Concerning “Effects of a supraphysiological dose of testosterone on physical function, fatigue, and mood in men with human immunodeficiency virus-associated weight loss”

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TO THE EDITOR: In their article on the effects of a supraphysiological dose of testosterone in HIV-infected patients with weight loss, Knapp et al. (6) found improvements in some parameters, such as fat-free mass, mood, fatigue, and certain quality of life measurements in treated compared with untreated control patients.

Inclusion criteria for the study were a weight loss of $\geq 5\%$ over the preceding 6 months or a body mass index of $< 20$ kg/m$^2$. However, the spectrum of weight loss has changed considerably since the introduction of combination antiretroviral therapy. In patients not treated with antiretroviral drugs, weight loss can be attributed to HIV wasting or HIV-associated opportunistic conditions in most cases.

On the other hand, the incidence of these conditions in patients receiving antiretroviral therapy has decreased substantially, whereas antiretroviral-related lipoatrophy, another cause of weight loss, occurs commonly (3–5, 9). Lipoatrophy is associated with other metabolic complications and represents a stigmatizing condition with a significant impact on the quality of life of the patients, for which no effective treatment exists. Even modification of the antiretroviral regimen responsible for lipoatrophy, usually thymidine analogs, has been associated with only modest improvements in this condition (4, 5, 10).

The authors state that patients with severe lipodystrophy were excluded from the study. However, it is not easy to differentiate weight loss due to lipoatrophy from HIV-related weight loss on clinical grounds, and in addition, lipopathic patients without severe signs of lipodystrophy did not seem to have been excluded from the study.

The authors also stated that $\sim 60\%$ of the patients received antiretroviral therapy, although this information was available only for a subset of patients. Therefore, at least two different causes, HIV related and antiretroviral related, were probably responsible for the weight loss of these patients, the latter due mainly to lipoatrophy as a consequence of the inhibition of the mitochondrial DNA polymerase gamma (2, 3, 8).

The beneficial effects of testosterone therapy in HIV-related weight loss are known (1, 7, 9), but its possible effects on antiretroviral-associated lipoatrophy are unclear (1, 5). The authors did not classify patients according to these two types of weight loss, despite their use of dual-energy X-ray absorptiometry (DEXA), which may be useful for this purpose. However, a rough approach to such a classification could be carried out considering the antiretroviral status of the patients: most untreated patients had presumably HIV-related weight loss, whereas in those who developed weight loss in the course of successful and sustained antiretroviral therapy the most common cause would presumably be lipoatrophy.

Therefore, it would be interesting to analyze separately the effects of testosterone vs. placebo in patients who had not received any antiretroviral therapy, and especially in those who developed weight loss during the course of such a therapy, to evaluate whether the improvements observed with exogenous testosterone in the overall cohort are similar or different in antiretroviral-treated and untreated patients.

REFERENCES