

crease in the cholesterol content of the blood was observed on December 17, 1934, and for a period of 6 weeks after this date 2 gm. of choline hydrochloride were added daily to the diet. In D24 a lowered cholesterol content of the blood was established on January 27, 1935, and for a period of 6 weeks thereafter the diet of this animal was supplemented with 250 gm. of raw pancreas daily.

The results obtained are shown in Charts 1 and 2. The addition of raw pancreas to the diet of D24 produced a rise in the cholesterol esters from 2 to 97 mg. and in the total cholesterol a rise from 120 to 243 mg.% in the space of 40 days. The administration of choline to D23 produced very little change in the cholesterol level of the blood. It has been emphasized by us previously⁵ that a notable effect of the pancreatic lipid factor is its ability to raise and maintain a cholesterol level in the blood, both total and esterified, far above the normal. The addition of choline to the diet of D23, in amounts far greater than the choline contained in the lecithin content of raw pancreas fed D24, failed to raise the total and esterified cholesterol content of the blood of D23 from a lowered level to a level above the preoperative or normal.

8644 C

Pancreatic Diabetes and Hypophysectomy in the Rat.

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The laboratory mammals used for pancreatectomy are the dog and the cat. The complete extirpation of the pancreas of the rat and related rodents is considered an impossibility because of the diffuse nature of this organ and the inaccessibility of certain branches of tissue. Nonetheless it seemed a matter of some interest and usefulness to investigate the effects of as complete an extirpation as is possible.

The rat pancreas consists roughly of 3 portions: (1) the head, or duodenal division located on the right of a line following the portal vein from the junction of the splenic and superior mesenteric veins to the point at which it passes behind the first part of the duodenum; (2) the tail, or splenic, division located on the left of a line passing from the junction of the splenic and superior mesen-

teric veins along the left border of the omental border of the pancreas; and (3) the body, or mid-portion, consisting of the rest of the pancreas between these 2 lines. We find that we can remove completely the tail and body and most of the head with the exception of certain tissues located in the mesenteries of part of the duodenum and transverse colon. This can be accomplished by an electro-cautery which is used to sever the exposed parts close to the duodenum and especially for cauterizing one by one the small blood vessels passing from the spleen into the tail of the pancreas. Ordinary methods of blood vessel ligation are unusable. The animals used were about 30 days old at operation since at this age in the rat the maximum islet number is attained (Overholser¹).

This operation should result in the removal of the great majority of the pancreatic islets since Overholser¹ has shown that in a linear unit of the head the islet number is 18.3, in the body 19.0, and in the tail 34.0. In cubic units the tail alone therefore contains $3\frac{1}{2}$ times the number of any other portion.

Blood sugar measurements were made on all the animals used before the operation and on a considerable number of control, unoperated animals. Sufficient blood for a microdetermination (method of Folin²) was obtained by heart puncture. Heart punctures can, with practise, be completed in 30 seconds without exciting the animals. The normal blood sugar concentration of the rats raised upon our standard laboratory diet is 101.8 mg. % and the

TABLE I.*
The Blood Sugar Concentrations of Rats at Various Intervals After Pancreatectomy and When Followed by Hypophysectomy.

Days after Pancreatectomy	No. of Animals	Mean blood Sugar	Standard Deviation
0	73	101.81	7.083
4	10	135.92	12.303
5	21	172.26	9.981
6	14	183.56	11.952
7½	23	199.88	15.604
13	15	216.57	17.866
18½	22	213.18	11.366
25½	18	211.42	10.643
34	25	218.79	11.704
62	16	211.81	12.600
3	3	180.72	—
5	9	169.10	—
12½	7	112.79	—
24	7	98.39	—

*Days after hypophysectomy are indicated below the blank line.

¹ Overholser, M. O., *Endocr.*, 1925, **9**, 493.

² Folin, O., *N. E. J. Med.*, 1932, **206**, 727.

low coefficient of variation (7%, see Table I) of the determinations taken by heart puncture indicates the reliability of this method.

After pancreatectomy the blood sugars of the operated animals were taken at intervals over a period of 2 months. These data are summarized in Table I and presented graphically in Fig. 1A. It

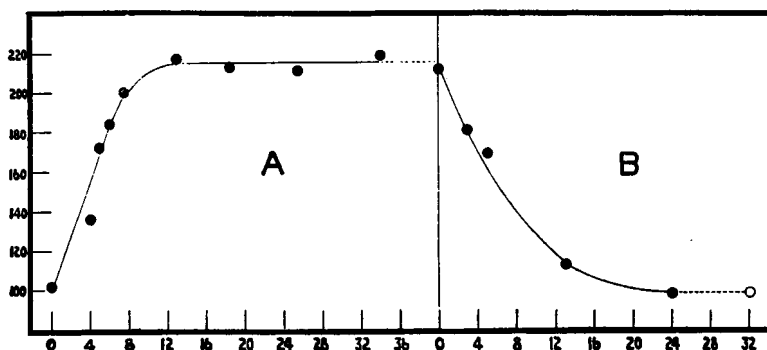


FIG. 1.

Ordinates: blood sugar in mg. %. 1A abscissa: time in days after pancreatectomy. 1B abscissa: time in days after hypophysectomy of pancreatectomized rats. The 0-day value for curve 1B is the mean blood sugar concentration at 62 days after pancreatectomy; the 32-day value is the mean of a group of 20 rats which had attained blood sugar equilibrium.

will be seen that there is a prompt rise in blood sugar concentration to a maximum of about 215 mg. % by 2 weeks after pancreatectomy, and that thereafter this level is constantly maintained. The constancy of this level is indicated by the fact that the coefficient of variation is about 5%, the extreme values, after the second week, being 190 and 233 mg. % respectively. These data imply therefore that there is no regeneration of islet tissue and that the remaining unexcised islets are sufficient to keep the blood sugar at a constant determined level. It should be noted that aside from a small mortality at operation due to occasional hemorrhage or overanæsthetization the animals recovered and remained perfectly healthy thereafter gaining weight and showing no detectable superficial symptoms. There were no deaths due to uncontrollable hyperglycemia and no indications of the attainment of lethal levels.

Hypophysectomy of the depancreatized animals results in a restoration of normal blood sugar levels (Table I and Fig. 1B). It is notable that the return to the equilibrium level (about 98 mg. %) also occurs in about 2 weeks. We find that among the animals hypophysectomized after the maximum hyperglycemic level has been attained there was a greater mortality at operation than in a group hypophysectomized at 4 to 6 days after pancreatectomy.

The equilibrium blood sugar level of the hypophysectomized-pancreatectomized animals is slightly more variable than that of normal animals. In a group of 20 depancreatized animals the blood sugars of which were taken at 24 to 42 days after hypophysectomy the mean level was 97.87 with a coefficient of variation of about 9% and extreme values of 84 and 117 mg. % respectively.

In attempting hypophysectomies to be followed by pancreatectomies we noted that a number of the hypophysectomized rats died within a few days and the rest within a few weeks. These deaths proved to be due to hypoglycemia, for in a group of hypophysectomized animals observed at 8 days after hypophysectomy and raised upon our standard diet the mean blood sugar was 73.02 mg. % whereas in a control group operated on at the same time but given additional sugar in the diet the mean value was 102.18 mg. %.

Summary: A constant hyperglycemic blood sugar level of about 215 mg. % is attained in about 2 weeks after removal of the tail, body, and most of the head portion of the pancreas of month-old rats. Hypophysectomy restores the blood sugar level to about 98 mg. % which is in the normal range (102 mg. %). Hypophysectomy without pancreatectomy results in hypoglycemia unless sugar additional to that used in the diet of normal rats is added.

8645 C

Bacteriologic Studies in Myasthenia Gravis.

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Boothby and his associates¹ have reported on their metabolic studies in cases of myasthenia gravis and on the beneficial effect of treatment with glycine and ephedrine. They have called attention to the fact that not infrequently the disease begins, or is made worse, following upper respiratory infections. We have coöperated in the study of this peculiar syndrome and have carried out bacteriologic studies in 49 cases by methods similar to those previously described.^{3, 4} A streptococcus which was very similar in

¹ Boothby, W. M., *J. Am. Med. Assn.*, 1934, **102**, 259.

³ Rosenow, E. C., *Internat. Clin.*, 1930, **2**, 29.

⁴ Rosenow, E. C., and Jensen, L. B., *J. Infect. Dis.*, 1933, **52**, 167.