factors for decreased BMD, they're not the only cause of osteopenia and osteoporosis among many living with the virus. "In HIV-infected individuals," the authors write, "low BMD has been linked most frequently to low body weight, but has also been linked to testosterone or estrogen deficiency, glucocorticoids [for example, prednisone], malabsorption, tobacco use, alcohol and opiate abuse, [lowest ever] CD4 cell count, duration of HIV infection, lipodystrophy, insulin resistance and [elevated lactic acid levels]."

Fortunately, the majority of causes of secondary osteoporosis can be suspected or diagnosed on the basis of a thorough history and physical examination, the authors add.

Maintaining Good Bone Health

People living with HIV and their health care providers, the *CID* authors write, should focus on factors important to bone health, including adequate nutrition, particularly calcium and vitamin D intake.

Because of the high prevalence of low BMD in HIV infection, the authors recommend people living with HIV take 1,000–1,500 mg of calcium and 800–1,000 IU of vitamin D daily. The amount of daily sun exposure sufficient for maintaining vitamin D levels without increasing the risk of skin cancer is unknown, they add.

Muscle strengthening and balance exercises to prevent falls should also be recommended. In postmenopausal women, exercise that puts a physical load on the bone has been shown to improve BMD and reduce fracture, according to at least one study. In turn, 30 minutes of weight-bearing exercise—including jogging or walking—at least three days a week is recommended.

Finally, any secondary causes of low BMD should be treated to slow, if not reverse, the development of osteopenia and osteoporosis. For example, patients with low testosterone levels may want to consider replacement therapy. They're also advised to drink less alcohol and quit

smoking.

Treatment for Low BMD

Two first-line treatments for osteoporosis—Fosamax (alendronate) and Zometa (zoledronic acid)—have been tested in HIV-positive people in randomized, clinical trials. The results of these studies, the *CID* authors stress, indicate that the drugs act similarly and aren't any more likely to cause side effects in people living with HIV compared with the general population.

"Given the prolonged effects of Bisphosphonates and the uncertainty of their long-term safety, the optimal duration of treatment with [these drugs] is unclear, but some experts recommend discontinuation after five years with careful observation," the authors write. "Because HIV-infected subjects are now expected to live for many decades, the decision as to when to start or stop therapy is difficult and deserves to be investigated in long-term clinical trials."

As for reversing BMD loss believed to be caused, at least in part, by ARV treatment, "there is currently no evidence to suggest that switching [an ARV regimen] will improve BMD and reduce fracture risk in HIV-infected patients," they write.

There is, however, the question of tenofovir—found in Atripla, Truvada and Viread—which has been associated with increased bone loss in people living with HIV receiving this drug. However, the authors say, "There have been no properly powered studies to date that have linked [tenofovir] use to fracture." They add: "At this juncture, there is insufficient evidence to recommend against [tenofovir] use in a patient with known low BMD prior to [ARV therapy] initiation. However, alternative [ARV] choice or closer bone monitoring after [tenofovir] initiation may be considered for subjects with fragility fractures or known osteoporosis."

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