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Production of Progestational Endometrium in Post-Menopause Women with Δ^4 Pregnen-in-17-on-3-ol-17 Administered Orally.

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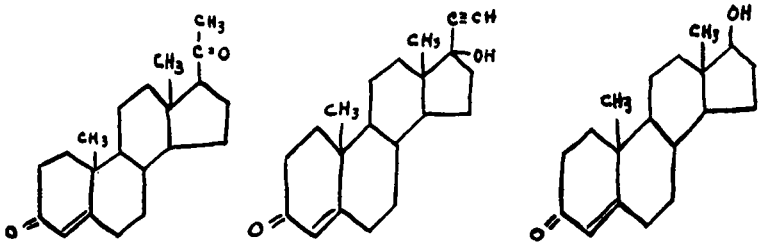
Inhoffen and Hohlweg[1] have reported the production of progestational endometrium in primed, immature rabbits following the oral administration of Δ^4 pregnen-in-17-on-3-ol-17† (pregneninolone, 17 ethenyl testosterone). This substance is a synthetic compound similar in structure to progesterone and testosterone.



Progesterone Δ^4 Pregnen-in-17-on-3-ol-17 Testosterone

The present study was undertaken to determine whether this compound was effective in women when administered orally. The production of progestational changes in the endometrium of post-menopause women was used as objective evidence of progesterone-like activity. Five post-menopause women, in whom endometrial biopsies revealed advanced atrophy of the endometrium, were selected, primed with estradiol-benzoate† and then given pregneninolone by mouth in doses varying from 105 to 480 mg over periods varying from 3 to 8 days. Endometrial biopsies were obtained by suction curettage during the administration of the estradiol-benzoate as well as after the pregneninolone.

The following are protocols of 2 typical cases:

Case I. C.R.; age 44; natural menopause, 7 months. A preliminary suction curettage was attempted but, because of atrophy of the cervix with stenosis of the cervical canal, no endometrium was obtained. The patient was then given 350,000 R. U. of estradiol-benzoate, intramuscularly, in divided doses over a period of 10

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1 Inhoffen, H. H., and Hohlweg, W., *Naturwissenschaften*, 1938, **26**, 96.

weeks. During the period of estrogen administration a suction curettage was performed and revealed a proliferative endometrium. The patient then received 140 mg of pregneninolone, orally, in divided doses, over a period of 4 days. Seven days after the beginning of the pregneninolone, another suction curettage was performed and revealed a definite progestational endometrium. These changes were characterized by: (a) nuclear shift in the glandular epithelium to the base; (b) subnuclear vacuolization; (c) tortuosity and serration of the glands; (d) edema of the stroma and increase in size of the stroma cells; (e) marked reduction in the number of mitotic figures. In many instances, glands in the proliferative stage were seen adjacent to glands exhibiting advanced progesterone effect.

Case II. E.V.; age 47; natural menopause, 2 years. A preliminary suction curettage revealed atrophic endometrium. The patient was then primed with a total of 655,000 R.U. of estradiol-benzoate over a period of 5 months. During this time 5 episodes of spontaneous bleeding, lasting from 1 to 5 days, occurred. Five endometrial biopsies were performed during the period of estrogen administration and revealed varying degrees of proliferation (Fig. 1). The

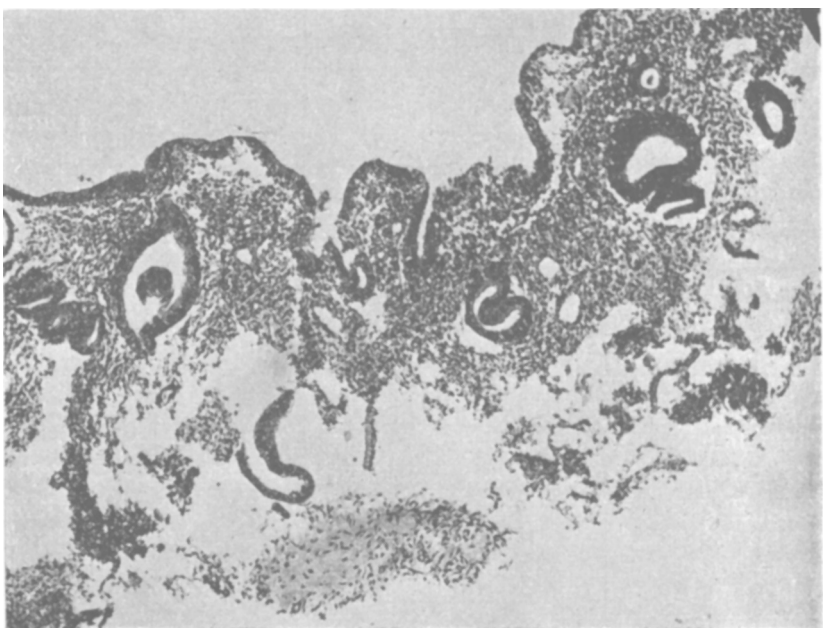

FIG. 1.
Case II. E.V. Age 47; natural menopause 2 years ago. Endometrial biopsy after priming with estradiol benzoate showing proliferative endometrium.

patient then received 60 mg of pregneninolone daily over a period of 8 days (480 mg). During the period of pregneninolone administration, 120,000 R.U. of estradiol-benzoate was given, intramuscularly, in divided doses. A suction curettage, performed on the 8th day after the beginning of pregneninolone administration, revealed a characteristic progestational endometrium (Fig. 2). Most of the glandular epithelium had the typical morphologic characteristics of progestational endometrium. In addition, the stromal changes were well marked and in some areas strongly suggestive of an early decidual reaction.

Of the 3 remaining cases, 2 showed striking progestational changes after 500 and 540 mg of pregneninolone given over periods of 8 and 10 days, respectively. In the third case, receiving only 105 mg of pregneninolone over a period of 3 days, the progestational effect was slight in degree with occasional glands exhibiting typical progestational characteristics.

Summary. Definite progestational changes were produced in the endometrium of post-menopause women with Δ^4 pregnen-in-17-on-3-ol-17, administered orally, after preliminary priming with estradiol-benzoate.

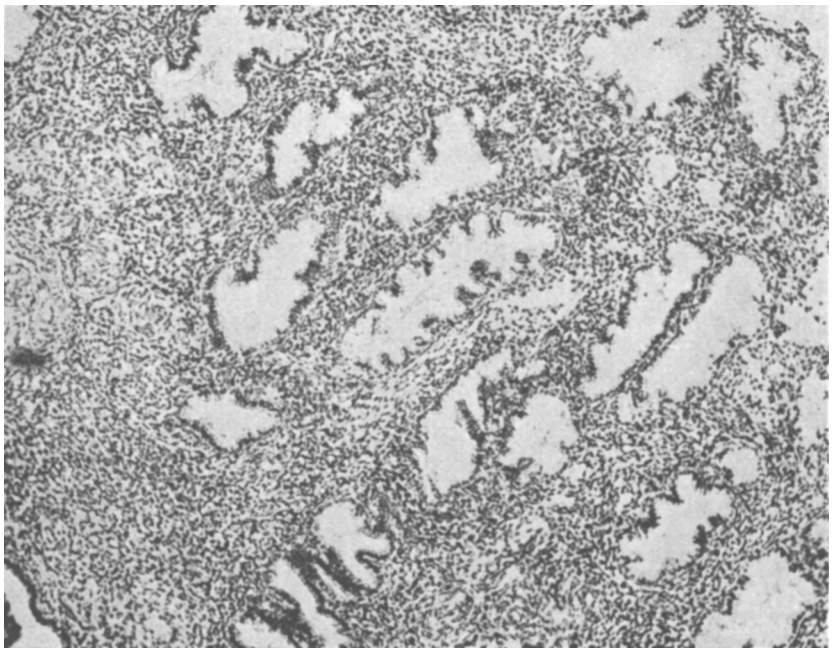

FIG. 2.
Endometrial biopsy performed 8 days after beginning of oral administration of pregneninolone. Total dosage 480 mg. Note typical progestational effect.