after short fixation in Zenker, was measured from serial sections.[3] Determinations were made on 4 groups of rats:

Group (I) Normal, untreated controls.
" (II) Normals, treated with parathyroid extract.
" (III) Partially nephrectomized, untreated rats.
" (IV) Partially nephrectomized rats, injected with parathyroid extract.

The individual data are shown on the scatter chart, and the mean values in the various groups are presented in Table I.

TABLE I.

Group	No. of rats	Mean volume of parathyroids in mm³	
		Abs.	Per 100 g
I	13	.1483	.0886
II	18	.1506	.0914
III	32	.2314	.1789
IV	11	.2413	.2222

It is obvious that the injection of parathyroid extract, even in large doses, does not bring about an involution of the normal glands, nor does it prevent the hyperplasia which follows partial nephrectomy.

We are greatly indebted to the Eli Lilly Co. for the parathyroid extract used in these experiments.

10013

Effect of Testosterone Propionate upon Endometrial Cycle of the Human.

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Experimental evidence is accumulating which indicates that male hormone counteracts the physiologic effects of estrogenic hormone. Ihrke and D'Amour[1] reported suppression of the estrous cycle in female rats while being injected with male hormone concentrates prepared from bull testes. Similar results were obtained by Robson[2]

[3] Jarrett, W. A., Peters, H. A., and Pappenheimer, A. M., PROC. SOC. EXP. BIOL. AND MED., 1935, **32**, 1211.

[1] Ihrke, I. A., and D'Amour, F. E., *Am. J. Physiol.*, 1931, **96**, 289.

[2] Robson, J. M., PROC. SOC. EXP. BIOL. AND MED., 1936, **35**, 49.

in mice and Browman[3] in rats with testosterone. Zuckerman[4] has reported that testosterone propionate inhibits follicle growth and luteinization in monkeys. The present investigation was undertaken to determine the effect of testosterone propionate upon the endometrial cycle of the menstruating human female.

A group of 6 women were selected and preliminary control endometrial (suction) biopsies were performed in each case to determine the presence of a normal endometrial cycle. In all of the cases selected for this study, the control biopsies performed during the latter half of the cycle showed, on one or more occasions, an endometrium in the secretory phase, indicating a regular estrogenic and corpus luteum effect.

These women were given testosterone propionate* in individual doses of 25 to 100 mg at intervals of 2 to 3 days. The total monthly dosage was varied from 175 mg to 800 mg. The androgen was administered intramuscularly in concentrations of 25 to 50 mg per cc of sesame oil. During the course of testosterone injections, suction biopsies of the endometrium were performed at intervals of 1 to 4 weeks, covering 1 to 3 monthly cycles.

Because of the lack of uniformity in the terminology employed in the literature to describe the morphologic variations of the endometrium, a brief description of the histologic criteria employed in this study is presented.

The normal monthly cycle may be divided into menstrual, proliferative and secretory phases. The *proliferative* phase occurs from the end of menstruation to the time of ovulation. In a 28-day cycle, this extends over a period of approximately 10 days, following a 4-day menstrual period. The endometrium is characterized by an increase in thickness, enlargement and tortuosity of the glands, numerous mitoses, pseudostratification of the epithelial cells, and increase in the number, size and mitotic activity of the stroma cells. There is abundant experimental evidence to indicate that this phase is the result of purely estrogenic stimulation of the endometrium resulting in progressive cellular activity and growth.

The *secretory* phase occurs from the time of ovulation to the beginning of menstruation. This phase is characterized by loss of epithelial pseudostratification, early realignment of the glandular epithelium with centralization of the nuclei, presence of subnuclear vacuolization and glycogen accumulation, papillary projections of

[3] Browman, L. G., PROC. SOC. EXP. BIOL. AND MED., 1937, **36**, 205.

[4] Zuckerman, S., *Lancet*, 1937, **2**, 676.

* We are indebted to Drs. Gregory Stragnell and Erwin Schwenk of the Schering Corporation for the testosterone propionate.

the glandular epithelium into the gland lumen, corkscrew outline of the glands, rare mitoses, and secretion within the gland lumen. The stroma shows increasing edema and lymphocytic infiltration. The stroma cells are enlarged and many of them contain glycogen. The glycogen stain, when used, is of great value in differential diagnosis, since the proliferative phase does not show the presence of glycogen except in the slightest degree. These secretory endometrial changes are the result of a combined estrogen and progesterone effect.

The term *hyperplastic* endometrium indicates an abnormally marked estrogenic effect. It excludes the presence of any corpus luteum stimulation. It represents a hyperproliferation beyond that seen in the average, late proliferative phase of a normal cycle.

The endometrial changes noted after the administration of testosterone propionate are the reverse of those observed in hyperplasia. In contrast, they suggest an inhibition or suppression of estrogen stimulation and proliferation. The term *hypoplasia* is proposed to describe a subnormal proliferative effect, that is, less than that seen in the average, early proliferative phase of the normal cycle. When the manifestations of cellular activity and growth are more strikingly reduced, the designation *marked hypoplasia* is used. *Atrophy*

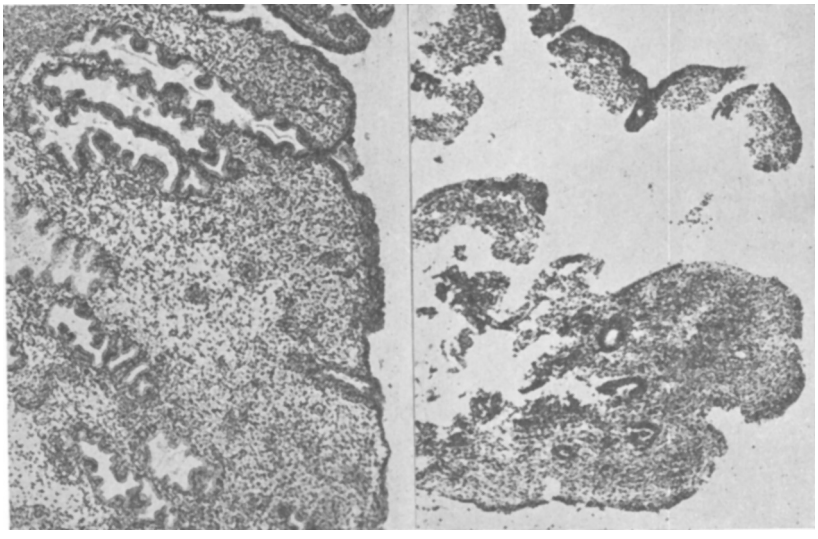

FIG. 1. FIG. 2.

FIG. 1.

Control suction curettage—taken premenstrually. Endometrium showing normal secretory phase.

FIG. 2.

Atrophic endometrium after the administration of testosterone propionate.

is suggested for the endometrial picture resembling that encountered long after the menopause of castration (Fig. 1).

With atrophy, only minute fragments of tissue are obtained despite vigorous curettage with the suction curette. The endometrium is reduced to a thin strip, as evidenced by the not infreqent presence of myometrial tissue a short distance below the surface epithelium. Fragmentation of the specimen is common in contrast to the well-preserved strips removed during normal phases. The endometrial glands are few in number and narrow or slightly dilated. The glandular epithelium does not show the presence of mitoses or pseudostratification. The epithelial nuclei are small, irregular in contour, dark-staining, and often pyknotic. Vacuolization of the cytoplasm and other evidences of plasmolysis are present. The stroma cells are not abundant and are spindle shaped, with small, dark nuclei. No mitoses are to be seen within the stroma cells.

In hypoplasia, the endometrium shows signs of definitely reduced cellular activity. The mitotic figures ordinarily seen within the stroma cells and glandular epithelium of the early proliferative phase are rare. The epithelial nuclei are not uniform, light-staining or vesicular, but small, dark and often irregular. Evidence of cellular degeneration is frequent. The cytoplasm is more acidophilic. The stroma cells are small and dark-staining. The picture is that of a quiescent or partly regressive state. Depending upon the extent to which the endometrium approaches the picture of atrophy, the terms slight or marked hypoplasia are used.

After the administration of testosterone propionate, the endometrial biopsies in all the 6 cases revealed absence of secretory phase or progesterone effect. In 2 of these cases the endometrium presented a picture of atrophy; in one, marked hypoplasia; in 2, slight hypoplasia; and in another, slight proliferation. Pseudomenstruation (bleeding from a non-secretory phase) occurred after the first month of testosterone injections in 2 cases. In a third case, very slight bleeding occurred on 3 occasions at regular monthly intervals. With continued testosterone administration, all of the 6 patients subsequently missed one or 2 menstrual periods.

It appears from these studies that after the administration of adequate doses of testosterone propionate, the following striking morphologic changes occur in the endometrium of cyclical women: (1) Disappearance of the secretory phase; (2) inhibition of the proliferative phenomena, often with regression to the hypoplastic or atrophic state.

These results may be interpreted as indicating either inactivation

of estrogen and progesterone or inhibition of follicle and corpus luteum development. Salmon[5] has shown that the hyperactive hypophysis of the human female castrate can be inhibited with testosterone propionate. It seems logical to assume, therefore, that the suppression of estrogen and progesterone effects in the endometrium, which occurred in the cases reported here, following the administration of testosterone propionate, may be brought about by a similar mechanism—*viz.*, inhibition of the gonadotropic factors (both follicle stimulating and luteinizing) of the hypophysis.

Loeser[6] reported the observation that diminution in bleeding occurred in cases of metrorrhagia following administration of testosterone propionate. He cites a case of irregular menstruation associated with endometrial hyperplasia in which the endometrium became atrophic after 500 mg of testosterone propionate, and suggests inhibition of the hypophysis as a possible explanation of the action of the testosterone propionate.

10014

Effect of Progesterone on Fallopian Tube Contractility.

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It has been previously shown that the Fallopian tubes in women after the menopause lose the rhythmic contractions which, in cyclical women, can be recorded on a kymograph.[1] It was further shown that regular rhythmic contractions can be restored to the Fallopian tubes by the administration of adequate doses of estrogenic hormone.

In the present investigation, an attempt was made to evaluate the effect of progesterone on the Fallopian tube contractility. Five postmenopause women were selected whose vaginal smear studies revealed definite estrogen deficiency. Preliminary control kymographic recordings of the tubal contractions were obtained at weekly intervals, employing the Rubin insufflation apparatus.[2] The patients were then each given a course of estrogen injections in the form of estra-

5 Salmon, U. J., PROC. SOC. EXP. BIOL. AND MED., 1937, **37**, 488.

6 Loeser, A. A., *Lancet*, 1938 (Feb. 12), 373.

1 Geist, S. H., Salmon, U. J., and Mintz, M. E., *Am. J. Obst. and Gyn.*, in press.

2 Rubin, I. C., *J. A. M. A.*, 1920, **75**, 661; 1928, **90**, 99.