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# Anabolic Effects of Nandrolone Decanoate in Patients Receiving Dialysis

## A Randomized Controlled Trial

Kirsten L. Johansen, MD

Kathleen Mulligan, PhD

Morris Schambelan, MD

**I**N THE UNITED STATES, THE AVERAGE life span of a patient entering a long-term dialysis program is less than half that of an age-matched control not receiving dialysis.<sup>1</sup> Although the cause of this discrepancy is probably multifactorial, both malnutrition and reduced muscle mass are common in dialysis patients<sup>2-6</sup> and have been shown to correlate with increased mortality.<sup>3,5-8</sup> Therapies designed to improve the nutritional status of dialysis patients might therefore be expected to improve outcome. Anabolic agents, such as human growth hormone, can improve nitrogen balance in patients undergoing dialysis and in other catabolic states.<sup>9-14</sup> Human growth hormone reduces urea generation and protein catabolic rate in long-term hemodialysis patients in short-term studies.<sup>12,13</sup> However, human growth hormone can exacerbate hyperglycemia in patients with diabetes, who represent a large percentage of malnourished hemodialysis patients. Moreover, human growth hormone is expensive and may have limited potential as a long-term treatment.

Anabolic steroids, such as nandrolone decanoate, might be expected to accomplish some of the same anabolic effects

See also pp 1282 and 1326.

**Context** Patients receiving dialysis commonly experience malnutrition, reduced muscle mass (sarcopenia), and fatigue for which no effective treatment has been identified. Anabolic steroids are known to increase muscle mass and strength in healthy individuals, but their effect on the sarcopenia and fatigue associated with long-term dialysis has not been evaluated.

**Objective** To assess the effects of an anabolic steroid, nandrolone decanoate, on lean body mass (LBM), functional status, and quality of life in dialysis patients.

**Design** Randomized, double-blind, placebo-controlled trial conducted between April 1996 and July 1997.

**Setting** Hospital-based outpatient dialysis unit.

**Patients** Twenty-nine patients undergoing dialysis for at least 3 months.

**Intervention** Nandrolone decanoate, 100 mg (n = 14), or placebo (n = 15) by intramuscular injection once a week for 6 months.

**Main Outcome Measures** Weight, LBM, fatigue, grip strength, walking and stair-climbing times, and treadmill performance after 3 and 6 months of treatment.

**Results** Lean body mass increased significantly in patients given nandrolone compared with patients given placebo (mean change [SD], +4.5 [2.3] kg;  $P < .001$  compared with baseline). This effect was significantly greater than the change in LBM in the placebo group (mean change [SD], +1.9 [1.6] kg;  $P = .003$  compared with baseline;  $P = .005$  compared with nandrolone group). Serum creatinine levels increased in the nandrolone group (+168 [203] mmol/L [1.9 {2.3} mg/dL];  $P = .02$ ) but not in the placebo group (-4.0 [177] mmol/L [0.04 {2.0} mg/dL];  $P = .95$ ), suggesting an increase in muscle mass. Time to complete the walking and stair-climbing test decreased from 36.5 to 32.7 seconds in the nandrolone group, while those in the placebo group increased from 38.7 to 42.1 seconds ( $P = .05$ ). Peak oxygen consumption increased in the individuals in the nandrolone group who performed treadmill tests, but not to a statistically significant degree. Grip strength did not change in either group.

**Conclusions** Treatment with nandrolone for 6 months resulted in a significant increase in LBM associated with functional improvement in patients undergoing dialysis.

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of human growth hormone without leading to hyperglycemia. Nandrolone and other anabolic steroids have been used by athletes to build muscle mass and enhance weight-lifting performance, and a recent placebo-controlled study showed that supraphysiologic dosages of testos-

**Author Affiliations:** Divisions of Nephrology (Dr Johansen) and Endocrinology (Drs Mulligan and Schambelan), Department of Medicine, San Francisco General Hospital, University of California, San Francisco.

**Corresponding Author and Reprints:** Kirsten L. Johansen, MD, Nephrology Section, Box 111J, San Francisco Veterans Affairs Medical Center, 4150 Clement St, San Francisco, CA 94121 (e-mail: johanse@itsa.ucsf.edu).

terone resulted in an increase in muscle mass and strength in normal subjects.<sup>15</sup> Although nandrolone was used previously to treat anemia associated with end-stage renal disease, no controlled trial has been performed to test for anabolic effects in dialysis patients. Furthermore, the widespread availability of recombinant human erythropoietin for the treatment of anemia associated with chronic renal failure has virtually eliminated the use of nandrolone in dialysis patients in the United States.

The present study was undertaken to determine whether a 6-month course of nandrolone could improve nutritional and functional status in patients undergoing dialysis, using a randomized, double-blind, placebo-controlled design. Changes in lean body mass (LBM) measured by dual-energy x-ray absorptiometry (DEXA), treadmill exercise performance, walking and stair-climbing tests, and several quality-of-life measures were compared in the groups receiving nandrolone and placebo.

## METHODS

### Study Subjects

All patients undergoing long-term dialysis at the San Francisco General Hospital Medical Center, San Francisco, Calif, between April 1996 and July 1997 were screened for possible study enrollment. Entry criteria included evidence of malnutrition by biochemical indexes or body composition measurements, or poor quality of life as assessed by questionnaire. Specifically, patients had to have 2 or more of the following to be considered malnourished: albumin level of less than 40 g/L, total cholesterol level of less than 3.88 mmol/L (150 mg/dL), transferrin level of less than 2 g/L, protein catabolic rate of less than 0.8 g/kg per day, predialysis serum urea nitrogen level of less than 21.4 mmol/L (60 mg/dL), or insulinlike growth factor 1 (IGF-1) level of less than 300 ng/mL. Patients were excluded if they had been receiving dialysis for fewer than 3 months or if they had other reasons for being in a catabolic state, such as human immunodeficiency virus (HIV) infection, known malignancy, corticosteroid treatment, surgery, or infection requiring in-

travenous antibiotics, within 3 months. Other exclusion criteria included participation in other studies or illicit drug use. All patients gave written informed consent for study participation and the protocol was approved by the Committee on Human Research at the University of California, San Francisco.

### Initial Evaluation

Study subjects underwent an initial evaluation in the General Clinical Research Center (GCRC) at San Francisco General Hospital that included a history taking and physical examination, measurements of body composition, tests of strength and endurance, and an assessment of physical performance and quality of life. Hemodialysis patients with edema had their dry weights adjusted until they were free of edema and had no orthostatic changes at the end of dialysis. Baseline measurements of indexes of nutritional status, including serum urea nitrogen, serum creatinine, albumin, total cholesterol, and transferrin levels, were performed by Spectra Laboratories, Fremont, Calif, and total and free testosterone, luteinizing hormone, follicle-stimulating hormone, and IGF-1 in the core laboratory of the GCRC using reagents purchased from Diagnostic Products Corp (Los Angeles, Calif) and Nichols Institute Diagnostics (IGF-1, San Juan Capistrano, Calif). Dialysis adequacy was assessed by Kt/V using single-pool kinetics (Quantitative Medical Systems, Emory, Calif).<sup>16</sup>

### Body Composition

Body weight was measured on an electronic scale (model 7101, Acme Medical Scale Co, San Leandro, Calif). Lean body mass and fat were measured by DEXA (Lunar model DPX, Madison, Wis). These measurements were made within 1 hour after hemodialysis or following drainage of peritoneal dialysis fluid. Patients wore only a hospital gown, underwear, and pajama bottoms that contained no snaps or other material that might interfere with attenuation. The same equipment was used for baseline, 3-month, and 6-month evaluations for all patients.

### Functional Testing

Patients without a history or symptoms of coronary artery disease or physical limitations to exercise underwent functional testing. A treadmill protocol that was designed for patients with limited ability to exercise was used.<sup>17</sup> Oxygen consumption ( $\text{VO}_2$ ) was measured continuously by indirect calorimetry using a Vmax 29 metabolic cart (Sensor-medics, Yorba Linda, Calif). Heart rate and blood pressure were monitored throughout the test, and the test was terminated when the patient expressed his or her inability to exercise further or when systolic blood pressure exceeded 240 mm Hg or diastolic blood pressure measured 120 mm Hg. Grip strength was measured using a handheld dynamometer (Lafayette Instrument Co, Lafayette, Ind). Each hand was tested 3 times and the highest value was recorded. A walking and stair-climbing test was performed in the 16 hemodialysis subjects who were enrolled after May 1996. Subjects were timed while walking a fixed distance at a normal pace and while climbing a flight of stairs at a normal pace, and the results were summed.

### Quality of Life

Quality of life was assessed by an instrument administered by personal interview. The questionnaire includes the Index of Overall Life Satisfaction,<sup>18</sup> as well as the eating dimension of the Sickness Impact Profile<sup>19</sup> and the fatigue and anger/hostility components of the Profile of Mood States.<sup>20</sup> In addition, questions were included about potential adverse effects of nandrolone treatment.

### Treatment

Subjects were randomly assigned to receive nandrolone decanoate, 100 mg/wk, by intramuscular injection or placebo injection of saline solution colored to resemble active study drug. Randomization was computer-generated in blocks of 4. Assignments were made sequentially by a research pharmacist who dispensed medications but was not otherwise involved in the study. Patients were given their injections at the di-

alysis unit by GCRC staff. Dialysis staff, patients, and investigators were blinded throughout the study to treatment assignment. Hematocrit and hemoglobin levels were measured monthly and erythropoietin dosages were adjusted to maintain hematocrit between 0.33 and 0.36. Monthly liver function tests were checked, and the dosage of study drug was reduced by half for any elevation of transaminases to more than 3 times the upper limit of normal. Dosages were also reduced for signs of virilization. After 3 and 6 months of treatment, patients returned to the GCRC for repeat testing of quality of life, body composition, functional performance, and hormone levels.

**Statistical Analyses**

Sample size was determined using change in LBM as the primary outcome measure and extrapolating expected changes and SDs from data in patients with HIV-associated wasting. The target sample size was 17 patients per group to detect a change in LBM of 2 kg with an SD of 2 kg, an  $\alpha$  level of .05, and a  $\beta$  level of .2. Comparisons between groups were made by unpaired *t* tests. Changes between baseline and follow-up variables within each group were compared with paired *t* tests. Univariate correlations were evaluated using Pearson regression analysis. Variables are reported as mean (SD) unless otherwise noted. Results were considered statistically significant at a 2-tailed  $P < .05$ . STATISTICA software (StatSoft Inc, Tulsa, Okla) was used for all analyses.

**RESULTS**

**Study Subjects**

All subjects who met the entry criteria were asked to participate. The most frequent reasons for ineligibility included recent access surgery or infection, inadequate length of dialysis treatment, infection with HIV, and inability to give consent. Six subjects who were otherwise eligible declined to participate in the study (FIGURE 1).

A total of 29 subjects were enrolled (TABLE 1). All subjects were either mal-

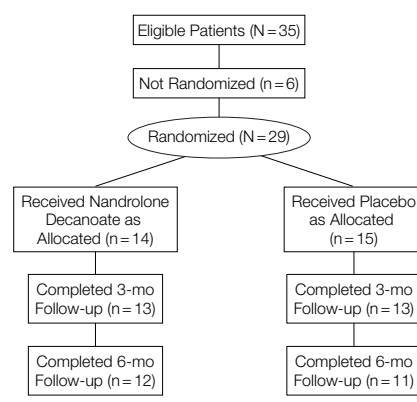
nourished (n = 20) or functionally impaired (n = 28) by study criteria and 19 met both criteria. Fourteen subjects received nandrolone and 15 received placebo injections. The treatment groups were quite similar, with no statistically significant differences in any of the parameters tested. The underlying cause of end-stage renal disease was diabetes in 11 subjects, hypertension in 9, nephrolithiasis and chronic pyelonephritis in 1, and unknown in the remaining 8. All but 1 subject required antihypertensive treatment at the time of study enrollment. A total of 6 women (2 premenopausal) were included in the study. Twenty-five subjects completed the 6-month protocol and 23 of these (12 in the nandrolone group and 11 in the placebo group) had all measurements made. Two subjects completed the study but were unable to have final measurements taken because of medical instability. Three subjects were withdrawn from the placebo group because of elevated transaminases (at 4 weeks), hematoma at the study drug injection site (at 3 months), and sudden death (at 4 months). One subject in the nandrolone group was withdrawn af-

ter developing unstable angina (at 3 weeks).

**Body Composition**

Changes in body composition are shown in FIGURE 2. By the end of the study, subjects who received nandrolone had gained 1.8 (2.3) kg of body weight ( $P = .03$  compared with baseline) and those given placebo had gained 1.4 (2.8) kg ( $P = .14$  compared with baseline). (These data do not include changes in body weight for 2 patients, 1 of whom had a

**Figure 1.** Flow Diagram of the Randomized Controlled Trial



**Table 1.** Baseline Characteristics of the Study Population\*

Characteristics	Total (N = 29)	Nandrolone Decanoate Group (n = 14)	Placebo Group (n = 15)
Hemodialysis/peritoneal dialysis	20/9	10/4	10/5
Age, y	47 (13)	44 (15)	50 (10)
Sex, male	23	11	12
Diabetes, No. (%)	11 (38)	5 (36)	6 (40)
Duration of ESRD, y	2.6 (2.3)	2.9 (2.7)	2.3 (2.0)
Hemodialysis, Kt/V	1.24 (0.25)	1.12 (0.09)	1.34 (0.29)
Weekly peritoneal dialysis, Kt/V	0.28 (0.02)	0.27 (0.02)	0.29 (0.03)
Residual renal function, mL/min	0.8 (1.2)	0.9 (1.1)	0.7 (1.3)
BMI, kg/m <sup>2</sup>	25.8 (6.6)	25.6 (3.8)	26.0 (8.5)
Serum albumin level, g/L	40 (5)	40 (4)	40 (5)
Serum urea nitrogen level, mg/dL†	67 (17)	66 (17)	69 (18)
Serum creatinine level, mg/dL†	12.7 (3.7)	13.0 (3.0)	12.5 (4.3)
Serum cholesterol level, mg/dL†	171 (39)	170 (49)	171 (29)
Transferrin level, g/L	2.19 (0.40)	2.15 (0.44)	2.23 (0.35)
IGF-1 level, ng/mL	270 (173)	306 (236)	239 (89)
nPCR, g/kg per day	1.09 (0.21)	1.06 (0.21)	1.12 (0.21)

\*Data are presented as mean (SD) unless otherwise specified. ESRD indicates end-stage renal disease; Kt/V, measure of dialysis dose; BMI, body mass index; IGF-1, insulinlike growth factor 1; and nPCR, normalized protein catabolic rate.

†To convert serum urea nitrogen, and cholesterol values to millimoles per liter, multiply by 0.357, and 0.02586, respectively. To convert creatinine to micromoles per liter, multiply by 88.4.

leg amputation and the other, a central venous stenosis resulting in massive arm edema. In these subjects, calculation of the changes in body composition excluded the affected limbs. Results are qualitatively similar if these 2 patients are excluded from the analysis.) Although there was no significant difference in the change in body weight between the groups, there were significant differences in the components of body composition. The nandrolone group gained 4.5 (2.3) kg of LBM ( $P < .001$ ) and lost 2.4 (2.9) kg of fat ( $P = .02$ ), while the placebo group gained 1.9 (1.6) kg of LBM ( $P = .003$ ) and lost 0.4 (2.5) kg of fat ( $P = .59$ ). The increases in LBM in the nandrolone group were significantly greater than in the placebo group after both 3 months ( $P = .05$ ) and 6 months ( $P = .005$ ) of treatment. Changes in body weight were almost exactly replicated by the combined changes in LBM and fat measured by DEXA ( $r = 0.94$ ;  $P < .001$ ; FIGURE 3).

The increase in LBM in the nandrolone group was accompanied by an increase in predialysis serum creatinine levels (168 [203] mmol/L [1.9 (2.3) mg/dL];  $P = .02$ ) whereas there was no significant change in serum creatinine levels in the placebo group (-4 [177] mmol/L [-0.04 (2.0) mg/dL];  $P = .95$ ). The change in serum creatinine levels correlated significantly with the change in LBM ( $r = 0.48$ ;  $P = .02$ ). There was

no significant change in Kt/V or predialysis serum urea nitrogen or correlation between either of these variables and the change in serum creatinine levels in the nandrolone group.

**Functional Status**

Fourteen subjects were able to undergo paired treadmill tests at baseline and 3 months and 11 subjects completed treadmill testing at baseline and after 6 months of treatment. Reasons for inability to undergo initial or follow-up treadmill testing included coronary artery disease (7 subjects); hospitalization at the time of planned evaluation (3 subjects); severe hypertension on the day of intended testing (2 subjects); study drop-out (2 subjects); and valvular heart disease, amputation, arthritis, abdominal hernia, and diabetic foot ulcer (1 subject each). TABLE 2 shows the exercise data. For all variables, the difference between the nandrolone and placebo groups was statistically significant at 3 months but not at 6 months. However, the difference at 3 months appeared to be due to both improvement in the nandrolone group and deterioration in the placebo group. There was no significant improvement in the nandrolone group compared with baseline after 3 or 6 months of treatment.

Walking and stair-climbing times improved significantly in the nandro-

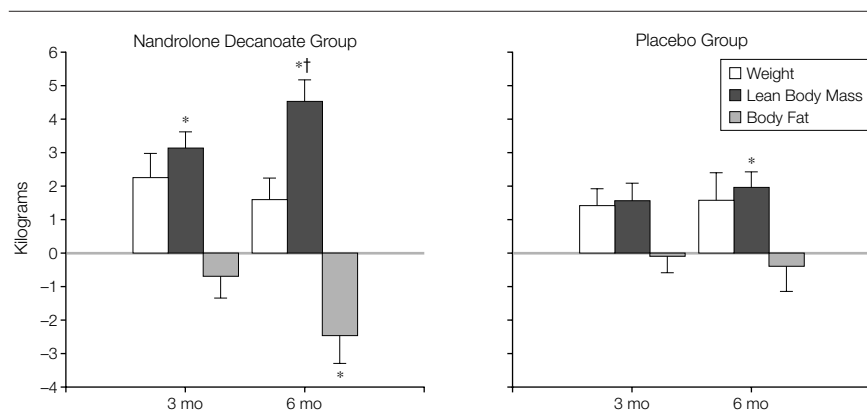
lone group compared with the placebo group after 6 months (Table 2). There were no changes in grip strength in either group.

**Biochemical and Hormonal Parameters**

Total serum testosterone, luteinizing hormone, and follicle-stimulating hormone levels decreased significantly in men who received nandrolone but not in men who received placebo (TABLE 3). Free testosterone levels also decreased in the group receiving nandrolone, but not to a statistically significant degree. There were no changes in dehydroepiandrosterone sulfate or estradiol levels. Too few women were enrolled to draw conclusions about changes in hormone levels with nandrolone.

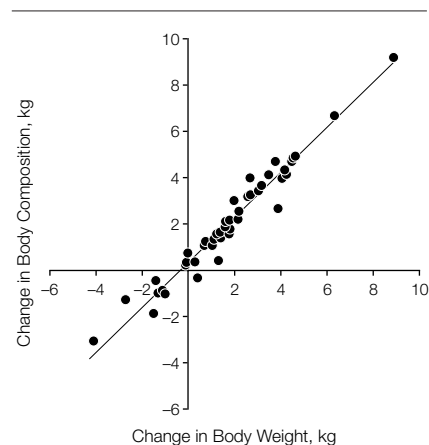
Hematocrit did not change significantly during the study in either group because erythropoietin dosage was adjusted to maintain hematocrit. By the end of the study, erythropoietin dosage had been reduced significantly in the group as a whole, but there was no significant difference in magnitude of the reduction between the nandrolone and placebo groups. Total cholesterol levels decreased by 0.39 (0.65) mmol/L (15 [25] mg/dL) in the nandrolone

**Figure 2.** Changes in Weight and Body Composition



Body composition was measured by dual-energy x-ray absorptiometry. Changes from the baseline values are expressed as mean ± SEM. Asterisks indicate statistical significance compared with baseline values by paired *t* test ( $P < .05$ ); dagger, statistical significance compared with the placebo group by unpaired *t* test ( $P < .01$ ).

**Figure 3.** Relationship Between Change in Body Weight and Change in Body Composition



There was a significant correlation between changes in body weight and changes in body composition (lean body mass + body fat as measured by dual-energy x-ray absorptiometry) ( $r = 0.94$ ;  $P < .001$ ).

group ( $P = .04$ ) but did not change in the placebo group (0.03 [0.54] mmol/L [-1 (21) mg/dL];  $P = .92$ ). Overall, the difference between the groups did not reach statistical significance ( $P = .06$ ). Cholesterol levels were not fractionated because the samples were not all collected under fasting conditions. Nevertheless, there were no changes in triglyceride levels in either group.

**Quality of Life**

Quality-of-life data were available in 19 patients (11 in the nandrolone group and 8 in the placebo group). The only significant change in quality of life was a reduction in the fatigue component of the Profile of Mood States in the nandrolone group at 6 months (from 6.1 [6.2] to 3.1 [4.5];  $P = .04$ ) compared with baseline and with the placebo group, which did not change (3.3 [1.4] to 4.5 [3.9];  $P = .85$ ). There were no significant changes in either group in the anger/hostility scale, but there was a trend toward an increase in the nandrolone group.

**Adverse Effects**

The study drug was generally well tolerated, but minor adverse effects occurred. Two subjects (1 receiving nandrolone and 1 receiving placebo) developed a hematoma at the injection site. In both cases, the hematoma resolved spontaneously. One nandrolone recipient complained of a reduction in testicular size that resolved with dosage reduction. Two men (both receiving placebo injections) complained of skin rash that did not resolve after the drug was discontinued. Of the 3 women who received nandrolone, 2 required dosage reduction for amenorrhea and acne, respectively.

Nandrolone did not appear to affect blood pressure control. All but 1 subject were receiving antihypertensive therapy. Six subjects required increases in antihypertensive medication during the study (3 in each group). Seven subjects had their antihypertensive medication dosages reduced during the study (4 receiving nandrolone and 3 receiving placebo).

**COMMENT**

The results of the present study demonstrate that treatment with nandrolone leads to anabolic effects and functional benefit in debilitated dialysis patients. During a 6-month treatment period, subjects who received nandrolone gained an average of 2.5 kg more LBM than those who received placebo. This gain was accompanied by an increase in serum creatinine levels, suggesting that nandrolone caused increased muscle mass. In addition, subjects who received nandrolone had a significant reduction in their reported symptoms of fatigue and a decrease in the times required for walking and stair-climbing.

Several short-term studies have examined the effects of anabolic agents, such as human growth hormone in patients undergoing dialysis, and have demonstrated positive effects on nitro-

gen balance.<sup>12-14</sup> To our knowledge, our study is the first to evaluate the long-term effects of anabolic therapy on body composition and the first to use nandrolone, a 19-nortestosterone derivative, for this purpose. Nandrolone offers several theoretical advantages over human growth hormone in the dialysis population. Human growth hormone has the potential to exacerbate hyperglycemia in patients with diabetes<sup>21,22</sup> and, because patients with diabetes make up a disproportionate number of the malnourished and debilitated dialysis patients most likely to benefit from anabolic therapy, human growth hormone may have limited utility. Another advantage of nandrolone is its lower cost. Treatment with human growth hormone costs approximately \$27 500 per year at the dosages used in most studies, while nandrolone costs approximately \$87 per year.

**Table 2.** Results of Treadmill Exercise, Walking, and Stair-Climbing Tests\*

Variables	Nandrolone Decanoate Group			Placebo Group		
	Baseline (n = 8)	3 mo (n = 7)	6 mo (n = 6)	Baseline (n = 6, 8)†	3 mo (n = 4, 6)†	6 mo (n = 4, 6)†
Treadmill time, min	14.7 (5.3)	17.6 (6.9)‡	16.8 (8.7)	12.5 (3.8)	8.9 (1.7)	14.7 (1.8)
Maximum work output, W§	95 (31)	120 (39)‡	110 (49)	74 (25)	48 (18)	87 (21)
Total work output, W§	706 (508)	1087 (747)‡	1080 (1045)	468 (307)	212 (140)	629 (175)
Peak oxygen consumption, L/min	1.4 (0.3)	1.6 (0.4)	1.5 (0.3)	1.3 (0.2)	0.9 (0.3)	1.1 (0.3)
Walking and stair-climbing time, s	36.5 (8.4)	35.6 (11.0)	32.7 (8.1)	38.7 (14.7)	40.6 (19.1)	42.1 (16.6)

\*Data are presented as mean (SD).  
 †Different numbers of subjects in the placebo group underwent treadmill exercise and walking and stair-climbing tests. The first number refers to the treadmill data and the second to the walking and stair-climbing data.  
 ‡Changes from baseline are significantly different from the placebo group ( $P < .05$ ).  
 §One watt = 1 joule per second.  
 ||Changes from baseline are significantly different from the placebo group and from baseline ( $P < .05$ ).

**Table 3.** Hormone Levels in Men at Baseline and After 3 Months of Treatment\*

Hormone Levels	Nandrolone Decanoate Group		Placebo Group	
	Baseline	3 mo	Baseline	3 mo
Total testosterone, ng/dL†	329 (160)	164 (129)‡	439 (210)	439 (104)
Free testosterone, ng/dL†	14.4 (7.3)	10.1 (4.9)	16.4 (5.8)	18.6 (5.0)
Luteinizing hormone, IU/L	4.4 (5.0)	1.2 (2.5)‡	5.9 (5.1)	6.0 (5.3)
FSH, IU/L	4.4 (2.4)	0.9 (2.0)‡	6.4 (5.0)	7.9 (5.0)
DHEA-S, µg/L†	336 (181)	284 (183)	177 (99)	168 (99)
Estradiol, pg/mL†	37.2 (15.7)	35.1 (15.7)	35.3 (16.3)	36.1 (12.5)

\*Data are presented as mean (SD). FSH indicates follicle-stimulating hormone; DHEA-S, dehydroepiandrosterone sulfate.  
 †To convert testosterone values to nanomoles per liter, multiply by 0.0347. To convert DHEA-S values to micromoles per liter, multiply by 0.027. To convert estradiol values to picomoles per liter, multiply by 3.67.  
 ‡Significant reduction compared with the baseline values by paired *t* test ( $P < .05$ ).

A potential disadvantage of anabolic steroid treatment is the possibility of adverse lipid effects. Some studies have shown decreases in high-density lipoprotein cholesterol levels or increases in triglyceride levels after treatment with anabolic steroids.<sup>23-25</sup> However, others, particularly with 17 $\beta$ -esterified preparations such as nandrolone, have not demonstrated adverse lipid effects.<sup>25-27</sup> In fact, there have been several reports that treatment with nandrolone results in lowering of lipoprotein(a),<sup>28,29</sup> a form of low-density lipoprotein cholesterol recently identified as an independent risk factor for atherosclerosis in dialysis patients.<sup>30-33</sup> Thus, the net effect of nandrolone on cardiovascular risk is not clear. In the present study, there was a trend toward reduction in total cholesterol levels in the nandrolone group and no change in triglyceride levels. Fasting blood samples were not obtained in these patients, so the full effects of nandrolone on lipid profiles cannot be determined. However, it is notable that total cholesterol levels decreased in the patients who received nandrolone while no such change was seen in those receiving placebo. Further studies evaluating anabolic steroids in patients receiving dialysis should include fasting lipid levels, including high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, and lipoprotein (a) levels.

A major feature of this study is the use of DEXA to measure LBM. Although DEXA cannot distinguish extracellular fluid from functional lean tissue, the increase in serum creatinine levels and the reduction in fat in the treatment group suggest a pharmacological effect of nandrolone resulting in an increase in muscle mass. In contrast, although LBM increased modestly in the placebo group, there was no accompanying increase in serum creatinine levels. These results suggest that the observed increase in LBM in the placebo group consisted, at least in part, of an expansion in extracellular fluid volume and did not represent a substantial increase in muscle mass.

The small number of subjects able to undergo and/or complete treadmill testing was a limitation of this study. Treadmill exercise protocols can be performed by only the healthiest dialysis patients, and many study subjects had relative contraindications to treadmill exercise at baseline. In those able to undergo initial treadmill testing, intercurrent illness frequently precluded testing at the 3-month or 6-month points. Furthermore, many patients who were able to exercise repeatedly on the treadmill were limited by symptoms such as leg fatigue and did not reach maximal  $\text{VO}_2$ , adding to the variability of the results. In those patients able to undergo treadmill testing, our baseline results are in accord with those of previous investigators who have demonstrated dramatically reduced peak  $\text{VO}_2$  in dialysis patients compared with age-matched sedentary controls.<sup>34-37</sup> The lack of a significant improvement in peak  $\text{VO}_2$  in the subjects treated with nandrolone despite evidence of increased muscle mass suggests that reduced muscle mass is not the limiting factor in maximal  $\text{VO}_2$  in patients receiving dialysis, but no definitive conclusions can be drawn from such a small group of patients tested.

Subjects treated with nandrolone had an improvement in walking and stair-climbing times. These results are not unexpected because these activities are dependent on lower extremity strength, and recent reports have shown increased strength with anabolic steroid treatment in subjects with normal renal function.<sup>15</sup> In addition, subjects reported significantly less fatigue after nandrolone treatment. Because more than 30% of dialysis patients need assistance in performing the normal activities of daily living<sup>38,39</sup> and because functional limitations are a major determinant of quality of life in dialysis patients,<sup>40</sup> this intervention may have an important impact on the functional capabilities and quality of life of patients undergoing dialysis.

In summary, treatment with nandrolone resulted in increased LBM and improved functional status in dialysis pa-

tients. Nandrolone was safe and well tolerated during 6 months of treatment, but further studies are needed to assess the long-term safety and benefits of such treatment.

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## REFERENCES

1. US Renal Data System. *USRDS 1994 Annual Data Report*. Bethesda, Md: National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases; 1994.
2. Woodrow G, Oldroyd B, Turney J, Tompkins L, Brownjohn A, Smith M. Whole body and regional body composition in patients with chronic renal failure. *Nephrol Dial Transplant*. 1996;11:1613-1618.
3. Pollock C, Allen B, Warden R, et al. Total-body nitrogen by neutron activation in maintenance dialysis. *Am J Kidney Dis*. 1990;16:38-45.
4. Coles G. Body composition in chronic renal failure. *QJM*. 1972;41:25-47.
5. Hakim R, Levin N. Malnutrition in hemodialysis patients. *Am J Kidney Dis*. 1993;21:125-137.
6. Lazarus J. Nutrition in hemodialysis patients. *Am J Kidney Dis*. 1993;21:99-105.
7. Kopple J. Effect of nutrition on morbidity and mortality in maintenance dialysis patients. *Am J Kidney Dis*. 1994;24:1002-1009.
8. Lowrie E, Lew N. Death risk in hemodialysis patients: the predictive value of commonly measured variables and an evaluation of death rate differences between facilities. *Am J Kidney Dis*. 1990;15:458-482.
9. Mulligan K, Grunfeld C, Hellerstein M, Neese R, Schambelan M. Anabolic effects of recombinant human growth hormone in patients with wasting associated with human immunodeficiency virus infection. *J Clin Endocrinol Metab*. 1993;77:956-962.
10. Tayek J, Brasel J. Growth hormone administration decreases urea nitrogen losses in malnourished cancer patients [abstract]. *Clin Res*. 1992;40:95A.
11. Manson JM, Wilmore D. Positive nitrogen balance with human growth hormone and hypocaloric intravenous feeding. *Surgery*. 1986;100:188-197.
12. Ziegler T, Lazarus JM, Young L, Hakim R, Wilmore D. Effects of recombinant human growth hormone in adults receiving maintenance hemodialysis. *J Am Soc Nephrol*. 1991;2:1130-1135.
13. Schulman G, Wingard R, Hutchison R, Lawrence P, Hakim R. The effects of recombinant human growth hormone and intradialysis parenteral nutrition in malnourished hemodialysis patients. *Am J Kidney Dis*. 1993;21:527-534.
14. Ikizler T, Wingard R, Breyer J, Schulman G, Parker R, Hakim R. Short-term effects of recombinant human growth hormone in CAPD patients. *Kidney Int*. 1994;46:1178-1183.
15. Bhasin S, Storer T, Berman N, et al. The effects of supraphysiologic doses of testosterone on muscle size and strength in normal men. *N Engl J Med*. 1996;335:1-7.

16. Sargent J. Control of dialysis by a single-pool urea model: the National Cooperative Dialysis Study. *Kidney Int.* 1983;13(suppl):S19-S25.
17. American College of Sports Medicine. *Guidelines for Exercise Testing and Prescription*. 4th ed. Philadelphia, Pa: Lea & Febiger; 1991.
18. Campbell A, Converse P, Rodgers W. *The Quality of American Life*. New York, NY: Russell Sage Foundation; 1976.
19. Bergner M, Bobbit R, Carter W, Gilson B. The Sickness Impact Profile: development and final revision of a health status measure. *Med Care.* 1981;19:787-805.
20. McNair D, Lorr M, Droppleman L. *EITS Manual for the Profile of Mood States*. San Diego, Calif: Educational and Industrial Testing Service; 1971.
21. Botero D, Danon M, Brown R. Symptomatic non-insulin-dependent diabetes mellitus during therapy with recombinant human growth hormone. *J Pediatr.* 1993;123:590-592.
22. Kollind M, Adamson U, Lins P, Efendis S. Diabetogenic action of GH and cortisol in insulin-dependent diabetes mellitus: aspects of the mechanisms behind the Somogyi phenomenon. *Horm Metab Res.* 1987;19:156-159.
23. Lindholm D, Fisher J, Vieira J, Dombeck DH, Bernal G, Lerthora J. Clinical effects of oral flouxymesterone in patients with dialysis-controlled uremia. *Trans Am Soc Artif Intern Organs.* 1973;19:475-483.
24. Hurley B, Seals D, Hagberg J, et al. High-density-lipoprotein cholesterol in bodybuilders v powerlifters: negative effects of androgen use. *JAMA.* 1984;252:507-513.
25. Thompson P, Cullinane E, Sady S, et al. Contrasting effects of testosterone and stanozolol on serum lipoprotein levels. *JAMA.* 1989;261:1165-1168.
26. Glazer G, Suchman A. Lack of demonstrated effect of nandrolone on serum lipids. *Metabolism.* 1994;43:204-210.
27. Hendler E, Goffinet J, Ross S, Longnecker R, Bakovic V. Controlled study of androgen therapy in anemia of patients on maintenance hemodialysis. *N Engl J Med.* 1974;291:1046-1051.
28. Teruel J, Lasuncion M, Rivera M, et al. Nandrolone decanoate reduces serum lipoprotein(a) concentrations in hemodialysis patients. *Am J Kidney Dis.* 1997;29:569-575.
29. Lippi G, Guidi G, Ruzzenente O, Braga V, Adam S. Effects of nandrolone decanoate (Decadurabolin) on serum Lp(a), lipids and lipoproteins in women with postmenopausal osteoporosis. *Scand J Clin Lab Invest.* 1997;57:507-512.
30. Cressman M, Heyka R, Paganini E, O'Neil J, Skibinski C, Hoff H. Lipoprotein(a) is an independent risk factor for cardiovascular disease in hemodialysis patients. *Circulation.* 1992;86:475-482.
31. Kronenberg F, Utermann G, Dleplinger H. Lipoprotein(a) in renal disease. *Am J Kidney Dis.* 1996;27:1-25.
32. Bartens W, Nauck M, Schollmeyer P, Wanner C. Elevated lipoprotein(a) and fibrinogen levels [corrected] increase the cardiovascular risk in continuous ambulatory peritoneal dialysis patients. *Perit Dial Int.* 1996;16:27-33.
33. Avram M, Sreedhara R, Patel N, Chattoopadhyay J, Thu T, Fein P. Is an elevated level of serum lipoprotein (a) a risk factor for cardiovascular disease in CAPD patients? *Adv Perit Dial.* 1996;12:266-271.
34. Bradley J, Anderson J, Evans D, Cowley A. Impaired nutritive skeletal muscle blood flow in patients with chronic renal failure. *Clin Sci.* 1990;79:239-245.
35. Painter P, Messer D, Widener C, Zimmerman S. Response to graded exercise testing in patients treated with CAPD. *Perit Dial Bull.* 1984;4(suppl):S94-S97.
36. Painter P, Messer-Rehak D, Hanson P, Zimmerman S, Glass N. Exercise capacity in hemodialysis, CAPD, and renal transplant patients. *Nephron.* 1986;42:47-51.
37. Moore G, Brinker K, Stray-Gundersen J, Mitchell J. Determinants of  $VO_{2peak}$  in patients with end-stage renal disease: on and off dialysis. *Med Sci Sports Exerc.* 1993;25:18-23.
38. Gutman R, Stead W, Robinson R. Physical activity and employment status of patients on maintenance dialysis. *N Engl J Med.* 1981;304:309-313.
39. Ifudu O, Paul H, Mayers J, et al. Pervasive failed rehabilitation in center-based maintenance hemodialysis patients. *Am J Kidney Dis.* 1994;23:394-400.
40. Churchill D, Torrance G, Taylor D, et al. Measurement of quality of life in end-stage renal disease: the time trade-off approach. *Clin Invest Med.* 1987;10:14-20.

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—Jacob M. Da Costa (1833-1900)