able media. Sulfapyridine in concentrations of 1-4000 definitely retards the growth of human tubercle bacilli. Sulfapyridine in concentrations of 1-6000 and 1-10000 affects little, or not at all, the growth of the organism.

We wish to express our appreciation to Dr. S. A. Petroff for his valuable advice.

11192 P

Insulin Hypoglycemia and Epinephrine Output from the Adrenal Glands.

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It has been shown that the severity of experimental pancreatic diabetes is not modified by reduction or suppression of the epinephrine output from the adrenal glands.[1] The insulin requirement under these conditions is not different from that of diabetic animals whose epinephrine secretion is not interfered with. Furthermore, it was found that depancreatized dogs, not subjected to interference with the adrenals, sooner or later develop reduced or suppressed secretion of epinephrine, which appears to be due primarily to the diabetic state.[2]

Our experimental investigations in progress have yielded results which indicate that epinephrine, when introduced intravenously at a constant rate in amounts corresponding to the ordinary rate of liberation from the adrenals in normal dogs, can elevate the level of blood sugar. The influence of similar amounts of epinephrine in animals previously subjected to operations for reduction or suppression of secretion from the adrenals is under investigation.

Although epinephrine secretion is not concerned primarily with the cause or progress of experimental pancreatic diabetes, it might, nevertheless, play a rôle, perhaps not indispensable, in normal carbohydrate metabolism. Cannon, McIver and Bliss[3] have suggested that epine-

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1 Rogoff, J. M., and Ferrill, H. Ward, *Arch. Int. Med.*, 1937, **60**, 805.

2 Rogoff, J. M., and Nixon, E. Nola, *Am. J. Physiol.*, 1937, **120**, 440.

3 Cannon, W. B., McIver, M. A., and Bliss, S. W., *Am. J. Physiol.*, 1924, **69**, 46.

phrine secretion from the adrenals constitutes a mechanism for mobilizing sugar in hypoglycemia. Their experimental evidence is in support of the view that as the level of blood-sugar declines to a "critical point" (between 110 and 70 mg % in cats, under chloralose anesthesia), an increased discharge of epinephrine from the adrenals is produced. They employed the Folin-Wu method for estimating blood sugar.

Since prolonged hyperglycemia can lead to reduction or suppression of epinephrine secretion, it appears probable that hypoglycemia might result in an increase in epinephrine output from the adrenals. Cannon, McIver and Bliss did not make quantitative measurements of the epinephrine output. They regarded acceleration of the so-called "denervated heart" as an indication of increased epinephrine discharge. Their conclusions rest on the observation that acceleration of the denervated heart did not occur at the critical point, following administration of insulin, if epinephrine secretion from the adrenals was interfered with.

Stewart and Rogoff[4] found no increase in epinephrine output, by direct measurement of the rate of liberation of epinephrine from the adrenals, in three cats under the influence of insulin. Blood sugar was estimated by the well-known Folin-Wu and the Shaffer-Hartmann methods, with good agreement. Since, in those experiments the blood sugar level did not decline to the aforementioned critical point, nor to a "hypoglycemic" level, we have performed similar experiments with the same method allowing a sufficient period for development of more marked insulin hypoglycemia. In addition, we have also performed experiments on animals with denervated heart. In these experiments the Shaffer-Hartmann method for blood-sugar was employed.

Quantitative determination of the rate of liberation of epinephrine from the adrenals was made on 2 cats and 2 dogs, after administration of effective doses of insulin. In one cat (nembutal anesthesia) the blood-sugar level remained high, in the other it declined to 36 mg %. In the 2 dogs it reached 40 mg and 37 mg %, respectively. Epinephrine output was determined at 0.00011 mg and 0.00022 mg per kg per minute for the cats, and 0.00018 mg and 0.0003 mg per kg per minute for the dogs. In each case the output was not different from that generally observed in normal animals, without insulin, under comparable experimental conditions.[5]

In the experiments on animals with the heart denervated by ex-

[4] Stewart, G. N., and Rogoff, J. M., *Am. J. Physiol.*, 1923, **65**, 331.

[5] Stewart, G. N., and Rogoff, J. M., *Am. J. Physiol.*, 1923, **66**, 235.

cision of the stellate ganglia and section of the vagi, some of our results were comparable with those reported by Cannon, McIver and Bliss. Others, however, demonstrated that it is possible to obtain excellent acceleration of the heart, following effective doses of insulin, in animals with one adrenal excised and the other denervated.

In one of the experiments, which in our opinion is conclusive, both adrenals were excised, the heart denervated and insulin was administered (chloralose anesthesia). The blood-sugar level declined markedly (121, 56, 14 mg %). The heart rate, before insulin, was 202 beats per minute. As the insulin hypoglycemia developed the heart rate became accelerated, reaching 238 beats per minute.

Since this acceleration occurred in the complete absence of the adrenal glands, we are convinced that the reaction can not be relied upon as an indicator for changes in the rate of epinephrine secretion. In view of these results and those obtained by direct, quantitative measurements of the epinephrine output, we are led to conclude that, regardless of its influence on the blood-sugar, insulin does not detectably alter the rate of liberation of epinephrine from the adrenals.

11193 P

Influence of Ingestion of Pancreatic Juice upon Liver Fat in Depancreatized Dog Maintained with Insulin.*

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Previous work has clearly established, first, that completely depancreatized dogs develop fatty livers despite their survival with insulin and a diet adequate in calories, proteins, salts and vitamins, and, second, that raw pancreas, when ingested, possesses not only preventive but curative action upon the deposition of the excessive amounts of lipids in the liver.[1] Moreover, it has been shown that ligation of the pancreatic ducts, a process which completely excludes the pancreatic juice from the intestinal tract and which results in

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1 Kaplan, A., and Chaikoff, I. L., *J. Biol. Chem.*, 1937, **119**, 435.