Age-related changes in the feedback regulation of gonadotrophin secretion by sex steroids in men

Kazuo Muta, Ken-ichi Kato, Yasuo Akamine and Hiroshi Ibayashi

Third Department of Internal Medicine, Faculty of Medicine, Kyushu University, Fukuoka 812, Japan

Abstract. In order to clarify the age-related functional changes of the hypothalamic-pituitary-gonadal axis in men, the negative feedback control of serum gonadotrophin by sex steroids was studied in 39 young (18–34 years) and 49 elderly (62–95 years) men. Mean basal LH and FSH levels and the responsiveness to synthetic LH were determined before and after daily injection of testosterone propionate (TP; 5, 10 or 50 mg/day) or oestradiol benzoate (OeB; 50, 100 or 500 μg/day) for 3 days. After the administration of TP or OeB, serum levels of testosterone or oestradiol were more elevated in the elderly than in the younger group. In the latter, basal LH level decreased significantly at 10 mg/day of TP and so did basal levels of both LH and FSH at 50 and 100 μg/day of OeB. Responses of serum LH and FSH to LH were inhibited significantly by TP at a dose of 50 mg/day and by OeB at doses of 100 and 500 μg/day. Whereas in the elderly group, basal LH levels and responses of both LH and FSH were not suppressed significantly by TP regardless of the dose. At a dose of 500 μg OeB, serum LH response was decreased remarkably. Per cent suppression of serum LH response at 50 mg TP, as well as those of serum LH and FSH responses at 500 μg OeB in the elderly group, was significantly less than in the younger group. These data indicate that in the elderly men the regulatory system of gonadotrophin secretion appears to manifest a more marked resistance to inhibitory effects of sex steroids, and also suggest that the set-point to sex steroids in the hypothalamic-pituitary axis is reset at a higher level in male senescence.

Senility is an irreversible phenomenon that develops with advancing age. Since Pedersen-Bjergaard & Tønnesen (1948) revealed quantitatively that urinary androgens in men began to decrease gradually after the fourth decade, several investigators (Hollander & Hollander 1958; Vermeulen et al. 1972; Stearns et al. 1974; Greenblatt et al. 1976) have indicated that there is a decline of testicular endocrine function in old age, and have thus demonstrated overwhelming evidence for a progressive decrease in plasma concentration of testosterone (T) and its unbound fraction with aging. On the other hand, significant increases in urinary and circulating gonadotrophin levels and excessive pituitary responsiveness to synthetic LH in the elderly male have been demonstrated (Rubens et al. 1974; Baker et al. 1976; Kato et al. 1977; Wasada 1978). These observations suggest that in the male reproductive system the mechanisms of senescence may primarily operate at the testicular level to decrease androgen synthesis, and that secondarily compensatory increases in gonadotrophin secretion may be caused by negative feedback control. Alternatively, it is possible to assume that in the negative feedback mechanism of gonadotrophin secretion, senescence may induce an elevation of set-point to sex steroids in the hypothalamic-pituitary axis, as has been suggested by Everitt (1976). From this viewpoint, on increasing serum concentration of testosterone (T) or oestradiol (Oe) with administration of testosterone propionate (TP) or oestradiol benzoate (OeB) in young and aged groups, the dynamic changes of serum gonadotro-
phin secretion were compared between two groups. In this manner, an attempt was made to elucidate functional changes in the hypothalamic-pituitary-gonadal axis occurring in the male with aging.

Material and Methods

Subjects

Thirty-nine younger males ranging in age from 18 to 34 years (average: 23.9 years) and 49 elderly males from 62 to 95 years (average: 76.6 years) volunteered for this study. All subjects were found to be healthy and in good condition at the time of the experiment, by both clinical and biochemical evaluations. None had received any medication known to exert influence upon the hypothalamic-pituitary-gonadal axis.

Study protocol

The younger and elderly groups were examined comparatively for basal LH and FSH levels, and for serum LH and FSH responses to LRH, before and after daily administration of TP (5, 10 or 50 mg/day) or OeB (50, 100 or 500 μg/day) for 3 days.

At 8.00 a.m. on the first day of the experiment, the initial iv injection of 100 μg of synthetic LRH was given to the volunteers after drawing blood samples for the determination of basal levels of serum LH, FSH, T, Oe and free testosterone index (FTI). As serum LH and FSH levels fluctuate spontaneously (Santer & Bardin 1973), samples for basal LH and FSH levels were taken 3 times (0, 10 and 20 min before LRH injection) to establish an accurate basal value. After LRH injection, blood samples were drawn from the contralateral arm vein at 15, 30, 60, 90 and 120 min. From the second to the fourth day, each group, young and aged, was divided into 6 subgroups, which were injected im with 5, 10 and 50 mg of TP and 50, 100 and 500 μg of OeB daily, respectively, for 3 days. Each daily dose was divided into two equal portions and administered at 9.00 a.m. and 6.00 p.m., respectively. On the morning of the fifth day, LRH injection was repeated in the same manner as that on the first day. Samples were immediately centrifuged and were kept frozen at −20°C until estimated. Synthetic LRH was supplied by Tanabe Pharmaceutical Co. Ltd., Osaka and TP and OeB were by Teikoku Hormone Co. Ltd., Tokyo.

Determination of hormones

Serum LH and FSH were measured using the double antibody RIA method with the 2nd IRP-HMG as standard (Odell et al. 1967). The sensitivity of this method for detection of LH and FSH was 1.5 mIU/ml for each. The coefficients of variation in inter- and intra-assay were 12.5 and 4.9% for LH and 13.7 and 6.3% for FSH, respectively. T was determined by RIA as previously described (Nawata et al. 1977), using an antibody against T-3-oxime-BSA. Serum Oe was estimated by RIA with an antibody against Oe-11-hemisuccinate-BSA after Sephadex LH-20 column chromatography prior to assay (Yoshida et al. 1973; Murakami et al. 1976). The variability in inter- and intra-assay were 12.8 and 9.3% for T and 10.3 and 8.6% for Oe, respectively. FTI was calculated by multiplying the per cent free T by the total T concentration for each subject (Rosenfield 1971). All samples from an individual were estimated in duplicate in the same assay in order to eliminate inter-assay variations.

The results obtained were expressed as mean ± SEM. The data were analyzed statistically for the significance of differences by Student’s t-test for inter-group comparison and by the paired t-test for intra-group comparison.

Table 1.

<table>
<thead>
<tr>
<th></th>
<th>No.</th>
<th>LH (mIU/ml)</th>
<th>FSH (mIU/ml)</th>
<th>Testosterone (ng/100 ml)</th>
<th>Free testosterone index</th>
<th>Oestradiol (pg/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Young</td>
<td>(39)</td>
<td>8.2 ± 0.9</td>
<td>8.0 ± 0.7</td>
<td>593 ± 27</td>
<td>315 ± 23</td>
<td>23.2 ± 2.2</td>
</tr>
<tr>
<td>Aged</td>
<td>(49)</td>
<td>42.7 ± 4.6**</td>
<td>38.7 ± 4.5**</td>
<td>401 ± 22**</td>
<td>129 ± 19*</td>
<td>38.9 ± 3.1*</td>
</tr>
</tbody>
</table>

The number of subjects is in parentheses. All values given are mean ± SEM.

* P < 0.01 compared to younger group. ** P < 0.001 compared to younger group.
Table 2.
Comparison of serum LH and FSH response to LRH 100 µg iv injection.

<table>
<thead>
<tr>
<th></th>
<th>No.</th>
<th>LH</th>
<th></th>
<th>FSH</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Δ Peak&lt;sup&gt;a&lt;/sup&gt; (mIU/ml)</td>
<td>Δ Area&lt;sup&gt;b&lt;/sup&gt; (mIU/2 h)</td>
<td>Δ Peak (mIU/ml)</td>
</tr>
<tr>
<td>Young</td>
<td>(39)</td>
<td>75.5 ± 8.3</td>
<td>140.5 ± 18.3</td>
<td>10.1 ± 1.3</td>
</tr>
<tr>
<td>Aged</td>
<td>(49)</td>
<td>123.2 ± 12.6&lt;sup&gt;c&lt;/sup&gt;</td>
<td>273.8 ± 32.7&lt;sup&gt;d&lt;/sup&gt;</td>
<td>26.3 ± 3.3&lt;sup&gt;d&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

The number of subjects is in parentheses. All values given are mean ± SEM.

<sup>a</sup> Δ Peak: maximal increment (peak value – basal value).
<sup>b</sup> Δ Area: the cumulative response corresponding to the areas circumscribed by the serum LH and FSH curves during the first 2 h after LRH injection.
<sup>c</sup> P < 0.01 compared to younger group.
<sup>d</sup> P < 0.001 compared to younger group.

Results

Comparison of basal hormone levels and pituitary responsiveness to LRH between younger and elderly groups

Table 1 shows that mean basal level of LH as well as FSH was significantly higher (P < 0.001) in the elderly than in the younger group. Serum T level and FTI value in the aged were significantly smaller (P < 0.001 and P < 0.01, respectively) than in the younger subjects. These data support our earlier results reported previously (Kato et al. 1977; Wasada 1978). On the other hand, serum concentration of Oe was significantly higher (P < 0.01) in elderly subjects as compared with younger ones.

Table 2 indicates the pituitary responsiveness to 100 µg synthetic LRH. Δ Peak means maximum increment (peak value – basal value). Δ Area means cumulative response corresponding to the areas circumscribed by the serum LH and FSH curves during the first 2 h after LRH injection from which the respective basal levels have been deducted (Franchimont et al. 1975). Both Δ peak and Δ area of LH and FSH in the elderly subjects were significantly higher than in the younger ones, about twice as large as those in the latter. The LH peak after LRH stimulation tended to appear later in the aged than in the younger group.

Effects of TP on basal LH and FSH levels and response to LRH

Fig. 1 shows changes in serum T levels and FTI values before and after TP administration. In the younger group, the serum T levels did not increase significantly after administration of TP at small doses (5 and 10 mg/day), but a large dose (50 mg/day) elicited a remarkable increase in serum T level from 708 ± 60 to 1716 ± 213 ng/100 ml with statistical significance (P < 0.01). FTI which is an index of free T, had a significant rise with 10 and 50 mg of TP, respectively. On the other hand, in the aged group serum T and FTI presented a more marked increase than in the young in all subgroups treated with 5, 10 and 50 mg of TP. At a dose of 50 mg the serum T level increased from 515 ± 105 to 2986 ± 466 ng/100 ml.

Table 3 shows changes of serum LH and FSH in the basal levels and responses to LRH before and after TP administration. In the younger group, 10 mg TP caused a significant rise in FTI value, whereas basal LH level was significantly suppressed (P < 0.05). In the elderly subjects, basal LH levels did not show a significant decrease after administration of 10 mg of TP, nor after a dose of 50 mg. Basal FSH levels were not suppressed by the increases in serum T concentration in either the younger or elderly group with the exception of the aged subgroup treated with 50 mg of TP (P < 0.05).

Serum LH and FSH responses to LRH of the younger group were not inhibited by small doses of 5 or 10 mg/day of TP, but were significantly suppressed by the large dose of 50 mg treatment for 3 days. In the aged group, the responses to LRH were not significantly inhibited even after the administration of 50 mg TP. Moreover, when compared the per cent suppression of Δ LH area
Serum testosterone levels and free testosterone indices before (open columns) and after (closed columns) administration of testosterone propionate in doses of 5, 10 and 50 mg/day for 3 days. Values are mean ± SEM. Number of subjects examined is in parentheses. ∗, ∗∗, ∗∗∗, statistically significant difference from the pre-treatment value; \( P < 0.05, P < 0.01, P < 0.001 \).

Effects of OeB on basal LH and FSH levels and response to LRH

Fig. 2 shows changes in serum Oe levels before and after OeB administration. Serum Oe concentrations increased almost in proportion to the dose of OeB in both young and aged groups. Table 4 indicates the basal LH and FSH levels and the responses to LRH estimated before and after OeB treatment. In both groups increased Oe depressed the basal levels of LH and FSH. In all subgroups of younger subjects, basal LH levels showed a significant dose-dependent decrease, being reduced to 76.6, 69.5 and 61.5% of each pre-treatment value, respectively. Basal FSH levels were also suppressed with 100 and 500 \( \mu \)g/day of OeB. On the other
**Table 3.**
Changes in basal level, \( \Delta \) peak and \( \Delta \) area of serum gonadotrophin with LRH before and after administration of testosterone propionate (TP).

<table>
<thead>
<tr>
<th>Dose of TP (mg/day)</th>
<th>Young</th>
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<th></th>
<th></th>
<th></th>
<th>Aged</th>
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<tr>
<td></td>
<td>No.</td>
<td>Before</td>
<td>After</td>
<td>No.</td>
<td>Before</td>
<td>After</td>
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<tr>
<td>LH</td>
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<td></td>
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<tr>
<td>Basal level (mIU/ml)</td>
<td>5</td>
<td>8.6 ± 1.3</td>
<td>8.2 ± 1.7</td>
<td>(4)</td>
<td>20.2 ± 4.7</td>
<td>13.0 ± 3.8</td>
<td></td>
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<tr>
<td></td>
<td>10</td>
<td>8.9 ± 3.6</td>
<td>2.6 ± 0.3(^c)</td>
<td>(7)</td>
<td>44.7 ± 12.7</td>
<td>21.5 ± 5.2</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>50</td>
<td>6.3 ± 0.4</td>
<td>2.6 ± 0.2(^d)</td>
<td>(6)</td>
<td>53.8 ± 15.6</td>
<td>25.5 ± 6.5</td>
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<tr>
<td>( \Delta ) Peak (mIU/ml)(^a)</td>
<td>5</td>
<td>34.4 ± 17.5</td>
<td>110.5 ± 37.0</td>
<td>(4)</td>
<td>79.5 ± 18.0</td>
<td>111.8 ± 32.8</td>
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<tr>
<td></td>
<td>10</td>
<td>61.4 ± 13.1</td>
<td>56.8 ± 5.9</td>
<td>(7)</td>
<td>189.4 ± 42.3</td>
<td>179.5 ± 41.0</td>
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<tr>
<td></td>
<td>50</td>
<td>44.7 ± 11.2</td>
<td>28.3 ± 6.2(^e)</td>
<td>(6)</td>
<td>142.7 ± 57.6</td>
<td>109.5 ± 38.5</td>
<td></td>
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<td></td>
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<tr>
<td>( \Delta ) Area (mIU/2 h)(^b)</td>
<td>5</td>
<td>251.8 ± 111.1</td>
<td>297.2 ± 108.3</td>
<td>(4)</td>
<td>187.4 ± 43.2</td>
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<td></td>
<td>10</td>
<td>134.3 ± 21.8</td>
<td>116.7 ± 18.6</td>
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<td>447.7 ± 84.7</td>
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<td></td>
<td>50</td>
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<td>67.2 ± 15.3(^f)</td>
<td>(6)</td>
<td>411.9 ± 183.9</td>
<td>316.3 ± 126.8</td>
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<tr>
<td>FSH</td>
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<td></td>
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<tr>
<td>Basal level (mIU/ml)</td>
<td>5</td>
<td>10.0 ± 2.0</td>
<td>8.1 ± 2.7</td>
<td>(4)</td>
<td>19.0 ± 5.0</td>
<td>16.6 ± 3.8</td>
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<td></td>
<td>10</td>
<td>8.9 ± 1.6</td>
<td>7.4 ± 1.3</td>
<td>(7)</td>
<td>38.5 ± 6.9</td>
<td>25.7 ± 4.4</td>
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<tr>
<td></td>
<td>50</td>
<td>4.7 ± 0.5</td>
<td>3.0 ± 0.3</td>
<td>(6)</td>
<td>21.1 ± 1.4</td>
<td>12.1 ± 2.4(^g)</td>
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<tr>
<td>( \Delta ) Peak (mIU/ml)</td>
<td>5</td>
<td>16.3 ± 7.8</td>
<td>21.6 ± 7.7</td>
<td>(4)</td>
<td>17.2 ± 4.8</td>
<td>16.8 ± 6.2</td>
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<tr>
<td></td>
<td>10</td>
<td>8.1 ± 1.3</td>
<td>11.4 ± 3.1</td>
<td>(7)</td>
<td>32.7 ± 7.8</td>
<td>36.6 ± 8.5</td>
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<tr>
<td></td>
<td>50</td>
<td>7.4 ± 2.0</td>
<td>3.9 ± 0.8</td>
<td>(6)</td>
<td>12.9 ± 4.0</td>
<td>8.9 ± 2.5</td>
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<td></td>
<td></td>
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<tr>
<td>( \Delta ) Area (mIU/2 h)</td>
<td>5</td>
<td>40.9 ± 22.3</td>
<td>35.0 ± 15.7</td>
<td>(4)</td>
<td>49.6 ± 14.9</td>
<td>26.8 ± 6.7</td>
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<tr>
<td></td>
<td>10</td>
<td>17.8 ± 4.2</td>
<td>28.4 ± 9.1</td>
<td>(7)</td>
<td>83.2 ± 23.0</td>
<td>94.9 ± 24.2</td>
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<tr>
<td></td>
<td>50</td>
<td>16.8 ± 5.2</td>
<td>5.8 ± 1.2(^h)</td>
<td>(6)</td>
<td>27.7 ± 8.9</td>
<td>25.1 ± 5.6</td>
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</tr>
</tbody>
</table>

The number of subjects is in parentheses. All values given are mean ± SEM.

\(^a\) \( \Delta \) Peak: maximal increment (peak value – basal value).

\(^b\) \( \Delta \) Area: the cumulative response corresponding to the areas circumscribed by the serum LH and FSH curves during the first 2 h after LRH injection.

\(^c\) \( P < 0.05 \) compared to pre-treatment value.

\(^d\) \( P < 0.01 \) compared to pre-treatment value.

hand, in elderly subjects, the inhibitory effects of OeB on basal LH and FSH levels were lower than in the younger ones. In the former, both LH and FSH exhibited a significant decrease only with 500 \( \mu \)g/day of OeB.

OeB diminished pituitary responsiveness to LRH stimulation (Table 4). In the young, \( \Delta \) areas of serum LH and FSH decreased significantly \( P < 0.05 \) with OeB at a small dose of 100 \( \mu \)g/day. And 500 \( \mu \)g of OeB produced a remarkable decrease in \( \Delta \) areas of them, about 53.3 and 70.1% of the values before OeB administration, respectively. \( \Delta \) Peak of serum LH decreased distinctly, but \( \Delta \) FSH peak was only slightly inhibited. Suppressive effects of OeB on the responses of both LH and FSH to LRH were weak in the aged rather than in the young. In the former, with 500 \( \mu \)g of OeB, \( \Delta \) peak and \( \Delta \) area of serum LH were significantly inhibited, but not of serum FSH. When per cent inhibition of serum LH and FSH in \( \Delta \) area was compared between younger and elderly groups, there were significant differences \( P < 0.05 \) with 500 \( \mu \)g of OeB (Fig. 3).

**Discussion**

The present study carried out in normal young subjects revealed that both T and Oe were inhibitory factors for gonadotrophin secretion in male.
displayed a stronger inhibitory action on serum LH than on FSH, as reported previously by several investigators (Lee et al. 1972; Stewart-Bentley et al. 1974). However, as demonstrated by Sherins & Loriaux (1973), Oe inhibited the secretion of both LH and FSH. The response of serum LH and FSH to LRH was not inhibited by small doses of TP (5, 10 mg/day), but was suppressed significantly by a large dose (50 mg/day). By constant infusion of a physiological dose of T, Santen (1975) found no significant changes in serum LH response to LRH. With chronic administration of T enanthate, there was no inhibitory effect of increased serum T on the response of serum LH and FSH to synthetic LRH early in the treatment (Robyn et al. 1976), but this response began to decrease gradually after 4 weeks of treatment (Caminos-Torres et al. 1977). These results suggest that T may not directly exert an inhibitory action upon the pituitary, but may act at the level of the hypothalamus, reducing the release of intrinsic LRH. In contrast to T, basal levels of serum LH and FSH and these responses to LRH were suppressed significantly with a small dose of OeB (100 µg/day). This finding suggests that Oe may directly exert an inhibitory effect not only upon the hypothalamus but also upon the pituitary. Franchimont et al. (1975) and Santen (1975) reported similar results. In the present experiment a large dose of TP induced a significant decrease in the response of serum LH and FSH to LRH. One of the reasons for this suppression may be decrease in intrinsic LRH secretion from the hypothalamus. Another reason may be that Oe displays a direct inhibitory effect on the pituitary since it increases after conversion from T by aromatization in peripheral tissues (Longcope et al. 1978) or in the central nervous system (Naftolin et al. 1971).

On the other hand, in this experiment the elderly subjects showed various changes differing from the younger ones in the dynamic condition of gonadotrophin secretion. The first of these changes was excessive secretion of LH and FSH from the pituitary with decrease in T secretion from the testis (Tables 1 and 2). Secondly, the hypothalamic-pituitary axis of the aged resists more strongly the effects of sex steroids. In the present experiment of TP administration, serum T and FTI values increased significantly in the subgroups administered with 50 mg of TP in both young and aged subjects.

![Fig. 2.](image)

Serum oestradiol levels before (open columns) and after (closed columns) in administration of oestradiol benzoate in doses of 50, 100 and 500 µg/day for 3 days. Values are mean ± SEM. Number of subjects studied is in parentheses. *, **, significantly differed from the pre-treatment value; \( P < 0.05, P < 0.001. \)
The basal LH level and serum LH response to LRH were significantly suppressed in the young, but not in the aged. Furthermore, there was a significant difference in the inhibitory effect of 50 mg TP on the serum LH response to LRH between the younger and the aged subgroups. These findings suggest the possibility that in the aged male there is decrease in the sensitivity of the central regulatory system of LH secretion to negative feedback effect of T. Besides, in the examination of OeB administration, the inhibitory effects of increased serum Oe on both of LH and FSH secretion were remarkably lower in the aged than in the young. It also indicates that in the elderly male there exists insensitiveness of the hypothalamic-pituitary axis to Oe in negative feedback control of gonadotrophin secretion. These results lend strong support to the presumption that there may be a rise in the set-point of the central nervous system to sex steroids with aging.

Dilman (1976) proposed a hypothesis that three types of imbalance of a homeostasis progress in the reproductive system of women in old age. These types consist of a central type in which the threshold in the hypothalamus is raised by an increase in gonadotrophin secretion, a peripheral type in which insufficiency in the secretion of classical oestrogens occurs, and a dysfunction type in which the spectrum of hormone secretion undergoes qualitative changes. It is naturally presumed that the similar changes as supposed in women may progress in the male reproductive system with aging, and our data suggest these existences in men. As pointed out by Pirke & Doerr (1973), the significant increase of serum Oe levels in the elderly group (Fig. 1) appears to be one of dysfunc-
### Table 4.
Changes in basal level, Δpeak and Δarea of serum gonadotrophin with LRH before and after administration of oestradiol benzoate (OeB).

<table>
<thead>
<tr>
<th>Dose of OeB (μg/day)</th>
<th>Young</th>
<th>Aged</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. Before</td>
<td>After</td>
</tr>
<tr>
<td><strong>LH</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Basal level (mIU/ml)</td>
<td>50</td>
<td>12.5 ± 1.3</td>
</tr>
<tr>
<td></td>
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</tr>
<tr>
<td></td>
<td>500</td>
<td>7.6 ± 1.1</td>
</tr>
<tr>
<td>Δ Peak (mIU/ml)&lt;sup&gt;a&lt;/sup&gt;</td>
<td>50</td>
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<td></td>
<td>100</td>
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<td>Δ Area (mIU/2 h)&lt;sup&gt;b&lt;/sup&gt;</td>
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<td>123.2 ± 17.0</td>
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<td>100</td>
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<td></td>
<td>500</td>
<td>124.4 ± 19.2</td>
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<td><strong>FSH</strong></td>
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<tr>
<td>Basal level (mIU/ml)</td>
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<td>9.0 ± 0.9</td>
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<td></td>
<td>100</td>
<td>10.3 ± 2.6</td>
</tr>
<tr>
<td></td>
<td>500</td>
<td>6.0 ± 1.4</td>
</tr>
<tr>
<td>Δ Peak (mIU/ml)</td>
<td>50</td>
<td>7.5 ± 1.7</td>
</tr>
<tr>
<td></td>
<td>100</td>
<td>15.3 ± 1.8</td>
</tr>
<tr>
<td></td>
<td>500</td>
<td>8.5 ± 1.7</td>
</tr>
<tr>
<td>Δ Area (mIU/2 h)</td>
<td>50</td>
<td>13.3 ± 1.9</td>
</tr>
<tr>
<td></td>
<td>100</td>
<td>32.2 ± 3.6</td>
</tr>
<tr>
<td></td>
<td>500</td>
<td>17.3 ± 3.8</td>
</tr>
</tbody>
</table>

The number of subjects is in parentheses. All values given are mean ± SEM.

<sup>a</sup> Δ Peak: maximal increment (peak value – basal value).

<sup>b</sup> Δ Area: the cumulative response corresponding to the areas circumscribed by the serum LH and FSH curves during the first 2 h after LRH injection.

<sup>c</sup> P < 0.05 compared to pre-treatment value.

<sup>d</sup> P < 0.01 compared to pre-treatment value.

Concerning this mechanism, there are interesting reports that in the aged males peripheral aromatization is increased (Hemsell et al. 1974; Baker et al. 1976) and that blood production rate of Oe is unchanged in connection with decreased metabolic clearance rate in male senescence (Pirke & Doerr 1973). It is possible to assume that the increase in serum Oe in the aged male partially participates to blunt the sensitivity of the hypothalamic-pituitary axis to falling of T synthesis. Further investigation is required for the verification of this assumption.

References


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