6652

The Two Main Types of Anterior Pituitary Gland Present in Different Species of Animals.*

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We have shown[1, 2, 3] that the anterior pituitary glands of various species of animals differ in their effects on the thyroid gland and on the sex organs. In accordance with the character and intensity of these effects, we could arrange the various anterior pituitaries in a definite order. We also included urine of pregnant women and assigned to it a place between cattle anterior pituitary, and rabbit and cat anterior pituitary. The differences between rat, rabbit, cat, and guinea pig anterior pituitaries depended only on differences in the quantities of the active substances present, which were especially pronounced, if we compared the anterior pituitary of the guinea pig with the anterior pituitaries of the other animals, but it was impossible to equalize by variations in the quantities of substance used the effects exerted by cattle anterior pituitary and by urine of pregnant women with the effects exerted by the anterior pituitaries of the 3 species mentioned.

We now have examined also the effects of the anterior pituitary glands of sheep and hog. We prepared extracts from these glands in exactly the same manner as in the case of cattle gland: 5 gm. of dried and powdered gland were extracted with 100 cc. of dilute acid during a period of 2 days. The final extracts were then made very slightly alkaline and filtered through a Seitz filter.

In additional experiments, we extracted the gland tissue directly with 0.9% NaCl solution for 2 hours and extracts obtained were filtered through Seitz filters. These latter extracts showed only very weak effects, owing to the short time of extraction.

The effects of these extracts were tested on 24 guinea pigs, each weighing about 190 gm. Daily injections were made during periods varying between 5 and 10 days. The ovaries were studied in serial sections, the other organs (uterus, cervix, vagina), thyroid gland and, in some cases, other organs were examined microscopically in the usual way, but not in serial sections.

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[1] Loeb, Leo, PROC. SOC. EXP. BIOL. AND MED., 1932, **29**, 642.

[2] Loeb, Leo, *Endocrinol.*, 1932, **16**, 129.

[3] Loeb, Leo, PROC. SOC. EXP. BIOL. AND MED., 1932, **29**, 1128.

The results were as follows: The regular extracts of anterior pituitary glands of sheep and hog behaved approximately in the same way as did the corresponding extracts of anterior pituitary of cattle. In the thyroid gland they produced a marked hypertrophy and hyperplasia of the acinus cells associated with irregularity in the shape of the acini and a very far going solution and absorption of the colloid. These effects were the more marked, the greater the quantity of the extract that was injected. With the very weak extracts these effects would be lacking or almost lacking.

The ovaries all underwent a very pronounced atresia of follicles, only very small follicles remaining preserved. Thus a hypotypical condition of the ovaries resulted. This may have been partly due to or accentuated by the loss in weight or the lack of a more considerable gain in weight of these guinea pigs during the period of injection. But it was also due, in all probability, to a direct injurious effect which these extracts exerted on the ovaries or to an absence of the normal growth-promoting and of the maturation-producing effect of the anterior pituitaries as found in other species. There was also a tendency to the production of usually small pseudo-corpora lutea, which owed their origin in the main to hypertrophic changes in the connective tissue elements and in the theca interna during the later processes of atresia, although we cannot exclude the possibility that in some cases remnants of the granulosa may have participated in these formations. Furthermore, the theca interna of quite atretic follicles often underwent a slight increase in size and thus produced a very rudimentary so-called interstitial gland; likewise connective tissue cells situated in the medulla of the ovary, especially in the neighborhood of the blood vessels, might show a certain hypertrophy, so that isolated strands of this so-called interstitial gland were produced. There was no very definite relation between the quantities of extract injected and the intensity of the changes produced in the ovaries comparable to what we had found in the case of the thyroid gland. The occurrence of these ovarian changes, except the hypotypical conditions which took place in all cases, was irregular. In some cases all these changes were found, in others one or the other alteration was lacking and in other animals all of these were absent.

The vagina was usually in an atrophic condition; there was no sign of increase in size of the epithelial cells, nor any proliferation of the lower cuboidal layer. The uterus did not usually show an active condition; in some cases it was relatively thin. However, occasionally a certain proliferative activity was noticed in the con-

nective tissue of the uterine mucosa and in the glands, perhaps due to the presence of small pseudo-corpora lutea or of interstitial gland in the ovaries. The mammary gland was not proliferating, but in certain of the acini there was occasionally some secretory activity noticeable. In one case a piece of sheep anterior pituitary gland, the size of a rabbit anterior pituitary, was inoculated subcutaneously into a guinea pig daily for 7 days. Hypertrophy of the thyroid gland was lacking. The ovary showed normally developed follicles; there was no hypotypical condition, but a pseudo-corpus luteum containing an ovum had formed. The uterus did not show any special reaction. The mammary gland was nonproliferating with some indication of secretion.

We see then that anterior pituitary glands of cattle, sheep and hog exert approximately the same effects on the thyroid gland and sex organs of the guinea pig. In contrast with these species, the pituitary glands of rabbits, cat, rat and guinea pig allow the follicles to grow to full size and bring about maturation of the granulosa. They may cause even premature maturation of follicles which have not yet reached full size. They also give rise to the production of pseudo-lutein bodies in which the luteinized granulosa and theca interna are invaded by connective tissue and blood vessels, a change that represents a modified, hypertrophic type of atresia. These anterior pituitaries lead to the production of much interstitial gland, at the expense (1) of the theca interna of the follicles in the late stage of atresia and (2) of the connective tissue in the medulla of the ovary. The amount of interstitial gland and the size of the individual cells in this formation exceeds by far the corresponding formation produced by the anterior pituitaries of the first group of animals. Moreover, the effects are attained much more regularly by these latter anterior pituitaries. Comparing the effects of equal weights of anterior pituitary in the first and second group of species, the effects in the thyroid gland are more pronounced in the second group. The vagina shows usually only a partial proliferation in the second group except in the cases in which ovulation occurs, when there is a complete keratinization. The mammary gland is usually proliferating under the influence of the second group of anterior pituitary glands. We have previously discussed marked quantitative differences between the effects of the different species constituting the second group, for example: Inoculation of one anterior pituitary of the guinea pig repeated daily during a period of from 5 to 10 days causes only maturation of follicles and a slight production of interstitial gland in the medulla. It has no effect on the thyroid gland.

Only daily inoculation of from 5 to 6 anterior pituitaries leads to changes similar to those produced by one-half or of a whole anterior pituitary of rabbit or of one anterior pituitary of the rat; but the latter exercise usually a stronger effect on the thyroid gland. As stated previously, the marked production of pseudolutein bodies and interstitial gland seems to inhibit a full proliferation of the vagina and inhibits perhaps also ovulation.

In contrast to the marked quantitative differences between the anterior pituitaries of the different species of the second group, equal weights of anterior pituitary of the first group seem to exert about the same effects, although it is possible that the anterior pituitary substance of the hog is slightly more effective than that of the sheep, if equal weights of both pituitaries are compared. In this connection, it may be of interest to compare the weights of the anterior pituitary glands of some of the species which we have considered in these investigations:

Average weights of the anterior pituitary glands of different species: †Cattle: 1115 mg. Sheep: 350 mg. Hog: 125 mg. Male rabbit (weighing 1300 to 1800 gm.): 12 mg. Male guinea pig (weighing 400-500 gm.): 7.5 mg. Male rat (weighing 120 gm.): 3 mg.

Summary. Different species of animals can be separated into 2 classes in accordance with the effects which their anterior pituitary glands exert on the thyroid gland and sex organs of the guinea pig, namely, Class I: Cattle, sheep, hog. Class II: Rabbit, rat, cat, guinea pig. The effects of the anterior pituitary glands of these two classes of animals on the thyroid gland and sex organs of the guinea pig are compared. We intend to investigate the possible effect of variations in the age of the donors of the anterior pituitary glands.

† The age of the cattle used in these experiments was on the average 3 yrs., while that of the sheep and hogs was 10 months.