from Kidd's procedure. That this is an unlikely factor is suggested by observations that the amount and state of the tumor tissue appeared to bear no definite relation to the presence or absence of the specifically acting antibodies. Our data indicated that the presence of antibody was often associated with the existence of spreading metastases, although 15 rabbits with metastases failed to show the specific antibody.

In a personal communication to the author Kidd has stated that no difficulty had been experienced in securing suitable antigenic material from any specimen of Brown-Pearce carcinoma provided that the tissue was not entirely necrotic. The antigens used in the present series gave positive reactions with at least one serum (Rockefeller or Harvard) but the possibility of the existence of quantitative differences was suggested by the fact in no case did any of the author's sera give positive reactions with all the antigens (Table I). Thus the possibility exists that saline extracts of various tumors may vary in their capacity to fix complement in the presence of sera containing the specific antibody.

Summary. In confirmation of Kidd's work it has been demonstrated that a substance associated with the Brown-Pearce carcinoma fixes complement in the presence of serum of some rabbits bearing the specific tumor. But an incidence of positive reactors considerably lower than that reported by Kidd was observed. Several possible explanations for this discrepancy are discussed.

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Biological Properties of Pregneninolone (17-Ethinyl Testosterone) in Women.

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Inhoffen, Longemann and Serini[1] have synthesized a compound (Δ^4 pregnenin-20-on-3-ol-17; also known as pregneninolone, 17-ethinyl testosterone; anhydro-hydroxy-progesterone) which possesses an unusual variety of biological properties.

This compound, which is chemically very closely related to testosterone and progesterone, has been shown to have: (a) a pro-

[1] Inhoffen, H. H., Longemann, W., and Serini, A., *Ber. Deutsch. chem. Ges.*, 1938, **71**, 1024.

gesterone-like action (progestomimetic) in immature rabbits being, furthermore, active when administered orally;[2, 3] (b) an estrogen-like action (estromimetic) on the uterus and vagina of adult and immature rats;[4, 5] and (c) an androgen-like action (andromimetic) in capons and rats.[4, 5, 6]

In humans, pregneninolone has been shown to produce a progestational effect on the estrogen-primed endometrium[7, 8] and to induce bleeding in cases of functional amenorrhea.[9] The study reported here was undertaken to determine if pregneninolone, administered to women, exhibited, in addition to the progestomimetic action, the same variety of biological properties (*viz.*, estromimetic and andromimetic) that it does in experimental animals.

Estromimetic. To determine whether pregneninolone had an estrogen-like action, a series of 20 post-menopausal and ovariectomized women, all of whom exhibited morphologic signs (by vaginal smears and endometrial and vaginal biopsies) of estrogen deficiency, were given doses of pregneninolone* (orally), varying from 30 to 60 mg per day, for periods varying from 35 to 56 days. The total doses administered varied from 2100 to 2940 mg. Vaginal smears were taken twice weekly; endometrial and/or vaginal biopsies at approximately 4-week intervals.

Results. No evidence of any estromimetic action was observed in the endometrium, vaginal mucosa or vaginal smears in the patients taking 30 mg per day. In 3 patients, taking 60 mg per day, slight estromimetic effects were noted in the vaginal smears after the ingestion of 3160, 3600 and 4200 mg of pregneninolone, in 8, 10 and 11 weeks, respectively. The smears in these cases revealed a scattering of large, squamous, epithelial cells among the "atrophy" cells. At no time, however, in spite of continued administration of the hormone, did the smears reveal a complete estrogenic effect. The endometrial biopsies revealed no evidence of a proliferative response.

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* For the pregneninolone used in this investigation, we are indebted to Dr. E. Schwenk, Schering Corporation, Bloomfield, N. J., and to Mr. R. C. Mautner, Ciba Pharmaceutical Products, Summit, N. J.

Andromimetic. To determine whether pregneninolone possessed androgen-like properties, the hormone was administered to a group of women with regular menstrual cycles. It has previously been shown that testosterone propionate, if administered to cyclical women (in adequate doses), causes: (a) suppression of menstruation;[10, 11] (b) regressive changes in the endometrium, resulting in hypoplasia or atrophy;[10, 12, 13] (c) regressive changes in the vaginal mucosa, manifested by the appearance of estrogen deficiency smears;[11, 13, 14] and (d) masculinization (arrhenomimetic) phenomena (coarsening of the voice and lowering of its pitch; facial hirsuties; enlargement of the clitoris).[10, 13, 15]

Sixteen patients were given pregneninolone in doses varying from 30 to 60 mg per day, for periods varying from 3 to 20 months. The total amounts administered varied from 760 to 10,480 mg.

Results. In no instance were the menstrual cycles significantly affected. The vaginal smears did not reveal any signs of regression in any of the cases. None of the patients developed any of the arrhenomimetic phenomena. It is interesting to note, furthermore, that none of the patients developed acne—a not infrequent result of the administration (by the intramuscular route) of 500 mg or more of testosterone propionate.

Summary and Conclusions. Pregneninolone, though chemically very closely related to both testosterone and progesterone, does not manifest in women the same multiplicity of biological properties that it does in experimental animals. In women, its most striking property is its progestomimetic effect on the estrogen-primed endometrium, when administered orally.

In contrast to its action in rats, in women pregneninolone appears to have: (a) no estromimetic effect on the endometrium and only a very slight effect on the vaginal epithelium if given in very large doses; and (b) no arrhenomimetic effects.

Two interesting observations emerge from this study that are worthy of note. First, the profound change in biologic activity that resulted from the introduction of the ethinyl group at the 17th

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carbon atom of the testosterone molecule, which is the only manner in which pregneninolone differs from testosterone. Second, the striking difference in the biological properties displayed by the same compound when administered to experimental animals and to humans.

The results of this study draw attention to the inadvisability of applying to humans, observations concerning the biological properties of hormones as determined in animal experiments and emphasizes the importance of determining (by means of objective studies) the biological properties of these compounds in humans before using them as therapeutic agents.

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Thermostable Oxidations in Tumor and Muscle Tissue.

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Hopkins and Dixon[1] showed that if a tissue was minced, thoroughly extracted with boiling water, dehydrated with alcohol, dried and finely ground, the resulting "thermostable powder" would not take up oxygen by itself, but in the presence of a little glutathione would take up considerable amounts of oxygen. Further work by Hopkins[2] indicated that the oxygen uptake of these thermostable powders was due to the oxidation of fat at an acid pH and the oxidation of protein at neutral or slightly alkaline pH.

We were interested in determining whether tumor tissue possessed any thermostable oxidative properties similar to those Hopkins found for muscle tissue. For our experiments we have used Flexner-Jobling rat carcinoma and have compared all results to those ob-

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2 Hopkins, F. G., *Biochem. J.*, 1925, **19**, 787.