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10/16/06 MON 11:22 [TX/RX NO 9417]
The clinical and endocrinological effect of hysterectomy and bilateral salpingo-oophorectomy at the time of ostearial implantation.
surgeons who did not use implants; these patients served as controls.

**Hormone assays**

Blood samples were placed in lithium-heparin tubes and the separated plasma stored at -23°C until assayed. Luteinizing hormone (LH) was estimated by radioimmunoassay using a double antibody technique (Midgeley, 1966). The antiserum used showed no cross-reaction with pure FSH or with thyroid stimulating hormone. 131I (Radiochemical Centre, Amersham) was used for iodination (Greenwood *et al.*, 1963). The second international reference preparation of human menopausal gonadotrophin (2nd IRP-HMG) was used as standard.

A double antibody radioimmunoassay was also employed for the assay of FSH. Cross-reaction of the antiserum with LH was eliminated by absorption of the antibody with pure human chorionic gonadotrophin (5 IU of HCG per ml of antiserum). The 2nd IRP-HMG was used as standard.

Total plasma oestrogen was estimated by radioimmunoassay (Hotchkiss *et al.*, 1971) without chromatographic separation of the oestrogens. This method is specific for endogenous oestrogens, there being no cross-reaction with synthetic steroids (Kharma *et al.*, 1972). The intra-assay coefficient of variation for the three hormones was 10 per cent and the recovery of oestrogen throughout the assay was between 70 and 90 per cent.

**Karyopyknotic index (KI)**

Vaginal wall smears were stained by Papanicolaou (1954) technique and the KI assessed on a count of 200 cells.

**Hot flushes**

Hot flushes were graded as severe if they occurred more than three times per day, moderate if they occurred under three times per day but above three times per week, and mild if they occurred under three times per week.

**RESULTS**

The mean age of the control patients was 46.4 years (S.D. = 4.3) and of patients receiving an implant was 47.6 years (S.D. = 4.1). There is no significant difference between the age of the two groups.

Plasma oestrogen levels after surgery are shown in Figure 1. The mean value of the control patients was 5.6 ng/100 ml (S.D. = 2.8). Thirty-four of the 42 patients with implant had a significantly raised plasma oestrogen level (more than two standard deviations above the mean of the control value), can be seen that all 23 patients studied during the first 15 months, and 11 out of 15 patients studied between 16 and 30 months after hysterectomy, had a significantly higher oestrogen level than the controls. No significant difference was noted between plasma LH and FSH in either group. Twenty-two oestrogen implants were used.
Note the 23 patients with an implant seen in the present study, and the patients treated with oestradiol therapy. Of these, 11 of the 14 patients with no apparent socio-emotional deterioration scored higher than the mean of the control value. However, only 1 of the 14 patients scored significantly lower than the mean. The mean value of the LH control patients was 7.2 ± 3.4 mg/ml (SD = 7.2, SD = 3.4). Thirty-three per cent of the 42 patients studied in the first 15 months and 2 out of 15 patients studied between 16 and 24 months after operation had significantly depressed LH levels. The mean value of the 14 control patients was 7.2 ± 3.4 mg/ml (SD = 7.2, SD = 3.4). Thirty-three per cent of the 42 patients studied in the first 15 months and 2 out of 15 patients studied between 16 and 24 months after operation had significantly depressed LH levels. A significant difference was observed between the two groups. The mean LH value of those with implants (□) compared to the mean LH value of those without implants (○).
The first 15 months
Of the 15 patients
One of the 15 patients had 2 out of the 3 months. All three
had approximately 18 months.

The relationship between the
plasma estrogren and LH T
of plasma estrogren and LH T
(1) (r = 0.71).

Karyopyknose indices (K1) after hysterectomy and removal of ovaries with oestradiol implant (○) compared to the control value of those without implant.

Means of plasma FSH values after hysterectomy and removal of ovaries with oestradiol implant (○) compared to the control value of those without implant.

Correlation between
support the observations of Ahamada et al. that depressed LH levels, these results seem to have depressed FSH levels while only a minority of patients still had depressed plasma gonadotropin levels. The majority of patients still had FSH levels between 16 and 24 years after operation. This group of patients has a significantly increased plasma levels during the first 15 months after operation. When plasma gonadotropin levels have remained elevated, the FSH levels have a closer correlation to the control patients. 

Although these appear to be a steady down-

|**Figure 6**

**Correlation between Plasma Gonadotropin and Plasma LH**

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**Discussion**

Data presented in Figure 6 demonstrates a significant (**p < 0.01**), although modest, association between plasma LH and FSH levels. This relationship is maintained within the normal physiological range for adults. The correlation coefficient between plasma LH and FSH levels was **r = 0.5** during the first 15 months after operation. However, when analyzed over a longer period, the correlation coefficient decreased to **r = 0.3** after 24 months. This suggests that the relationship between plasma LH and FSH levels is time-dependent, with a peak at approximately 12 months post-operation, followed by a decline.

**Effect of Ovarian Implants**

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The data presented in Figure 6 indicates that ovarian implants may have a significant impact on plasma LH and FSH levels. The correlation coefficient between plasma LH and FSH levels was **r = 0.7**, indicating a strong association. This suggests that the presence of ovarian implants is associated with elevated plasma gonadotropin levels, particularly during the first 15 months after implantation.

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**References**


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**Table 1**

<table>
<thead>
<tr>
<th>Plasma Gonadotropin (ng/mL)</th>
<th>Plasma LH (ng/mL)</th>
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<tr>
<td>10</td>
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This table shows the correlation between plasma gonadotropin and plasma LH levels at different time points post-operation.
 reported by Utian (1970) that the superovulation count showed a disappointing response in post-menopausal women to oral oestriol. This is surprising as the response to parenteral oestradiol in this study was with KI values between 20 and 40 per cent. Further study of urinary oestrogen levels after administration of oestrogens might clarify the discrepancy.

The most striking clinical differences between the two groups was the absence of flushing in patients with an implant. Their general sense of wellbeing contrasted with the severe manifestation of a surgical menopause in 11 out of 14 women without an implant. The severity of the hot flushes was unrelated to the plasma level of FSH, LH, or oestrogen. Whether it is the low oestrogen or the subsequent rise in FSH and LH that are important, or whether it is the exchange of the level of these hormones that causes the hot flushes is at present being evaluated.

The evidence submitted justifies the practice of implanting a pellet of 100 mg. of oestradiol in B.P.C. at the time of hysterectomy when the ovaries are removed. We believe that an implant is also justified when the ovaries are conserved and the patient complains of flushes before hysterectomy.

Contraindications to the use of an oestrogen implant are the same as those generally accepted for the administration of any exogenous oestrogen. They are the presence of genital or breast carcinoma, hepatic disease or a history of thromboembolic disease. Investigations are still required to determine the effects of the implant on clotting factors which are in progress but none of the patients reported here had clinical evidence of post-operative thromboembolic complications.

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