

that these may be involved in the release or utilization of the components necessary to maintain the probable physiological imbalance created by hemicastration. Hence it can be said that there is a de novo synthesis of hydrolytic and oxidative enzymes.

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### Bilateral ovarian hypertrophy in pituitary-grafted rats<sup>1</sup>

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**Summary.** Large masses that looked like tumours were found in place of the ovaries in rats with isotransplants of pituitaries, 11 months after this procedure. They were interpreted as being due to massive bilateral cystic hyperplasia and hypertrophy of both ovaries.

There are many experimental and clinical reports showing that prolactin excess or deficit influences ovarian function in women and in experimental animals<sup>2-9</sup>. As it is known that pituitary isografts, placed under the renal capsule, induce increased prolactin production in the rat<sup>10,11</sup>, it was considered interesting to use this method to observe the effects of chronic prolactin excess on ovarian function in the rat.

Pituitary isografts were placed under the kidney capsule in 15 normal female Wistar rats, 3 months old. 1 pituitary was grafted in each kidney. Another 10 female rats from the same group were kept as controls.

Vaginal smears were performed daily during the first 2 months and afterwards during 10 consecutive days each month, during the 11-month experimental period. After the operation the normal vaginal cycle and the estrus and

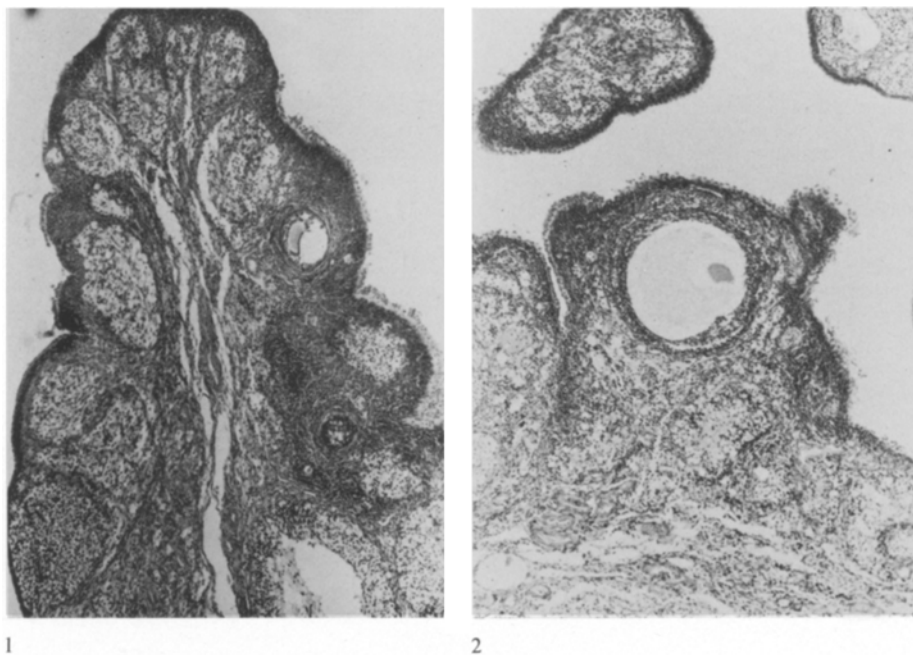
proestrus disappeared in the experimental animals, the vaginal smears presenting a metaestrus-like picture with residues of cornified cells, some navicular cells and many leucocytes; the latter sometimes predominated and the smears looked like diestrus.

Blood was extracted from the heart 2.5 months after the operation. Prolactin was assayed in the serum by radioimmunoassay using a rat NIAMDD prolactin kit, which was generously sent by A.F. Parlow. The serum prolactin level of the 10 control rats was  $5.80 \pm 0.92$  ng/ml while that of the 17 pituitary-grafted ones it was  $22.47 \pm 5.39$ , the difference being significant ( $p < 0.01$ ). But looking at the individual data it could be seen that only 7 out of 15 pituitary-grafted rats were clearly hyperprolactinemic.

The most outstanding feature in the autopsy was the bilateral presence, in place of each ovary, of a large,

Fig. 1. Histologic section of tumoral-looking mass showing ovarian tissue with follicles in different degrees of development. Clumps of clear cells of luteinic aspect are also seen.

Fig. 2. A section with greater magnification showing a well developed ovarian follicle and clear cells of luteinic aspect.



tumoral-looking mass, that was as big as the kidney. The average weight of these masses was  $18.8 \pm 2.8$  g while the ovarian weight of the controls was  $26.3 \pm 2.20$  mg. These tumoral-looking masses could be solid or cystic, but more often showed a combination of these features. The cysts contained a transparent liquid. The masses were well vascularized.

In most animals a hypertrophy of renal arteries and veins was found. The kidneys had some irregularities in the place where the graft had taken place, but we were unable to find evidence of surviving pituitary tissue there in the histological study. The uterus and vagina had a macroscopic appearance similar to that of normal female controls.

The ovarian masses were fixed in 15% formalin and prepared for histological study with hematoxylin eosin. The solid masses consisted of cellular cords included in a massive fibrosis. The cells were dense with a xanthomatous aspect that reminded us of luteinized theca cells. There were also cellular groups around a central cavity, as if they were follicles deformed by the fibrosis (figures 1 and 2).

Besides the cysts filled with transparent liquid, other cystic cavities were filled with pus, as shown histologically. We interpreted these macro- and microscopical findings as a large bilateral cystic hyperplasia and hypertrophy of both ovaries. It was found in all the 8 pituitary-grafted animals which survived until the end of the experiment and in none of the controls. Out of the 8 animals which survived, 6 had

been found to be clearly hyperprolactinemic in the measurement made 2.5 months after the graft. Unfortunately, no prolactin assay was done at the autopsy.

These striking ovarian changes may perhaps be due to changes in the gonadotrophin or prolactin secretion. Further histological and hormonal studies should be made in order to clarify this point.

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