even though the axis of the cardioelectrical impulse remains unchanged. Results when both ventricles are in contact serve to emphasize that the character of the electrocardiogram is influenced more by the left than by the right ventricle.

8114 C

Effects of Human Anterior Pituitary Gland on Sex Organs and Thyroid of the Guinea Pig.*

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Two types of effects of anterior pituitary gland on the sex organs can be distinguished.[1] The first type is represented by the anterior pituitaries of cattle, hog and sheep. Extracts from these glands cause in the guinea pig a rapid atresia of follicles, a slight production of interstitial gland in the medulla of the ovary and in some atretic follicles a moderate enlargement of the theca interna and sometimes also of the connective tissue which organizes the central cavity of the follicles. Occasionally small or medium sized pseudocorpora lutea may develop. The thyroid gland undergoes a marked hypertrophy. If instead of injection of extract, pieces of anterior pituitary from these species, each one about the size of a pea, are implanted, similar effects are obtained. On the other hand, implantation of pieces from rabbit, rat, and cat anterior pituitary induces in addition to the marked luteinization of the theca interna and the increased production of interstitial gland in the medulla of the ovary an early maturation and luteinization of the follicular granulosa, and the subsequent transformation of this hypertrophic granulosa and theca interna into lutein bodies and pseudocorpora lutea. This occurs if larger follicles are thus affected; somewhat smaller follicles including those which are in process of atresia are changed into interstitial gland bodies in which the theca interna and perhaps also the granulosa undergo luteinization. Daily im-

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[1] Loeb, Leo, PROC. SOC. EXP. BIOL. AND MED., 1932, **29**, 642, 1128; *Endocrinology*, 1932, **16**, 129; Loeb, Leo, and Friedman, Hilda, PROC. SOC. EXP. BIOL. AND MED., 1933, **30**, 741.

plantation of one or 2 guinea pig anterior pituitary glands causes merely a growth of follicles to large size with subsequent granulosa maturation and formation of strands of interstitial gland in the medulla. It does not as a rule induce hypertrophy of the thyroid gland, whereas similar quantities of rat and rabbit anterior pituitaries are effective in this respect. The action of extracts prepared from anterior pituitaries of the second (rabbit) group in the same way as extracts from the first group has not yet been studied.

It was of interest to determine what would be the effects of human anterior pituitary and whether this kind of gland belongs to one of these 2 groups. Zondek and Aschheim in a few implantations of human anterior pituitary glands into mice,[2] noticed enlargement of the ovaries, uterus and occurrence of estrus. They concluded that both hormones A and B are present in human anterior pituitary glands. Schultze-Rhonhof and Niedenthal[3] transplanted pieces of human anterior pituitaries into mice and rats and obtained similar results. They noted keratin formation in the vagina, and the formation of corpora lutea and pseudocorpora lutea in the ovaries. However, these investigators did not yet distinguish between different types of anterior pituitaries, because they used as test animals mice and rats which are not suitable for the analysis of finer differences in the action of the anterior pituitary, probably because in these species the granulosa of follicles is much more resistant than it is in the guinea pig.

We implanted human anterior pituitary glands obtained at autopsies into 9 female guinea pigs with an initial weight varying between 180 and 205 gm. As a rule, each animal received daily one-fourth of a human anterior pituitary for 4 consecutive days; examination took place on the fifth day. A tenth guinea pig received daily one-fourth of a gland for 8 consecutive days, 2 glands being used altogether; the last animal received daily one-half of an anterior pituitary gland from 5 different anterior pituitaries, the gland from a different case being inoculated each day and the examination taking place on the sixth day. Three additional guinea pigs were injected daily with 1 cc. of an extract prepared from a larger number of human anterior pituitaries in exactly the same way as our acid extract of cattle anterior pituitary. These animals received 2, 4 and 8 injections respectively of this extract. In all cases the ovaries

[2] Zondek, B., *D. Hormone des Ovariums und des Hypophysen vorderlallen*, Berlin, 1931.

[3] Schultze-Rhonhof, F., and Niedenthal, R., *Zentralblatt f. Gynaekol.*, 1928, **52**, 1892.

were cut into complete serial sections and sections of uterus, vagina, mammary gland, thyroid and adrenal gland were likewise studied.

In all essential respects the same results were obtained in all these cases, although some minor differences were observed. The weight of the guinea pigs remained in the majority of cases approximately stationary during the experiment; in 3 cases, there was a loss of 10 to 15 gm. and in 2 other cases a slight gain; in the animal receiving 8 injections the weight increased from 195 to 250 gm.

The changes in the ovaries induced by human anterior pituitary gland are as follows: 1. There is a marked tendency of the granulosa of follicles to mature and to luteinize; this applies not only to large but even to small or medium sized follicles.

2. Associated with this process of luteinization in the granulosa is a luteinization of the theca interna. Somewhat later connective tissue and capillaries may grow through the enlarged granulosa and into the central cavity of the follicles. The degree of maturation and luteinization of the granulosa varies in different follicles; it is usually less marked than the luteinization of the theca interna. This leads to an hypertrophic type of follicular atresia.

3. The connective tissue growing into the center of the cavity of follicles during the process of ordinary atresia and especially that surrounding the egg may enlarge and assume the character of epithelioid tissue.

According to the size of the follicles thus affected and the rapidity and intensity of luteinization of the granulosa, either pseudolutein bodies or luteinizing atretic follicles develop. The large pseudolutein bodies become gradually transformed into pseudocorpora lutea. Around follicles in the later stages of connective tissue atresia a considerable amount of luteinized tissue develops; how far this consists solely of enlarged theca interna or also of remnants of luteinized granulosa is difficult to decide.

4. In the medulla of the ovary strands of large interstitial gland tissue develop; the degree of their development corresponds, on the whole, to the degree of luteinization of the theca interna.

The difference between the effects of anterior pituitaries obtained from different cases was not striking; however, some differences were noted as to the presence of large follicles, the greater or lesser tendency of follicles to mature and the number of pseudolutein bodies and pseudocorpora lutea which developed. In one case in which a guinea pig received 8 injections of extract of human anterior pituitary we found what were apparently true corpora lutea, in which we could not discover any retained eggs. Extracts of

human anterior pituitary acted essentially like implanted gland tissue. We may therefore conclude that the process of preparing the extract does not cause a destruction of the hormone acting on the granulosa of the follicles.

Corresponding to the ovarian effects were the changes in the secondary sex organs. In the vagina in a number of cases there was a moderate proliferation of the cuboidal epithelium, leading to the formation of 2 or 3 layers covered by a layer of vacuolar cylindrical cells. As pointed out previously a complete development of squamous and keratin forming epithelium does not take place under these conditions, notwithstanding the presence of a number of mature follicles. In contrast with this relative inactivity of the vagina under these conditions is the active proliferation in this organ which we find at the time of normal estrus, when a single mature follicle readily calls forth very active proliferation and keratinization. We may assume that the luteinized theca interna tissue inhibits the full effect which during normal estrus the mature granulosa exerts on the vaginal epithelium. In still other cases the proliferation in the vagina is lacking altogether; this is found especially in instances in which large mature follicles are absent. However, these relations are not always clear cut; it is probable that simultaneous action of the mutually inhibiting systems, namely mature granulosa and luteinized theca interna, introduces certain complications.

The uterine mucosa has a tendency to form predecidual tissue, especially in cases in which pseudolutein bodies and pseudocorpora lutea are prominent; but here also certain variations occur. In the mammary gland, we find in the majority of cases more or less proliferation which may be associated with signs of secretion; but the latter may be noted also in cases in which proliferation is lacking.

The thyroid gland was in all cases hypertrophic, although the degree of hypertrophy varied in different cases. It was usually quite marked, but in some instances only moderate. It was least marked in the animal which received 8 injections of extract; in this guinea pig correspondingly the gain in weight was greatest. As to the adrenal cortex, accurate counts of the number of mitoses present were not made; but it was evident that in quite a number of animals the proliferative activity in this organ was much increased.

Conclusion. The human anterior pituitary exerts about the same effects in the guinea pig as the anterior pituitary glands of rabbit and rat and it differs markedly in its effects from the anterior pituitaries of cattle, hog and sheep. This is true especially as far as

the effects on ovaries and secondary sex organs are concerned; both types of anterior pituitaries produce a stimulation of thyroid and adrenal glands. Injection of extracts of human anterior pituitaries act in about the same way as implantations of pieces of gland tissue.

8115 C

Effects of Cattle Anterior Pituitary Extracts and KI on Liver Glycogen in Guinea Pigs.*

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Silberberg[1] has shown that oral administration of KI inhibits the hypertrophic changes in the thyroid gland which are produced by injections of extracts of anterior pituitary gland of cattle. A similar inhibiting effect was shown by Siebert and Thurston to be exerted by KI administration in respect to the rise in metabolism which otherwise would have been produced by injections of such extracts of anterior pituitary. We now wished to determine whether KI exerts an inhibiting effect on the changes in carbohydrate metabolism which, according to Eitel and Loeser[2] as well as Holden,[3] are called forth when extracts of cattle anterior pituitary gland are injected into guinea pigs. These changes consist in a marked diminution in the liver glycogen and an increase in blood sugar which Holden finds is of a very transitory character.

Male guinea pigs (190-220 gm.) kept under optimum conditions were used in the majority of tests. In certain cases females were used. The experiments were divided into 2 parts. In the first part, 13 guinea pigs were injected with anterior pituitary extract and simultaneously fed KI. In the second part, 14 guinea pigs were given KI alone. The amount of extract of cattle anterior pituitary gland injected daily intraperitoneally was 1 cc. Two or more animals were injected for each period, namely 2, 4, 6, and 8 days. For 4 days previous to the first injection and continuing throughout

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1 Holden, Raymond F., PROC. SOC. EXP. BIOL. AND MED., 1934, **31**, 773.

2 Eitel, H., and Loeser, A., *Arch. Exp. Path. u. Pharm.*, 1932, **167**, 381.

3 Shaffer, P. A., and Somogyi, M. J., *Biol. Chem.*, 1933, **100**, 695.