In an 18-month randomized placebo-controlled study of patients with human immunodeficiency virus (HIV) having abdominal fat accumulation and relative growth hormone (GH) deficiency, low-dose, long-term GH reduced visceral adipose tissue (VAT) but worsened glucose control. To investigate changes in VAT and other parameters after GH discontinuation, data from an extension in which participants crossed over from their initial treatment (months 0-18) to the opposite treatment (immediately after the month 18 visit through month 36) were analyzed.

**Methods.** Of 21 participants originally assigned to receive GH who finished initial treatment (months 0-18), 20 crossed over to receive placebo, 17 of whom (85%) completed the 36-month study. Of 27 participants originally assigned to placebo who finished initial treatment (months 0-18), 24 crossed over to receive GH, 20 of whom (83%) completed the study. Participants who dropped out were not different from completers. Patients but not researchers remained blinded to treatment status.

Determination of aggregate change for months 24, 30, and 36 vs initial baseline was performed as previously described for months 6, 12, and 18, using longitudinal mixed modeling and repeated-measures analysis of variance including all available data. All P values are 2-sided and P < .05 was significant. Power calculations were previously reported. Analyses were performed using SAS version 9.2 (SAS Institute, Cary, North Carolina).
North Carolina). The study was approved by the Massachusetts General Hospital institutional review board, and participants provided written informed consent.

Results. Among participants who received GH during the first 18-month period, VAT increased 9.3% (95% confidence interval [CI], 2.9%-15.8%) within 6 months of crossover to placebo (P = .007 vs 18 months) (FIGURE). The rebound in VAT after GH discontinuation (months 24, 30, and 36) was large, with an aggregate increase over initial baseline of 8.3% (95% CI, 0.6%-15.9%; P = .046), much larger than the small decrease in VAT seen among those who received placebo during months 0 through 18 (P = .008) (FIGURE). This result remained significant in sensitivity analyses controlling for age, sex, physical activity, and dietary intake.

After discontinuation of GH, insulin-like growth factor 1 (IGF-1) returned rapidly to initial baseline levels (FIGURE). For metabolic variables that had changed significantly with GH during the primary efficacy phase, the aggregate changes in triglyceride and diastolic blood pressure values after crossover to placebo were not significantly different from initial baseline. However, aggregate 2-hour glucose levels were significantly higher by 9.8% (95% CI, 0.6%-19.0%; P = .048) after crossover compared with initial baseline, suggesting residual adverse effects after GH discontinuation. A detailed table of all outcome data is available from the authors on request.

None of the patients switching to placebo changed antiretroviral class after GH discontinuation.

Comment. Low-dose GH for 18 months significantly reduced VAT, but after GH was discontinued, VAT rebounded rapidly to a level that was significantly above initial baseline values. Rapid rebounds in VAT were seen in studies of HIV-infected patients receiving much higher-dose GH, but this study is the first to investigate the withdrawal of long-term, low-dose GH in this population. The change in VAT was larger in participants receiving placebo after GH crossover than in those receiving placebo in the first half of the study, and thus likely represents more than the natural history of change in visceral fat among HIV patients.

Levels of IGF-1, which is responsible for certain actions of GH, were not lower than baseline after GH withdrawal, but further studies are necessary to determine whether low-dose GH reduces endogenous GH activity, accounting for the changes seen after GH discontinuation. The conclusions in this study are limited to low-dose GH, and HIV patients using higher doses of GH may experience different changes in VAT and glucose during and after GH discontinuation.

Growth hormone is not approved by the Food and Drug Administration for use to reduce visceral fat in HIV and may be associated with a deleterious rebound in visceral adiposity after discontinuation.

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CORRECTION
Unreported Potential Competing Interest: In the book review of Acute Care Surgery: A Guide for General Surgeons, published in the June 9, 2010, issue of JAMA (2010;303[22]:2299-2300), information about a potential competing interest should have been reported. On page 2300, after the Financial Disclosures section, the following information should have been included: “Additional Information: Dr Alam is a faculty member of the academic division in which Dr Velmahos, one of the 4 editors of the book he reviewed, is the division chief.”