Marked gender differences in ambulatory morning growth hormone values in young adults

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The influence of gender on serum concentrations of growth hormone (GH) and 12 other endocrine analytes was investigated in sera drawn from 291 healthy medical students in the ambulatory state in the morning, after fasting overnight. GH was measured with a sensitive noncompetitive fluoroimmunoassay. The median GH value was 80-fold higher in women 21–26 years old than in age-matched men (14.4 vs 0.18 mIU/L), compared with a female/male ratio of 2.2 for 17β-estradiol and a male/female ratio of 14 for testosterone. Furthermore, the values for sex hormone-binding globulin, follicle-stimulating hormone, luteinizing hormone, prolactin, and insulin-like growth factor 1 (IGF-1) were higher, whereas the values for free thyroxine, triiodothyronine, thyroid-stimulating hormone, and parathyroid hormone were lower in the women. The median GH value was 68-fold higher in women 27–43 years old than in age-matched men (10.9 vs 0.16 mIU/L). Women taking contraceptives with ethinyl estradiol and desogestrel or levonorgestrel had higher GH values, and the desogestrel group had lower IGF-1 values than women not taking contraceptives. The median GH values in these groups were 125- and 117-fold higher, respectively, than in men 21–26 years old. The results suggest that routine morning activity produces a marked GH response in >90% of young women but in very few age-matched men. The effect on GH was even more pronounced in women taking oral contraceptives, suggesting that the intake of ethinyl estradiol contributes to higher GH concentrations in these women.

More than 90% of growth hormone (GH) production is secreted in a pulsatile mode in both men and women (1). The pattern of this GH secretion in humans is rhythmic and oscillatory rather than episodic (2). There are significant gender differences in GH secretion (3, 4). The mean serum GH concentration over 24 h is ~2–3 times higher in premenopausal women than in men of the same age. This difference is mainly because of higher GH secretory burst amplitudes (1, 2, 5). GH release has also been reported to be consistently more irregular in women than in men, both in light and dark periods (5). In contrast, the frequency of GH secretory bursts during a 24-h period, the half-life of GH, and the estimated GH basal release have been reported to be similar in men and women (1, 2). Estrogen has been suggested as the dominant factor underlying the sex difference in the human GH axis (4).

As part of the training in clinical chemistry for medical students at Uppsala University Hospital, blood samples were obtained from ~120 students each year. The samples were taken on an ambulatory basis in the morning, after an overnight fast. The concentrations of various hormones, including GH, in the serum were measured according to the clinical chemistry routine. Late in 1993, a more sensitive time-resolved sandwich fluoroimmunoassay for GH was introduced in our laboratory. It then became apparent that the difference in serum GH concentrations between healthy young men and women was considerably larger than the differences that we observed with our competitive radioimmunoassay or that had previously been reported in the literature, in samples taken under similar conditions (6, 7).

The female students had ~60- to 100-fold higher median GH concentrations than the male students. Such a large difference had not been documented for any other hormone or other compound. The highest values were found in women taking oral contraceptives. To rule out the possibility that this was a coincidence, a prospective 3-year study on the influence of gender on GH and other hormones was initiated. GH and 12 other hormones and hormone-related analytes were measured consecutively in blood samples obtained from medical students in the ambulatory state in the morning, after an overnight fast. Age-matched groups of healthy men and eumenorrheic women were compared.
Because ~40% of the female students used hormonal contraceptives, an analysis of the influence of such drugs was included. The majority of these female students took oral doses of either levonorgestrel (LEV) or desogestrel (DES) in combination with ethinyl estradiol (EE); they were divided into two study groups on this basis.

Materials and Methods
Sera were drawn in 1994, 1995, and 1996 from medical students. Written informed consent was given by the students. Those who were not healthy or were taking any medication that could influence hormone concentrations (except for the women on oral contraceptives) were excluded. Also excluded were amenorrheic women and pregnant female students. In women, the samples were taken at random in the menstrual cycle. The study population was divided into six groups according to gender, age, and the use of contraceptives (Fig. 1).

In the younger age interval, samples were obtained from 125 male students (mean age, 23.6 years; median age, 23.0; range, 21–26) and from 75 female students (mean age, 23.4 years; median age, 23.0; range 21–26). Forty-one of 67 female medical students using hormonal contraceptives were included: 19 women taking a combination of 30–40 mg of EE and 50–150 mg of LEV (EELEV women) and 22 women taking a combination of 20–30 mg of EE and 150 mg of DES (EEDES women). All women on hormonal contraceptives had a free interval of 7 days. The mean ages of the EELEV and EEDES women were 23.0 years (median, 23.0; range, 21–26) and 22.5 years (median, 22.5; range, 21–24), respectively.

In the higher age interval, samples were obtained from 25 male students and 25 age-matched female students. In both groups, the mean age was 32.6 years (median, 32.0; range, 27–43).

The serum samples were obtained in the morning when the subjects came to the hospital, in the ambulatory state and after overnight fasting. The sampling procedure was part of the teaching in clinical chemistry, where the students drew sera from one another. The situation was the same in all years. Sera were analyzed for 12 different hormones and sex hormone-binding globulin (SHBG).

Methods
GH in 50 μL of serum (S-GH, 22 kDa) was measured with a noncompetitive sandwich time-resolved fluoroimmunoassay (AutoDELFIA™ hGH kit, Wallac Oy) specific for the pituitary GH 22-kDa isoform. Two different mouse monoclonal antibodies directed to different sites on the GH 22-kDa molecule were used. One antibody was immobilized onto the walls of microtiter plates, and the other, labeled with europium chelate, was in solution. The results were expressed in mIU/L, using as a reference standard the 1st international reference preparation of GH (80/505). The minimal detection limit was 0.009 mIU/L. The within- and between-assay coefficients of variation were 1.1% and 2.3%, respectively.

Insulin-like growth factor 1 (IGF-1) was measured, after acid-ethanol extraction of 100 μL of serum, with the use of a double antibody radioimmunoassay (IGF-1 By extraction kit, Nichols Institute Diagnostics), based on the competition between 125I-labeled IGF-1 and sample IGF-1. The immunocomplex was precipitated with goat anti-rabbit IgG antibodies. The results were expressed in μg/L, using as a reference the 1st International Reference Preparation of IGF-1 (87/518). The minimal detection limit was 30 μg/L. The within- and between-assay coefficients of variation were 6% and 8%, respectively.

The serum concentrations of cortisol, 17β-estradiol, free thyroxine, triiodothyronine (T3), and testosterone were measured with competitive immunoassays (AutoDELFIA Cortisol kit, AutoDELFIA Estradiol kit, AutoDELFIA FreeThyroxin [FT4] kit, and AutoDELFIA Triiodothyronine [T3] kit from Wallac Oy; Coat-A-Count® Total Testosterone kit from Diagnostic Products Corporation).

The serum concentrations of follicle-stimulating hormone (FSH), luteinizing hormone (LH), thyroid-stimulating hormone, prolactin, SHBG, and parathyroid hormone were measured with noncompetitive sandwich immunoassays (AutoDELFIA hFSH kit, AutoDELFIA hLH Spec kit, AutoDELFIA hTSH Ultra kit, AutoDELFIA Prolactin kit, and AutoDELFIA SHBG kit from Wallac Oy; INTACT PTH kit from Nichols Institute Diagnostics).

Statistics
The median and the 2.5th and 97.5th percentiles of the hormone concentrations were calculated for each group of individuals. The Mann–Whitney nonparametric test was used to calculate the significance of differences between groups.

Results
The median values and the 2.5th and 97.5th percentiles for all hormones assayed in 125 men, 75 women, 19 EELEV women, and 22 EEDES women 21–26 years of age are shown in Table 1, and those in 25 men and 25 women of ages 27–43 years are shown in Table 2. Degrees of significance of differences between groups are indicated. The women not taking oral contraceptives served as a reference group for the EELEV and EEDES women in the younger group of students.

Differences Between Women and Men
Ages, 21–26 years. The distributions of the GH values in the different groups of students are illustrated in Fig. 1. There was a difference in the skewness of the data between men and women, the data being skewed toward higher values in the men and in the opposite direction in the women. The median GH value was 14.4 mIU/L in the group of 75 women, ages 21–26 years, a value 80-fold higher than that in the 125 men of that age, in whom it was 0.18 mIU/L. The corresponding median IGF-1 values were 322 and 290 μg/L, i.e., the value was 1.1-fold higher (P <0.01) in the women than in the men.
Fig. 1. Distributions of GH concentrations (mIU/L) in sera obtained in the ambulatory state in the morning, after an overnight fast, from 291 medical students divided into different groups: 125 men and 75 women, ages 21–26 years; 19 women, ages 21–26 years, taking EE and LEV contraceptives (EELEV women); 22 women, ages 21–24 years, taking EE and DES contraceptives (EEDES women); and 25 men and 25 women, ages 27–43 years.
The male/female and female/male ratios for all median hormone values in the men and women, ages 21–26 years, are shown in Fig. 2. The gender difference was largest for GH, with a ratio of 80. The ratios for the sex hormones testosterone and 17β-estradiol were 14 and 2.2, respectively. The median values for GH, SHBG, 17β-estradiol, FSH, LH, prolactin \( (P < 0.001) \), and IGF-1 \( (P < 0.01) \) were higher in women than in men, whereas those for testosterone, free thyroxine \( (P < 0.001) \), T3 \( (P < 0.01) \), thyroid-stimulating hormone, and parathyroid hormone \( (P < 0.05) \) were lower. The median value for cortisol did not differ significantly between men and women (Table 1). The corresponding IGF-1 values were 256 and 218 µg/L, which did not differ significantly. The median IGF-1 values were lower in older men and older women than in younger men and women \( (P < 0.001) \). The median values for GH, SHBG, 17β-estradiol \( (P < 0.001) \), FSH, LH, and prolactin \( (P < 0.01) \) were higher in women than in men, whereas the median testosterone value was lower \( (P < 0.005; \) Table 2).

**WOMEN 21–26 YEARS OF AGE TAKING ORAL CONTRACEPTIVES VS REFERENCE GROUP**

The median GH value was 21.0 mIU/L in 19 EELEV women and 22.5 mIU/L in 22 EEDES women. These values were 117- and 125-fold higher than in the men 21–26 years of age. The corresponding median IGF-1 values were 256 and 218 µg/L, which did not differ significantly. The median IGF-1 values were lower in older men and older women than in younger men and women \( (P < 0.001) \). The median values for GH, SHBG, 17β-estradiol \( (P < 0.001) \), FSH, LH, and prolactin \( (P < 0.01) \) were higher in women than in men, whereas the median testosterone value was lower \( (P < 0.001; \) Table 2).

### Table 1. Median values and 2.5th and 97.5th percentiles (in parentheses) of serum concentrations of analytes in samples obtained in the ambulatory state in the morning after an overnight fast.

<table>
<thead>
<tr>
<th>Analyte</th>
<th>Men 125&lt;sup&gt;a,b&lt;/sup&gt;</th>
<th>Women 75&lt;sup&gt;b,e&lt;/sup&gt;</th>
<th>EELEV women 19&lt;sup&gt;e&lt;/sup&gt;</th>
<th>EEDES women 22&lt;sup&gt;d&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>GH, mIU/L</td>
<td>0.18&lt;sup&gt;e&lt;/sup&gt;</td>
<td>14.4</td>
<td>21.0&lt;sup&gt;f&lt;/sup&gt;</td>
<td>22.5&lt;sup&gt;e&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td>(0.06–4.40)</td>
<td>(0.37–53.0)</td>
<td>(2.40–60.0)</td>
<td>(5.70–6.0)</td>
</tr>
<tr>
<td>IGF-1, µg/L</td>
<td>290&lt;sup&gt;e&lt;/sup&gt;</td>
<td>322</td>
<td>305</td>
<td>280&lt;sup&gt;e&lt;/sup&gt;</td>
</tr>
<tr>
<td>Cortisol, nmol/L</td>
<td>509</td>
<td>487</td>
<td>837&lt;sup&gt;a&lt;/sup&gt;</td>
<td>873&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Testosterone, nmol/L</td>
<td>23.0&lt;sup&gt;e&lt;/sup&gt;</td>
<td>1.60</td>
<td>0.83&lt;sup&gt;e&lt;/sup&gt;</td>
<td>1.00&lt;sup&gt;e,h&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td>(13.0–36.0)</td>
<td>(0.70–3.00)</td>
<td>(0.20–1.51)</td>
<td>(0.86–3.40)</td>
</tr>
<tr>
<td>SHBG, nmol/L</td>
<td>31.2&lt;sup&gt;e&lt;/sup&gt;</td>
<td>60.2</td>
<td>119&lt;sup&gt;e&lt;/sup&gt;</td>
<td>231&lt;sup&gt;e,i&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td>(15.9–61.3)</td>
<td>(30.1–124)</td>
<td>(57.0–214)</td>
<td>(90.3–408)</td>
</tr>
<tr>
<td>17β-estradiol, pmol/L</td>
<td>120&lt;sup&gt;e&lt;/sup&gt;</td>
<td>259</td>
<td>81.2&lt;sup&gt;e&lt;/sup&gt;</td>
<td>70.5&lt;sup&gt;e,h&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td>(69.9–166)</td>
<td>(76.8–1170)</td>
<td>(50.0–1000)</td>
<td>(27.0–114)</td>
</tr>
<tr>
<td>FSH, µg/L</td>
<td>0.56&lt;sup&gt;e&lt;/sup&gt;</td>
<td>0.86</td>
<td>0.55&lt;sup&gt;f&lt;/sup&gt;</td>
<td>0.30&lt;sup&gt;e&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td>(0.19–1.36)</td>
<td>(0.23–2.00)</td>
<td>(0.01–1.51)</td>
<td>(0.02–1.20)</td>
</tr>
<tr>
<td>LH, µg/L</td>
<td>0.67&lt;sup&gt;e&lt;/sup&gt;</td>
<td>0.96</td>
<td>0.38&lt;sup&gt;e&lt;/sup&gt;</td>
<td>0.08&lt;sup&gt;e,h&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td>(0.26–1.22)</td>
<td>(0.06–5.40)</td>
<td>(0.01–1.87)</td>
<td>(0.02–0.97)</td>
</tr>
<tr>
<td>Prolactin, µg/L</td>
<td>6.90&lt;sup&gt;e&lt;/sup&gt;</td>
<td>8.90</td>
<td>8.70</td>
<td>10.8</td>
</tr>
<tr>
<td></td>
<td>(3.80–14.5)</td>
<td>(3.60–34.0)</td>
<td>(6.30–18.0)</td>
<td>(3.70–24.0)</td>
</tr>
<tr>
<td>TSH, mIU/L</td>
<td>2.00&lt;sup&gt;f&lt;/sup&gt;</td>
<td>1.67</td>
<td>2.30&lt;sup&gt;f&lt;/sup&gt;</td>
<td>2.33</td>
</tr>
<tr>
<td></td>
<td>(0.89–4.60)</td>
<td>(0.70–4.50)</td>
<td>(1.23–4.30)</td>
<td>(0.30–5.30)</td>
</tr>
<tr>
<td>FT4, pmol/L</td>
<td>14.4&lt;sup&gt;e&lt;/sup&gt;</td>
<td>12.1</td>
<td>10.6</td>
<td>11.5</td>
</tr>
<tr>
<td></td>
<td>(11.0–18.1)</td>
<td>(9.10–16.0)</td>
<td>(9.20–14.9)</td>
<td>(9.50–15.4)</td>
</tr>
<tr>
<td>T&lt;sub&gt;3&lt;/sub&gt;, nmol/L</td>
<td>1.97&lt;sup&gt;f&lt;/sup&gt;</td>
<td>1.83</td>
<td>2.40&lt;sup&gt;e&lt;/sup&gt;</td>
<td>2.52&lt;sup&gt;e&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td>(1.57–2.50)</td>
<td>(1.21–2.50)</td>
<td>(2.00–3.50)</td>
<td>(1.81–3.30)</td>
</tr>
<tr>
<td>PTH, ng/L</td>
<td>25.0&lt;sup&gt;f&lt;/sup&gt;</td>
<td>28.0</td>
<td>23.0</td>
<td>24.5&lt;sup&gt;f&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td>(12.4–46.0)</td>
<td>(14.8–50.0)</td>
<td>(16.2–43.0)</td>
<td>(9.30–59.0)</td>
</tr>
</tbody>
</table>

<sup>a</sup> n = 93 for IGF-1; n = 119 for cortisol; n = 118 for 17β-estradiol.
<sup>b</sup> Age range, 21–26 years.
<sup>c</sup> n = 74 for IGF-1; n = 68 for cortisol and 17β-estradiol.
<sup>d</sup> Age range, 21–24 years.
<sup>e</sup> P < 0.001 vs women.
<sup>f</sup> P < 0.05 vs women.
<sup>g</sup> P < 0.01 vs women.
<sup>h</sup> P < 0.05 vs EELEV women.
<sup>i</sup> P < 0.001 vs EELEV women.
<sup>j</sup> TSH, thyroid-stimulating hormone; FT4, free thyroxine; and PTH, parathyroid hormone.

*Ages, 21–26 years.* The median GH value was 10.9 mIU/L in the group of 25 women, ages 27–43 years, and 0.16 mIU/L in 25 age-matched men, which meant a 68-fold higher median value in the women (Fig. 1). The corresponding IGF-1 values were 256 and 218 µg/L, which did not differ significantly. The median IGF-1 values were lower in older men and older women than in younger men and women \( (P < 0.001) \). The median values for GH, SHBG, 17β-estradiol \( (P < 0.001) \), FSH, LH, and prolactin \( (P < 0.01) \) were higher in women than in men, whereas the median testosterone value was lower \( (P < 0.001; \) Table 2).

The male/female and female/male ratios for all median hormone values in the men and women, ages 21–26 years, are shown in Fig. 2. The gender difference was largest for GH, with a ratio of 80. The ratios for the sex hormones testosterone and 17β-estradiol were 14 and 2.2, respectively. The median values for GH, SHBG, 17β-estradiol, FSH, LH, prolactin \( (P < 0.001) \), and IGF-1 \( (P < 0.01) \) were higher in women than in men, whereas those for testosterone, free thyroxine \( (P < 0.001) \), T3 \( (P < 0.01) \), thyroid-stimulating hormone, and parathyroid hormone \( (P < 0.05) \) were lower. The median value for cortisol did not differ significantly between men and women (Table 1).
women, the IGF-1 concentration was lower (P < 0.05) than in the reference group of women. In both the EELEV and EEDES women, the median values for cortisol, SHBG, and T₃ were higher (P < 0.001) than those in the reference group, whereas the median values for testosterone, 17β-estradiol, LH (P < 0.001), and FSH (P < 0.05) were lower (Table 1).

**EEDES WOMEN VS EELEV WOMEN**

The median SHBG value was almost twice as high (ratio 1.9; P < 0.001) in the EEDES than in the EELEV women, whereas the values for testosterone, 17β-estradiol, and LH were lower (P < 0.05).

**Discussion**

The most remarkable observation in the present study is the large difference in GH concentrations between healthy young men and women when the blood samples were taken on an ambulatory basis in the morning, around 0830, after an overnight fast. The young women not using hormonal contraceptives had an 80-fold higher median value than the men, and the two groups of women taking oral contraceptives had 117- to 125-fold higher median GH concentrations than the men. Median values were used for the comparisons, not arithmetic or geometric mean values, because the distributions were far from gaussian, as shown in Fig. 1.

The gender difference in the GH values observed in this study was considerably larger than previously reported in the literature (1, 2, 5–7). There are several possible explanations for our observations: (a) the high sensitivity of the GH method, (b) the samples were taken in the morning, after an overnight fast, (c) the samples were taken in the ambulatory state preceded by routine activity in the morning and not in a resting state, and (d) the study was carried out on young adults.

In a 1965 study by Frantz and Rabkin (6) on the effect of gender and ambulation on plasma GH, a competitive RIA for plasma GH was used. They found that women had approximately sixfold higher concentrations than men in the ambulatory state. The detection limit of their assay was ~0.3 μg/L, and most of the values for men were below or close to the limit of detection of the assay. When the labeled antibody methods based on a noncompetitive principle (also called sandwich, two-site, or non-competitive immunometric assays) were introduced (8, 9), it was shown that they were at least 10-fold more sensitive than the competitive radioimmunoassays (9). With the noncompetitive assay used in the present study, all men had GH concentrations above the detection limit (0.009 mIU/L). The higher sensitivity of the GH assay method is one explanation for the much larger gender difference in GH values in the present study compared with previous ones.

Highly sensitive noncompetitive GH immunoassays have been used in some studies on serum or plasma GH concentrations in samples taken frequently (at 10- to 20-min intervals) during 24-hour periods. The reported gender differences in GH concentrations were small compared with those observed in the present study. However, in those studies, the subjects were generally older; they came to the hospital the day before sampling; they were resting in the beginning of the 24-hour sampling period; and in two studies, they were not fasting at the start. The gender ratio for the mean GH concentration during a 24-hour period ranged from 1.45 to 2.9 (1, 2, 5). In another study, the subjects (age range, 18–34 years) came to the hospital in the morning after fasting overnight, and the blood sampling started after 1 h of rest. The gender ratio of the baseline median GH values was 10 (7). It seems that the main difference between these studies and ours is that in our study the samples were taken in the ambulatory state in the morning.

More than 90% of the young women and <10% of the young men had GH concentrations above 1.6 mIU/L.
corresponding to about 1 \( \mu G/L \). The estimated GH basal secretion, the half-life of GH, and the frequency of GH peaks during 24 h have been reported to be similar in the two sexes \( (1, 2) \). Thus, the most likely explanation for the high concentrations of GH in the women in our study is that something in the morning triggered a GH burst in almost all of the women but in very few of the men. This could be because of gender differences in the sensitivity of the pituitary or hypothalamus to the GH-releasing effects of mild physical activity. It would be of great interest to compare the GH concentrations in young men and women during days with routine daily stress, including both physical activity and mental stress.

Both fasting and physical activity are known to raise GH concentrations in the blood \( (10–14) \). In the present study, the samples were taken after an overnight fast, at 0830 in the morning, which may be regarded as very mild stress of fasting. The physical activity that preceded the blood sampling was, in most cases, the usual daily journey to the hospital on foot or by bicycle. Participation in the training in clinical chemistry, in which they drew blood samples from one another, may have constituted mild stress for some of the students. To what extent men and women differ in their reactions to such mild fasting, mild stress, or moderate physical activity remains to be clarified.

All the women examined in the present study were healthy and premenopausal. They had 17\( \beta \)-estradiol concentrations within the reference range for their age. There is ample evidence in the literature to suggest that estrogens play a major role in increased GH secretion in women compared with men \( (3, 4, 15–18) \). When estrogen was given in pharmacological doses to men, their plasma GH rose to concentrations similar to those in women \( (6) \). Estrogen seems to increase the growth hormone releasing hormone-stimulated GH secretion, and a difference in response to growth hormone-releasing hormone has been reported in premenopausal but not postmenopausal women compared with men \( (19) \).

The gender ratio of 80 for GH is even more impressive when compared with the ratio of 14 for testosterone and 2.2 for 17\( \beta \)-estradiol. The IGF-1 concentrations were significantly higher \( (P < 0.01) \) in women than in men 21–26 years of age, but the median value was only 11% higher. Some previous studies found higher IGF-1 concentrations in female adolescents than in male adolescents \( (20, 21) \), whereas several investigators did not observe any gender difference in adults \( (20, 22) \). In the present study, we found lower IGF-1 values in the men and women \( (27–43 \text{ years}) \) than in younger ones \( (P < 0.001) \), in agreement with earlier studies \( (23) \). In the older group of students, no significant gender difference was detected.

The group of women taking EE + DES (EDES women) had a median GH value that was 125-fold higher than that of the men 21–26 years of age and ~50% higher \( (P < 0.01) \) than that of the reference group of women (not taking hormonal contraceptives). The IGF-1 concentration was significantly lower \( (P < 0.01) \) in the EDES group than in the female reference group. The effects of EE + LEV (EELEV women) on the GH and IGF-1 concentrations were similar to those in the EDES women, but less pronounced. The median GH value was 117-fold higher than that in the men and ~50% higher than that in the reference group of women \( (P < 0.05) \), whereas the IGF-1 concentrations did not differ significantly between these groups. The difference between EDES and EELEV women may be caused by a weak androgen effect of LEV \( (24) \). This was even more pronounced for the SHBG concentrations. The median value was twice as high \( (P < 0.001) \) in EDES women as in EELEV women. In contrast, no corresponding large difference in the cortisol

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**Fig. 2.** The male/female and female/male ratios of median serum concentrations of 12 hormones and SHBG in samples taken in the ambulatory state in the morning, after an overnight fast.

PTH, parathyroid hormone; TSH, thyroid-stimulating hormone; and fT4, free thyroxine.
values was observed between the EELEV and EEDES women, confirming the results from previous studies, in which different kinds of gestagens were found to have similar effects on the liver synthesis of cortisol-binding globulin, which seems to be stimulated by the oral EE therapy (24–26).

In conclusion, the median serum GH concentration in young women was 80-fold higher than in young men when the samples were taken on an ambulatory basis in the morning, after an overnight fast. The very high GH concentrations in the women were probably effects of endogenous estrogen in combination with moderate physical activity, mild stress, and a mild fasting state. Because the basal secretion and peak frequency have been reported to be similar in men and women (1, 2) and such a large gender difference in GH concentrations has not been observed in earlier studies under resting, fasting conditions (1, 2, 5), it seems that the circumstances in the morning in the present study (i.e., routine activity) produced marked GH peaks in the women but not in the men. Additional studies are needed to investigate to what extent men and women differ in their responses to the mild stress and moderate physical activity experienced during a routine day.

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References