# Serum Leptin Levels and Leptin Expression in Growth Hormone (GH)-Deficient and Healthy Adults: Influence of GH Treatment, Gender, and Fasting

Kurt Kristensen, Steen B. Pedersen, Sanne Fisker, Helene Nørrelund, Anne Mette Rosenfalck, J.O.L. Jørgensen, and Bjørn Richelsen

**Growth hormone (GH) treatment is associated with a reduction in fat mass in healthy and GH-deficient (GHD) subjects. This is mainly mediated via a direct GH action on adipose cells and stimulation of lipolysis. Leptin is secreted from adipose tissue and may be involved in signaling information about adipose tissue stores to the brain. Hormonal regulation of leptin is still not fully elucidated, and in the present study, we investigated both the long-term (4-month) and short-term (28-hour) GH effects on serum leptin and leptin gene expression in subcutaneous adipose tissue. In GHD adults (n = 24), leptin correlated with most estimates of adiposity ($r = .62$ to $.86$), as previously found in healthy subjects. However, no correlation was observed with intraabdominal fat determined by computed tomographic (CT) scan (INTRA-CT). GH treatment for 4 months had no independent effect on either serum leptin or leptin gene expression. In a short-term study, we found that fasting gradually reduced leptin levels in both healthy men and GHD adults, with a maximum reduction of 58% to 60% ($P < .01$) after 31 hours. No independent effect of GH suppression or GH substitution on serum leptin was found during fasting. Adipose tissue leptin mRNA correlated with serum leptin ($r = .51$, $P < .01$) and the body mass index ([BMI] $r = .55$, $P < .05$). Serum leptin levels and gene expression were significantly higher in women compared with men ($26.6 \pm 5.8$ *v* $10.0 \pm 1.30$ ng/mL, $P < .05$). However, in regression analysis accounting for the gender differences in subcutaneous femoral adipose tissue (FEM-CT), the difference in serum leptin disappeared, indicating that subcutaneous femoral fat or factors closely related to femoral fat (eg, sex hormones) may be causal factors for the gender difference in leptin.**


THE PHYSIOLOGICAL regulation of leptin is currently being investigated. Since a large variation is observed in leptin levels among humans with the same amount of adipose tissue, other determinants obviously may be of importance in regulating leptin levels. Most studies have shown that women have higher leptin levels than men even after adjusting for body fat.[1,2] Insulin and dexamethasone have been shown to increase leptin mRNA expression and leptin secretion in human preadipocytes.[3] Glucocorticoids increase leptin levels in most human in vivo studies,[4-6] whereas more prolonged insulin exposure is required to increase leptin levels and leptin gene expression in vivo.[7,8]

Adipose tissue is recognized as an important target tissue for growth hormone (GH). GH is a substantial factor for adipose tissue growth and differentiation,[9] and moreover, it has marked metabolic effects, especially on lipid and protein metabolism. In adipocytes, GH receptors are present and binding of the ligand seems to have both insulinomimetic and insulin antagonistic effects. During short-term incubation of adipocytes, insulinomimetic actions seem to dominate, with stimulation of lipogenesis, glucose transport, and antilipolytic activity.[10] Long-term in vitro incubations revealed lipolytic action and inhibition of glucose transport and glucose metabolism, inhibition of lipoprotein lipase, and activation of hormone-sensitive lipase.[11,12] Investigations in vivo support the presence of lipolytic action, with increased serum free fatty acid levels and reduced triglyceride accumulation together with increased lipid oxidation and energy expenditure leading to a reduction in adipose tissue mass.[13]

GH deficiency (GHD) in adults is associated with increased fat mass, and GH substitution promotes a marked change in body composition with a reduction of adipose tissue and an increase in lean body mass (LBM).[14] In rodents, both leptin and GH appear to have a weight-regulating effect and to increase energy expenditure. In addition, leptin and GH act on receptors found in a variety of tissues that belong to the same cytokine receptor superfamily of single transmembrane receptors.[15,16] Hence, we found it of interest to study whether GH, with its pronounced effect on adipose cell metabolism, regulates adipocyte leptin gene expression and secretion. Therefore, we investigated the effect of GH on leptin levels during GH treatment in (1) a long-term (4-month) study in GHD patients and (2) a short-term study (28-hour) in GHD patients and healthy young men during fasting, GH suppression, and GH substitution.

## SUBJECTS AND METHODS

### *Subjects*

Thirty-two adults with GHD for at least 1 year and eight healthy adults participated in the study, which was approved by the local Ethics Committee and the National Board of Health. GHD was defined as a peak stimulated serum GH level less than 5 μg/L. The diagnosis was based on two positive GH stimulation tests (L-arginine, insulin tolerance, clonidine, or heat tests). In cases with a deficiency of other hormones, at least 1 year of stable substitution was required before inclusion in the study. The patients were included in the study after informed consent in accordance with Helsinki Declaration II.

### *Study Design*

Two investigations were performed. In study 1, the design was double-blind and placebo-controlled. Twenty-four GHD patients never

*From the Department of Endocrinology and Metabolism, Aarhus University Hospital, Aarhus Amtssygehus; Aarhus Kommunehospital, Aarhus; and Department of Endocrinology, Hvidovre University Hospital, Denmark.*

*Submitted February 23, 1998; accepted May 13, 1998.*

*Supported by Fonden til lægevidenskabens Fremme, Danish Medical Research Council, the Aarhus University—Novo Nordisk Center for Research in Growth and Regeneration, and The Danish Diabetes Association.*

*Address reprint requests to Kurt Kristensen, MD, Department of Endocrinology and Metabolism, University Hospital Aarhus, Aarhus Amtssygehus, DK-8000 Aarhus C.*



*0026-0495/98/4712-0015$03.00/0*

previously treated with GH were randomized into two groups that received either GH 2 IU/m$^2$/d (Norditropin; Novo Nordisk, Copenhagen, Denmark) or placebo administered as daily subcutaneous injections for 4 months. In study 2, eight GHD patients and eight healthy men were investigated for 28-hour periods. GHD patients received GH replacement until 2 days before the examinations. The participants were admitted to the hospital after 12 hours of fasting. Blood parameters were evaluated during the following 28 hours. Healthy men were investigated for 28 hours during (1) fasting, (2) fasting and endogenous GH suppression with somatostatin (200 $\mu g \cdot h^{-1}$) and replacement with insulin (0.1 $mU \cdot kg^{-1} \cdot min^{-1}$) and glucagon (1.5 $ng \cdot kg^{-1} \cdot min^{-1}$), and (3) endogenous suppression as in (2) supplemented with 1.5 mg GH during the study period (half administered as six bolus injections and the other half as a continuous infusion). GHD patients were studied during (1) 28-hour fasting and (2) fasting and GH substitution.

### *Anthropometry*

Anthropometric examinations were performed at the beginning of the study and after 4 months. Height and body weight were measured, and the body mass index ([BMI] weight in kilograms divided by height in meters squared) was calculated. Body composition was evaluated by dual-energy x-ray absorptiometry (DEXA) using a QDR-2000 densitometer (Hologic, Waltham, MA). The following measurements were used: total fat mass (FM-DEXA), relative fat mass (FM%-DEXA), and LBM-DEXA. Intraabdominal/subcutaneous adipose tissue was assessed by computed tomography (CT) with a Somatom Plus-S scanner (Siemens, Erlangen, Germany). The area was scanned in 10-mm cross-sectional slices at the femora 10 cm proximal to the patella and at the umbilical level using 120 kV and 330 mA. The following measurements were used: subcutaneous abdominal fat (ABD-CT), intraabdominal fat (INTRA-CT), subcutaneous femoral fat (FEM-CT), and the muscle to fat ratio at the midthigh (MU/FAT-CT).

### *Adipose Tissue Biopsy and Leptin Expression*

Adipose tissue from each patient in study 1 was obtained from the abdominal region by liposuction before and after 4 months of treatment. Briefly, the skin was anesthetized using 10 mL lidocaine (10 mg/mL). A small incision was made, and isotonic NaCl was injected into the adipose tissue. The liposuction cannula was inserted and the vacuum applied. A total amount of 4 to 6 g was obtained and immediately frozen in liquid nitrogen. RNA was isolated using the trizol reagent (GIBCO-BRL, Gaithersburg, MD). Reverse transcription and amplification was performed using random hexamer primers as described by the manufacturer (GeneAmp PCR kit; Perkin Elmer-Cetus, Norwalk, CT). The leptin primers used in the polymerase chain reaction (PCR) spanned a cDNA product of 352 base pairs. The sense OB-primer corresponds to OB-cDNA 85 to 107 and the antisense strand of the OB-cDNA 417 to 437.[17] β-Actin mRNA was amplified as a housekeeper marker, and the semiquantitative multiplex PCR method "primer-dropping"[18] was used to monitor mRNA expression. The β-actin primers were added after 11 cycles (primer-dropping), and initial studies have shown that the reaction was linear between 30 and 36 cycles for both sets of primers, and 33 cycles were therefore chosen. Finally, 8 μL of the PCR product was loaded on a 2% agarose gel and stained with ethidium bromide, and the band intensity was scanned in a Bio-Rad 1000 gel scanner (Richmond, CA). Figure 1A demonstrates the linear amplification of β-actin and OB-PCR products, and Fig 1B shows that increasing amounts of OB-RNA are detectable with the primer-dropping method. The coefficient of variation was 5.4%. Serum leptin was measured with a radioimmunoassay method (Linco Research, St Charles, MO) in serum samples obtained from subjects after 10 hours of fasting. The range of the standard curve in this assay is 0.5 to 100 ng/mL. The intraassay coefficient of variation was 3.7%.

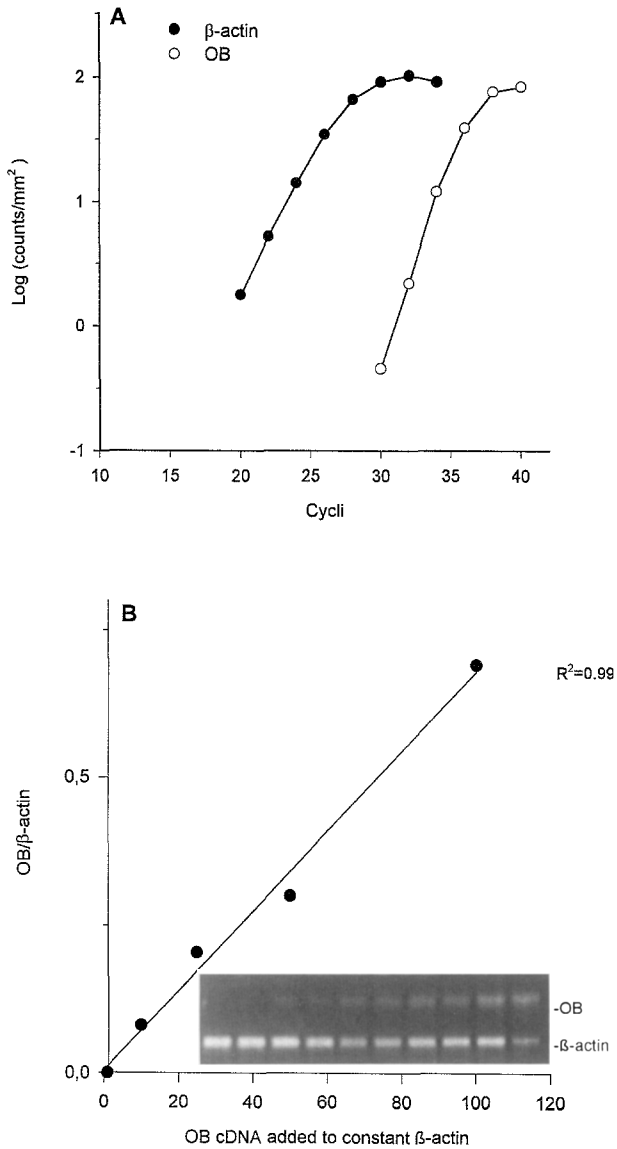


**Fig 1. (A) PCR with β-actin primers shows linear amplification from 20-27 cycles and with OB primers from 28-36 cycles. (B) Quantitation of the relative amount of OB PCR products. Increasing amounts of OB cDNA product are added to a constant amount of β-actin. Photograph of EtBr gel shows PCR products in duplicate.**

### *Statistics*

All analyses were performed using SPSS statistical software (SPSS, Chicago, IL). Differences between groups were tested with Student's unpaired and paired *t* test where appropriate. If necessary, data were logarithmically transformed to obtain normality. Leptin was log-transformed in all correlations and calculations. Multiple and linear regression analyses were used to relate variables. Backward stepwise regression analysis was performed to evaluate the contributions of independent variables to the determination of leptin levels. A *P* value of .05 was used as the criterium for entry at each step. Covariance analyses were used to adjust log-leptin for different estimates of body composition, and the significance of differences between groups was assessed by the F statistic. Results are expressed as the mean ± SEM. *P* values less than .05 were considered significant (two-way significance).

**Table 1. Characteristics of the GHD Subjects**

| Characteristic | GH | | Placebo | |
|---|---|---|---|---|
| | 0 mo | 4 mo | 0 mo | 4 mo |
| Sex ratio (male/female) | 11/2 | 11/2 | 7/4 | 7/4 |
| Weight (kg) | 93.9 ± 5.2 | 92.4 ± 5.4* | 77.1 ± 4.9 | 77.1 ± 4.9 |
| BMI (kg/m²) | 29.9 ± 1.5 | 29.4 ± 1.5* | 27.0 ± 1.9 | 26.9 ± 1.8 |
| s-Leptin (ng/mL) | 11.6 ± 2.0 | 10.0 ± 2.1* | 15.5 ± 4.3 | 17.5 ± 5.9 |
| s-FFA (mmol/L) | 525 ± 61 | 578 ± 63 | 659 ± 209 | 593 ± 176 |
| s-IGF-I (μg/L) | 111.6 ± 16.7 | 318.2 ± 30.5† | 109.7 ± 16.7 | 103.4 ± 17.7 |
| s-Insulin (mU/L) | 38.4 ± 8.4 | 55.3 ± 9.6* | 39.4 ± 8.8 | 40.4 ± 6.0 |
| s-Glucose (mmol/L) | 5.03 ± 0.07 | 5.38 ± 0.16* | 4.99 ± 0.01 | 4.97 ± 0.12 |
| INTRA-CT (cm³) | 160.0 ± 18.5 | 119.3 ± 12.5* | 160.1 ± 19.3 | 163.9 ± 22.9 |
| ABD-CT (cm³) | 300.2 ± 33.0 | 269.8 ± 34.9* | 266.7 ± 40.2 | 256.7 ± 44.0 |
| MU/FAT-CT ratio | 2.13 ± 0.26 | 2.70 ± 0.47* | 2.01 ± 0.28 | 2.22 ± 0.29 |
| FM-DEXA (kg) | 32.4 ± 2.7 | 28.1 ± 2.9† | 26.9 ± 2.0 | 26.6 ± 1.9 |
| LBM-DEXA (kg) | 58.3 ± 3.2 | 61.0 ± 3.3† | 47.6 ± 3.9 | 47.8 ± 4.0 |
| FM%-DEXA | 34.09 ± 1.81 | 29.65 ± 2.11† | 35.04 ± 0.02 | 35.06 ± 0.02 |

NOTE. Data are the mean ± SEM. Blood samples were obtained after an overnight fast.
Abbreviations: s, serum; FFA, free fatty acid.
*$P < .05$, †$P < .001$ *v* time 0. Insulin, FFA, leptin, and IGF-I were log-transformed to obtain normality.

## RESULTS

### Study 1: GH Treatment for 4 Months

Descriptive data are listed in Table 1 for subjects in study 1. The sex ratio was equal in the two study groups ($P = .27$). The mean age was 39.1 ± 11.6 years in the GH group and 36.8 ± 9.4 years in the placebo group (NS). No age difference was observed between men and women ($P = .45$).

#### *Effect of GH Treatment on Estimates of Body Composition*

At baseline, the BMI was equal between men and women (28.15 ± 1.43 *v* 29.12 ± 2.51) but FM% was significantly lower in men (31.9% ± 1.11% *v* 43.0% ± 2.61%, $P < .0001$). In the GH-treated group, weight loss occurred (93.9 ± 5.2 *v* 92.4 ± 5.4 kg, $P < .05$) during 4 months of GH treatment. FM-DEXA decreased by 4.3 ± 0.5 kg ($P < .001$) and LBM-DEXA increased by 4.7%, or 2.7 ± 0.6 kg ($P < .001$). The MU/FAT-CT ratio increased by 26.8% (2.1 ± 0.3 *v* 2.7 ± 0.5, $P < .06$) in GH-treated GHD patients. GH did not significantly increase the relative loss of INTRA-CT fat mass compared with the other depots (subcutaneous or peripheral fat). No changes were observed in the placebo group.

#### *Effect of GH Treatment on Serum Leptin and Leptin Gene Expression*

At baseline, serum leptin levels were significantly higher among women (n = 6) versus men (n = 18) (26.6 ± 5.8 *v* 10.0 ± 1.3 ng/mL, $P < .05$). When adjusting log-leptin for FEM-CT, the difference between men and women disappeared (significance of F = .27), whereas ABD-CT did not have the same effect (significance of F = .06). If log-leptin was adjusted for differences in INTRA-CT, there was still a difference between men and women (significance of F < .01). Leptin correlated positively with the BMI in all GHD patients ($r = .45$, $P < .05$). There was also a positive correlation with most indices of adiposity (Table 2). However, there was no correlation with INTRA-CT (Fig 2) or LBM-DEXA. There was a significant negative correlation with the MU/FAT-CT ratio (−.74, $r = .0001$).

GH treatment for 4 months significantly decreased ($P < .05$) serum leptin from 11.6 ± 2.0 to 10.0 ± 2.1 ng/mL (Table 1). This difference in the leptin level did not remain significant after adjustment for FM-DEXA. When comparing the change in leptin in placebo versus GH-treated subjects, a significant difference between the two groups was found ($P = .03$), but adjusting this difference in leptin for the change in fat mass also caused the difference to disappear (significance of F = .43). To verify whether the findings for serum leptin were reflected at the transcriptional level, subcutaneous abdominal adipose tissue biopsies were taken. Determination of leptin mRNA confirmed that no change in leptin gene expression occurred during the 4-month GH treatment (Fig 3). The correlation between leptin mRNA in subcutaneous adipose tissue and the serum leptin level was .51 ($P = .01$) and twofold higher leptin expression was found in women compared with men ($P = .03$). A significant correlation was also observed between leptin mRNA and the BMI even when adjusting for sex ($r = .55$, $P < .05$).

After 4 months, similar correlations between serum leptin and estimates of body fat were observed as found initially in the GH-treated group. A significant correlation was observed between the relative change in leptin and the relative change in FEM-CT for both the GH-treated and placebo groups combined ($r = .62$, $P < .003$).

Multiple linear stepwise regression analyses were performed with leptin as the dependent variable and the following indepen-

**Table 2. Pearson's Correlation Coefficient Between Leptin and Estimates of Body Fat at Baseline in 24 GHD Patients**

| Parameter | *r* | *P* |
|---|---|---|
| FM%-DEXA | .86 | <.0001 |
| FM-DEXA | .62 | <.001 |
| ABD-CT | .73 | <.0001 |
| FEM-CT | .74 | <.0001 |
| BMI | .45 | <.05 |
| LBM-DEXA | .25 | .24 |
| INTRA-CT | .00 | .99 |
| MU/FAT-CT | −.74 | <.0001 |

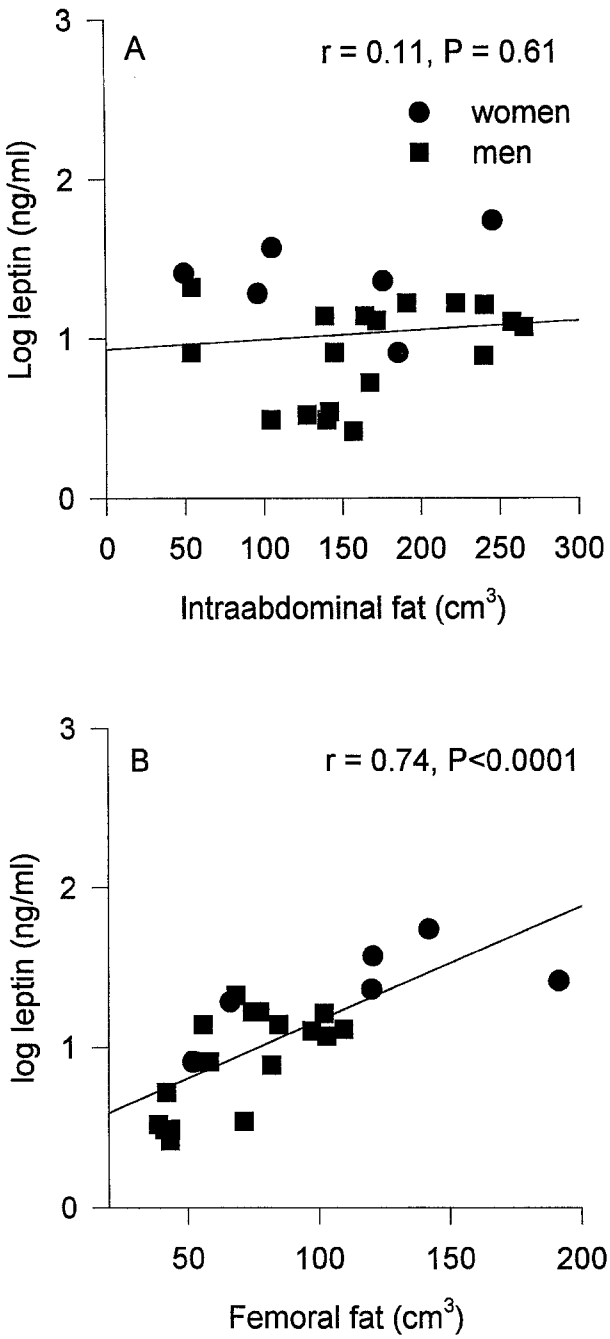


**Fig 2. (A) Correlation between leptin and intraabdominal adipose tissue and (B) subcutaneous adipose tissue in 24 GHD patients.**

dent variables: an estimate of body fat, insulin-like growth factor-I (IGF-I), insulin, age, and gender. The different estimates of body fat were introduced separately in multiple stepwise regression analyses because of colinearity. Most estimates of body fat (FM-DEXA, FM%-DEXA, FEM-CT, and ABD-CT) were independent significant determinants of serum leptin levels with similar partial correlation coefficients. In addition, gender remained an independent significant determinant of leptin in all equations. IGF-I, INTRA-CT, fasting insulin, and age did not contribute significantly to the prediction of leptin levels (data not shown).

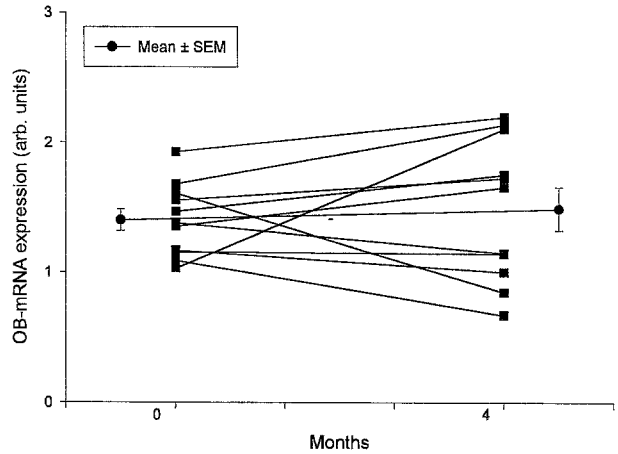


**Fig 3. OB-mRNA expression in subcutaneous adipose tissue before and after 4 months of GH treatment.**

*Leptin and Blood Parameters*

At baseline and after 4 months, no correlation was found between leptin and nonesterified fatty acid (NEFA), glucose, insulin, or IGF-I, respectively. In the placebo group and GH group, no correlations were observed between the differences in leptin and the differences in insulin. In the intervention group, insulin increased by 11% ($P < .005$) and IGF-I by 24% ($P < .0001$) (Table 1). Glucose increased significantly after 4 months of GH treatment (5.03 ± 0.03 *v* 5.38 ± 0.16, $P < .05$). No change was observed for NEFA. Serum insulin, IGF-I, and glucose levels were significantly increased in the GH group.

## Study 2: Short-Term Effects of GH

Basal characteristics are listed in Table 3. In GHD and healthy men, we did not find any significant difference in baseline leptin levels, and there was no difference in FM-DEXA. This is probably explained by the daily GH replacement therapy in GHD subjects prior to the investigation. The age difference was not considered a problem, as the subjects were their own controls in the three situations studied. Among healthy non-obese young men, the alterations in serum leptin were similar in the three situations studied: (1) fasting, (2) fasting + GH suppression, or (3) fasting + endogenous GH suppression with GH substitution (Fig 4). No differences were observed among the three situations, and the leptin values were pooled. The mean value decreased by 28% within the first 7

**Table 3. Characteristics of GHD and Healthy Men in Study 2**

| Characteristic | GHD (n = 8) | Healthy (n = 8) |
|---|---|---|
| Age (yr) | 46.5 ± 3.9 | 24.4 ± 0.3* |
| Weight (kg) | 75.9 ± 0.7 | 74.6 ± 0.2 |
| BMI (kg/m²) | 25.4 ± 1.6 | 23.4 ± 0.8 |
| Serum-leptin (ng/mL) | 6.7 ± 1.9 | 4.6 ± 1.0 |
| Serum-insulin (mU/L) | 43.4 ± 17.9 | 37.6 ± 4.4 |
| LBM-DEXA (kg) | 58.3 ± 4.8 | 61.0 ± 1.3 |
| FM-DEXA (kg) | 15.9 ± 2.2 | 12.5 ± 0.9 |

NOTE. Data are the mean ± SEM. Blood samples were obtained after an overnight fast.

*$P < .001$ *v* GHD. Insulin and leptin were log-transformed to obtain normality.

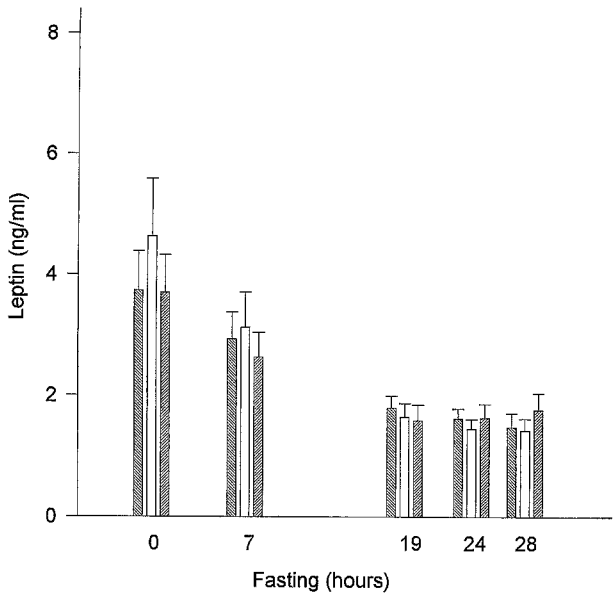


**Fig 4. Leptin levels in healthy men influenced by (▨) fasting, (□) fasting + endogenous GH suppression, and (▨) fasting + endogenous GH suppression supplemented with GH infusion. Fasting reduced serum leptin by 58%.**

hours of fasting after admittance (4.02 ± 0.43 *v* 2.90 ± 0.27 ng/mL, $P < .0001$) and a further 42% decrease in leptin was found from 7 to 19 hours (2.90 ± 0.27 *v* 1.67 ± 0.63 ng/mL, $P < .0001$), but from 19 to 24 hours, the decrease plateaued (1.67 ± 0.63 *v* 1.57 ± 0.10 ng/mL, $P = .07$) and reached steady state after 24 hours of fasting. The effects of GH were also studied in eight GHD subjects with an identical protocol (GH suppression was omitted). The same results were found as in healthy men, with no influence of GH substitution on leptin levels. Fasting caused a 36% decrease in leptin from 0 to 7 hours ($P < .001$) and a further 32% decrease from 7 to 19 hours ($P < .005$). Then, a steady state was reached. There were no differences in insulin levels at the different examination times between the fasting condition and fasting with GH substitution (data not shown).

## DISCUSSION

The impact of gender, GH status, and fasting on the serum leptin level and leptin expression in both healthy subjects and GHD adults was studied. Among GHD subjects, women have higher leptin levels compared with men, in accordance with previous data in healthy subjects.[2] In a multiple regression analysis in which estimates of body fat were included, gender remained a significant determinant of leptin levels. This strong influence of gender was observed in some previous reports[2,19,20] but not all.[21] At baseline in study 1, women had a significantly higher leptin level than men and adjusting leptin for INTRA-CT did not affect the difference, whereas adjusting for FEM-CT eliminated the gender difference. This may suggest that the gender difference in leptin is related to topographical differences in body fat and especially differences in subcutaneous fat particular to the femoral region.

Leptin expression in subcutaneous adipose tissue biopsies was measured, and we found higher expression in women compared with men. This might, on the other hand, suggest that factors other than adipose tissue topography influence leptin expression. We had no opportunity to measure adipose cell size, but correcting mRNA levels for the subcutaneous adipose tissue mass caused the difference to disappear ($P = .11$), indicating that cell size may be an explanation, as previously found.[22]

When investigating the two sexes together, most estimates of body fat correlated well with leptin levels; however, the INTRA-CT mass did not, suggesting that visceral fat is of minor importance for the circulating leptin level. This is in accordance with a previous report in healthy subjects wherein leptin mRNA expression was lower in intraabdominal compared with subcutaneous adipose tissue.[23] In GHD patients, leptin reflects total body fat stores and especially the percentage of adipose tissue mass.

Serum leptin levels decreased significantly after 4 months of GH treatment, but no change was found after placebo. After controlling leptin levels for the decrease in total adipose tissue mass, there was no change during GH treatment, and in accordance with these findings, leptin gene expression in abdominal adipose tissue was unaffected by 4 months of GH treatment. This supports the notion that the effect of GH on leptin is secondary to reductions in fat mass. This is in agreement with one previous study[24] but not another.[25] In a case-control study, GHD patients had a higher serum leptin level than BMI-matched healthy controls, indicating that GH might decrease leptin levels.[25] This could reflect the differences in study design (follow-up *v* case-control, GHD *v* GHD and healthy) or the difficulties inherent to BMI or bioelectrical impedance measurements in assessing body fat compared with DEXA scanning. The BMI does not provide any precise information on the amount of fat, especially in lean subjects, and bioelectrical impedance measures total body water content, which is decreased in GHD compared with normal subjects.[26] These problems might be indicated by the lack of difference in body composition between GHD subjects without GH replacement and healthy controls in the study by Al-Shoumer et al[25] but found in most other studies.[26,27] In addition, bioelectrical impedance provides no information on body fat topography (leptin does not correlate with intraabdominal fat).

No correlation was found between leptin and fasting insulin as previously demonstrated in GHD subjects.[24,25] GH increased insulin levels by 11% and in most studies, insulin seems to increase plasma leptin after several hours.[7,8] Hence, an indirect stimulating effect of GH, via insulin, on leptin levels could be expected but was not found.

We also studied the impact of short-term GH treatment on leptin levels (study 2). The participants fasted for 12 hours before admission to the hospital, and serum leptin levels were measured the following 28 hours at the hospital. We found that leptin decreased rapidly during the first 36 hours of fasting, and afterward, it remained constant at 42% of the initial level. This is in agreement with our recent study wherein leptin in obese subjects was reduced to 40% of the prefasting level.[28] Suppression of endogenous GH secretion with somatostatin did not influence the decline in serum leptin during fasting in healthy men. The same was also found when suppressing endogenous GH secretion and substituting with GH infusion. GH infusion to GHD patients showed the same results, with no influence on the fasting-induced decline in leptin levels. The decline was similar in healthy and GHD subjects and remained at the same level.

This is in contrast to another study in which GH and IGF-I were administered to GHD patients for 5 days. A diverse effect of IGF-I and GH was found. Leptin decreased during IGF-I treatment and lagged behind the prompt reduction of insulin secretion by 24 to 48 hours, whereas GH treatment increased leptin after 2 days and also with a 24-hour later response compared with the increase in insulin.[29] An explanation for the incomparable results of the two studies may be that the change in leptin was caused by the action of GH/IGF-I on insulin levels, which we did not observe during fasting, wherein insulin levels were similar during the two situations in GHD patients.

In the present study, we found no influence of GH on leptin levels or leptin gene expression. Serum leptin levels in GHD adults were related to estimates of adiposity, as in healthy subjects. In women, significantly higher levels of serum leptin and leptin gene expression were observed as compared with men. This gender difference persisted when taking the total fat mass into account. Adjusting leptin for subcutaneous adipose tissue, particularly in the femurogluteal region, caused the difference to disappear. This could be due to the fact that subcutaneous adipose tissue in the femurogluteal region is responsible for gender differences in leptin per se, or to factors related to femurogluteal fat deposition, eg, sex hormones (estrogens or androgens). Fasting reduced leptin levels by 58% to 60% in healthy men and GHD subjects, and the levels were unaffected by short-term GH treatment.

## ACKNOWLEDGMENT

The technical assistance of Lenette Pedersen and Dorte Phillip is gratefully appreciated. Novo Nordisk Pharmaca kindly provided GH and placebo.

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