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Effect of Administration of Estrogenic Factor upon Hypophyseal Hyperactivity in the Menopause.

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In a previous communication[1] we demonstrated by improved methods[1, 2] the presence of considerable quantities of both follicle stimulating and luteinizing principles or reactions in the blood and urine of menopause patients and castrates.

The present study was undertaken in order to determine whether injection of large quantities of estrogenic substance would influence the secretion and correlated excretion of the gonadotropic factors, as well as to prove or disprove whether such changes actually take place, and whether amelioration of symptoms, as claimed by Sevringhaus,[3] ran parallel to these changes.

Fourteen cases were studied—4 spontaneous menopause, 8 surgical castrates, 2 X-ray menopause.

As in our previous study,[1] fluctuations in excretion were noted in individual women. A long period of preliminary observation was deemed necessary. In 3 cases, this preliminary period was 26, 52, and 63 days. In the other cases, it varied between 2 and 14 days.

From 4,000 to 22,000 R.U. of estrogenic factor (Progynon Benzoate, obtained through the courtesy of Dr. Stragnell of the Schering Corporation) were used. During the preliminary period the daily output of luteinizing factor in the urine varied from an undeterminable quantity to 40 R.U., that of the follicle-stimulating factor from an undeterminable quantity to 56 R.U. In 3 cases in which the gonadotropic factor was determined in the blood, the concentration found during the preliminary study was 25 R.U. per liter.

The estrogenic factor (Progynon B) was administered by intramuscular injection every 2nd or 3rd day until the entire amount had been given.

In 2 cases the gonadotropic factor disappeared from the urine 4 days after the injection and did not reappear for 24 and 26 days

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1 Frank, R. T., Salmon, U. J., and Friedman, R., PROC. SOC. EXP. BIOL. AND MED., 1935, **32**, 1666.

2 Salmon, U. J., and Frank, R. T., PROC. SOC. EXP. BIOL. AND MED., 1935, **32**, 1236.

3 Sevringhaus, E. L., *J. Am. Med. Assn.*, 1935, **104**, 624.

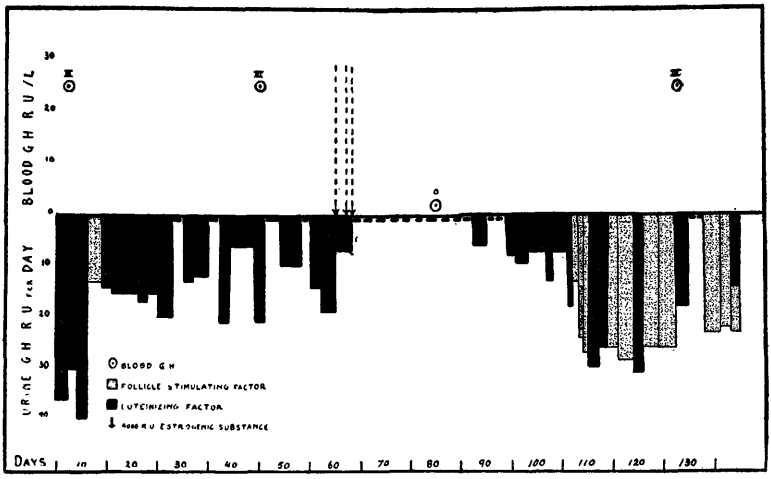

FIG. 1.

Spontaneous Menopause. Age 52. 9 years' duration. Each arrow signifies injection of 4,000 R.U. of Progynon B.
G.H.—Gonadotropic factor.
Total duration of observation 135 days.

respectively. In the remaining cases the gonadotropic factor disappeared for 28 to 47 days. In 2 cases the observation was continued for 101 days after the first injection had been given.

Summary. In 14 menopause cases in which a hyperexcretion of gonadotropic factor was observed, injection of 4,000 to 22,000 R.U. of estrogenic factor was followed by a rapid decrease of gonadotropic factor in the blood and urine. The disappearance of the prepituitary hormone persisted for from 28 to 70 days but was regularly followed by a return to the condition noted before treatment. The amelioration of subjective symptoms roughly paralleled the decrease of the gonadotropic factor in the urine.

From these studies it appears that the hypophyseal hyperactivity which follows castration or appears in the spontaneous menopause (Zondek,[4] Fluhman[5]) can be temporarily ameliorated by the administration of estrogenic factor in high dosage.

Graph of a typical case is appended.

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[4] Zondek, B., *Klin. Woch.*, 1930, **10**, 2121.

[5] Fluhman, C. F., *Endocrinology*, 1931, **15**, 177.