The adrenal tumors which are produced in some strains of mice and rats following gonadectomy may be prevented either by hypophysectomy (2) or by the administration of some steroid hormones, namely, estrogens (4, 6), androgens (4, 5), and desoxycorticosterone in oil (5) but not when administered in pellet form (5).

Dietary caloric restriction in C3H female mice did not prevent the tumor formation but retarded or prevented its gonadal function, as judged by the lack of stimulation of the secondary sex organs (1).

In the present experiments the influence of the removal of one adrenal at the time of gonadectomy on the development of cortical tumors in the remaining gland was studied in female mice of the CSH stock.

MATERIALS AND METHODS

In total, 68 female mice of the CSH strain were gonadectomized at 4 weeks of age, and at the same time either the left or the right adrenal gland of 34 of them was removed. The remaining 34 were kept as gonadectomized controls.

Starting at 3 months after the operation, vaginal smears were taken from both groups by the lavage method. This procedure was repeated at monthly intervals during 4 consecutive days. The appearance of a continuous mixed type of vaginal smear characterized by numerous leukocytes and with nucleated epithelial and cornified cells outnumbering the nucleated cells was recorded and interpreted as indicative of gonadal stimulation. At different postoperative time points mice from both groups were sacrificed and their adrenals as well as the uterus and vagina studied macro- and microscopically.

RESULTS

Chart 1 shows the monthly incidence of positive vaginal smears in both groups of animals. As can be seen, the incidence was greater in the gonadectomized group than in the group which gonadectomy plus unilateral adrenalectomy was performed. In fact, at 4 months after the operation the incidence of positive vaginal smears was 40 per cent, while it was only 3 per cent in the group in which one adrenal was removed. At the end of the 10th month the incidence was 87 and 30 per cent, respectively. However, the macro- and microscopic study of the adrenal glands in both groups of mice revealed the typical postcastrational changes for CSH mice (Fig. 1), indicating that in the unilaterally adrenalectomized animals, the remaining gland developed tumors similarly to the group having both glands, but without showing gonadal stimulation, as judged by the atrophy of the uterus and the absence of positive vaginal smears.

In an attempt to find out whether the lack of stimulation in the unilaterally adrenalectomized group was due to an insufficient release of gonadotrophin by the pituitary gland, ten gonadectomized-

Postcastrational Adrenal Tumors in Unilaterally Adrenalectomized C3H Mice*

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FIG. 1.—Histological section of the adrenal gland of a gonadectomized-unilaterally adrenalectomized mouse (1), and of an adrenal gland of a gonadectomized control (2), at 7 months after the operation.
unilaterally adrenalectomized animals were treated for 7 days with pituitary extract prepared from male pituitary glands of the same stock of mice and suspended in saline. The treatment was begun by the subcutaneous injection of one gland per mouse the 1st day, two glands the 2d, and three glands the 3d, with this amount maintained for 7 consecutive days. Daily vaginal smears were taken from all mice during treatment. None of the mice showed vaginal stimulation either during or immediately after the treatment.

DISCUSSION

It seems clear that, in C3H female mice, the removal of one adrenal gland at the time of gonadectomy did not prevent the development of the typical postcastrational adrenal tumor in the remaining gland, but most of these tumors did not produce sex hormones, as judged by the lack of stimulation of the secondary sex organs.

It is rather difficult at this time to give an explanation of the phenomenon observed. The fact that the treatment with anterior pituitary extract failed to induce stimulation in the unilaterally adrenalectomized group might perhaps be an indication that an insufficient production or release of gonatrophin by the pituitary gland is no the factor involved. It is possible that the unilaterally adrenalectomized animals may have a lower sensitivity of the uterus and vagina to the amount of sex hormones produced by the tumorous adrenals, or that the amount of sex hormones put out by a single gland might be less than that necessary to produce stimulation. None of these possibilities has been investigated.

At any rate, the fact that in the unilaterally adrenalectomized mice, as with mice subjected to caloric restriction, tumors can occur without evidence of sex hormone production may give further support to the theory formulated by Casas, King, and Visscher (1) that perhaps the factors responsible for the anatomical alterations of the adrenals and those responsible for their functional activity may not be identical.

SUMMARY

The removal of one adrenal gland at the time of gonadectomy in female mice of the CSH strain did not prevent the development of tumors in the remaining gland, but most of those tumors did not show signs of the production of sex hormones.

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