

of growing guinea pigs. The various layers of the cartilage cells become hypertrophic and hyperplastic, and are subsequently quickly calcified and replaced by bone. The epiphyseal line undergoes, therefore, premature closure under the influence of the extract.

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Effect of Various Anterior Pituitary Gland Preparations on Thyroidectomized Guinea Pigs.

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It has been shown that following repeated injections of cattle anterior pituitary extract a very extensive atresia of follicles takes place in the ovary of the guinea pig, which is in contrast to the growth and maturation of follicles that occurs after implantation of anterior pituitary glands of rabbit, rat and guinea pig.¹ A similar, though less pronounced atresia of follicles may be produced through undernourishment of guinea pigs (development of hypotypical ovaries).² It was of interest to determine whether the thyroid gland which is rendered strongly active by these extracts is concerned in this effect on the ovarian follicles. This question was of interest, because it has been shown that some of the effects of anterior pituitary extracts are mediated by the thyroid gland; and furthermore, that thyroid hormone increases basal metabolism and may lead to a loss of weight in the animal in which it is present in excess.

We first carried out control experiments in which we thyroidectomized 21 guinea pigs with an original weight varying between 175 and 205 gm. (except one guinea pig which weighed 260 gm.). Autopsies were performed at intervals between 6 and 38 days following thyroidectomy. The thyroidectomy was complete in 13 animals, while in the remaining 8 some remnants of the thyroid were found. The operation caused a loss in weight or prevented a normal gain, especially in guinea pigs with an original weight less than 190 gm. The heavier animals had an initial loss of weight for

¹ Loeb, Leo, PROC. SOC. EXP. BIOL. AND MED., 1932, **29**, 642, 1128; *Endocrinology*, 1932, **16**, 129.

² Loeb, Leo, *Biol. Bull.*, 1917, **32**, 91.

the first few post-operative days followed by a rapid gain. It was found that complete thyroidectomy does not interfere with the normal development of the ovarian follicles and of the secondary sex organs when the weight remains normal. Loss in weight may cause an incomplete development of the follicles (hypotypical ovaries); but this condition is less marked than that caused by injections of cattle anterior pituitary extracts. The latter cause a very pronounced atresia of follicles even in guinea pigs in which the general state of nourishment would permit growth of the follicles to medium and large size. In completely thyroidectomized guinea pigs spontaneous ovulation may take place when a weight approximating 300 gm. has been reached. In one of these animals, a placental body developed in the ovary as the result of parthenogenetic development of an ovum. This condition was probably independent of the preceding thyroidectomy. The 8 guinea pigs in which the thyroidectomy had been incomplete showed no loss of weight following the operation, presumably because in all these animals the initial weight was relatively high. The ovarian follicles and the secondary sex organs behaved in the normal manner. The remnants of thyroid tissue underwent compensatory hypertrophy in the course of time.

Sixteen thyroidectomized guinea pigs were injected with cattle anterior pituitary extract. In 9 of these animals, no remnants of thyroid gland were found at autopsy, while in 7 the thyroidectomy had not been quite complete. The weight of the guinea pigs at the time of operation varied between 190 and 205 gm., with the exception of one animal which weighed 180 gm. Following the operation, an interval varying between 6 and 37 days was permitted to elapse before the injections of extract were commenced. During the first 10 days following the operation, the weight of the guinea pigs remained stationary or showed a slight loss with a subsequent gain in weight of about 50 to 90 gm. The period of injections during which one injection of extract was given daily, varied between 2 and 11 days. During the first 4 days of injection, there was in some animals a loss in weight amounting to between 5 and 25 gm.; the others gained 10 to 35 gm. The amount of extract injected daily, varied from $1\frac{1}{2}$ cc. to 3 cc.

The results of the injection of acid extract were typical. A very extensive atresia of follicles occurred soon after the beginning of the injections and only in very small, or small to medium-sized follicles did the granulosa remain preserved, and even in these follicles there was a tendency for the granulosa cells to dissolve. The follicles reached medium to somewhat larger size before atresia

set in, in only 2 cases. In some of the atretic follicles, the theca interna and part of the connective tissue growing into the follicular cavity luteinized, and in some cases smaller pseudolutein bodies and pseudocorpora lutea developed. In one of the larger animals, in which ovulation had taken place prior to the commencement of the injections of extract, these corpora lutea underwent retrogressive changes. In the medulla of the ovary rudimentary strands of interstitial gland were seen quite commonly. Vagina, uterus and mammary gland were in a resting condition; but in the uterine mucosa some activity was noticeable in some cases, leading to the formation of predecidual connective tissue in one case. The activity in the uterine mucosa seemed to be correlated with the luteinization processes which took place in the ovary.

We may then conclude that in thyroidectomized guinea pigs extract of cattle anterior pituitary gland has the same effects on the ovary as in normal animals and the effects of this extract on the ovary are not mediated by the thyroid gland but take place independently of the latter.

The same applies to the effects obtained by implanting anterior pituitary glands of rabbit, rat and guinea pig into young female guinea pigs. In 8 guinea pigs such glands were implanted daily during a period of 4 or 5 days. In 2 of these animals no remnants of thyroid were found at autopsy, while some small remnants of isthmus were found in the others. In all of them the typical effects on the granulosa and theca interna were obtained, *viz.*, large mature follicles, pseudolutein bodies and pseudocorpora lutea as well as interstitial gland bodies developed. In some cases, a premature luteinization of the granulosa began in the follicles which had not reached full size. The results varied typically in accordance with the kind of anterior pituitary which was implanted and the amount of gland tissue used, as has been described previously. Here also thyroidectomy did not modify the results in a noticeable manner.

Conclusion. The changes which extract of cattle anterior pituitary gland and anterior pituitary of rabbit, rat and guinea pig exert on the ovary and on the secondary sex organs take place independently of the thyroid gland. It is due to a direct effect on the ovary and is not noticeably modified by the lack of thyroid function.