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Effect of Adrenalin on Insulin Sensitivity of Partially Adrenalectomized and of Hypophysectomized Dogs.

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In a previous report[1] it was pointed out that after partial adrenalectomy in dogs, the animals became abnormally sensitive to insulin similar to that which is observed after hypophysectomy. This study was undertaken to see if adrenalin injections would delay or prevent the insulin convulsions in partially adrenalectomized and in hypophysectomized dogs. Adrenalin was injected intravenously at a constant rate for a period of 2 hours or less following a single injection of insulin intravenously. The adrenalin was diluted in sterile saline to a concentration such that one cubic centimeter per kilogram of body weight per hour would contain the desired quantity. After adrenalin was discontinued the dogs were observed for several hours for indications of hypoglycemia. Blood sugars were sometimes estimated at intervals during the experiment.

Seven dogs were used in which the dosage of insulin causing convulsions had been carefully determined. A dose of insulin was selected for each animal which consistently produced convulsions in less than 2 hours, usually within one hour. In 3 animals with both adrenals denervated and most of the medullas destroyed, this dose of insulin could be increased 2-4 times without causing convulsions during the injection of adrenalin. In one case, although the animal appeared normal when the injection of adrenalin was stopped at the end of 2 hours, convulsions occurred later. In 2 animals one adrenal had been removed and the other denervated with extensive destruction of the medulla. These animals reacted similarly to the 3 previous ones, one receiving 5 times his usual convulsive dose without showing evidence of hypoglycemia. Two animals which had been hypophysectomized several months before were quite sensitive to insulin. Injections of less than 0.5 unit per kilo regularly produced convulsions. During the administration of adrenalin these animals were able to tolerate much larger doses of insulin, although they were more likely to show convulsions when the adrenalin injection was stopped than the animals with impaired adrenal medulla.

[1] Barnes, Scott, Ferrill and Rogoff, PROC. SOC. EXP. BIOL. AND MED., 1934, **31**, 524.

A discussion of the antagonism existing between insulin and adrenalin will not be given in this preliminary report. Adrenalin dilutions were made only at the beginning of an experiment and it is not known how much deterioration occurred. However, the rate of injection at the beginning of the experiment was within the range of epinephrine secretion found by Stewart and Rogoff[2] in blood coming from the adrenal glands (0.00015-0.001 mg. per kilo per minute). More experiments are being conducted, but our results so far seem to indicate that the hypophysectomized animals require more adrenalin to prevent convulsions following insulin than animals subjected to suppression of epinephrine secretion from the adrenals. Further, it would seem probable that the hypophysectomized animal does not liberate effective amounts of adrenalin during insulin hypoglycemia.

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Studies of Renal Excretion of Creatinine. II. Volume of Distribution.

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By studying the time change of the concentration of a substance in the plasma and of its simultaneous rate of excretion in the urine, the conclusion has been reached[1, 2] that both these quantities decrease exponentially to the pre-ingestion level and furthermore, that the coefficients of the time in both exponential functions are equal, on an average, for a given substance. From these 2 facts it follows that the rate of excretion of a substance obeying such laws is proportional to the plasma concentration at any time. The above statements have been verified so far only for creatinine and xylose.

In symbols we have

$$\eta = ae^{-\alpha t} \quad (1)$$
$$\xi = be^{-\beta t} \quad (2)$$
$$\alpha = \beta \quad (3)$$
$$\eta = A\xi \quad (4)$$
$$A = (a/b) \quad (5)$$
$$\eta = y - y_e \quad (6)$$
$$\xi = x - x_e \quad (7)$$

[2] Stewart and Rogoff, *Am. J. Physiol.*, 1919, **48**, 397.

[1] Dominguez, R., and Pomerene, E., *J. Biol. Chem.*, 1934, **104**, 449.

[2] Dominguez, R., and Pomerene, E., *Proc. Am. Physiol. Soc.*, New York, March, 1934.