

# Is There a Role for Androgenic Anabolic Steroids in Medical Practice?

Adrian Sandra Dobs, MD, MHS

**A**NDROGENIC ANABOLIC STEROIDS (AASs) HAVE BEEN touted as either a poison or a panacea. Members of the lay community, particularly athletes, have long claimed that the anabolic steroids have muscle-building potential that results in improved physical functioning. The medical community has countered that these drugs are dangerous and are associated with multiple adverse effects. At long last, some quality clinical research is being done to determine whether AASs have any legitimate role in medical therapeutics and, if so, in which patient populations.

Anabolic steroids have been used by the medical community in rare situations. For instance, in the 1960s before recombinant human growth hormone became available, oxandrolone was used to treat short stature in Turner syndrome.<sup>1</sup> Most studies of boys and girls with short stature or delayed puberty showed growth acceleration but no increase in final height.<sup>2,3</sup> Therefore, although recombinant human growth hormone is expensive and needs to be taken as a subcutaneous injection, it is unlikely that anabolic steroids will replace growth hormone in treating short stature.

A more relevant question is whether AASs have a role in treating specific disease states and, if so, in whom and when. There is some suggestion that body composition affects health outcomes. For example, just as excessive abdominal obesity is a strong cardiovascular risk factor, loss of lean body mass also may have importance as a prognostic risk factor. Best studied in human immunodeficiency virus (HIV)-associated wasting syndromes, loss of lean body mass is a strong predictor of increased mortality.<sup>4</sup> Several studies have shown that when hypogonadism occurs in conjunction with weight loss in patients with HIV infection,<sup>5</sup> treatment with testosterone<sup>6,7</sup> or oxandrolone<sup>8</sup> results in increased lean body mass. Although it has not been definitively proved, maintaining or increasing lean body mass may be beneficial for long-term survival in HIV-infected individuals.

Clinicians caring for cachectic patients will agree that it is important to maintain energy intake during illness, not just to maintain weight but to maintain lean muscle mass, although how lean body mass provides protection is not yet

clear. It may be a direct effect whereby muscle mass improves the effectiveness of chemotherapy or antiviral agents; or it could be a surrogate marker for weight or other factors known to affect survival.

In this issue of THE JOURNAL, Strawford et al<sup>9</sup> show the importance of AASs in treating HIV-associated wasting and Johansen et al<sup>10</sup> report on the benefits of using AASs in patients with chronic renal failure. These studies join others that have shown the merits of AASs in chronically ill patients who have lost body mass, including patients with cirrhosis,<sup>11</sup> pulmonary disease,<sup>12,13</sup> and burns.<sup>14</sup> Strawford et al recruited 24 eugonadal men with HIV infection who had lost a mean of 9% of their baseline weight. Volunteers whose therapy included a combination of exercise and testosterone were randomized to take either oxandrolone or placebo. The addition of oral oxandrolone, 20 mg/d, provided some additional benefit over exercise alone in increasing nitrogen retention, lean body mass, weight, and muscle strength. This is an intriguing study design because all participants had normal serum testosterone levels prior to randomization and all were administered low-dose testosterone to prevent the decline in this hormone that often occurs when AASs are used alone.

However, it is not clear that the administration of “physiologic testosterone replacement” to both groups was necessary. Serum testosterone levels after treatment with only testosterone were not statistically significantly different from the pretreatment values, yet it did result in suppression of serum gonadotropin levels, suggesting supraphysiologic androgen replacement. Therefore, the study may have compared 2 levels of AASs, rather than comparing oxandrolone with physiologic androgen concentrations.

Johansen et al<sup>10</sup> took a slightly different tack by enrolling malnourished men and women, not necessarily those who had lost weight, and randomized them to receive intramuscular nandrolone or placebo. Although the increase in weight was similar between groups, subjects treated with nandrolone had a significant increase in lean body mass and in serum creatinine levels. Functional status was improved as tested by walking and stair climbing. Such data are po-

See also pp 1275 and 1282.

**Author Affiliation:** Department of Medicine, The Johns Hopkins University School of Medicine, Baltimore, Md.

**Corresponding Author and Reprints:** Adrian Sandra Dobs, MD, MHS, Department of Medicine, The Johns Hopkins University School of Medicine, Baltimore, MD 21287-4906 (e-mail: adobs@jhu.edu).

tentially important for an increasingly large patient population whose quality of life is often low. As expected, serum testosterone levels decreased in the group treated with steroids due to suppression of luteinizing hormone and follicle-stimulating hormone levels. Although the authors note that patients in the actively treated group reported reductions in fatigue, they did not report on sexual function. Moreover, 3 of the women also developed amenorrhea and acne.

Both studies are limited by absence of an exercise treatment arm alone. Exercise is associated with an increase in muscle mass and, except for sports-related injuries, is clearly the safest and least expensive approach to prevent muscle wasting. Also, the important distinction between anabolic and androgenic effect was not fully explored in either study.

Before AASs can be adopted in clinical practice, additional studies are necessary. Among the key issues that need investigation are (1) to understand the effect of lean body mass on disease progression in different disease states and to determine whether augmenting lean body mass changes the prognosis; (2) to evaluate the long-term safety of AASs; (3) to define which patients might benefit most from AASs, ie, those with advanced illness vs those with milder disease; (4) to determine whether AASs are best used intermittently or as a continuous low dose; and (5) to identify the anabolic drug of choice, eg, testosterone enanthate or an oral androgen product. Knowing that there is only 1 androgen receptor,<sup>15,16</sup> clinicians and researchers need a better understanding of the differences between androgenic and anabolic effects of AASs, especially if these drugs are to be used in women.

Moreover, reports of complications associated with use of AASs as performance enhancing drugs among athletes may represent an important warning. Even though the incidence of these complications is unclear since the denominator of drug use in athletes is not well defined, the physiologic effects of virilization, irregular menses, and hirsutism in women and testicular atrophy and infertility in men are common.<sup>17</sup> Likewise, the risk of AAS-associated premature epiphyseal closure in teenaged users or reductions in serum high-density lipoprotein levels can have long-term consequences. Reports of cardiomyopathy,<sup>18</sup> hypercoagulation,<sup>19</sup> tendon tears, hepatocellular carcinoma,<sup>20</sup> psychiatric disorders, and sudden death<sup>21</sup> have been documented. Although these complications are unacceptable in a healthy population, they may be acceptable risks in selected patients with advanced illness and muscle wasting, especially if other measures have failed.

The results from the separate studies of Strawford et al and Johansen et al suggest a benefit of AASs in 2 different patient groups and are a promising addition to the growing body of knowledge on the therapeutic use of AASs in disease states. Nonetheless, at this time, it is still reasonable to take a conservative approach. Physicians need to be cogni-

zant of the important problem of muscle wasting and the contribution of reduced lean body mass to prognosis. Measures to maintain energy intake and to increase resistance exercises needed to increase body mass should be a routine part of clinical care. However, more data on greater numbers of subjects and for longer periods of exposure are necessary to define more clearly the role AASs may have in improving the functional status and prognosis in eugonadal patients with secondary wasting syndromes.

#### REFERENCES

- Marti-Henneberg C, Buuruabnen AK. Oxandrolone treatment of constitutional short stature in boys during adolescence: effect on linear growth, body age, pubic hair, and testicular development. *J Pediatr*. 1975;6:783-788.
- Bareille P, Massarano AA, Stanhope R. Final height outcome in girls with Turner syndrome treated with a combination of low dose oestrogen and oxandrolone. *Eur J Pediatr*. 1997;156:358-362.
- Rosenfeld RG, Frane J, Attie KM, et al. Six year results of a randomized prospective trial of human growth hormone and oxandrolone in Turner syndrome. *J Pediatr*. 1992;121:49-55.
- Kotler D, Tierney AR, Wang J, Pierson RN. Magnitude of body cell mass depletion and the timing of death from wasting in AIDS. *Am J Clin Nutr*. 1989;50:44-47.
- Dobs AS, Few WL III, Blackman MR, Harman SM, Hoover DR, Graham NMH. Serum hormones in men with HIV-associated wasting. *J Clin Endocrinol Metab*. 1996;81:4108-4112.
- Grinspoon S, Corcoran C, Askari H, et al. Effects of androgen administration in men with the AIDS wasting syndrome. *Ann Intern Med*. 1998;129:18-26.
- Bhasin S, Soror TW, Asbel-Seth N, et al. Effects of testosterone replacement with a nongenital transdermal system, androderm, in human immunodeficiency virus-infected men with low testosterone levels. *J Clin Endocrinol Metab*. 1998;83:3155-3162.
- Berger JR, Pall L, Hall CD, Simpson DM, Berry PS, Dudley R. Oxandrolone in AIDS-wasting myopathy. *AIDS*. 1996;10:1657-1662.
- Strawford A, Barbieri T, Van Loan M, et al. Resistance exercise and supraphysiologic androgen therapy in eugonadal men with HIV-related weight loss: a randomized controlled trial. *JAMA*. 1999;281:1282-1290.
- Johansen KL, Mulligan K, Schambelan M. Anabolic effects of nandrolone decanoate in patients receiving dialysis: a randomized controlled trial. *JAMA*. 1999;281:1275-1281.
- Meneshall CL, Moritz TE, Roselle GA, et al, for the Veterans Affairs Cooperative Study Group. 275. Protein energy malnutrition in severe alcoholic hepatitis: diagnosis and response to treatment. *JPN J Parenter Enteral Nutr*. 1995;19:258-265.
- Schols AM, Soeters PB, Mostert R, Plummers RJ, Wouters EF. Physiologic effects of nutritional support and anabolic steroids in patients with chronic obstructive pulmonary disease: a placebo-controlled randomized trial. *Am J Respir Crit Care Med*. 1995;152(4 pt 1):1268-1274.
- Ferreira IM, Verreschi IT, Nery LE, et al. The influence of 6 months of oral anabolic steroids on body mass and respiratory muscles in undernourished COPD patients. *Chest*. 1998;114:19-28.
- Demling RH, DeSanti I. Oxandrolone, an anabolic steroid, significantly increases the rate of weight gain in the recovery phase after major burns. *J Trauma*. 1997;43:42-51.
- Tilley WD, Marcelli M, Wilson JD, et al. Characterization and expression of a cDNA encoding androgen receptors. *Science*. 1989;86:327-331.
- Zhou ZX, Wong CI, Sar M, et al. The androgen receptor: an overview. *Recent Prog Horm Res*. 1994;49:249-274.
- MacIndoe JH, Perry PJ, Yates WR, Holman TL, Ellingrod VS, Scott SD. Testosterone suppression of the HPT axis. *J Invest Med*. 1997;45:441-447.
- Ferrera PC, Putnam DL, Verdile VP. Anabolic steroid use as the possible precipitant of dilated cardiomyopathy. *Cardiology*. 1997;88:218-220.
- Fisher M, Applyby M, Rittoo D, Cotter L. Myocardial infarction with extensive intracoronary thrombus induced by anabolic steroids. *Br J Clin Pract*. 1996;50:222-223.
- Kosaka A, Takahashi HJ, Yajima Y, et al. Hepatocellular carcinoma associated with anabolic steroid therapy: report of a case and review of the Japanese literature. *J Gastroenterol*. 1996;31:450-454.
- Dickerman RD, Schaller F, Prather I, McConathy WJ. Sudden cardiac death in a 20-year old bodybuilder using anabolic steroids. *Cardiology*. 1995;86:172-173.