7699 C

Pregnancy Cells in Rat Pituitary: Influence of Lipoidal Corpus Luteum Extract.

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Modifications of the histological picture of the anterior pituitary in the mammal have been shown to be dependent upon extra-hypophyseal somatic changes. The cellular alterations of this gland during pregnancy and following castration are well known. Examination of the anterior hypophysis from clinical cases of hydatidiform moles and of chorio-epitheliomata has demonstrated histological changes similar to those occurring during pregnancy (Rössler,[1] Novak and Koff,[2] Heidrich, Fels and Mathias[3]). Similar effects have been obtained experimentally in the pituitaries of rabbits, guinea pigs, and rats by the injection of foetal and placental extracts (Berblinger,[4] Lehman,[5] Baniecki[6]). Experimental ovarian luteinization by means of the injection of fresh anterior pituitary tissue also has been shown to produce pregnancy changes in the mouse pituitary (Haterius and Charipper[7]).

The histological changes of the anterior pituitary involving the appearance of pregnancy cells, experimentally induced, appear to be related to the presence of some product of gestation. Haterius and Charipper[7] have indicated that the ovary is necessary as an intermediate agent for the production of pregnancy cells in the anterior hypophysis and, furthermore, that in the luteinization of the ovary lies the factor essential for the production of these cells. With the development of a potent lipoidal extract of the corpus luteum it appeared possible to test this hypothesis.

All animals used were sexually mature. The various groups of 5 each were made up of mates from not more than 2 litters of the same age. In all cases, daily vaginal smears were made for several weeks to determine the oestrous cycles. Only those with regular

[1] Rössler, H., *Z. f. Geburtsh. u. Gynäk.*, 1929, **96**, 516.

[2] Novak, E., and Koff, A. K., *Am. J. Obst. and Gynec.*, 1930, **20**, 481.

[3] Heidrich, L., Fels, E., and Mathias, E., *Bruns. Beitr. z. klin. Chir.*, 1930, **150**, 349.

[4] Berblinger, W., *Verhandl. d. dtsch. pathol. Ges., München*, 1914, 184.

[5] Lehman, J., *Virchow' Arch. f. path. Anat. u. Physiol.*, 1928, **286**, 346.

[6] Baniecki, H., *Arch. f. Gynäk.*, 1928, **134**, 693.

[7] Haterius, H. O., and Charipper, H. A., *Anat. Rec.*, 1931, **51**, 85.

normal cycles were used. The animals were divided and given 15 daily injections of 0.5 cc. as indicated in Table I.

TABLE I.

Group No.	Animal	Treatment
1	Normal females	*Lipo-lutin
2	Bilaterally castrated females	"
3	Normal females	Estrogen
4	Bilaterally castrated females	"
5	Normal males	Lipo-lutin
6	Bilaterally castrated males	"
7	Normal males	Estrogen
8	Bilaterally castrated males	"
9	Normal females	Minced brain tissue in normal saline
10	" males	Minced brain tissue in normal saline

* The lipo-lutin and estrogen utilized in this investigation was kindly donated by Parke, Davis and Co. The lipoidal extract of the corpus luteum obtained from this source gave a positive reaction when biologically assayed for deciduomata formation.

At the end of the fifteenth day the animals were all sacrificed and their pituitaries fixed in Guthrie's modification of Zenker's fluid; sectioned in paraffin and stained with Delafield's haematoxylin and eosin. Similarly fixed and stained pituitaries were obtained from untreated pregnant, non-pregnant and castrate females and untreated normal and castrate males.

Histological examination of the anterior pituitaries from the estrogen treated animals and those injected with minced brain tissue in normal saline showed no apparent irregular changes. The cells in every case appeared normal when compared to those from the control animals.

Examination of the anterior pituitaries from animals treated with a lipoidal extract of the corpus luteum were all uniform in their histological appearance when compared one to the other within the respective groups. They all showed the presence of large ovoid cells with a deeply eosin-stained homogeneous cytoplasm surrounding a usually eccentrically placed vesicular nucleus. These cells appear to be identical with those found in the anterior pituitary obtained from pregnant animals. It is of further interest to note that the pituitaries obtained from both male and female castrate animals treated with lipo-lutin contained beside the cell type just described, many small poorly delineated castration cells, indicating a tendency toward the correction of castration cell types in this gland. This phenomenon has been shown, previously, to obtain in male rats receiving ovarian implants (Haterius and Nelson[8]).

[8] Haterius, H. O., and Nelson, W. O., *J. E. Z.*, 1932, **61**, 175.

Summary. Evidence is offered that the essential factor for the production of pregnancy cells in the anterior pituitary of the rat is contained in the luteinized ovary and, further, that this factor is not sex specific.

7700 P

Effects of Thyreotropic and Adrenotropic Hormones on Hypophysectomized Frog Tadpoles.

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Twenty-four specimens of *Rana sylvatica* and *Rana pipiens* hypophysectomized at the tail-bud stage, and kept in the laboratory for 525 days, whose normal mates had metamorphosed at 65-70 days, were divided into 3 groups. Seven animals were kept as controls, 7 were treated with Collip's adrenotropic[1] hormone, batch AI, and the remaining 10 with his thyreotropic[2] hormone, batch TG. As a result of his own bio-assays (on rats) Collip stated that the thyreotropic hormone was not free from adrenotropic material but that the adrenotropic hormone was 'fairly pure'. The hormones were administered by intraperitoneal injection, using special fine needles, in 0.05 cc. doses, given once daily, 6 days a week. For the injection an animal was removed from its aquarium and placed on a pad of absorbent cotton wet with ice water. It was then immobilized, ventral side uppermost, by a smaller sheet of wet cotton having a slit cut in it through which the injection could be made. Following the injection the animal was quickly returned to its aquarium.

In 4 days both of the treated groups were dark in color. The adrenotropic group was decidedly darker than the thyreotropic. The only other change noted in the first 5 days was a slight reduction of the tail fin in a few cases.

On the 6th day the hind legs of one animal in the thyreotropic group appeared to be lengthening and by the 10th day all but 2 of this group showed definite growth of the hind legs. From then on the changes normally seen at metamorphosis appeared rapidly. Forelegs emerged from the 11th day on, the tail shortened, the mouth became a transverse slit, characteristic frog spots (*R. pipiens*) ap-

[1] Collip, Anderson and Thompson, *Lancet*, 1933, **2**, 347.

[2] Anderson and Collip, PROC. SOC. EXP. BIOL. AND MED., 1933, **30**, 680.