

series differed only in the amount of the daily yeast supplement and it was concluded that the increased tolerance for benzoate, observed in the second series, was due partly to more efficient utilization of the food and partly to the presence of glycine in the additional yeast protein.

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Effect of Hormones of Anterior Pituitary on Thyroid Gland in the Guinea-Pig.

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In former investigations Loeb^{1, 3} and Loeb and Kaplan² have shown that feeding of tablets of anterior pituitary substance (Armour & Co.) prevents, in the guinea pig, compensatory hypertrophy which otherwise occurs in many cases after the greater part of the thyroid has been extirpated. H. A. McCordock⁴ through feeding of these tablets prevented the marked cell proliferation which occurs in the guinea pig after administration of potassium iodide. There are also prevented the slight changes in colloid and in the size of the acinus cells caused by iodine. These experiments proved that in Armour's Anterior Pituitary preparation there is present a substance which prevents growth processes (hypertrophy and hyperplasia) in the thyroid of the guinea pig.

However, in larvae of amphibia, it has been shown that removal of the anterior pituitary may cause atrophic changes in the thyroid gland (B. M. Allen,⁵ P. E. Smith⁶) or, conversely, that injection of acid extracts of anterior pituitary may stimulate the thyroid gland and cause morphological changes indicative of active secretion (E. Uhlenhuth and S. Schwartzbach⁷). These facts suggested to us the possibility that there may be present, also, in the mammalian anterior pituitary, substances which have a stimulating effect on the thyroid gland.

¹ Loeb, Leo, *J. Med. Res.*, 1920, xli, 481.

² Loeb, Leo, and Kaplan, E. E., *J. Med. Res.*, 1924, xliv, 557.

³ Loeb, Leo, *Am. J. Pathol.*, 1929, v, 71.

⁴ McCordock, H. A., *Am. J. Pathol.*, 1929, v, 171.

⁵ Allen, B. M., *Anat. Rec.*, 1917, xi, 486.

⁶ Smith, P. E., *Anat. Rec.*, 1917, xi, 57.

⁷ Uhlenhuth, E., and Schwartzbach, S., *Brit. J. Exp. Biol.*, 1927, v, 1.

We prepared, from dried and powdered anterior pituitary of cattle, acid as well as alkaline extracts (subsequently neutralized) of which we injected daily 1 cc. intraperitoneally in each of a series of 19 guinea pigs, an additional animal as well as animals used in other series serving as controls. We used 2 different concentrations in both the alkaline and the acid extract. The injections extended over periods varying between 7 and 19 days. There resulted in every case hypertrophy of the thyroid gland; it varied in intensity in different animals but on the average was very pronounced and exceeded considerably the average obtained in cases of compensatory hypertrophy following extirpation of the thyroid gland. Especially in the younger animals the changes were very pronounced. All the signs of compensatory hypertrophy were thus imitated: Enlargement of the acinus cells; the appearance of granules in the portion of the cell directed towards the lumen of the acinus; softening and absorption of colloid; an irregular and often slit-like shape of the acini and, in certain cases, a great increase in mitoses. The hypertrophy exceeded considerably that found after administration of iodine in the guinea pig, where the mitotic proliferation is the principal effect obtained. Both acid and alkali extracts were able to produce this hypertrophy.

Of great interest is the relative or absolute loss in weight associated with the injections in the large majority of cases. It is especially marked in the heavy animals, while in the small (young) guinea pigs the majority retained approximately their weight or lost only a small amount. However, the relative loss of weight as indicated in the failure of the animals to gain during the period of injection is very great also in the young guinea pigs. In those animals which showed a distinct gain during the course of the experiments, the average intensity of hypertrophy is much less than in the others. This parallelism between intensity of hypertrophic changes and the weight curve of the guinea pigs suggests very strongly the conclusion that administration of the extracts caused an increased elimination of thyroid hormones into the circulation and thus caused an increase in metabolism. However, there remains the possibility that the extracts may affect the metabolism also directly and not merely by way of the thyroid.

We have, then, to deal with 2 opposite effects on the thyroid gland of substances obtained from the anterior pituitary. Feeding of Armour's tablets of anterior pituitary inhibits growth processes and function in the thyroid gland, whereas intraperitoneal injection of acid or alkaline extracts stimulates markedly the growth processes and apparently also the function of this organ. We have now a

simple method which allows, in the guinea pig, the production of very intensive hypertrophy of the thyroid gland within a relatively short period of time.

Thus far these results apply only to the guinea pig, where the thyroid gland seems more responsive to stimulation than in certain other animals.

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Studies on Growth. II. Effect of Liver Extract on Food Consumption, Food Utilization and Growth.

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In certain of our experiments it has been necessary to investigate the effect of the addition of liver to the diet of growing rats. Osborne and Mendel¹ have recently called attention to the marked acceleration of the growth rate which occurs under these circumstances. It was possible from our experiments to show the difference between the action of yeast and of liver on the consump-

TABLE I.
Effect of Liver Extract and of Yeast on Food Consumption, Food Utilization and Growth.

Diet	No. of rats*	Aver. increased wt., 40 day period	Aver. food intake	Calories per gm. increase in weight	Remarks
Mixed stock control diet	17	gm. 115	cal. —	—	Diet fed <i>ad libitum</i> .
B + 0.3 gm. yeast	10	118	1345	11.4	" " " "
B + 0.3 gm. yeast and liver extract	10	161	1630	10.1	" " " "
B + 0.15 gm. yeast	17	62	975	15.7	Restricted food intake
B + 0.3 gm. yeast	16	80	975	12.2	" " "
B + 0.3 gm. yeast and liver extract	10	73	975	13.4	" " "

* Males, 30 days of age, were used.

¹ Osborne, T. B., and Mendel, L. B., *J. Biol. Chem.*, 1926, lxi, 661.