URINARY FOLLICLE STIMULATING HORMONE AND LUTEINIZING HORMONE IN NORMAL ADULT MEN

By

Peter Christiansen

ABSTRACT

The normal range of the excretion of follicle stimulating hormone (FSH) and luteinizing hormone (LH), as well as the relation between these values and those in aging subjects was investigated by specific bioassays in 50 normal adult men with an age range of 21 to 82 years. The FSH rose significantly but did not reach the levels observed in postmenopausal women. The LH showed no significant rise and consequently the FSH/LH ratio rose. Normal values and the 95% fiducial limits in the decades from 21 to 70 years are shown.

In contrast to the many reports about FSH and LH excretion in women, little has been published about FSH and LH in men and especially in normal men. We therefore studied this problem and it is the purpose of this report to show the excretion of FSH and LH in normal men as measured by specific bioassays.

The development of radioimmunoassays in recent years has made it possible to investigate the plasma levels of FSH and LH from hour to hour and day to day. Peterson et al. (1968) found in 4 normal men no systematic day to day variation, as occurs in normal women and found in 2 normal men examined every hour for 24 hours no special diurnal rhythm. However, Saxena et al. (1968) found in 3 normal men, morning values of FSH higher than evening values and in 2 of the men a similar variation of LH levels. In our study any influence of such variations was eliminated as combined extracts from urine collected over 12-14 days were assayed.
MATERIAL AND METHODS

Subjects
All the subjects were healthy adult males with an age range of 21–82 years. They had testes of normal size, were normally virile without any sign of endocrine disorder and those who were married and wanted children had proved their fertility by having at least 1 child. Altogether 50 subjects were investigated. All the collected 12–14 24 hour urine samples were extracted by the method of Johnsen (1958), and then pooled and divided into 3 portions for the 3 bioassays.

Bioassays
1. Total urinary hypophyseal gonadotrophins (HG) were measured by the mouse uterus test (Johnsen 1958) and expressed in mouse uterus units (MUU) per 24 hours. One ampoule of the 2. international reference preparation for human menopausal gonadotrophin (2. IRP-HMG) contains 40 IU FSH, 40 IU LH and 183 MUU.
2. The urinary follicle stimulating hormone (FSH) was measured by the rat ovarian augmentation test (Steelman & Pohley 1953) and performed in the following way: 26–28 days old female rats of the Serum Institute strain (originating from the Wistar strain), weighing 45–55 g were injected twice daily for 3 days subcutaneously, each time with a volume of 0.5 ml. Autopsy was performed on the 4th day. Both ovaries were dissected free of surrounding tissue and weighed on a torsion balance to the nearest 0.5 mg. The test material together with human chorionic gonadotrophin (Physex® LEO) was mixed in vitro in such a way that each rat got 20 IU HCG as total dose for augmentation. The extracts were assayed against the 2. IRP-HMG with a 3+3 design expressing the activity in IU per 24 hours. Five rats per dose.
3. The urinary luteinizing hormone (LH) was measured by the ventral prostate weight method (VPW) (Greep 1941) and performed as previously described (Christiansen 1967). The extracts were assayed against the 2. IRP-HMG in a 2+2 design expressing the activity in IU per 24 hours. 5–8 rats were used per dose. The bioassays were calculated according to a computer programme for bioassays (McArthur et al. 1966). Only statistically valid assays were accepted.

Significant responses were obtained with all urine samples.

RESULTS
As the excretion of hypophyseal gonadotrophins shows a log-normal distribution all the values were transformed into logarithms in the statistical calculations. The correlation between levels of gonadotrophins and age was calculated, the 4 men above 70 years, however, being excluded as this number was too small to allow of any conclusions about the sequence of events in very old men. From the equation of age correlation all the remaining 46 values were transformed to a standard age (45 years was chosen as being in the middle of the period). This provisional elimination of the age factor allowed the whole series to be investigated as an entity. Histogram plots for both FSH and LH showed no trends of formation of more than one population and the normal distribution of the log values was again confirmed. The mean, SD and
95% fiducial limits were calculated for the standard age (45 years). From the equations of the age correlations the means for all groups were then calculated. As seen from the plots there was no reason to believe that the individual variation changes with age. Accordingly, the standard deviation obtained for the standard age was used for all ages for a calculation of the 95% fiducial limits for all age groups.

The urinary total hypophyseal gonadotrophins in this group of normal men showed the same normal range and relationship to age as that published earlier by Johnsen (1959). The correlation to age is statistically highly significant (log HG = 0.846 + 0.009 × age, t = 3.10, P < 0.001).

Urinary FSH rises with age in normal men (Fig. 1). The plot is in semilogarithmic scale. The positive correlation between FSH levels and age is statistically highly significant (log FSH = 0.473 + 0.010 × age, t = 4.37, P < 0.001). Table 1 shows the mean excretion of FSH in decades from 21 to 70 years and the 95% fiducial limits reflect the wide range of values among these men.

Fig. 1.
Urinary follicle stimulating hormone in 50 normal males 21–82 years old.
Semilogarithmic scale.
Table 1.
Urinary follicle stimulating hormone (FSH) and aging in normal men.

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>N</th>
<th>Mean IU/day</th>
<th>95% limits</th>
</tr>
</thead>
<tbody>
<tr>
<td>21-30</td>
<td>14</td>
<td>5.3</td>
<td>1.6-17.7</td>
</tr>
<tr>
<td>31-40</td>
<td>12</td>
<td>6.8</td>
<td>2.0-22.4</td>
</tr>
<tr>
<td>41-50</td>
<td>5</td>
<td>8.5</td>
<td>2.6-28.4</td>
</tr>
<tr>
<td>51-60</td>
<td>9</td>
<td>10.8</td>
<td>3.3-35.9</td>
</tr>
<tr>
<td>61-70</td>
<td>6</td>
<td>13.7</td>
<td>4.1-45.4</td>
</tr>
</tbody>
</table>

Urinary LH rises much less than FSH with age in normal men. The rise is only at the borderline of statistical significance \( \log \text{LH} = 0.703 + 0.003 \times \text{age} \), \( t = 1.77, P < 0.10 > 0.05 \). Table 2 shows the mean excretion and the 95% fiducial limits.

As a consequence, the FSH/LH ratio increases in aging males. Table 3 shows the mean and the 95% fiducial limits. The correlation between FSH/LH and age is statistically significant \( \log \text{FSH/LH} = -0.229 + 0.007 \times \text{age} \), \( t = 3.08, P < 0.001 \).

A correlation between FSH levels and LH levels has been found, the coefficient of correlation being 0.54 \( (t = 4.40, P < 0.001) \).

**DISCUSSION**

The data presented indicate that in aging men the urinary FSH increases significantly whereas LH shows no significant rise and consequently the FSH/LH ratio rises. These findings are in agreement with Johnsen (1959) who – using the mouse uterus test – found that total urinary hypophyseal gonadotrophins

Table 2.
Urinary luteinizing hormone (LH) and aging in normal men.

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>N</th>
<th>Mean IU/day</th>
<th>95% limits</th>
</tr>
</thead>
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<tr>
<td>21-30</td>
<td>14</td>
<td>6.2</td>
<td>2.4-16.1</td>
</tr>
<tr>
<td>31-40</td>
<td>12</td>
<td>6.7</td>
<td>2.6-17.4</td>
</tr>
<tr>
<td>41-50</td>
<td>5</td>
<td>7.2</td>
<td>2.8-18.9</td>
</tr>
<tr>
<td>51-60</td>
<td>9</td>
<td>7.9</td>
<td>3.0-20.5</td>
</tr>
<tr>
<td>61-70</td>
<td>6</td>
<td>8.5</td>
<td>3.3-22.2</td>
</tr>
</tbody>
</table>
Table 3.
FSH/LH ratio and aging in normal men.

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>N</th>
<th>Mean</th>
<th>95% limits</th>
</tr>
</thead>
<tbody>
<tr>
<td>21–30</td>
<td>14</td>
<td>0.87</td>
<td>0.29–2.57</td>
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<td>31–40</td>
<td>12</td>
<td>1.01</td>
<td>0.34–3.00</td>
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<td>41–50</td>
<td>5</td>
<td>1.18</td>
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<td>51–60</td>
<td>9</td>
<td>1.38</td>
<td>0.47–4.08</td>
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<tr>
<td>61–70</td>
<td>6</td>
<td>1.61</td>
<td>0.54–4.76</td>
</tr>
</tbody>
</table>

rise with age. The mouse uterus test (Johnsen 1958) in our laboratory reflects FSH rather than LH (Christiansen & Johnsen, to be published). It should be noted, however, that the gonadotrophin rise with age in men is very much smaller than the rise in women from the pre- to postmenopausal state.

The FSH and LH levels found are in agreement with those reported by Rifkind et al. (1967) but disagree with those reported by McArthur et al. (1958) and Becker & Albert (1965) who found higher values when the reported values were converted to equivalents of the 2. IRP-HMG. However, Becker & Albert (1965) selected subjects with the highest levels of total gonadotrophins and this factor may account for the difference in the results obtained.

It is surprising that urinary FSH rises with age in men. Rosen & Weintraub (1971) and Christiansen (1971) found – in idiopathic oligospermic young men – a monotrophic increase in plasma and urinary FSH, respectively. In normal men spermatogenesis is maintained during aging almost throughout life though some changes in the histological picture have been reported (Tillinger 1957). However, probably normal spermatogenesis in aging males requires higher FSH stimulation. Another possibility is that the hypothalamus is less sensitive to the inhibitory substance assumed to be produced by the germ cells.

LH is maintained at approximately the same level in normal men till at least the 8th decade. As Hamburger (1948) and Pincus (1956) have shown there is a progressive fall in the excretion of 17-KS with aging. However, Kent & Acone (1965) found no decrease in the level of testosterone in plasma in aging males up to the 8th decade despite a decrease in the testosterone production rate, suggesting a concomitant fall in the utilization of this hormone. If plasma testosterone remains constant with age, a constant LH level is to be expected.

Our results showing a nearly constant level of LH and a rise in FSH far
less than that seen in postmenopausal women argues against the existence of a male climacteric and support the concept that in man FSH and LH are regulated independently.

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REFERENCES


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