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.

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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.

destruction of the acinar elements of the pancreas, is likewise followed by the appearance of fatty livers.[2] These observations would seem to suggest that a factor (or factors) which is capable of controlling the lipid content of the liver resides in the external secretion of the pancreas. It was recognized, however, that proof for this belief is lacking and might be obtained by observing the effects of the ingestion of the *external secretion* of the pancreas upon the liver lipids of the completely depancreatized or duct-ligated dog. The present investigation was undertaken to test this view. It shows that pancreatic juice, when fed over periods of 20 weeks, is quite active in preventing the appearance of excessive deposits of fat in the liver of the completely depancreatized dog maintained with insulin.

The maintenance of depancreatized dogs in this laboratory has been described elsewhere.[1] For a variable period following pancreatectomy each dog received twice daily a diet containing 250 g of lean meat, 50 g of sucrose, 5 g of bone ash and 125 g of raw pancreas from which all visible fat had been removed. Vitamin supplements were furnished twice weekly.† When a vigorous appetite appeared, the feeding of raw pancreas was discontinued and each dog then received pancreatic juice twice daily (Table I) in addition to the meat, sucrose, bone ash and vitamin constituents listed above. The feeding of pancreatic juice was continued for a period of 20 weeks, since it has been shown[1] that this interval is necessary to insure a consistent finding of an excess of 14% fatty acids in the liver of depancreatized dogs when pancreas or other curative agents are withheld.

The pancreatic juice was collected by means of the Elman-McCaughan fistula[3] in dogs that were maintained in good condition with a diet that contained lean meat, raw pancreas, salts and vitamin sup-

TABLE I.
Liver Lipids of Depancreatized Dogs Fed Pancreatic Juice.

Dog	Weight		Period depancreatized, weeks	Pancreatic juice		Liver	
	Initial, kg	Final, kg		Period fed, weeks	Amount daily, avg cc	Wt, g	Fatty acid content, %
D 228	10.5	9.5	28	20	377	530	3.70
D 229	9.9	9.8	28	20	377	540	7.00
D 230	10.1	9.0	28	20	377	570	5.79
D 234	16.7	11.1	24	20	377	535	3.11

[2] Montgomery, M. L., Entenman, C., and Chaikoff, I. L., *J. Biol. Chem.*, 1939, **128**, 387.

† Vitamins A and D were supplied in the form of cod liver oil; the B complex as a rice bran concentrate.

[3] Elman, R., and McCaughan, J. M., *J. Exp. Med.*, 1927, **45**, 561.

plements. Fluid loss was replaced by the daily administrations of 1000 to 1500 cc of Ringer's solution.

At the end of the 20 weeks' period, during which they received pancreatic juice, the depancreatized dogs were sacrificed and the entire liver was removed for lipid analyses. The preparation of the liver for analysis has been recorded elsewhere.[2] The fatty acid content of the livers of 4 dogs is recorded in Table I. It should be noted that these livers contained between 3.1 and 7.0% fatty acid. In 2 of the animals values below 4% were found. These observations are in direct contrast with the results of the previous study, in which it was shown in 30 depancreatized dogs kept alive with insulin, that (although fatty livers may appear as early as 3.5 weeks after excision of the gland) a fatty acid content between 14.4 and 29.2% (average 24%) appeared in the liver when animals were maintained on diets containing no raw pancreas for 19.5-21 weeks.

The observations recorded here show that a factor (or factors) possessing the property of inhibiting the infiltration of excessive deposits of fat in the liver of the completely depancreatized dog maintained with insulin is present in the external secretion of the pancreas. They do not support the contention of Dragstedt, *et al.*,[4,5] that the factor is unrelated to the external secretion of the pancreas.

[4] Van Prohaska, J., Dragstedt, L. R., and Harms, H. P., *Am. J. Physiol.*, 1936, **117**, 166.

[5] Dragstedt, L. R., van Prohaska, J., and Harms, H. P., *ibid.*, 1936, **117**, 175.