TABLE II.
Reversibility of Detoxification by Acetylation.

	Dose, cc	Acetylated* suspension	Control suspension (not acetylated)
Gonococcus suspension injected immediately after ketenization	0.5	2/6	6/6
Same gonococcus suspension injected 6 days after ketene treatment	0.5	6/6	

* Numerators indicate the number of mice killed by the injection. Denominators show the total number of mice injected in this experiment.

Effect of acetylation on the antigenic properties of gonococci. Three rabbits were immunized by a series of intravenous injections with suspensions of gonococci treated with ketene immediately before each injection. These rabbits survived weekly intravenous injections, increasing from 0.5 cc to 4.0 cc of the concentrations previously mentioned, without mortality. At the end of 6 weeks antiserum showed about the same antibody content by precipitin test and the same degree of specificity as that made by injections of unacetylated organisms or gonococcus protein.[9]

Conclusions. The toxicity of gonococcus and meningococcus cells is appreciably but temporarily reduced by acetylation with ketene.

10476 P

Experimental Intersexuality: Masculinization of Female Rats by Postpartum Treatment with Anterior-Pituitary-Like Hormone.*

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Papanicolaou and Falk[1] reported a masculinization of female guinea pigs due to treatment with anterior-pituitary-like hormone. This masculinization consisted of growth and enlargement of the clitoris. They also noted a "masculinizing effect" on the skeletal musculature due to the same treatment.[2] These "masculinizing" effects were associated with a marked development of the interstitial

[9] Boor, A. K., and Miller, C. P., *J. Exp. Med.*, 1934, **59**, 63.

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[1] Papanicolaou, G., and Falk, E. A., PROC. SOC. EXP. BIOL. AND MED., 1934, **21**, 750.

[2] Papanicolaou, G., and Falk, E. A., *Science*, 1938, **87**, 238.

cells of the guinea pig ovary. Presumably the hypertrophied interstitial tissue produces an androgenic substance. Hill[3] demonstrated that ovaries transplanted to the ears of castrated male mice produced an androgenic substance. He believes that the ability of these grafts to produce androgenic substance is conditioned by the relatively low temperature to which they are exposed.[4] Hill mentioned a "luteinization of the transplants." Deanesly[5] has repeated this work in rats and believes that the androgenic output is directly related to the amount of thecal luteinization present in the grafted ovaries. Selye, Collip and Thomson[6] have demonstrated that when treatment of female rats with APL is started at 6 days of age, a marked thecal luteinization is found by the 16th day. If daily treatment is continued, granulosal luteinization is not found until the animal is 30 to 40 days old. However, from the data presented by these authors one gains the impression that the theca lutein cells produce estrogenic substance (persistent estrus smears in the experimental rats). They do not mention any change in the clitoris. This literature appears, on the surface, to be discordant and for this reason we have undertaken to repeat Papanicolaou's work, using the rat instead of the guinea pig and making histological studies of the changes occurring in the ovary as well as in the clitoris.

Sixteen newborn female rats were treated daily with APL† in increasing dosages varying from 50 to 800 R.U. The period of treatment varied from 6 to 50 days. The total dosage varied from 600 to 13,000 R.U. Ovaries of animals treated for 6, 10, 30, 36, and 50 days have been examined microscopically. The remaining animals were killed at the age of 6 to 9 months. In the treated animals, at 17-18 days, the clitoris was noticeably enlarged as compared with control littermates (5 animals) and normal stock animals. At 19-21 days, the clitoris was enlarged to such an extent that the organ was evertable. At autopsy, 5-8 months after cessation of the treatment, the clitorides were still noticeably larger than normal and were still evertable.

A preliminary microscopical study of the ovaries revealed little or no change in the animal killed after 6 days of treatment. In animals killed after 10 days of treatment, definite thecal luteinization has been found. After 30, 36 and 50 days of treatment, marked thecal

[3] Hill, R. T., *Endocrin.*, 1937, **21**, 495.

[4] Hill, R. T., *Endocrin.*, 1937, **21**, 633.

[5] Deanesly, Ruth, *Proc. Roy. Soc.* (Series B), 1938, **126**, 122.

[6] Selye, H., Collip, J. B., and Thomson, D. L., PROC. SOC. EXP. BIOL. AND MED., 1933, **30**, 780.

† The APL was furnished by Ayerst, McKenna and Harrison, Ltd.

luteinization has been found in some areas together with large bodies of lutein cells, some with a central cavity and with degenerating ova.

The 3 adult clitorides (7-8 mos.) which have been examined microscopically show structural modifications. A well developed *os priapi* with anterior process is present in each. This structure is not found in the normal adult female, although a homologue exists in the newborn female. Treatment with APL during the first few weeks of life has stimulated this homologue to develop into the typical male structure. There is also some stimulation of the glans epithelium in these animals in that papillae are more numerous than in the normal clitoris. In one animal differentiation of the papillae into spines has taken place. These spines are typical male structures. Some stimulation of the cavernous structures was also noted.

Both Deanesly and Hill have concluded that the androgen produced by ovaries grafted into males is not testosterone. Lamar[7] and the present authors[8] have shown that progesterone, in large amounts, is androgenic in the rat. Progesterone is presumably produced by lutein cells. It is not known whether, in the normal female rat, progesterone is produced by the luteinized granulosa or by the luteinized theca cells. At any rate, it is conceivable that the androgen produced by the ovaries of these experimental animals may be progesterone.

Summary. The administration of APL to infantile female rats causes masculinization of the clitoris consisting of gross enlargement and the development of an *os priapi.*

10477 P

Melanophore Hormone of the Pituitatry Gland and Metabolic Stimulation.*

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Collip and coworkers have recently reported metabolic stimulation in rabbits, guinea pigs, and rats occurring within a few hours following injection of certain pituitary extracts.[1, 2, 3] The substance in

7 Lamar, J. K., *Anat. Rec.*, 1937, **70**, Suppl. p. 45.

8 Greene, R. R., Burrill, M. W., and Ivy, A. C., *Endocrin.*, 1939, **24**, 351.

* Aided by a grant from the Otho S. A. Sprague Memorial Institute.

1 O'Donovan, D. K., and Collip, J. B., *West. J. Surg.*, 1937, **45**, 564.

2 O'Donovan, D. K., and Collip, J. B., *Endocrin.*, 1939, **23**, 718.

3 Billingsley, L. W., O'Donovan, D. K., and Collip, J. B., *Endocrin.*, 1939, **24**, 63.