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Effects of Injecting Pregnancy-Urine Extracts in Hypophysectomized Rats. II. The Female.*

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The results reported from the injection of P.U. into hypophysectomized female rats are conflicting. Reichert *et al.*¹ report no effect with such treatment; Wade *et al.*² agree, though reporting some luteinization and oestrus; Noguchi³ reports thecal proliferation, follicular destruction and oestrus; Freud⁴ reports similar effects as with A.P. treatment; Collip *et al.*^{5,6} report thecal luteinization and induction of "a continuous oestrus from a shrinking ovary" in the adult, but not in the immature female.

We have injected over 40 mature and immature hypophysectomized female rats exclusive of controls with Antuitrin S (P.U. extract). Treatment was begun immediately or postponed 16-81 days after operation.

Animals injected immediately after operation, whether mature or immature, run a cornified (with an occasional mixed) type of vaginal smear.‡ In the postponed treatments, definite oestrus effects were invariably present as evidenced by larger uteri and oc-

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¹ Reichert, F., Pencharz, R., Simpson, M., Meyer, K., and Evans, H. M., *Am. J. Physiol.*, **100**, 157.

² Wade, N. J., Katzman, P. A., and Jorgensen, M., *Proc. Am. Soc. Biol. Chem.*, 1933, xevi.

³ Noguchi, K., *Japan J. Med. Sc.*, 1931, Trans. IV, *Pharm.* **5**, 104.

⁴ Freud, J., *Deutsch. Med. Wochn.*, 1932, **58**, 974.

⁵ Collip, J. B., and Selye, H., *Nature*, 1933, **131**, 56.

⁶ Selye, H., and Collip, J. B., *Proc. Soc. Exp. Biol. and Med.*, 1933, **30**, 647.

⁷ Collip, J. B., Selye, H., Thomson, D. L., and Williamson, J. E., *Proc. Soc. Exp. Biol. and Med.*, 1933, **30**, 665.

⁸ Selye, H., Collip, J. B., and Thomson, D. G., *Proc. Soc. Exp. Biol. and Med.*, 1933, **30**, 780.

⁹ Collip, J. B., Thomson, D. L., and Selye, H., *Proc. Am. Soc. Biol. Chem.*, 1933, xxxi.

‡ The animals were definitely immature as evidenced by the closure of the vagina and immature condition of the uterus and ovaries. We have not experimented upon rats as young as 22 days. These might fail to show an oestrus response.

asionally by the appearance of a mixed or cornified vaginal smear. §

The ovaries *always enlarge*, though with prolonged treatment they decrease again as in similarly-treated normal females. Ovaries of females treated immediately after operation showed hypertrophied interstitial cells and new corpora lutea, which were difficult to distinguish from those already existing in the case of the adult. The ovaries of females with postponed treatment showed the same marked interstitial cell hypertrophy and often corpora lutea formation. We are not prepared to state that these bodies arise only from thecal cells. Careful studies such as that of Corner on the corpus luteum of the sow will have to be made before the participation of the granulosa can be eliminated. In no case were follicles stimulated to grow. With continued treatment, and more rapidly with cessation of treatment, the ovaries diminished in size, leaving persistent corpora as discrete bodies surrounded by the involuted interstitial tissue.

POSTPONED INJECTIONS.

Immature Rats. Two littermates, 31 days old at hypophysectomy. No treatment for 16 days. One then autopsied. Weight of *both* ovaries, .0065 gm. Other injected for 10 days (25 R.U./day). *Left* ovary, .0102 gm., treated 19 days more, *right* ovary, .0081 gm. Two littermates, 39 days old at hypophysectomy. No treatment for 70 days. *Left* ovary, .0015 gm. Injected 6 days (25 R.U./day), *right* ovary, .0110 gm. The other injected 10 days, *left* ovary, .0095 gm. Treated 15 days more, *right* ovary, .0081 gm.

Mature Rats. Three littermates, 91 days old at hypophysectomy. No treatment for 78 days. *Left* ovary of each removed, weights, .0048, .0077, .0054 gm, respectively. All treated 10 days (10 R.U./day), weights of *right* ovaries, .0140, .0146, .0128 gm. respectively, percentage increases, of 192, 90, and 137.

IMMEDIATE INJECTIONS.

Immature Rats. Four littermates. 41 days old at hypophysectomy. One autopsied at beginning of experiment. Ovaries, .0123 gm. Two treated for 10 days (25 R.U./day). One autopsied at end of treatment, ovaries, .0510 gm. or 314% increase. Untreated operated sister, ovaries, .0083 gm. The other autopsied 11 days after treatment was stopped, ovaries, .0140 gm.

Mature Rats. Five littermates, 119 days old at hypophysectomy. One autopsied at beginning of experiment, ovaries, .0343 gm. One treated for 8 days (25 R.U./day), ovaries, .0485, or 41% over reference control. Another treated for 19 days, ovaries, .0460 gm., a 34% increase over the reference control. Another treated for 10 days, then a no-treatment period of 10 days, ovaries, .028 gm., an 18% decrease. The other, untreated, was autopsied after a 10 day post-operative period, ovaries, .0217 gm., a decrease of 37%.

§ It seems clear that the oestrus was not due to the presence of oestrin, since 5 cc. (500 R.U.) of the Antuitrin S uniformly failed to induce oestrus in sensitized spayed female rats.