The average percentage length of the second segment in the 4 animals is 17.7, 15.5, 20.7 and 23.9% respectively. The average for the entire series of 60 tubules is 19.5%.

The evidence for the subdivision of the mammalian proximal convoluted tubule into at least 2 cytologically distinct segments is entirely convincing. A more extensive segmental differentiation has been postulated by Suzuki,[8] but no critical cytological proof in support of his contention has yet been adduced.

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Effect of Combined Administration of Oestrone and Progesterone in Adult Ovariectomized Rats.

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Previous experiments[1, 2, 3, 4] have shown that the mucification of the vagina which is usually observed in pregnant rats may be elicited during lactation if large doses of oestrin are administered. Since administration of similar doses of oestrin in ovariectomized rats would lead to cornification of the vaginal epithelium, the mucification reaction was ascribed to the simultaneous action of oestrin and corpus luteum hormone. Similarly the epithelial lining of the uterus shows only a moderate degree of progestational proliferation during lactation or pseudo-pregnancy in the rat, while in the second half of pregnancy the proliferation of the endometrium and the growth of the uterus *in toto* is much more marked and of a different nature. Various reasons which are discussed in more detail in the papers quoted above led us to the conclusion that the endometrial changes during lactation, pseudo-pregnancy, and early pregnancy, are mainly due to the hormone of the corpus luteum, and we called this reaction "the first stage of pro-

8 Suzuki, T., Zur Morphologie der Nierensekretion unter physiologischen und pathologischen Bedingungen, Jena, 1912.

1 Selye, H., Harlow, C., and McKeown, T., PROC. SOC. EXP. BIOL. AND MED., 1935, **32**, 1253.

2 Selye, H., Collip, J. B., and Thomson, D. L., *Endocrinol.*, 1935, **19**, 151.

3 Selye, H., Collip, J. B., and Thomson, D. L., PROC. SOC. EXP. BIOL. AND MED., 1935, **32**, 1377.

4 Selye, H., and McKeown, T., *Proc. Roy. Soc.*, B, 1935, **119**, 1.

gestational proliferation." The "second stage of progestational proliferation" is that observed during late pregnancy, which we believed to be caused by the simultaneous action of corpus luteum hormone and oestrin. We concluded from indirect evidence that oestrin is produced in large quantities during late pregnancy in the rat but not during lactation or early pregnancy. This would explain why vaginal mucification and the second stage of progestational proliferation appears in late pregnancy only and not during early pregnancy or lactation.

Meyer and Allen[5] stated that vaginal mucification may be obtained in the ovariectomized mouse by the simultaneous administration of oestrone and a corpus luteum extract. But this corpus luteum extract contained oestrin and gave either mucification or cornification by itself, depending on the dose given. Similar results have been obtained by Desclin[6] in non-castrate guinea pigs with a corpus luteum extract which also caused mucification by itself. Fels,[7] however, found that purified corpus luteum hormone preparations have no effect on the vagina of the rat, while small doses of oestrin will cause mucification, as had already been established by previous investigators. He concludes that mucification is an oestrin reaction. He states, furthermore, that although oestrin may inhibit the action of corpus luteum hormone, corpus luteum hormone cannot inhibit the effect of oestrin. He considers the experiment of Fremery, *et al.*,[8] who inhibited the vaginal effect of slightly more than one mouse-unit of oestrin with 3 rabbit-units of corpus luteum hormone in ovariectomized rats, as insignificant because of the large quantity of corpus luteum extract which had to be injected, and might have had a non-specific oestrus-inhibiting effect. Brouha and Simonnet,[9] on the other hand, state that corpus luteum extracts inhibit the oestrus cycles in normal females but do not inhibit the vaginal effect of oestrin in the ovariectomized rat; from which they conclude that corpus luteum hormone acts through the ovary. In an endeavor to obtain further evidence concerning the factors responsible for the changes occurring in the uterus and the vagina of the rodent during late pregnancy we performed a series of experiments on 6 adult ovariectomized rats which received 30 γ of oestrone in 0.5 cc. and 400 γ of progesterone in 0.4 cc. of oil

[5] Meyer, R. K., and Allen, W. M., *Anat. Rec.*, 1933, **56**, 321.

[6] Desclin, L., *Compt. rend. Soc. Biol.*, 1933, **115**, 439.

[7] Fels, E., *Arch. f. Gynäkol.*, 1934, **158**, 364.

[8] Fremery, P. de, Luchs, A., and Tausk, M., *Pflüger's Arch.*, 1932, **231**, 341.

[9] Brouha, L., and Simonnet, H., *Ann. de Physiol.*, 1929, **5**, 567.

daily by means of subcutaneous injections. The progesterone was prepared from pregnandiol by the method of Butenandt and Schmidt.[10] During the experiment the vaginal smear remained dioestric, except in one case in which cornified cells predominated. Histological examination after autopsy on the 20th day of treatment showed that the vagina was lined with a very high mucified epithelium in all cases and the uterus was in the second stage of progestational proliferation in all but 2 cases. These last 2 showed the picture of full oestrus, although the vagina was mucified. It seems from these experiments that progesterone changes the vaginal effect of oestrin and causes mucification. The mucification thus obtained was extremely marked and should not be confused with the slight mucin secretion which may be obtained by sub-threshold doses of oestrin in the castrate rodent. In the latter case, the mucification and the development of the epithelium will always be poor and cannot be improved by raising the dose, since this would lead to cornification. We may conclude, therefore, that both the uterine and the vaginal changes of the late-pregnant rodent are the result of the combined action of oestrin and corpus luteum hormone. It is of interest to mention in this connection that the mammary glands of our animals showed only a very slight development—hardly more than that which the oestrone in itself would have caused.

Summary. The effect of 30 γ of oestrone per day on the vagina and uterus of the ovariectomized rat is modified by the simultaneous administration of 400 γ of synthetic progesterone. The vaginal epithelium shows mucification and the uterus is in the second stage of progestational proliferation. The vaginal effect of oestrone may be modified even in cases in which the uterine effect is not changed.

[10] Butenandt, A., and Schmidt, J., *Ber. deutsch. chem. Ges.*, 1934, **67**, 1901.