HIV-Positive Men Should Test ‘Free’ Testosterone Levels

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To check whether an HIV-positive man’s sex glands produce too little testosterone—a condition called male hypogonadism—doctors must look at morning blood draws and levels of “free” testosterone, according to a study by Johns Hopkins University investigators presented in July at the 14th International Workshop on Comorbidities and Adverse Drug Reactions in HIV, held in Washington, DC. The study’s presenter, Anne Monroe, MD, MPH, explained that if health care providers relied solely on “total” testosterone levels to diagnose hypogonadism in men living with HIV, they would miss roughly 30 percent of the cases.

Male hypogonadism can contribute to weight loss, fatigue, bone mineral decreases, mood changes and dwindling libido. The condition is common among men living with HIV, including those taking antiretrovirals. According to Monroe, prevalence rates vary considerably, from as low as 20 percent in some studies to as high as 70 percent in others.

“The cause of low testosterone in HIV-infected men is multifactorial,” Monroe explained, “and may be related to poor clinical or nutritional status, certain prescription or illicit drugs such as methadone and opiates, pituitary dysfunction, [chronic hepatitis C virus infection], body composition changes and increasing age.”

To diagnose hypogonadism, the Endocrine Society recommends morning tests to determine the total amount of testosterone in a deciliter of blood. The problem is that, compared with HIV-negative men, men living with HIV have elevated sex-hormone binding globulin (SHBG), which can bind to testosterone and prevent it from working as it should. Therefore, Monroe explained, measuring the amount of free testosterone—testosterone that is not bound to any other chemicals—may more accurately diagnose hypogonadism in men living with HIV.

Monroe said that other groups have noted the importance of testing for free testosterone levels in men living with HIV, but that this recommendation hasn’t been readily incorporated into HIV clinical care guidelines. In turn, her group conducted a new study to determine the prevalence of hypogonadism among HIV-positive and HIV-negative men participating in the Multicenter AIDS Cohort Study (MACS). They also wanted to compare the use of total and free testosterone testing to diagnosis hypogonadism.

The analysis included 508 men—342 HIV-positive men and 166 HIV-negative men. The HIV-

negative men were older (51.6 versus 48.1 years old) and had higher body mass indexes (25.8 versus 25.2 kg/m2). About 67 percent were white, and roughly 10 percent had hepatitis C virus infection. Among the men living with HIV, the lowest-ever (nadir) average CD4 count was 268 cells; at the time of the study, the average CD4 count was 495 cells, and 29 percent had viral loads above 400 copies. Sixteen percent were not on HIV treatment at the time of the study.

Morning total testosterone levels averaged 650.4 nanograms (ng) per deciliter (ng/dL) among the HIV-negative men, compared with 627.8 ng/dL among the HIV-positive men—this difference was not statistically significant, meaning it was small enough to have occurred by chance. Free testosterone levels were, however, significantly higher among the HIV-negative men compared with those living with HIV: 107.3 picograms per milliliter (pg/mL) versus 100.6 pg/mL, respectively. Similarly, SHBG levels were also significantly higher among those living with HIV compared with the HIV-negative men.

More HIV-positive men had hypogonadism, defined as having a total testosterone level below 300 ng/dL or a free testosterone level below 48 pg/mL. This outcome was documented in 9.1 percent of the men living with HIV, compared with 7.2 percent of the HIV-negative men. This difference, however, was not statistically significant.

When Monroe and her colleagues included 70 men from the MACS who were receiving testosterone replacement therapy—presumably for hypogonadism—and therefore didn't qualify for the main analysis, 24.5 percent (101 of 412 HIV-positive men) were suspected of having hypogonadism.

Focusing specifically on the original 43 HIV-positive and HIV-negative men with hypogonadism, Monroe and her colleagues looked at those who had a normal testosterone level coupled with a low free testosterone level and compared them with those who had a low total testosterone level with either a low or normal free testosterone level.

"Among the HIV-infected hypogonadal men," Monroe said, "a full third [32.3 percent] of them had normal total testosterone, but low free testosterone," compared with none of the HIV-negative men. "This means that if total testosterone [was the only measurement] used for diagnosis, about one-third of hypogonadal men would have been missed."

Monroe's group then looked only at the 31 hypogonadal men living with HIV. "We wanted to explore characteristics of the men who had a normal total testosterone but low free testosterone, compared with the men who had a low total testosterone," she said, noting that "more men with normal total testosterone had hepatitis C" and, as expected, "their SHBG was much higher."

There was no difference by CD4 count status, viral load or antiretroviral therapy status.

"In conclusion," Monroe finished, "using [morning] total testosterone to diagnose hypogonadism in HIV-infected men will result in missing about 30 percent of the cases. Morning free testosterone should be measured in all HIV-infected men in whom hypogonadism is suspected," which, she

added, is particularly important among men coinfected with hepatitis C and HIV.
