Body composition response to exogenous GH during training in highly conditioned adults

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Crist, Douglas M., Glenn T. Peake, Peter A. Egan, and Debra L. Waters. Body composition response to exogenous GH during training in highly conditioned adults. J. Appl. Physiol. 65(2): 579–584, 1988.—The effects of biosynthetic methionyl-human growth hormone (met-hGH) on body composition and endogenous secretion of growth hormone (GH) and insulin-like growth factor I (IGF-I) were studied in eight well-trained exercising adults between 22 and 33 yr of age. By the use of double-blind procedures, met-hGH (2.67 mg/0.5 ml diluent, 3 days/wk) and bacteriostatic water (placebo, 0.5 ml, 3 days/wk) were administered in a repeated-measures design that counterbalanced treatment order. Duration of each treatment was 6 wk. Subjects trained with progressive resistance exercise throughout and were maintained on a high-protein diet monitored by extensive compositional analyses of daily dietary intake records. Hydrodensitometry revealed that met-hGH significantly decreased percent body fat (%fat) and increased fat-free weight (FFW) and FFW/fat weight (FW), whereas the placebo treatment did not change any of these measures. Changes in FFW/FW correlated with the relative dose of meth-hGH but did not correlate with either the peak GH response to L-dopa/arginine stimulation or IGF-I levels obtained after treatment with placebo. There were no differences between treatments in the dietary intakes of total kilocalories, protein, carbohydrates, and fat. Mean IGF-I levels were elevated after treatments in the dietary intakes of total kilocalories, protein, carbohydrates, and fat. Mean IGF-I levels were elevated after treatment with met-hGH compared with postplacebo levels. After treatment with met-hGH, five of seven subjects had a suppressed GH response to stimulation from either L-dopa/arginine or submaximal exercise. We conclude that supraphysiological doses of met-hGH will alter body composition in exercising adults in a relative dose-dependent manner and that such treatment may suppress endogenous release of GH in some individuals.

GROWTH HORMONE (GH), a potent regulator of somatic growth, promotes proteinogenesis and fat mobilization and oxidation (16, 24). With the use of a two-compartment model of body composition, the physiological actions of GH will presumably increase the fat-free weight (FFW) and decrease the fat weight (FW) compartments. In this regard, it has been reported previously that GH replacement therapy reduces the excessive fat mass observed in short-statured children with isolated GH deficiency (22). Recently, we have reported that physiological GH replacement therapy will significantly increase FFW and decrease FW in sedentary older women with an impaired GH response to pharmacological stimulation (5).

Progressive resistance exercise (PRE) (31) and aerobic exercise (AE) (11, 29) of different intensities and durations will stimulate endogenous GH release. This response, along with the known physiological actions of GH, suggests that the hormone might mediate, in part, some of the manifestations of regular exercise training on body composition and that exogenous human GH might produce additional changes in those whose body composition response to exercise has plateaued from years of exercise training.

Thus we performed a double-blind, placebo-controlled experiment which investigated the effects of chronic alternate-day treatment with supraphysiological doses of biosynthetic methionyl-human GH (met-hGH) on FFW, percent body fat (%fat), and FFW/FW in well-trained, exercising young adults whose body composition response to exercise was presumably attenuated from extensive training. Moreover we monitored the effects of such treatment on the stimulated endogenous secretion of GH and another potent anabolic hormone dependent on GH release, insulin-like growth factor I (IGF-I).

METHODS

Subjects. After explanation of the nature and design of the experiment and the risks involved, informed voluntary consent was obtained from eight subjects ranging from 22 to 33 yr of age. All subjects were given a physical examination and considered in good health, and they were not taking any medications known to compromise the parameters of the study. Base-line physical characteristics for the male and female subjects, along with the study group characteristics for all subjects combined, are presented in Table 1. Intensive screening interviews revealed that all subjects were well trained in PRE, having had a group mean of 6.5 yr of experience in such training. Subjects well trained in PRE were selected for the study to achieve a high degree of homogeneity in their responsiveness to exercise training, skill level, and motivational state. These subjects were chosen since their exercise and performance had been at high levels and chronically sustained over many years, and they were not expected to change appreciably over the duration of the present study. Novice subjects may have had a rapid change in body composition (i.e., increased FFW) in response to
and throughout the study period as an adjunct to their training. Females also performed steady-state AE training before and throughout the study period. PRE training averaged five sessions per week. Four of the eight subjects (1 male and 3 females) performed steady-state AE training before and throughout the study period. PRE training was initiated on alternate days (3 days/wk) in 0.5 ml of bacteriostatic water delivered subcutaneously on alternate days (3 days/wk). The met-hGH (experimental) treatment consisted of 8.0 mg (2 U/mg) per week of met-hGH (Protropin; Genentech, San Francisco, CA), which was divided into three doses (2.07 mg/dose) and delivered on alternate days (3 days/wk) in 0.5 ml of bacteriostatic diluent. Because of differences in the body weights of the subjects, the relative dose range varied between 0.03 and 0.05 mg/kg per injection. Injections were given between 0800 and 1500, and their delivery was rotated among four to six sites throughout the study period. Treatments were administered on a double-blind basis with neither the experimental subject nor the person administering the injections knowing which treatment was being delivered. The total weekly dose of met-hGH used in this study (8.0 mg) was considered supraphysiological, since the spontaneous release of human GH during a 24-h period is purportedly -0.68 mg (4.8 mg/wk) in men and 0.79 mg (5.5 mg/wk) in women (30), similar to amounts reported by others (6).

All eight subjects were engaged in steady-state PRE training before and throughout the study period. PRE consisted of conventional weight-training exercise applied to single and multiple joint actions of the upper and lower extremities. PRE training averaged five sessions per week. Four of the eight subjects (1 male and 3 females) also performed steady-state AE training before and throughout the study period as an adjunct to their PRE training. In these subjects, AE training averaged 5 days/wk, at moderate intensity, with a variable duration of 35–90 min/session. Subjects were instructed on the necessity of maintaining the same training regimen during the entire study period, and their training was directly monitored on a frequent basis for consistency.

It is not an unusual practice for well-trained individuals undergoing PRE to ingest increased amounts of dietary protein in an attempt to increase their FFW. This practice may be of benefit since a high level of protein intake (>2 g·kg⁻¹·day⁻¹), during periods of intense PRE training, will improve nitrogen retention (13). Thus to maintain consistency with preexisting protein intakes in some of the subjects and to ensure sufficient protein and kilocaloric intakes under an increased potential for hormone-induced tissue anabolism in response to exercise, our subjects were instructed to ingest 2 g·kg⁻¹·day⁻¹ of protein and a recommended minimum of kilocalories to maintain body weight throughout the entire study period. Kilocaloric requirements were determined by routine methods, adjusting for physical activity patterns (17). Daily dietary-intake records were maintained by each subject throughout both treatment periods, and these records were analyzed on a weekly basis for total protein, carbohydrate, fat, and kilocaloric intakes. Subjects were given feedback each week concerning their actual protein and kilocaloric intakes as a means of ensuring compliance with the study's dietary requirements. The repeated-measures, counterbalanced design optimized internal consistency with regard to dietary intakes, exercise training, and other potential uncontrollable influences, minimizing the potential for these variables to bias the effects from either the placebo or met-hGH treatment.

Endogenous GH secretion. Preliminary investigations were performed to assess effects of the placebo and met-hGH treatments on the endogenous GH secretory response to stimulation. Secretory status in the first group of subjects was studied by L-dopa/arginine stimulation at the end of each treatment condition, whereas secretory status was studied in the second group by exercise stimulation after each treatment and by L-dopa/arginine stimulation before delivery of any treatment (base line). Thus these procedures provided a means of monitoring effects from the two treatments on endogenous GH secretion in response to stimulation (L-dopa/arginine and exercise) while also permitting an evaluation of secretory status in all subjects without bias from the met-hGH treatment (pooled results from the base line and postplacebo L-dopa/arginine studies).

All GH secretion studies were conducted between 24 and 72 h after the last treatment injection or, for baseline determinations, 3–7 days before delivery of any treatment. These secretory studies began between 0700 and 0900. Since L-dopa/arginine stimulation is used to categorize GH secretory responses (32), the postplacebo treatment results in the first group of subjects were pooled with the base-line results of the second group to evaluate the secretory status of the study population as a whole.

L-Dopa/arginine stimulation was performed, after a 12- to 14-h fast, by oral administration of 500 mg of L-dopa, taken at the beginning of L-arginine monohydro-
chloride infusion through an indwelling intravenous catheter placed in an antecubital vein; 0.5 g/kg body wt (up to a 30-g maximum) of L-arginine monohydrochloride was infused over a 30-min period, and blood samples (2 ml) for GH were obtained at study times -5, 0, 30, 45, 60, 90, and 120 min.

Release of GH in response to exercise stimulation was quantitated after predetermination of an appropriate submaximal exercise intensity, defined by an estimation of maximal O₂ uptake (VO₂max, ml·kg⁻¹·min⁻¹) during maximal exercise tolerance testing (ETT). Seven to 10 days before study of the GH response to exercise, ETT was conducted with the use of a modified Balke incremental-workstage protocol (18) on a motor-driven treadmill (Quinton Instruments, Seattle, WA). The treadmill speed was held constant at 5.44 km/h with a 2% grade elevation occurring each minute up to a maximum of 24%. Thereafter the grade was held constant and the speed increased 0.32 km/h until test termination. Subjects were exercised to exhaustion, and their VO₂max was derived from the treadmill work load at test termination (1).

After a 12- to 14-h fast, GH secretion in response to exercise was evaluated at a stimulation threshold of ~75% VO₂max, since such a level of effort is highly effective for provoking endogenous GH release (29). Steady-state exercise was maintained at this level of effort for 20 min (29), after a progressive two-stage warm-up lasting ~4 min. Blood samples (2 ml) for GH were obtained from an antecubital vein at study times -5, 0, 10, 15, 20, 25, 35, and 45 min.

In all the endogenous GH studies, human GH was assayed from serum according to the method developed in our laboratory by Peake et al. (20).

*Endogenous IGF-I secretion*. In the absence of poor nutritional status, diabetes mellitus, diseases of the brain and liver, and use of neuroactive drugs (27), circulating concentrations of IGF-I indirectly reflect the total 24-h integrated levels of GH (3, 7). Since our study population was healthy and well nourished, plasma IGF-I concentrations were determined after each treatment to study whether the met-hGH treatment produced a physiological effect, different from that of the placebo, and to aid in the assessment of endogenous GH secretory status by L-dopa/arginine stimulation. Thus fasting blood samples (2 ml) for IGF-I were withdrawn from an antecubital vein, between 0700 and 0900, on the day after the last injection of each treatment condition. EDTA-treated plasma samples were assayed for IGF-I concentration using the radioimmunoassay kit of Nichols Institute Diagnostics (San Juan Capistrano, CA). With the use of this assay, the normal ranges are 0.45–2.20 U/ml for women and 0.34–1.90 U/ml for men.

**Body composition.** Fat-free weight (FFW) and %fat were evaluated by hydrodensitometry to estimate whole-body density (9). Underwater weights and dry body weight were measured by a Chatillon autopsy scale and Detecto platform scale, respectively. Vital capacity (VC) was measured by conventional spirometry while the subject was seated in a chair submerged in a large tank of water to a depth where the water level was at the clavicles of the subject. Total lung capacity (TLC) was derived from appropriate calculations with VC and an estimate of residual volume (RV) by the method of Goldman and Becklace (8). Underwater weighing was conducted by instructing the subject to expire a comfortable volume of air after having inspired to TLC and then submerging underwater by leaning forward and downward (15). Whole-body density was determined by use of an adjustment for air trapped in the gastrointestinal tract (100 ml). The test-retest reliability coefficient for this method of determining body density exceeds 0.96, with a coefficient of variation of <2% (10).

Ten submersion trials were performed, and the two highest and two lowest densities were deleted, leaving the mean of six trials to determine %fat by the Keys and Brozek equation (12). FFW was calculated by the following equation: (%fat/100) wt.

In all cases, hydrodensitometry was performed within 2–5 days immediately before and after each treatment. Weighings were conducted between 0800 and 1000 h after a 12- to 14-h fast.

*Study design considerations and statistical analyses*. Data obtained from pre- and posttesting for each treatment (body composition analyses) or only from posttesting for each treatment (IGF-I and dietary analyses) were paired and subjected to analyses of statistical difference between means using nonparametric inferential statistics for paired data. These analyses assessed only the isolated effects of each treatment, thus avoiding potential bias from a treatment-order interaction. Moreover, potential gender differences in responsiveness to the treatments or differences produced by other uncontrolled factors were avoided by employing a repeated-measures design, balancing these possible biasing effects across both treatment conditions. Thus the purpose of this study was to compare effects between treatments rather than specifically to assess potential subject differences within each treatment. Correlational analyses were performed by standard methods of bivariate regression. Descriptive statistics are presented for the preliminary data regarding human GH secretion in response to stimulation. All statistics were generated by the MSUSTAT statistical program (Montana State University, Bozeman, MT).

**RESULTS**

Data presented in Table 2 reveal a significant decrease in %fat and significant increases in FFW and FFW/FW as a result of the met-hGH treatment. Regressing the

**TABLE 2. FFW, %fat, and FFW/FW in subjects studied before and after 6 wk of treatment with placebo and met-hGH**

<table>
<thead>
<tr>
<th>Body Composition</th>
<th>Placebo</th>
<th>met-hGH</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pre</td>
<td>Post</td>
</tr>
<tr>
<td>FFW, kg</td>
<td>60.8±4.5</td>
<td>61.2±4.0</td>
</tr>
<tr>
<td>%Fat</td>
<td>13.4±1.6</td>
<td>13.0±0.9</td>
</tr>
<tr>
<td>FFW/FW</td>
<td>7.5±1.9</td>
<td>6.9±0.6</td>
</tr>
</tbody>
</table>

Values are means ± SE; n = 8 subjects. FFW, fat-free weight; %fat, percent body fat; FFW/FW, ratio of fat-free weight to fat weight; met-hGH, methionyl-human growth hormone. *Significant difference between pre- and posttest means (P < 0.05).
hormone-induced percent change in \( \text{FFW/FW} \) with the relative dose of each injection (2.67 mg/kg body wt) revealed that the magnitude of change in body composition was positively influenced by the relative dose (\( r = 0.77; P < 0.05 \)). There were no apparent relationships between the hormone-induced percent change in \( \text{FFW/FW} \) and either endogenous GH response to L-dopa/arginine stimulation (\( r = 0.18; P > 0.05 \)) or postplacebo IGF-I concentration (\( r = -0.23; P > 0.05 \)).

Daily mean (±SE) dietary intakes for kilocalories were the same (\( P > 0.05 \)) for the placebo (2,534 ± 363 kcal) and met-hGH (2,501 ± 325 kcal) treatment conditions. Similarly no changes were observed in dietary composition between treatment conditions for intakes of protein (placebo 148 ± 20 g vs. met-hGII 145 ± 17 g; \( P > 0.05 \)), fat (placebo 91 ± 16 g vs. met-hGH 89 ± 14 g; \( P > 0.05 \)), and carbohydrate (placebo 280 ± 44 g vs. met-hGH 272 ± 38 g; \( P > 0.05 \)). Actual protein intake averaged 2.10 g/kg during placebo treatment and 2.05 g/kg during met-hGH treatment.

The peak serum endogenous GH response to L-dopa/arginine stimulation, for the group as a whole (pooled base line and postplacebo) was normoresponsive at 14.7 ± 3.0 ng/ml, exceeding a hyposecretory response of ≤10 ng/ml (14). Similarly the postplacebo plasma IGF-I concentration for the group was 0.67 ± 0.09 U/ml, which exceeds the deficiency range of <0.25 U/ml (27). In three subjects, however, peak levels of GH were <10 ng/ml, presumably because of an impairment in the response to stimulation (3) rather than a true physiological impairment in the spontaneous release of the hormone. This view is supported by the finding of normal IGF-I levels (≥0.34 U/ml) in all the subjects.

When potential treatment-related changes in endogenous GH secretion were evaluated by L-dopa/arginine and exercise stimulations, mean peak responses were suppressed after met-hGH treatment in both stimulation groups (Table 3). However, the response was not suppressed in one subject of each group after treatment with met-hGH.

Posttreatment comparisons of mean IGF-I levels for all the subjects revealed that circulating concentrations of this hormone were significantly elevated as a result of treatment with met-hGH (placebo 0.67 ± 0.09 U/ml vs. met-hGH 1.51 ± 0.23 U/ml; \( P < 0.05 \)), but the increased level was below the upper limit of 2.20 U/ml for young adults (26).

**Table 3. Peak serum concentrations of endogenous GH in response to L-dopa/arginine and exercise stimulations in subjects studied during base-line conditions and/or treated with placebo and met-hGH**

<table>
<thead>
<tr>
<th>L-Dopa/Arginine</th>
<th>Exercise</th>
</tr>
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<tbody>
<tr>
<td>Base line</td>
<td>Placebo</td>
</tr>
<tr>
<td>Placebo</td>
<td>11.2±2.7</td>
</tr>
<tr>
<td>met-hGH</td>
<td>18.3±2.6</td>
</tr>
</tbody>
</table>

Values are means ± SE in ng/ml; \( n = 1 \) female, 3 males (group 1) and 2 females, 2 males (group 2). GH, growth hormone; met-hGH, methionyl-human GH; * 2 females, 1 male. NS, not studied.

**DISCUSSION**

In the present study, we found that alternate-day treatment with met-hGH altered body composition in highly conditioned, exercising adults by increasing FFW, decreasing %fat, and increasing FFW/FW. These changes were significantly greater than those produced by exercise alone. Findings from this experiment corroborate those from another recent investigation, which reported that daily replacement therapy with physiological amounts of human GH increased FFW and decreased FW in women with an impaired endogenous GH response to L-dopa/arginine stimulation (5). When combined, these studies suggest that treatment with physiological or supraphysiological doses of GH will produce changes in body composition in sedentary or exercising adults of various ages. Moreover we found that supraphysiological amounts of met-hGH were sufficient to significantly elevate circulating concentrations of IGF-I in all our subjects, confirming that the changes in body composition were indeed due to real alterations produced in vivo by the hormone treatment.

As a means of assessing whether retention of extracellular fluid may have contributed to our observed increase in FFW, four of our subjects (2 females and 2 males) were given 5.33 mg of met-hGH on alternate days for 6 wk (16 mg/wk) and FFW was measured by hydrodensitometry 2 and 21 days after cessation of treatment. Since the mean difference between the two measures of FFW was 0.37 ± 0.25 (SE) kg (unpublished observations), it is unlikely that the gains in FFW reported here were biased significantly from the retention of extracellular fluid. Although this observation differs from others reporting such an effect (4), the latter finding occurred only in some obese, sedentary subjects, and it appeared to be a transient response during a short treatment period (3 wk). In the present study, it is plausible that our longer treatment period was sufficient to permit recovery from the acute effects of met-hGH on fluid retention and/or regular exercise may have acted to retard this response through the loss of body fluid by sweat production.

In this study, the stimulated release of endogenous GH and circulating concentrations of IGF-I were used to assess secretory status of the hormone and to study potential changes in status due to the treatments employed. Although it is unclear whether the stimulation of human GH secretion will adequately reflect status for the spontaneous release of the hormone over a 24-h period (3, 21), hepatic secretion of IGF-I is stimulated by GH, and thus levels of IGF-I are positively correlated with the 24-h integrated concentration of GH (3, 7). This IGF-I response is rapid, attaining peak levels within 24 h (28). Thus both measures of GH secretion were used to assess status in our study group and, of principal concern, to monitor responses in vivo to the two treatments.

There were no apparent relationships between hormone-induced changes in body composition and either the endogenous human GH response to L-dopa/arginine stimulation (used in all subjects) or the postplacebo IGF-I concentration. This was somewhat unexpected, since it has been previously reported that nitrogen retention and
circulating concentrations of IGF-I in response to GH treatment are inversely related to GH secretory status in adults (25, 26). However, it is possible that quantitative differences in tissue sensitivity to the hormone in male and female subjects with normal GH hormone secretion (measured by stimulation or IGF-I) were not demonstrable when supraphysiological doses of the hormone were given.

It has been reported previously that exogenous GH will suppress endogenous release of the hormone (19, 23) and that this effect may be mediated in part by elevated levels of IGF-I (23). On a preliminary basis, we found that treatment for 6 wk with supraphysiological doses of met-hGH produced an impaired endogenous GH response to stimulation in some, but not all, of our subjects. This variable response may be related to the amount of hormone used in the study. Although a significant group elevation in IGF-I levels occurred during the met-hGH treatment, this response was still below the upper limit of normal (2.2 U/ml) for the study group. Thus it is plausible that the treatment dose of met-hGH used and the subsequent moderate increase in IGF-I levels led to feedback suppression of endogenous GH release in five of the seven subjects measured for this effect, whereas these physiological events were insufficient to produce this effect in two of the subjects.

In this study, biological activity of the total weekly met-hGH dose was equivalent to 16.0 U (2.0 U/mg). Thus the weekly relative dose for the present subjects averaged 0.23 U·kg⁻¹·wk⁻¹ (16 U·70.4 kg mean body wt⁻¹·wk⁻¹). Others have reported the need for higher doses (~20.8 U/wk or 0.41 U·kg⁻¹·wk⁻¹, using our mean population weight) to significantly elevate IGF-I levels (26) or increase nitrogen retention (25) in normosecretory adults. Although we did find that changes in body composition varied according to the relative total weekly dose of met-hGII, it is clear that this effect varied over a low dose range (0.18–0.30 U·wk⁻¹·kg⁻¹) in subjects who were, in general, normoresponsive to L-dopa/arginine stimulation. One possible explanation for the disparity between our findings and those of others (25, 26) is that the stress of long-term, intensive exercise training could induce alterations in vivo, which might potentiate tissue sensitivity to the physiological actions of GH (2). In any case, it is clear from our findings that supraphysiological doses of met-hGH increased circulating concentrations of IGF-I and increased FFW and decreased FW in highly conditioned, exercising adults.

The possibility does exist that there may have been gender differences in the body composition response to met-hGH. As one example of this, the met-hGH induced a 2.3 ± 0.6-kg increase in FFW in the males and a 3.1 ± 0.8-kg increase in the females. Although this could initially be attributed to a sex-related difference, the females were lighter in body weight than the males (Table 1), and this probably was responsible for the effect, since we found a significant positive correlation between the relative dose of met-lGH and percent change in FFW/FW (r = 0.77). However, further studies are warranted to differentiate between the possible independent influences of body weight and gender on the body composition response to met-hGH in healthy adults.

There are two principal adverse reactions associated with excessive amounts of human GH, carbohydrate intolerance, and soft-tissue overgrowth. In the present study, we measured fasting blood glucose levels periodically throughout each treatment and found no real changes suggestive of a hyperglycemic response to met-hGH. Because soft-tissue overgrowth is associated with abnormally high levels of IGF-I, the normal responses observed suggest that the chance for soft-tissue overgrowth occurring in our subjects was minimal. However, it is unreasonable to conclude that use of met-hGH is safe as an adjunct to exercise in healthy adults until more subjects are studied over longer periods of time and with more stringent tests for detecting changes in glucose tolerance and soft-tissue overgrowth.

Dietary intake was strictly monitored, since potential differences between treatments in protein and kilocaloric intakes could bias the treatment-related IGF-I and body composition responses. In this regard, we found that there were no significant differences in either dietary kilocaloric intake or intake of protein, fat, and carbohydrate. Previous studies have suggested that a high protein intake improves nitrogen retention in individuals undergoing intensive PRE (13) and that adequate protein intake is required, despite a hypokilocaloric intake, to produce a positive nitrogen balance, from exogenous GH, in healthy nonexercising subjects (16). To avoid compromising the dietary requirements for optimal tissue anabolism during PRE and the met-hGH treatment, our subjects ingested between 2.05 and 2.10 g·kg⁻¹·day⁻¹ of protein and a minimum number of kilocalories to maintain body weight. The kilocaloric requirement removed the potential bias from a dietary-induced FW loss. Since there were no significant differences in dietary intake between treatments, the findings obtained from this study cannot be attributed to uncontrolled changes in diet quantity or composition.

We conclude that treatment with supraphysiological doses of met-hGH will significantly alter body composition in adults who are highly conditioned from years of exercise training. The magnitude of this effect, however, is dependent in part on the amount of hormone given per body weight of the individual rather than endogenous GH secretory status. Changes in body composition are directly related to met-hGH administration, but the manifestations of treatment may be mediated in part by increased production of IGF-I or other GH-dependent serum anabolic factors. Moreover, supraphysiological treatment with met-hGH in exercising adults may produce impairments in the stimulated release of endogenous GH in some individuals.

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REFERENCES


