We hope to demonstrate by further experiments that the coagulation time which is prolonged in obstructive jaundice can be shortened sufficiently to reduce the operative risk.

4818

Comparison of Effects of Various Preparations of Anterior Pituitary Gland on Thyroid of Guinea Pig.

LEO LOEB AND R. B. BASSETT.

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

In a former communication,[1] we reported that the thyroid gland of guinea pigs which received injections of acid or alkaline extract of the anterior pituitary gland within a short time showed such a remarkable hypertrophy that it closely resembled the thyroid seen in pronounced cases of Graves disease. These findings were in marked contrast to the fact that the feeding of Armour's tablets of anterior pituitary prevented or greatly inhibited compensatory hypertrophy in thyroidectomized guinea pigs.

We now report further observations on the effect of the anterior pituitary gland.

Preparation of Extracts. The anterior pituitary of cattle was freed completely from other parts of the hypophysis, then dried and powdered. Five grams of the dried powder were extracted with 100 cc. of 0.5% acetic acid or with 100 cc. of 0.1% sodium hydroxide for a period of 24 hours, in ice chest. The fluid was separated from the residue by filtration, neutralized to pH 7.8 (Phenol Red), refiltered to remove a protein precipitate which falls out at the isoelectric point. The filtrate was then passed through a Seitz bacterial filter to render it sterile.

Experimental. Silberberg,[2] in the course of experiments carried out in this laboratory observed that there was a distinct hypertrophy in the thyroid gland of the guinea pig as early as one day after the injection of 1 cc. of acid extract of the anterior pituitary. Following this, we made a comparative study of the action of acid and alkaline extracts on the thyroid gland and also on the sex organs. One group of animals was injected daily with 1 cc. acid extract, and another

[1] Loeb, Leo, and Bassett, R. B., PROC. SOC. EXP. BIOL. AND MED., 1929, xxvi, 860.

[2] Silberberg, Martin, PROC. SOC. EXP. BIOL. AND MED., 1929, xxvii, 166.

with 1 cc. of alkaline extract. On each day, beginning with the second day of the experiment and ending with the seventh, we removed the thyroid gland from one guinea pig of each set. On the whole, we observed that the curves representing hypertrophic changes were the same for both extracts. A noticeable hypertrophy was seen even after one injection. The hypertrophy increased with the number of injections until the fifth or sixth day when the maximum was reached. But at the end of the second or third day the maximum of mitotic proliferation was reached, at which time the number of mitoses was exceedingly great. After this, the mitoses decreased while the solution of the colloid and the hypertrophy of the acinus cells progressed. Thus hypertrophy takes place with a surprising rapidity and the maximum increase in mitotic activity is reached before the stage of maximum hypertrophy and absorption of colloid. There is no marked difference in these respects between the action of acid and alkaline extracts.

In one experiment, an intravenous injection of 1 cc. of acid extract was given and one day later the thyroid removed for microscopic examination. A study of the gland showed the presence of early hypertrophy.

Other experiments were performed in which several cc. of extract were injected daily to compare the intensity of hypertrophy with that caused by 1 cc. daily. Contrary to expectation, the former procedure did not cause any greater hypertrophy than the latter.

In contrast to the thyroid of the guinea pig, which responds with remarkable regularity to the effect of anterior pituitary extracts, the rat thyroid does not show distinct hypertrophic changes after daily injections of 0.5 to 1 cc. of acid extract. At the most, only a trace of hypertrophy was demonstrable. We may conclude then, that the thyroid of the guinea pig is much more responsive to the injection of the extracts than that of the rat.

After determining the principal effects of acid and alkaline extracts on the thyroid of the guinea pig, we studied the effect of daily subcutaneous inoculations of a whole anterior pituitary gland taken from another guinea pig and also, of small pieces taken from cattle gland. In the greater number of the experiments, 6 to 10 inoculations were made on successive days, in the remaining, the number of inoculations was less. It was found that the subcutaneous inoculation of cattle gland was much more effective in causing hypertrophic changes in the thyroid than was the guinea pig gland. This may have resulted from the use of a comparatively greater amount of gland substance in the former case. This mode of ap-

plication was, however, less effective than the intraperitoneal injection of either the acid or alkaline extract.

We have also investigated the effect of these substances on the sex organs of the guinea pig. This phase of our studies is not yet complete and we shall report on it more fully at a later date. But we may state that the effects on the thyroid gland and those on the sex organs do not parallel each other. For example, inoculation of anterior pituitary gland of the guinea pig is very effective in causing ovulation, hypertrophy of the uterus and the opening of the vagina, whereas, it has only a relatively slight effect in causing hypertrophy of the thyroid. Inoculation of anterior pituitary of rabbit is likewise effective on the sex organs of the guinea pig. On the other hand, inoculation of anterior pituitary of cattle apparently does not produce changes in the sex organs as observed above, yet it is effective in causing hypertrophy of the thyroid. Acid or alkaline extracts, as prepared in our laboratory, do not cause ovulation or opening of the vagina in the guinea pig, but do lead to the production of structures which correspond to the so-called interstitial gland in the ovary of the rabbit. Such marked hypertrophy of the theca constituents of atretic follicles may lead even to the production of structures which somewhat resemble small corpora lutea. However, these structures contain degenerating ova.

These findings suggest that there may possibly be several constituents in the anterior pituitary gland, each of which acts in a specific manner on the thyroid gland and on the sex organs.

4819

Interaction Between Substances in Tissue Extracts and Blood Sera. Effect of Mixtures of these Substances on Coagulation of Blood.

E. L. BURNS, F. H. SCHARLES AND L. F. AITKEN. (Introduced by Leo Loeb.)

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

Loeb[1, 2] and subsequently Hewlett,[2] Muraschew,[2] and Nolf,[2] have shown that tissue coagulins (thrombokinase of Morawitz, tissue fibrinogen of Wooldridge and Mills, thromboplastic substances of

[1] Loeb, Leo, *Montreal Med. J.*, 1903, xxxii, 507; *Virchow's Archiv.*, 1904, clxxvi, 10.

[2] Loeb, Leo. See review of older literature in *Biochem. Centralblatt*, 1907, vi, 829.