

an increasing negativity from the surface to the subcortical white matter suggests a predominance of downwardly directed impulses. The facilitation to a second stimulus accompanying this potential presumably involves a cortico-thalamic discharge.

9188

Effects of Sugar, Glycerin and Urea on Hormones of Cattle Anterior Pituitary Glands.*

S. J. HAYWARD AND LEO LOEB.

From the Department of Pathology, Washington University School of Medicine, St. Louis, Mo.

In a series of former investigations we have distinguished essentially 3 types of effects of anterior pituitary glands on the ovary: (1) The destruction of follicles; (2) various luteinization processes, and (3) the full growth and maturation of follicles, followed in some cases by ovulation and formation of true corpora lutea. We also studied the relation of the thyroid-stimulating hormone to the substances affecting the ovaries. At first we noticed a close association between the thyroid-stimulating hormone and the substances inducing atresia and luteinization processes in the ovary. We considered it, therefore, probable that the thyroid-stimulating hormone and atresin, which is responsible for the destruction of ovarian follicles, were one and the same substance.¹ However, subsequently we developed a method which made possible the analysis of the effects produced by the anterior pituitary glands of various species by subjecting these organs *in vitro* to the action of various solutions.² The results of these experiments indicated that the effects of hormones on the thyroid gland were distinct from those acting on the ovary. In the present investigation we extended the application of this method by immersing the anterior pituitary glands of cattle in glycerin and in solutions of cane sugar and urea before transplanting them subcutaneously into guinea pigs. One cattle gland, or parts of a cattle gland were immersed in 80 cc. of the fluid for various periods of

* These experiments were carried out with the aid of a grant from the International Cancer Research Foundation and of a grant for research in science made to Washington University by the Rockefeller Foundation.

¹ Loeb, Leo, Volume jubilaire dédié an Prof. Lina Stern, Moscow, 1935, p. 405.

² Loeb, Leo, Anderson, H. C., Saxton, John, Hayward, S. J., and Kippen, A. A., *Science*, 1935, **82**, 331.

time. One-fourth of a gland was implanted daily, on 4 consecutive days, into immature female guinea pigs weighing approximately 175-180 gm. Previous to transplantation the gland was freed from adhering solution by rinsing it in sterile 0.9% NaCl solution. If fresh, non-treated cattle anterior pituitary is thus implanted and examination of the guinea pig is made on the day following the fourth implantation, it is found that atresin effects, in some cases accompanied by slight luteinization processes, predominate.

I. *Experiments with cane sugar.* (12 experiments). In most experiments saturated cane sugar solutions, and in a few cases 20% solutions were used. The glands were left in the different solutions for one hour, 4 hours, one, or 2 days. Some of the glands which were left in for one hour, and a few of the others, produced mainly atresin effects together with a slight theca luteinization, such as formation of interstitial gland in the medulla of the ovary and a mild luteinization of theca in quite atretic follicles; in one case also pseudolutein bodies developed. In the other cases various combinations of theca and granulosa luteinization predominated. In addition to the above named luteinization changes, luteinization in the theca of smaller preserved follicles, formation of lutein rings during the stage of early connective tissue atresia and of luteinizing connective tissue atresia occurred. Also interstitial gland bodies and transitions between some of these formations were occasionally noted. There was, as a rule, a definite hypertrophy of the thyroid gland.

The characteristic effect of these solutions consists in the preservation of those substances in the treated gland which produce the various luteinizations.

II. *Experiments with glycerin.* (11 experiments.) In the majority of cases pure glycerin, but in a few instances 50% glycerin, was used. The anterior pituitary glands were left in the solutions 4 hours, one, 2, or 3 days. The results were essentially the same as with cane sugar. In a few cases, especially in the experiments with shorter immersion of the glands in the solution, atresin effects together with slight luteinization were observed, but as a rule, the various combinations of theca and granulosa luteinization predominated. In addition to the above named changes in a few cases a premature maturation or luteinization of the granulosa of smaller, preserved follicles was seen, and in one case we observed ingrowth of connective tissue into the not enlarged granulosa, which was thus divided into parcels. In the majority of cases the thyroid gland showed much hypertrophy, but in some experiments this was only moderate.

III. *Experiments with urea solutions.* (66 experiments.) Saturated, as well as weaker solutions of urea (up to 10%) were used; in the majority of the experiments the solution contained 50% urea; the solutions with the immersed glands were kept mostly at room temperature, but some at 37°C., and others at 40°C., for one, 4, 10, 15 hours, one, 2, 3, or 4 days. The results differed in this series quite markedly from those obtained in Series I and II. The luteinization changes which were characteristic of sugar and glycerin action, were rather inconspicuous in the case of urea solutions; the latter produced principally maturation of follicles without any other changes in the ovaries, but sometimes also pseudolutein bodies, due perhaps in certain instances to an ingrowth of connective tissue and vessels into the mature granulosa; other luteinization processes were rare and slight. Maturation processes in full-sized follicles were found in 26 animals, that is, in more than one-third of all the guinea pigs. In these experiments the urea had caused to a large extent the elimination of the substances responsible for atresin action and luteinization, especially theca luteinization. In 22 cases the action of the urea solution went still further, leading to the entire elimination of all the hormones acting on the ovaries. In the remaining experiments, mainly pseudolutein bodies, either with or without other luteinization products, developed; in some cases the animals were sick and thus hypotypical ovaries were produced. In a few instances atresin action was noted, especially in some experiments in which the glands had been left only for one hour in the urea solutions. The greatest number of mature follicles was observed after an immersion for from 10 hours to 2 days in the solution. After 3 days, the ovaries in which mature follicles were observed were fewer, while those in which no hormone effects were seen, had increased in number. After 4 days, large mature follicles, without any other changes, were found. Of special interest is one case in which mature follicles had just ruptured and in which, in addition, a pseudolutein body was present. However, usually pseudolutein bodies developed as the result of ingrowth of connective tissue and blood vessels into the mature or maturing granulosa of large follicles.

As to the thyroid gland, in the large majority of cases in which fully mature follicles were found in the ovaries, the thyroid-stimulating hormone had been eliminated; but in some of these animals the thyroid showed moderate or even more marked hypertrophy. Also in those guinea pigs, in which the treated anterior pituitary glands no longer exerted any hormone effects on the ovary, thyroid stimulation was lacking in the large majority of cases; but moderate hypertrophy was found in some of the experiments. Thyroid stim-

ulation was more frequently associated with the third group of experiments, in which granulosa luteinization (pseudolutein bodies) or atresin effects predominated. We may then conclude that the thyroid-stimulating hormone, while in many cases associated with theca luteinization or atresin effects, is distinct from the hormone producing these ovarian effects. This conclusion is in agreement with views previously expressed by us.³

Summary. 1. When the anterior pituitary glands of cattle are kept *in vitro* in cane sugar solutions or in glycerin, luteinization processes in theca and granulosa predominate; but if the glands are left in the solution for only one hour atresin effects may still be noticeable. Thyroid hypertrophy is found in the majority of cases. 2. When, instead of cane sugar or glycerin, solutions of urea are used, formation of mature follicles is induced by the glands thus treated in more than one-third of the cases. In another third the action of the urea was so strong that all the ovarian hormones were eliminated. In the majority of these animals also the thyroid hormone had been lost, but in some cases the formation of mature follicles was associated with thyroid hypertrophy. In somewhat less than one-third of the cases formation of pseudolutein bodies, with or without other luteinization processes, and in a few cases atresin effects were observable. 3. While thus glycerin and cane sugar solutions make possible the production of luteinizing effects by the implanted glands, after application of urea solutions only maturation processes are produced, or luteinization effects mainly of the granulosa, or in still other cases all the hormones are eliminated.

9189 P

Relationship Between Blood Amylase and Urinary Amylase in Man.

S. H. GRAY AND MICHAEL SOMOGYI.

From the Laboratory, Jewish Hospital, St. Louis.

Somogyi¹ has shown that the amylase content in the blood is rather constant for the individual, while the variations from individual to individual are considerable. The study of the amylase content of the urine, however, reveals great irregularity in the same individual at various periods of the day, without any apparent regu-

³ Loeb, Leo, Saxton, John, and Hayward, S. J., *Endocrin.*, 1936, **20**, 511.

¹ Somogyi, Michael, *Proc. Soc. Exp. Biol. and Med.*, 1934, **32**, 538.