

whose ovaries were intact and in which injections were begun 2 to 4 days after hypophysectomy showed no mammary gland growth.

Conclusion: Progynon-B injected subcutaneously into 5 female and 4 male, immature, hypophysectomized albino rats in dosages varying from 25 to 500 International Units per day, produced no evidence of mammary gland growth.

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Action of Oestrin on the Vagina During Lactation.

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The injection of oestrin during lactation has resulted in contradictory opinions regarding the vaginal reaction. Previous experiments on the ovarian hormonal antagonism¹ have shown that the injection of 18, 10, 6, 4, and 2 rat units of oestrin, in oily solution, daily during the first 5 days of lactation always provoked typical oestrus as indicated by vaginal smears. Doses of less than one rat unit have demonstrated the existence of different thresholds of anti-luteinic action of oestrin, the vaginal reaction of oestrus being the first to appear.

Recently, Selye and co-workers have observed that doses of thirty micrograms of Oestrone, in oily solution, daily from the fifth to the tenth day of lactation have failed to provoke vaginal oestrus.^{2, 3} They also reported that 100 or 500 micrograms of Oestrone, injected daily from the fourth to the fourteenth day, had no influence on the vaginal smear which remained typical of dioestrus. "The vaginal epithelium showed a high degree of mucification, a condition regularly seen in pregnancy but not in lactation." It seems difficult to accept this hypothesis of complete antagonism of corpora lutea to the vaginal reaction due to oestrin since a decidual reaction is not maintained under conditions of follicular dominance.

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¹ Votquenne, M., *Compt. Rend. des Seances de la Soc. de Biol.*, 1934, **117**, 1121.

² Selye, H., Harlow, C., and McKeown, T., *Proc. Soc. Exp. Biol. and Med.*, 1935, **32**, 1253.

³ Selye, H., Collip, J. B., and Thomson, D. L., *Proc. Soc. Exp. Biol. and Med.*, 1935, **32**, 1377.

Further experiments with the injection of oestrin during lactation confirm earlier work.¹ The typical vaginal histology of oestrus has been obtained with 0.2 rat unit of oestrin injected daily during the first 4 days of lactation, and the animal sacrificed on the fifth day, even though the vaginal smear remained falsely negative. Particular attention must be paid to the fact that the vaginal smear during lactation does not correspond to the true state of the vaginal epithelium since complete rut is not attained with doses of oestrin of less than one rat unit (Allen and Doisy). Even if the vaginal epithelium is keratinized during lactation marked leucopedesis may occur and the smears show either typical dioestrus or a mixture of leucocytes and cells at all possible stages of keratinization, or even complete desquamation in casts. Vaginal keratinization seems to be the primary effect of oestrin during lactation and the leucocytes disappear only after it is complete.

Injections made during the first 5 days of lactation act when corpora lutea are progressively developing their power. However, similar results have been obtained by injecting oestrin ("Theelin in oil"—Parke, Davis & Co.) daily from the fifth to the ninth day, i. e. when the corpora lutea are fully developed (Criterium: Loeb's deciduoma). The observations of Selye and his co-workers can not be duplicated using smaller, more physiological doses of oestrin. Histological examination of the vaginal wall has shown that the typical picture of oestrus is obtained by the daily injection of 0.75 to 1 rat unit of theelin in oil from the fifth to the ninth day of lactation.

It seems difficult to defend the hypothesis of the anti-oestral action of corpora lutea during lactation under these circumstances. The injection of theelin during lactation may induce the typical histological reaction of oestrus in the vaginal epithelium without characteristic changes in the smear. The oestrin and progesterin may act simultaneously either on different organs (vaginal oestrus and deciduoma) or on the same organ (leucocytes and keratinized cells at all stages). These results confirm the interrelationship of the differential and reciprocal thresholds of action between oestrin and progesterin.

Summary. The anti-oestral action of corpora lutea of lactation is observed only when doses of less than one rat unit are given. The vaginal mucification observed by Selye and his co-workers is probably due to the large doses of Oestrone injected, rather than being the expression of a physiological anti-oestral action of the corpora lutea.