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Prolongation of Pseudopregnancy by Induction of Deciduomata in the Rat.

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Pseudopregnancy is a condition characterized by many of the phenomena of early pregnancy: a prolonged leucocytic vaginal smear, presence of large functional corpora lutea, reduced spontaneous activity, increased body weight, increased food consumption, development of the mammary glands, and progestational changes in the uterine mucosa with susceptibility to deciduomata formation. In the rat its length is subject to considerable variation but its duration is usually 13 to 15 days. Long and Evans¹ from an analysis of 151 cases have pointed out that the average duration of this condition from its induction to the succeeding estrus was 14.38 days. Slonaker² in an analysis of 475 cases found the average duration to be 14.53 days. This represents a material lengthening of the estrous cycle but is still considerably short of the period of pregnancy.

Maintenance of luteal function is essential throughout pregnancy in the rat. This is borne out by the fact that bilateral ovariectomy invariably terminates gestation.³⁻⁶ Removal of the pituitary gland during the first half of pregnancy is likewise followed by death and resorption of the fetuses, whereas pregnancy continues if hypophysectomy is performed after the tenth or eleventh day.^{7,8} This indicates that maintenance of corpora lutea is under the control of the pituitary gland (more specifically of lactogenic hor-

³ Harris, R. G., and Pflüger, J. J., *Anat. Rec.*, 1929, **44**, 205.

⁴ Johnson, G. E., and Challans, J. S., *Anat. Rec.*, 1930, **47**, 300.

⁵ Nelson, W. O., and Haterius, H. O., *Physiol. Zool.*, 1930, **3**, 231.

⁶ Hain, A. M., *Quart. J. Exp. Physiol.*, 1934, **24**, 101.

⁷ Pencharz, R. I., and Long, J. A., *Am. J. Anat.*, 1933, **53**, 117.

⁸ Selye, H., Collip, J. B., and Thompson, D. L., *Proc. Soc. Exp. Biol. and Med.*, 1933, **30**, 589.

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¹ Long, J. A., and Evans, H. M., *Memoirs of the Univ. of Calif.*, 1922, **6**.

² Slonaker, J. R., *Am. J. Physiol.*, 1929, **80**, 406.

none⁹) for the first half of pregnancy; but during the second half is controlled by some extra-pituitary factor, elaborated according to Astwood and Greep¹⁰ by the fetal placenta. Inasmuch as the pseudopregnant rat lacks an extra-pituitary luteotrophin, pseudopregnancy terminates rapidly after cessation of lactogenic hormone secretion.

In the present experiment pseudopregnancy was prolonged to the period of normal pregnancy in the rat following traumatization of the endometrium and subsequent formation of decidualomata and metrial glands.

Material and Technic. Fifty-six female rats 3 to 4 months of age were used in the following experiment. Vaginal smears were taken daily for a period of 2 weeks and the regularity of the estrous cycle determined. Animals showing fully cornified vaginal smears were selected on the first day of an experiment. The cervix uteri of each rat was stimulated for 1 or 2 seconds by an alternating current of 60 volts. Four days after the cervical stimulus was applied, the endometrium of the right uterine horn was traumatized by inserting a silk thread for a distance of 1 or 2 cm through the uterine lumen. Animals were autopsied (8 in a group) 4, 6, 8, 10, 13, 16, and 18 days after endometrial traumatization. Uteri and ovaries were fixed in formol, and sections prepared stained with hematoxylin and eosin and Mallory fluid. In addition 24 animals of similar age and weight were made pseudopregnant but their endometrium was not traumatized. Vaginal smears were taken daily in all cases, and the length of time from induction of pseudopregnancy until the succeeding estrus determined. Whole mounts of mammary glands were also prepared.

Results. In animals whose endometrium was not traumatized the period of pseudopregnancy (from electrical stimulation to the subsequent vaginal cornification) was 13.7 days (range, 12-15 days). In animals whose endometrium was traumatized, vaginal cornification did not recur before the twenty-second

day (18th day post-traumatization).[†] Associated with this prolongation of pseudopregnancy were maintenance of the corpora lutea,[‡] inhibition of follicular development (as determined histologically), leucocytic vaginal smears, and a structure in the insertion region of the uterus which Selye and McKeown¹¹ have termed "the metrial gland." The first evidence of metrial gland formation was observed 6 days post-traumatization.[§] The gland attained maximum diameter 10 days post-traumatization and regressed subsequent to this time. By the sixteenth day (20 days after the induction of pseudopregnancy) the structure was still grossly visible and well developed.^{||} Even by the eighteenth day gross enlargement of the insertion region marked the site of the metrial gland although typical "metrial cells" were not observed.

Mammary glands developed in the traumatized pseudopregnant rat to the same extent as they did in the untraumatized animal. The presence of decidualomata and metrial glands did not prevent mammary regression subsequent to the twelfth day of pseudopregnancy.

Summary. The induction of decidualomata resulted in prolongation of pseudopregnancy to the period of normal pregnancy in the rat. This prolongation occurred in the absence of fetal tissue and was associated with the presence of metrial glands, maintenance of corpora lutea, and inhibition of follicular development.

[†] On this day 5 of the 8 animals in this group came into estrus.

[‡] Attempts to induce secondary decidualomata were unsuccessful. Traumatization of the untraumatized horn 4, 6, 8, or 10 days subsequent to initial traumatization failed to induce a decidual growth although metrial glands were present at the site of original traumatization.

¹¹ Selye, H., and McKeown, T., *Proc. Royal Soc. B.*, 1935, **119**, 1.

[§] Development of the metrial gland occurred at the same time as decidual regression. First evidence of decidual regression was observed 6 days post-traumatization. On the 8th and 10th day post-traumatization decidual necrosis was increasingly more evident. By the 13th day post-traumatization no decidual stroma cells were observed.

^{||} Administration of trypan blue revealed that this dye was not ingested by the metrial cell before the 16th day post-traumatization.

⁹ Lyons, W. R., Simpson, M. E., and Evans, H. M., *Proc. Soc. Exp. Biol. and Med.*, 1943, **52**, 134.

¹⁰ Astwood, E. B., and Greep, R. O., *Proc. Soc. Exp. Biol. and Med.*, 1938, **38**, 713.