A Dangerous Age

Two new conditions -- osteoporosis and diabetes -- are hitting HIVers. Whether caused by the virus, the meds or both, these ailments have researchers alarmed about a graver syndrome -- premature aging. Jennifer Block reports on how to keep Old Man Time at bay.

October 1, 2001 By Jennifer Block

Treatment types love to construct neat metaphors for life with HIV. There's the old standby: train (you), ravine (opportunistic infections) and bridge (anti-HIV meds). *POZ*, of course, prefers the party analogue: You're throwing a glam gala. You've invited select guests from that famous family, HAART (highly active antiretroviral therapy). But suddenly some crashers are making a mess of things -- there's diarrhea dancing under the disco ball and nausea sporting a lampshade hat. You expected depression and anxiety to slip in -- they're out on the balcony with a half-gallon of Absolut -- but you never thought you would see Lady Lipo and Buffalohump Bill.

Call the promoters for back-up bouncers, baby, because osteoporosis and diabetes just toppled the red-velvet rope. Unfashionably late and low on theHAART side-effects list (see "Side FX," *POZ* September 2000), these *arrivistes* can still be 86'd if you act now.

No Bones About It

You may hear *osteoporosis* and think *Golden Girls*, but new research suggests that the condition -- marked by weaker, fracture-prone bones -- is likely increasing among HIVers. Lacking conclusive data, it's still too early to put all the blame on your combo, but the prevalence of bone-tissue loss is apparently significantly higher in people taking protease inhibitors (PIs) than in those on non-PI combos. What's not yet clear is whether it's HAART or some combination of the drugs, HIV and advancing age that's to blame.

Osteoporosis is a common complaint in an aging body: 50 percent of women and 12 percent of men actually lose bone after age 50. Say what? The problem is that while pre-midlife, the body continuously loses bone cells and continuously replenishes them in equal measure, with aging the number of cells made doesn't match the number gone -- there's a gradual loss of bone tissue. The result is thinner, weaker bones that may become brittle and break easily.

Pablo Tebas, MD, of the Washington University School of Medicine in St. Louis, is on the case. In 1999, he began looking for a link between HAART and bone-mineral density (BMD), a measure of bone strength used to diagnose osteoporosis. In a small study of HIV positive men, he found that of all HAART-takers, those on a PI were at greatest risk: Half of the protease poppers had osteopenia -- the prelude to osteoporosis. But the increase in PI-taking men was not statistically

significant when compared to neggies. The trouble is, there are no symptoms of osteopenia. “Lots of people with HIV are walking around undiagnosed,” says Lori Panther, MD, an HIV specialist in Boston. A full-body x-ray, called a DEXA scan, can be used to determine your baseline bone density, which is expressed as a “T score.” That score -- taken *before* you break a bone -- will help catch deterioration. But while osteopenia has been reversed in post-menopausal women, whether or not that will be true in HIVers is still unclear. What we do know is that osteoponic bones are twice as likely to fracture or break, and osteoporotic bones are four to five times more likely to do so.

Tebas has yet to absolutely establish a causal connection between HAART and BMD loss, but he hypothesizes a notably chilling scenario and synergy: HAART, HIV or both are effectively speeding aging’s inevitable toll. “Several years of HAART may accelerate the typical loss of bone mineral that occurs with advancing age,” he says. Unfortunately, some common collateral damage caused by HAART and HIV also increases the likelihood of bone loss, including fatigue (leading to decreased weight-bearing exercise), nausea (leading to bad nutrition) and hormone decreases (in both men and women). Of course, booze and cigarettes, those time-honored solaces, only up your risk.

But don’t get out that walker just yet. This doesn’t mean that if you have osteopenia, you’ll sneeze and break a rib. But it does mean that your bones could be more likely to break than you’d expect at your age, and so monitoring is important. And, anyway, just how serious is a fractured finger or a broken rib compared with HAART-related liver and heart damage or the consequences of HIV progression itself? “Not that serious yet,” says William Powderly, MD, a professor of medicine and Tebas’ colleague at Washington University. “There is no reason to stop or even change treatment based on these findings. We are convinced there is a link, but it is still not clear how severe or progressive treatment-induced osteoporosis is.”

That’s easy for a whitecoat to say, but bone-breaking PWAs might see it differently, if their input is sought. In Boston, Sonia Nagy, MD, and others at Beth Israel Deaconess Medical Center are trying to nail down more specific stats through a larger study of both men and women, which they hope will uncover additional risk factors. (They’re still enrolling participants in the area, so call 617.632.0769 for details.) Another unknown is how bone loss affects HIV positive men and women differently. Because women are more prone to osteoporosis in general, it’s reasonable to expect that women with HIV, who often experience the premature onset of menopause, are at greater risk and need early, effective intervention.

For now, garden-variety advice must suffice, but generally HIVers on HAART should start following guidelines for older neggies now: regular exercise (weight-bearing activity such as walking, running or weight-training -- not biking or swimming -- is best) and a diet rich in bone-building nutrients, along with nutrient supplementation to ensure adequate calcium (1,000 mg daily for men; 1,000 to 1,500 mg for women) and magnesium (500 to 1,000 mg per day; excess magnesium can cause loose stools) and vitamin D (400 to 800 IU a day). Good foods for this include milk, yogurt, cheese, salmon, soy or white beans and tofu made with calcium. Drugs prescribed for bone-loss prevention include Fosamax, Actonel, Raloxifene, Calcitonin and, for

women, hormone-replacement therapy, but of course all these treatments come with their own party crashers, too.

Sweet and Sour

Feeling a little bit *sensitive* about lipodystrophy's humps, paunches and ballooning bosoms? Tell that to your cells. An old theory about lipo is that it is the result of cells becoming desensitized, or "resistant," to insulin. But looks aside, this is a serious condition that may put you at risk for type II diabetes and cardiovascular disease.

You eat. You digest. Your body extracts glucose (the simple sugar needed by cells for energy) from food and dispatches it into the bloodstream. Your pancreas produces insulin to escort the glucose into the cells, which keeps your motor purring. But the insulin receptors in an HIVer's cells -- especially those of HAART takers -- may start boycotting the insulin and, with it, the glucose. Because your body needs that glucose, it compensates by signaling the pancreas to produce more insulin. For a time, this works: The cells absorb the energy.

Recent studies have shown that many HIVers with lipo overwork their pancreas because they need to make twice as much insulin as normal to sustain normal glucose levels. This worries researchers for two reasons: Either the pancreas could exhaust itself or the cells could become increasingly resistant. If either happens, then blood sugar is unabsorbed and levels skyrocket, which means that your cells are essentially starving to death. Behind both doors No. 1 and 2 lie diabetes and its fearsome risks: damage to blood vessels throughout the body, resulting in complications from top (blindness) to bottom (neuropathy and leg amputations) to in-between (heart-attacks, strokes and kidney failure). The early symptoms alone -- extreme thirst, hunger, weight loss, fatigue and itchy skin -- could make you feel worse than if you spent the night singing drunken karaoke.

While such high glucose is more obviously dangerous, the effects of high insulin levels may be subtler but ultimately just as worrisome. It is believed that they directly harm the blood vessels, even when blood glucose is not high. So consider that elevated insulin level to be a red flag for cardiovascular disease. There is evidence that PIs, particularly indinavir (Crixivan), may have a direct effect on glucose transport, which would in turn affect insulin sensitivity. But researchers also suspect that insulin resistance is connected to lipo-related fat changes. "Understanding the connection between fat and insulin is extremely important for HIV-infected patients with lipodystrophy," says Steven Grinspoon, MD, assistant professor of medicine at Harvard Medical School. "But we just don't know why insulin resistance is happening or how much it increases the risk for diabetes and heart disease."

The sad truth is, if your regimen includes protease inhibitors and you have lipodystrophy, you have a 50-50 chance of also having insulin resistance. But you'll have to give blood to be sure. Then you'll undergo tests for insulin and glucose levels on an empty stomach ("fasting levels") and then retest after downing a high-glucose drink ("post-prandial levels") to determine your degree of resistance. A high post-prandial glucose level suggests that insulin receptors are becoming increasingly resistant. But the neon alarm flashes when your fasting glucose levels are elevated -- this signals that your cells are not getting the energy they need. It could mean a diagnosis of type

II diabetes.

That’s what Dominic Hamilton-Little, an HIVer in New York City, got just one year after he failed a fasting glucose test. “I was permanently hungry and constantly thirsty, and it was gradual. I didn’t realize it until the doctor said, ’Whoa, your blood sugar is way too high.’” Within a year he was diagnosed with diabetes.

If you do have high insulin levels, you should exercise and eat a high-protein, high-fiber, moderate-fat diet, with a reasonable amount of carbs, as directed by your doc. As for switching to a no-protease combo, that’s a delicate decision only you and your doc can make. In a few small studies, ditching their protease inhibitors for efavirenz (Sustiva), nevirapine (Viramune) or abacavir (Ziagen) helped people increase insulin sensitivity.

Certain drugs aimed at reducing blood glucose, including metformin (Glucophage) and two drugs from the glitazone group, rosiglitazone (Avandia) and pioglitazone (Actos), have been used with some success. Metformin decreases the liver’s glucose production; glitazones up cells’ glucose absorption. Both drugs are used to treat overt diabetes, but recent studies on their lipo and insulin-resistance effectiveness show reduction not only of insulin and glucose levels but also of blood pressure as well as belly size. Some docs have started prescribing these drugs even to nondiabetic HIVers, and while it is too early to tell if the benefits of improving insulin sensitivity outweigh the drugs’ potential risks -- weight loss, diarrhea and lactic acidosis -- signs point to yes. “My hunch is that we will be using insulin-sensitizing agents more routinely in the future,” Grinspoon says. So don’t pack up that party just yet. First treat the osteo and insulin crashers to the old kill-’em-with-kindness routine -- kindness to your body, that is.

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