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Effects of Anterior Pituitary Extracts of Cattle on Carbohydrate Metabolism in the Guinea Pig.*

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In view of preceding observations that injections of anterior pituitary glands of cattle cause a marked stimulation of the thyroid gland in guinea pigs,¹ leading to a loss of weight by the animals² and to an increase in the basal metabolic rate,³ it was of interest to investigate the effects of such extracts on the carbohydrate metabolism.

Artundo and Mazzocco⁴ found no change in the glycogen reserves of white rats after injections of fresh rat hypophysis in saline. Eitel and Loeser⁵ have reported studies on guinea pigs, using anterior pituitary extracts containing thyroid stimulating hormone. They noted a fall in liver glycogen, reaching minimal values in 11 days, with a slow increase subsequently. They report no change in muscle glycogen. Our results are somewhat different in certain respects. We likewise used guinea pigs, which had served for the large majority of experiments carried out by Loeb and Siebert.⁶ Male guinea pigs (190-200 gm.) kept under optimal conditions were used in all experiments. The extract was that used previously in this department.⁷ Injections were made intraperitoneally with sterile precautions. The animals were killed 24 hours following the last injection and glycogen determined by a modification of the Pflüger method,⁸ blood sugars after Shaffer and Somogyi.⁹ Two or more animals were employed for each interval recorded and all glycogen determinations were made in duplicate. The points in the accompanying graphs represent averages.

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¹ Loeb, Leo, and Bassett, R. B., *Proc. Soc. Exp. Biol. and Med.*, 1929, **26**, 860.

² Loeb, Leo, and Friedman, Hilda, *Ibid.*, 1931, **29**, 14.

³ Siebert, Walter J., and Smith, R. S., *Ibid.*, 1930, **27**, 622.

⁴ Artundo, A., and Mazzocco, P., *Compt. Rend. Soc. Biol.*, 1930, **105**, 713.

⁵ Eitel, H., and Loeser, A., *Arch. Exp. Path. and Pharm.*, 1932, **167**, 381.

⁶ Loeb, Leo, and Siebert, Walter J., *Loc. cit.*

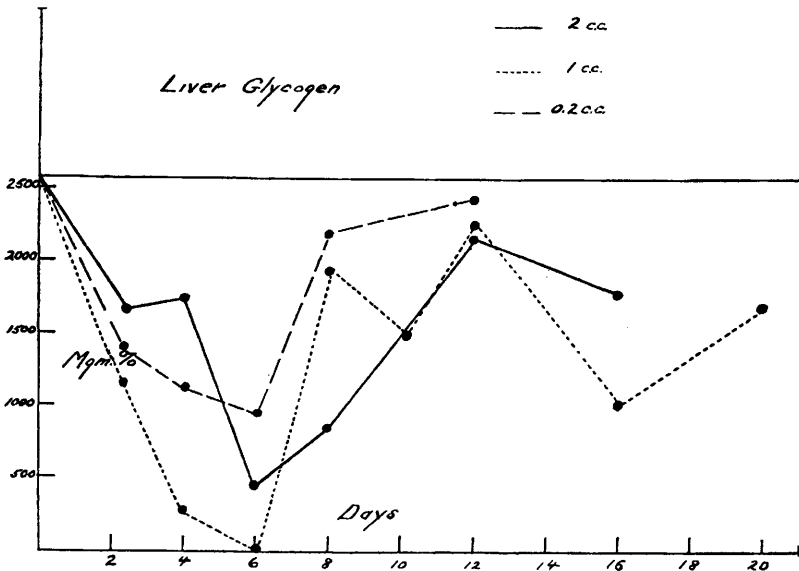
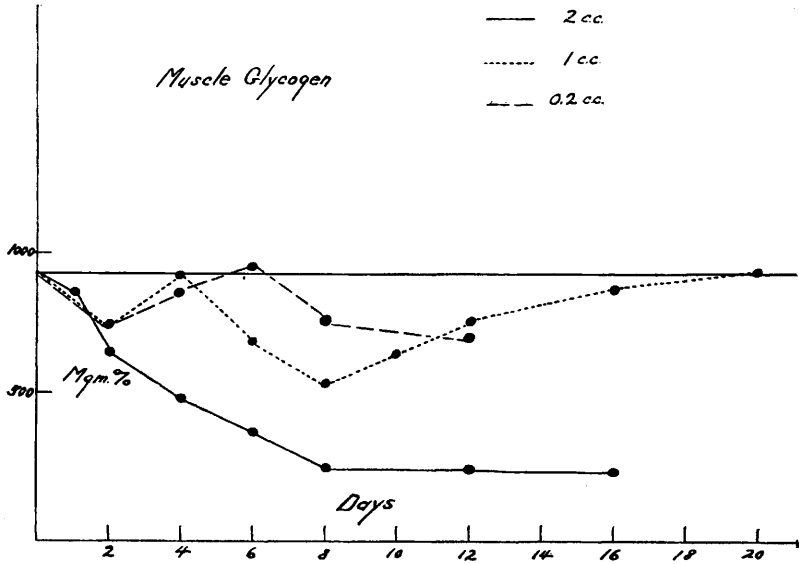
⁷ Loeb, Leo, and Bassett, R. B., *Proc. Soc. Exp. Biol. and Med.*, 1930, **27**, 490.

⁸ Good, C. A., Kramer, H., and Somogyi, M., *J. Biol. Chem.*, 1933, **100**, 485.

⁹ Shaffer, P. A., and Somogyi, M., *J. Biol. Chem.*, 1933, **100**, 695.

The following normal values were established :

		(Eitel and Loeser)
Liver glycogen	2540 mg. %	2590 mg. %
Muscle glycogen	930 mg. %	520 mg. %
Blood sugar	90-126 mg. %	68-120 mg. % (Hagedorn-Jensen)



Liver glycogen determinations were made after injections of 2 cc., 1 cc., and 0.2 cc. of acid extract. In each case, a rapid decline in the liver glycogen occurred, reaching a minimum in about 6 days. A slow recovery then occurred, notwithstanding continued injections. In no case did the liver glycogen return completely to normal. With injections of 2 cc. and 1 cc., the effects were similar, while with 0.2 cc. a less marked response obtained. The character of the liver glycogen curve was essentially the same in each case. No significant change in liver weight could be detected. The animals injected with the larger amounts tended to lose weight, as recorded previously.¹

With injections of 2 cc. daily, a fall in muscle glycogen (samples taken from thigh muscles) was noted. A subnormal level persisted during the course of the experiment. With 1 cc. and 0.2 cc. injections no significant change in muscle glycogen occurred.

Blood sugar determinations made concurrently with the glycogen estimations were not consistent, ranging from 92-384 mg. %. However, in one-third to one-half of the determinations, values were obtained exceeding the highest normal levels. This suggested that possibly the time factor might enter as a variable in these determinations and that the optimum might have been passed in many cases when the blood samples were taken 24 hours following the last injection. We, therefore, determined the blood sugar values as early as 4, 8 and 13 hours following a single injection of acid extract. The following figures were obtained: After 4 hours, 170 mg. %; after 8 hours, 232 mg. %; after 13 hours, 204 mg. %; after 24 hours, 138 mg. %.

Our results are in agreement with those of Eitel and Loeser in that we found a rather prompt fall in liver glycogen following the initial injections. However, our results differ in the following aspects:

(1) In our experiments, the liver glycogen reached a minimum in each case at 6 days, whereas according to Eitel and Loeser the minimum is reached in 11 days.

(2) We found a rather rapid recovery of the liver glycogen to slightly subnormal levels, notwithstanding continuation of the injections; whereas they report continued low glycogen values during the period of injections. Our results may perhaps be best explained by assuming a high activity of the extract employed and a rapid compensation on the part of the animal. Our curves are in agreement with the findings of Loeb and Bassett¹ that the maximum stimulation of the thyroid gland, as evidenced by the curve of the

mitotic activity, is reached about 6 days following the initial injection, or is reached during the first week, to be followed by a decrease.

(3) We find considerable quantitative differences in the diminution of liver glycogen depending upon the amount of extract given.

(4) We note a definite effect on muscle glycogen, provided sufficiently large doses have been injected.

As to the blood sugar level, a rise has been observed in the experiments of Houssay, *et al.*,¹⁰ in the dog; and by Barnes; Evans; and Baumann and Marine¹⁰ in the rabbit. However, these authors have obtained their effects after repeated injections of large amounts of anterior pituitary extracts. This is in contrast with the sharp rise and fall of blood sugar values observed in our preliminary experiment. This matter is being investigated further.

¹⁰ Houssay, B. A., Biassotti, A., Rietti, C. T., *Compt. Rend. Soc. Biol.*, 1932, **111**, 479. Barnes, B. O., Reported by E. I. Evans, *Proc. Soc. Exp. Biol. and Med.*, 1933, **30**, 1370. Evans, E. I., *Loc. cit.* Baumann, E. J., and Marine, D., *Ibid.*, 1932, **29**, 1220.