

per day for 21 days. The loss of weight and the average amount of glucose excreted were significantly greater in the adrenalectomized animals. The incidence of gross pathology, especially kidney changes and stomach ulcers, was greater in the adrenalectomized animals of all 3 experimental groups. It was concluded that adrenalectomized rats are more sensitive to an excess of cortisone acetate than are non-adrenalectomized rats.

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Ovarian Retention Cysts in Hypothyroid Rats Treated with Diethylstilbestrol.* (19316)

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It was reported earlier (Janes)(1) that cystic ovaries were encountered in rats which had been thyroidectomized for 8 months and that the incidence of their occurrence was increased when diethylstilbestrol was given for 20 days at the end of the period. Recently, Bourg and Simon(2) found cystic follicles in normal rats which had been given relatively large doses of estradiol for 10 or 20 days.

The present work is a continuation of the earlier study and includes observations on more thyroidectomized rats as well as rats treated with thiourea.

Materials and methods. Two hundred and twenty-nine adult female rats of the Long-Evans strain were used. Ninety-eight of these were thyroidectomized for 8 to 12 months, and

46 were rendered hypothyroid by the administration of 0.5% thiourea in the drinking water for 8 months. The remaining 85 were normal as far as thyroid function was concerned. For the last 20 days of the experiment, some of the rats in each group were given diethylstilbestrol either as daily injections of 100 γ or were implanted subcutaneously with 10 mg pellets (95% diethylstilbestrol, 5% cholesterol). At the end of the experiment, the ovaries were fixed for microscopic study. In certain instances the pituitaries were saved and assayed for gonadotrophins in immature female Sprague-Dawley rats.

Results. Rats with a chronic hypothyroidism, resulting from the addition of thiourea to their drinking water or from thyroidectomy, had a greater number of ovarian cysts than normal rats. The incidence of cyst formation in normal rats was increased when diethyl-

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TABLE I. Ovarian Retention Cysts.

Treatment	No. rats	No. rats with cysts	% with cysts
Normal	40	1	3
Normal stilbestrol 20 days	35	3	9
" " 40 "	10	0	0
Thyroidectomized 8-10 mo	39	7	18
" " 8-10 mo	59	32	54
stilbestrol 20 days			
Thiourea 8-10 mo	28	2	7
Thiourea 8-10 mo	18	6	33
stilbestrol 20 days			

stilbestrol was given for 20 days, but the cysts became even more numerous when this estrogen was given to the hypothyroid animals (Table I).

Grossly the cysts appeared as clear vesicles and varied in size (Photomicrographs were shown in earlier paper, Janes(1). The cysts were classified as such only if they were at least twice the size of mature follicles. In many cases the cysts measured as much as 8 mm in diameter. The granulosa cells originally present around the follicles disappeared during cyst formation and the cysts were lined with simple squamous epithelium. The theca interna adjacent to the cysts was luteinized in rats which had received diethylstilbestrol but such luteinization was generally lacking in cystic ovaries of untreated animals. In some rats given diethylstilbestrol pathologic changes such as hydrosalpinx, hydrometra or pyometra were present along with cystic ovaries. This was particularly prone to occur in the hypothyroid rats.

In order to observe the condition of the ovaries during the estrogen injection phase, some animals were laparotomized on the 10th day. At this time the ovaries showed cysts which were not as large or as numerous as at the end of the 20-day period of estrogen treatment.

An effort was made to determine what effect a more prolonged treatment with diethylstil-

bestrol might have on the structure of the ovaries. One hundred gamma of diethylstilbestrol was given daily to 10 normal rats for a period of 40 days. The ovaries were larger than normal in these rats but contained only a few healthy corpora lutea and the medium and large follicles showed atretic changes. However, no ovarian cysts were found (Table I). This indicates that the hypothyroidism is prerequisite for the cystic changes which are accentuated by the estrogen treatment.

The chronic hypothyroidism lead in many instances to atrophic ovaries. Other ovaries contained only a few small follicles and an occasional corpus luteum. Histologically there was no evidence of granulosa cell or other follicular stimulation. Assays of the pituitaries from rats with cystic follicles failed to reveal any significant differences in gonadotrophic hormone content so there is no evidence that changes in gonadotrophic hormones might account for the cyst formation.

Although the conditions of the experiments were not identical, Bourg and Simon(2) found some evidence of retrogressive changes in the ovaries of normal rats which had received large doses of estradiol. It appears, therefore, that the cystic ovaries which have been observed, may not result from pituitary stimulation, but are degenerative changes concomitant with chronic hypothyroidism and estrogen therapy.

Summary. Ovarian cysts were encountered in rats with a chronic hypothyroidism but their frequency was increased when such animals were given diethylstilbestrol. The cyst formation is probably associated with degenerative changes in the ovary.

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