TREATMENTS FOR WASTING IN PATIENTS WITH THE ACQUIRED IMMUNODEFICIENCY SYNDROME

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WASTING was an early identifying characteristic of human immunodeficiency virus (HIV) infection, originally termed “slim disease” in Africa.1 As defined by the Centers for Disease Control and Prevention (CDC), wasting in patients with the acquired immunodeficiency syndrome (AIDS) is the involuntary loss of more than 10 percent of base-line body weight in combination with diarrhea, weakness, or fever. Wasting is considered an AIDS-defining condition. However, there is considerable controversy about the appropriate definition of AIDS wasting (whether it should be defined as the loss of 5 or 10 percent of usual weight) and whether changes in body composition, rather than weight alone, better define the syndrome. For example, the initial characterization of AIDS wasting involved the disproportionate loss of lean body mass and muscle wasting in men3 (Fig. 1). Recent data suggest that women may lose relatively more fat than lean body mass4 and that changes in body composition may be related to the initial amount of body fat before weight loss in HIV-infected patients.5

Potential mechanisms of AIDS wasting include increased energy expenditure,6 decreased energy intake,7 inefficient use of energy substrate,8 and hormonal factors.9,10 AIDS wasting can lead to diminished functional capacity and death.11-13 Substantial progress has been made in the development of successful treatments for both men and women with AIDS wasting (Table 1).

BODY COMPOSITION
AND FUNCTIONAL CAPACITY

AIDS wasting was initially characterized in men as a decrease in body weight and lean body mass with relative sparing of fat.3 Although the quantification of weight loss is used most often to characterize wasting in a given patient, the assessment of body composition may be a valuable adjunct (Table 2).36 In this regard, body cell mass, a component of lean body mass that represents metabolically active lean tissue, exclusive of extracellular water and nonfat intercellular connective tissue, is a particularly useful index of wasting but is not usually available.

Wasting may be mild (loss of up to 5 percent of body weight), moderate (6 to 10 percent), or severe (more than 10 percent). The intensity of therapy can be adjusted according to the severity of wasting. Substantial loss of body cell mass and lean body mass may occur early in the course of HIV disease,36 at 95 percent of normal body weight,37 suggesting the need to consider treatments for wasting. Although the specific cellular mechanism for the loss of lean body mass is not known, the rate of muscle-protein synthesis is low among men with AIDS wasting.38 Recent data suggest that the change in body composition may be a function of base-line body composition, with men who have relatively high levels of adiposity losing more fat and less lean body mass than men with lower levels of adiposity.5 In women, a disproportionate loss of body fat occurs at all stages of the wasting syndrome, but substantial depletion of lean body mass occurs in women with advanced HIV disease and a body weight that is less than 90 percent of ideal weight.4

Diminished functional capacity is an important consequence of decreased lean body mass in patients with AIDS wasting. In a study of men with AIDS wasting (mean weight loss, 15 percent), muscle wasting was demonstrated by a reduced cross-sectional area of the quadriceps muscle, and the muscle area was highly predictive of the strength and functional capacity of the leg muscles13 (Fig. 2), suggesting a rationale for treatments to increase muscle mass in such patients.

EFFECTS OF HIGHLY ACTIVE ANTIRETROVIRAL THERAPY ON WASTING

Highly active antiretroviral therapy is a potentially important treatment for AIDS wasting.39 Before such therapy was available, two thirds of men with
AIDS weighed less than 90 percent of their ideal body weight or lost more than 10 percent of their usual weight. Weight loss and malnutrition may be less severe in patients receiving the potent new antiretroviral drugs, an effect that is concomitant with an improvement in immune function. Several factors, however, may limit the efficacy of highly active antiretroviral therapy as a treatment for AIDS wasting. First, loss of body cell mass occurs even in patients who are receiving protease inhibitors. Second, some patients in whom antiretroviral therapy results in an undetectable viral load have relapses because of the development of resistance or the inability to comply with a complicated medical regimen. Finally, highly active antiretroviral therapy may be associated with weight gain and redistribution of fat in a dorsocervical pattern (Fig. 3) and a truncal pattern, with no change in lean body mass. The mechanism of fat redistribution is not known and may be unrelated to antiretroviral therapy. The potential long-term consequences of the accumulation of visceral fat in HIV-infected patients are unknown.

**NUTRITIONAL SUPPLEMENTS AND APPETITE-STIMULATING DRUGS**

An important initial approach to the treatment of patients with AIDS wasting is to ensure that the caloric intake is adequate to meet the high metabolic demands associated with the infection. Energy ex-
penditure at rest is moderately increased in ambulatory HIV-infected men and women who are in stable condition and is further increased during secondary infection.\textsuperscript{50,51} The mechanism of increased energy expenditure during secondary infection is unknown, but it may be related to the effects of inflammatory cytokines on energy metabolism.\textsuperscript{51} Inadequate caloric intake in patients with increased energy expenditure is thought to contribute to the energy imbalance and wasting during opportunistic infection.\textsuperscript{7}

Nutritionally based strategies have been developed to restore the energy balance in patients with AIDS wasting. In a two-month, randomized comparison of total parenteral nutrition with dietary counseling in severely malnourished men who had lost more than 10 percent of their usual weight and who had concomitant diarrhea, weight increased by a mean of 8 kg in the parenteral-nutrition group and decreased by a mean of 3 kg in the dietary-counseling group (P<0.001 for the comparison between the two groups).\textsuperscript{52} Similarly, the administration of total parenteral nutrition for 4 to 42 weeks increased body cell mass in a study of men with AIDS wasting and malabsorption or gastrointestinal disease.\textsuperscript{53} In contrast, men with AIDS wasting and secondary infection, but without obvious malabsorption, continued to lose body cell mass despite treatment with total parenteral nutrition.\textsuperscript{53} A reduced ability to gain lean body mass despite adequate nutritional intake is thought to contribute to wasting in some HIV-infected patients. In addition, nutritional supplements may be useful in patients with AIDS wasting. In a preliminary 12-week study, patients with AIDS wasting who received glutamine (40 mg per day given orally) had an increase in mean body cell mass (1.7 kg, as compared with 0.4 kg in the placebo group; P<0.01 for the comparison between groups) but did not gain weight.\textsuperscript{15}

**Megestrol Acetate**

Of the appetite-stimulating drugs used to treat patients with AIDS wasting, megestrol acetate, a synthetic progesterational steroid, has been studied most extensively. In a 12-week randomized, placebo-controlled study of treatment with megestrol acetate (100 mg, 400 mg, or 800 mg per day given orally) in 271 patients with AIDS wasting (defined by a body weight that was less than 90 percent of ideal, with a loss of more than 20 percent of usual weight), the patients who received the 800-mg dose of megestrol acetate had a significantly larger mean increase in caloric intake than the placebo group (646 kcal per day, as compared with a decrease of 107 kcal per day in the placebo group; P=0.001 for the comparison between the two groups), with a weight gain of 3.5 kg as compared with a weight loss of 0.7 kg in the placebo group (P<0.001 for the comparison between the two groups).\textsuperscript{17} Furthermore, the overall quality of life improved in association with increased weight. In a 12-week randomized study of 100 patients with AIDS wasting, megestrol acetate (800 mg a day) resulted in a mean weight gain of 4.2 kg as compared with a loss of 0.6 kg in the placebo group (P<0.001 for the comparison between the two groups), but the increase in caloric intake was not sustained after eight weeks.\textsuperscript{18} In addition, both studies were performed mainly in men, and the weight gained in response to treatment with megestrol acetate was attributed primarily to increased fat mass.

Megestrol acetate has several side effects. It has

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**Table 2. Methods Routinely Available to Assess Lean Body Mass.**

<table>
<thead>
<tr>
<th>Method</th>
<th>Description</th>
<th>Radiation Involved</th>
<th>Advantages</th>
<th>Disadvantages</th>
<th>Precision (Coefficient of Variation)</th>
<th>Cost*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Measurement of skin-fold thickness</td>
<td>Thickness of subcutaneous adipose tissue is measured as an indication of fat and fat-free mass</td>
<td>No</td>
<td>Easily performed with portable equipment</td>
<td>Possibility of error and interobserver variability in measurement</td>
<td>5–10%</td>
<td>$5</td>
</tr>
<tr>
<td>Bioimpedance analysis</td>
<td>Low-level current is introduced, and measurements of impedance are used to calculate fat and fat-free mass</td>
<td>No</td>
<td>Easily performed with portable equipment, used to calculate body cell mass</td>
<td>Results may be affected by hydration</td>
<td>&lt;5%</td>
<td>NA</td>
</tr>
<tr>
<td>Dual x-ray absorptiometry</td>
<td>Soft-tissue attenuation of low-level radiation source is used to determine bone, fat, and lean body mass</td>
<td>Yes (&lt;5 mrem)</td>
<td>Noninvasive, takes 20–30 min to complete, negligible amount of radiation</td>
<td>Results may be affected by hydration; regional measurements not standardized</td>
<td>3%</td>
<td>$150†</td>
</tr>
</tbody>
</table>

*NA denotes not available.
†This cost corresponds to the current Medicare reimbursement rate. The actual cost may differ.
glucocorticoid activity and can therefore induce or exacerbate diabetes mellitus and cause Cushing’s syndrome. Because megestrol acetate decreases corticotropin secretion, adrenal insufficiency may occur if it is discontinued abruptly after long-term use. Furthermore, megestrol acetate decreases gonadotropin secretion and can therefore cause hypogonadism, which may explain, in part, its effects on fat mass in men with AIDS wasting.

Dronabinol

Dronabinol (delta-9-tetrahydrocannabinol) is approved for the treatment of anorexia in patients with AIDS. Treatment with dronabinol stimulates appetite, but weight gain is minimal. In a 12-week study comparing dronabinol (2.5 mg given orally twice a day) and megestrol acetate (750 mg per day) in patients with AIDS wasting (defined by a body-mass index [the weight in kilograms divided by the square
of the height in meters) of less than 20.5 or loss of more than 10 percent of usual weight), the patients receiving dronabinol had a mean weight loss of 2.0 kg, whereas those receiving megestrol acetate had a mean weight gain of 6.5 kg (P<0.001 for the comparison between the two groups).

TESTOSTERONE AND TESTOSTERONE ANALOGUES

Testosterone deficiency may contribute to wasting in both men and women with HIV infection. In early studies, approximately 50 percent of men with AIDS as defined by the CDC had hypogonadism. However, the prevalence of hypogonadism may be lower now, because HIV-infected patients receiving highly active antiretroviral therapy are healthier. Hypogonadism in HIV-infected men is most often due to the effects of undernutrition, chronic illness, or medications, such as megestrol acetate, on gonadotropin secretion. However, 25 percent of HIV-infected men with hypogonadism have primary hypogonadism. It is most often idiopathic but may be due to opportunistic infection, malignant infiltration of the testes, or the testicular effects of HIV infection or medications.

Hypogonadism in HIV-infected men causes muscle wasting. In one study of men with hypogonadism and AIDS wasting, muscle mass was 75 percent of the predicted value according to height, whereas weight was 92 percent of the predicted value — findings consistent with a preferential loss of muscle mass. In addition, hypogonadism may contribute to fatigue and decreased muscle strength in men with AIDS.

In a randomized, placebo-controlled study of treatment with testosterone (300 mg given intramuscularly every three weeks for six months) in men with hypogonadism (defined as a serum free testosterone concentration below the lower limit of the normal range) and AIDS wasting (mean weight loss, 18 percent), the men who received testosterone had a mean increase of 2.0 kg in lean body mass, whereas those who received placebo had a mean loss of 0.6 kg (P<0.05 for the comparison between the two groups) (Fig. 4). Treatment with testosterone was not associated with a change in weight or exercise capacity, but it did result in an improvement in the quality of life and had no side effects. Continuation of testosterone treatment for a total of 12 months resulted in a mean net increase of 3.7 kg in lean body mass (76 percent) as compared with the base-line value (P<0.05) and an increase in the hematocrit of 3.5 percent (P<0.01), and it was well tolerated.

In a randomized, placebo-controlled study of transdermal testosterone therapy (5 mg per day for three months) in ambulatory HIV-infected men with hypogonadism, lean body mass increased by a mean of 1.4 kg in the testosterone-treated men (P<0.05 for the comparison with the base-line value), but by only 0.2 kg in the men given placebo. In a study of relatively androgen-deficient men with 5 percent weight loss, testosterone given in a dose of 200 mg intramuscularly every two weeks increased well-being but not weight. Therefore, in men with AIDS wasting and hypogonadism, testosterone treatment is indicated to increase lean body mass and to improve the quality of life. This treatment is not currently indicated in men who have AIDS wasting without hypogonadism.

Synthetic testosterone analogues, including oxandrolone and nandrolone, have also been studied in men with AIDS wasting. In a randomized, dose-ranging study of the oral administration of oxandrolone (15 mg per day for 16 weeks) in men with AIDS wasting (defined as loss of more than 10 percent of usual weight), there was a mean weight gain after 14 weeks of 1.8 kg in the men who received oxandrolone as compared with 0.7 kg in those who received placebo (P<0.05 for the comparison between the two groups), but body composition was not determined. In contrast, the administration of a lower dose (5 mg daily) was not associated with weight gain. In a 12-month open-label study of oxandrolone (20 mg per day given orally) in HIV-infected men with weight loss (the degree was unspecified), weight was increased by a mean of 5.2 kg (P<0.01 as compared with the base-line value) and body cell mass by 3.5 kg (P<0.05 as compared with the base-line value).

In a 16-week open-label study of nandrolone de-
canoate, a synthetic, injectable testosterone analogue, a dose of 100 mg given intramuscularly every two weeks resulted in a mean weight gain of 2.3 kg (P<0.05 as compared with the base-line value) and an increase in lean body mass of 3.0 kg (P<0.01 as compared with the base-line value) in HIV-infected men who had lost 5 to 15 percent of their body weight.25 These steroids can cause liver dysfunction,64 and although they may result in an increase in weight and lean body mass in men with AIDS wasting, they are no more effective than testosterone. Therefore, testosterone rather than testosterone analogues should be used as therapy for hypogonadism in HIV-infected men.

Androgen deficiency also occurs in HIV-infected women.4,65 In a cross-sectional study of 43 HIV-infected women, serum free testosterone concentrations were below the lower limit of the normal range for sex and age in more than half the women with wasting.4 The effect of testosterone administration in androgen-deficient women with AIDS wasting has rarely been studied, because of concern about its safety. In a recent pilot study, transdermal administration of two doses of testosterone for 12 weeks (estimated delivery rates, 150 and 300 µg per day) was found to be a safe and effective means of increasing serum testosterone concentrations in HIV-infected women, without causing virilization, hirsutism, or changes in serum lipid concentrations or immunologic function.66 The lower, but not the higher, dose of testosterone resulted in normal serum testosterone concentrations, a mean weight gain of 1.9 kg as compared with 0.6 kg in the placebo group (P<0.05 for the comparison between the two groups), and an improvement in the quality of life. In contrast to the findings in studies of men with AIDS wasting, the weight gained during testosterone administration in women was primarily fat. Because HIV-infected women with AIDS wasting are depleted of fat, fat repletion may be beneficial.5,67

**GROWTH HORMONE**

Recombinant human growth hormone is another potential anabolic treatment for patients with AIDS wasting. Limited data suggest that these patients have resistance to the action of growth hormone, which is probably related to undernutrition, as demonstrated by high serum growth hormone concentrations and low serum insulin-like growth factor I concentrations.9,68 The administration of growth hormone increases lean body mass and protein synthesis and reduces urinary nitrogen excretion in pa-

![Figure 4. Mean (±SE) Changes in Body Composition in Men with AIDS Wasting and Hypogonadism Who Received Testosterone (300 mg Intramuscularly Every Three Weeks) or Placebo for Six Months.](image-url)

Fat-free mass was determined by dual-energy x-ray absorptiometry, lean body mass was calculated on the basis of total body potassium, and muscle mass was calculated on the basis of urinary creatinine excretion. The P values are for the difference in the change from base-line values between the testosterone group and the placebo group, calculated by analysis of covariance. The numbers in parentheses are the numbers of men for whom data were available both at base line and at the end of the study. Adapted from Grinspoon et al.21 with the permission of the publisher.

- **Testosterone**
  - Fat-free Mass: N=21
  - Lean Body Mass: N=22
  - Muscle Mass: N=21

- **Placebo**
  - Fat-free Mass: N=19
  - Lean Body Mass: N=19
  - Muscle Mass: N=18

**Figure 4**
patients with acquired growth hormone deficiency or conditions associated with catabolic states, including critical illness, burns, and sepsis.69-71

In a seven-day, open-label study of growth hormone (0.1 mg per kilogram of body weight per day given subcutaneously) in men with AIDS wasting (mean weight loss, 19 percent), weight increased by a mean of 2.0 kg (P<0.001 for the comparison with baseline values).9 Although the weight increase was highly correlated with the increase in total body water, urinary nitrogen excretion decreased, suggesting that growth hormone had a true anabolic effect on protein metabolism. In an open-label study of 2.5 or 5.0 mg of growth hormone administered subcutaneously every other day for three months in men with AIDS wasting, only the higher dose resulted in increases in weight (3.2 kg), lean body mass (3.8 kg), and total body water (2.5 kg) (P<0.05 for all three comparisons with baseline values).72 The doses used in these studies are significantly higher than those required for replacement therapy in patients with growth hormone deficiency, again suggesting a resistance to growth hormone.69

In a randomized, placebo-controlled trial of growth hormone (0.1 mg per kilogram per day given subcutaneously for 12 weeks, with an average dose of 6 mg per day) involving 178 patients with AIDS wasting (mean body weight, 87 percent of ideal weight), the growth hormone–treated patients gained weight (mean gain, 1.6 kg, vs. 0.1 kg in the placebo group; P=0.01 for the comparison between the two groups) and lean body mass (3.0 kg, vs. 0.1 kg in the placebo group; P<0.001) and lost fat (a decrease of 1.7 kg, vs. an increase of 0.3 kg in the placebo group; P<0.001) (Fig. 5).27 Total body water and intracellular water increased in the growth hormone–treated patients, but the hydration coefficient (the ratio of total body water to lean body mass) remained unchanged. In addition, treadmill performance increased significantly in the growth hormone–treated patients as compared with the patients given placebo. Although a small portion of the increased work output was a direct function of increased weight in the patients treated with growth hormone, the increase in exercise capacity was larger than the expected increase from weight gain. Common side effects were edema, arthralgias, and myalgias, resulting in dose reductions in 15 patients, as well as increased blood glucose concentrations and glycosylated hemoglobin values. The carpal tunnel syndrome developed in three patients.

Other studies have evaluated lower doses of growth hormone given in combination with insulin-like growth factor I. In a randomized, placebo-controlled study of combined treatment with growth hormone (0.34 mg given subcutaneously twice a day for 12 weeks) and insulin-like growth factor I (5 mg given subcutaneously twice a day) in patients with AIDS wasting (defined as a loss of more than 10 percent of usual weight), weight, muscle strength, and endurance did not increase, despite a significant increase in the concentration of serum insulin-like growth factor I.73 In a similar 12-week randomized, placebo-controlled study, patients receiving 1.4 mg of growth
hormone daily and 5 mg of insulin-like growth factor I subcutaneously twice a day had a sustained mean increase of 3.2 kg in lean body mass (P<0.01 for the comparison with the base-line value) but without a significant change in weight or quality-of-life scores. In addition, total body water increased significantly in the combined-treatment group, whereas muscle strength decreased.

Taken together, these data suggest that high-dose growth hormone may be of value in the treatment of patients with AIDS wasting but that the addition of insulin-like growth factor I provides no further benefit. The long-term safety and tolerability of growth hormone therapy, however, remain unknown. Other potential uses of growth hormone that have not been approved by the Food and Drug Administration—for example, to prevent wasting during acute opportunistic infection and to reduce fat accumulation in patients with the lipodystrophy syndrome—have not yet been adequately studied and may have adverse effects, such as hyperglycemia, especially in patients receiving protease inhibitors.

**EXERCISE**

Supervised exercise training is a potentially promising anabolic strategy for patients with AIDS wasting. In a controlled study of 24 ambulatory men with AIDS who were recovering from pneumocystis pneumonia, progressive resistance training three times a week for six weeks increased muscle function in the arms and legs (P<0.01 for the comparison with the control group) and weight (+1.7 kg vs. −1.9 kg, P<0.001). Similarly, a controlled study of 12 weeks of bicycle exercise and strength training (three sessions per week) in HIV-seropositive men resulted in significant increases in muscle strength in the arms and legs in association with an improvement in cardiorespiratory fitness. In addition, an eight-week program of progressive exercise for HIV-infected patients resulted in increases in strength and lean body mass (mean gain, 2.1 kg; P<0.001 for the comparison with the base-line value). These results suggest that a supervised program of progressive resistance and fitness training increases muscle strength and lean body mass in HIV-infected patients. However, weight loss was not a specific criterion for enrollment in these studies, and the effects of exercise in patients with AIDS wasting remain unknown.

**CYTOKINE MODULATION**

A potential strategy in the treatment of patients with AIDS wasting is the administration of cytokine modulators such as thalidomide or pentoxifylline. Although the role of inflammatory cytokines in AIDS wasting is not well established, preliminary data suggest the presence of increased serum concentrations of tumor necrosis factor during periods of acute illness and secondary infection. Increased production of cytokines may contribute to the increase in energy expenditure and wasting, but this hypothesis remains to be proved.

In an eight-week, open-label study of patients with AIDS, as defined by the CDC, the administration of pentoxifylline (400 mg given orally three times a day) decreased tumor necrosis factor messenger RNA in peripheral blood mononuclear cells from 10 of 16 patients (P=0.02 for the comparison with base-line values) but was associated with decreased weight (median loss, 1.4 kg; P=0.001). The administration of thalidomide (300 mg given orally once a day for 21 days) in men with AIDS wasting decreased serum tumor necrosis factor concentrations in the men who had tuberculosis but did not alter the concentrations in those without tuberculosis. In an open-label study of thalidomide given in a dose of 200 mg a day for 14 days in 13 HIV-infected men without wasting, weight increased by a mean of 3.1 percent (a gain of 2.7 kg over the base-line value, P<0.01), and there was a trend toward increased body cell mass, as well as extracellular fluid, and a significant decrease in urinary nitrogen excretion. Serum tumor necrosis factor concentrations tended to increase in the patients in this study and also in patients with advanced HIV disease and aphthous ulcers who received 200 mg of thalidomide a day in a four-week, placebo-controlled study.

In a placebo-controlled, 12-week study involving 28 patients with AIDS wasting, thalidomide given in a dose of 100 mg four times daily resulted in a significant increase in median weight (4.1 kg [P<0.01 for the comparison with the base-line value]), whereas the placebo group had a loss of 1.3 kg), but 11 patients receiving thalidomide reported somnolence and a similar number reported rash, which was life-threatening in 1 patient. The viral load and CD4 count did not change. The mechanism of action of thalidomide as an anabolic agent in patients with AIDS wasting is unknown, as is the long-term efficacy of such treatment. Thalidomide is contraindicated in women who could become pregnant, because of its teratogenic actions, and is not currently approved for the treatment of AIDS wasting.

**TREATMENT RECOMMENDATIONS**

A nutritional evaluation is recommended for all patients with AIDS wasting to ensure that the intake of protein, fat, and carbohydrates is adequate and that they are receiving the recommended daily allowances of essential vitamins and minerals. Evaluation for underlying opportunistic infection and for cancer and gastrointestinal disease is important in all such patients. Appetite-stimulating drugs should be reserved for patients with weight loss and reduced food intake; such drugs tend to increase fat but not lean body mass. Specific nutritional supplements may be useful to increase lean body mass in patients with AIDS wasting, but such treatment remains experimental.
Screening for hypogonadism is also a reasonable early step in the evaluation of men with AIDS wasting, and testosterone therapy should be initiated if androgen deficiency is confirmed (on the basis of the age-adjusted reference range for serum free testosterone). Treatment with testosterone (either intramuscular administration of testosterone esters or transdermal preparations), not synthetic testosterone analogues, is the therapy of choice in men with AIDS wasting and androgen deficiency. Oral testosterone preparations may have hepatotoxic effects and should therefore not be used. Long-term testosterone therapy has a sustained benefit, but gonadal function should be reassessed after one year of therapy, if body weight remains stable. Monitoring of the prostate is also necessary in patients receiving long-term testosterone therapy, particularly those who are over 50 years of age, with rectal examinations every year and measurements of serum prostate-specific antigen three to six months after the initiation of therapy and yearly thereafter. In men with AIDS wasting who do not have hypogonadism, anabolic steroids such as oxandrolone may increase lean body mass, but the long-term safety and efficacy of such treatment are not known; these compounds should be used cautiously, if at all, in patients with liver disease. The administration of androgen in women must still be considered experimental.

Although high-dose growth hormone (0.1 mg per kilogram per day) is now approved for short-term administration and may be useful for reducing nitrogen loss and building lean body mass in patients with AIDS wasting, careful monitoring for side effects is important. Given the high cost and reported side effects of growth hormone therapy at the doses required to treat the resistance to growth hormone that characterizes this disease, it is best reserved for patients with severe weight loss in whom other therapies are ineffective. Routine administration of growth hormone in patients with minimal-to-moderate weight loss is not recommended.

In addition, exercise may be beneficial if it is appropriately supervised, but there are insufficient data to recommend the routine use of exercise therapy for patients with AIDS wasting. Cytokine modulators are not currently approved for AIDS wasting and should be viewed as experimental.

CONCLUSIONS

Treatment with nutritional agents, testosterone or testosterone analogues, growth hormone, and exercise, when used selectively and appropriately, may induce weight gain and increase lean body mass in patients with AIDS wasting. The increasing use of highly active antiretroviral therapy will probably reduce but not eradicate wasting associated with HIV disease. Preliminary data suggest that antiretroviral therapy is not associated with increased lean body mass but may be associated with deleterious fat redistribution in some patients. Future research should focus on the development of treatments for women and long-term strategies that increase the functional status of both men and women with AIDS wasting.

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