the least trace of cataract. The older fish were used in Exps. 1-3. Of these, those that were fed pig spleen exclusively showed an average of 13.7% with cataract. The younger fish were used in the other experiments. Of these, those fed on spleen exclusively showed an average of 20.2% with cataract. From this it would seem that the younger the fish are when they are placed on an exclusive diet of spleen, the larger will be the percent of fish that develop cataract in a given time. No opacities appeared in the lenses of fish given the spleen-liver-heart diet (Exp. 8).

Since, as Table I shows, more fish with cataract were found in the covered troughs than in the uncovered troughs, it seems quite clear that exposure to light cannot be considered to be a cause of cataract in these fish.

Since the incidence of cataract was greater among trout obtained from wild stock (Exps. 4 and 5) than among those from hatchery stock, it appears that trout from wild stock are fully as susceptible to cataract as those from hatchery stock.

Hence, we must conclude that cataract in these fish is due to an unbalanced diet. The data above show that a dietary deficiency is responsible rather than any toxic substance since an exclusive spleen diet causes cataract while spleen in combination with other foods does not cause it.

## 9551

## Pancreatic Diabetes in the Rabbit.*

PAUL O. GREELEY. (Introduced by D. R. Drury.) (With the technical assistance of G. Jacobson and M. Kamins.)

*From the Department of Physiology, School of Medicine, University of Southern California.*

The diffuse distribution of the pancreas in the rabbit and the attending problems of surgical removal have prevented the study of pancreatic diabetes in this animal. In fact, it has been pointed out that "in rabbits the operation itself is impossible, because of the spread-out condition of the pancreas."[1] However, a method for

* We wish to express our sincere appreciation for the generous gifts of insulin from the Eli Lilly Co., and for nembutal from the Abbott Laboratories.

This work was aided by grants for technical assistance from the National Youth Administration.

[1] Macleod, J. J. R., *Carbohydrate Metabolism and Insulin*, 1926, p. 78.

complete pancreatectomy is presented here together with data pertaining to insulin requirements, glycosuria, blood sugar levels, etc.

The pancreas in general, is a thin sheet of tissue lying in the mesoduodenum with one large mass on the right between the portal vein and the vena cava and another mass in the mesentery of the spleen.

At operation it is essential to use a Beebe binocular loupe to pick up the small fragments of pancreas which break off and to prevent injury to small intestinal blood vessels. For rabbits of about 2 kilos the anesthetic used is 1 cc. of nembutal intravenously, 0.2 cc. of 1% atropine subcutaneously and sufficient ether at the beginning to allow opening of the abdomen.

Complete removal of the pancreas at one operation usually results in a very high mortality in from 24 to 60 hours from severe diarrhea, gastric detension, surgical shock, or unknown causes. A 3-stage operation with 3-4 weeks intervening between operations gives very satisfactory results. Three different abdominal incisions are used; for the first stage, about 1 inch to the left of the mid-line; for the second, a mid-line, and for the third about 1 inch to the right of the mid-line. Twenty-day chromic catgut size 00 is used for closing the abdomen.

In the first stage, all pancreas in a pocket formed roughly by the transverse colon, stomach and duodenum is removed. A splenectomy may be done by ligating and sectioning the larger vessels, or the pancreas can be gently pulled off from the splenic vessels. The mesentery and pancreatic tissue is removed from the transverse colon, the stomach raised up and the mesentery and pancreas covering the blood vessels carefully pulled free. The small pancreatic blood vessels which are broken stop bleeding in a few minutes. In this stage the gastro-duodenal mesentery is not broken through.

In the second stage all pancreas between the stomach, the inferior pancreatico-duodenal vessels and the vena cava is removed. As the duodenum is held up out of the abdominal cavity, the lateral layer of mesentery and pancreatic tissue is removed. This leaves the medial layer of mesentery to support the blood vessels. Both layers of mesentery may be removed where this support is not essential.

In the third stage, the duodenal loop is freed by cutting a small mesentery attachment which holds the distal portion to the descending colon. The loop is then spread out on a piece of gauze moistened with saline and all the remaining pancreas removed. This is readily accomplished by dissecting free and removing the upper layer of mesentery and pancreas. This prevents the blood vessels supplying the duodenal loop from being injured.

Blood sugars usually rose within a few hours following pancreatectomy.[2] (Table I.) Exceptions occurred in rabbit 9 in which the rise was delayed for 3 days and in rabbit 1 for 9 days. This delayed rise may have been due to incomplete pancreatectomy. At autopsy

TABLE I.
Time of Blood Sugar Increase Following Pancreatectomy.

| Date and Time of Pancreatectomy | Date | Blood Sugars Time | mg. % | Date and Time of Pancreatectomy | Date | Blood Sugars Time | mg. % |
|---|---|---|---|---|---|---|---|
| No. 1 | 1-11 | 2:00 P.M. | 160 | No. 7 | 4-23 | 12:15 P.M. | 154 |
| 1-11-37 | 1-12 | 5:00 " | 117 | 4-23-37 | 4-24 | 9:30 A.M. | 236 |
| 11:30 A.M. | 1-13 | 9:30 A.M. | 90 | 12:10 P.M. | 4-26 | 10:00 " | 260 |
| | 1-15 | 9:00 " | 110 | | 4-27 | 10:00 " | 300 |
| | | 3:40 P.M. | 100 | | | | |
| | 1-18 | 9:00 A.M. | 138 | No. 8 | 4-23 | 4:00 P.M. | 154 |
| | 1-19 | 10:00 " | 129 | 4-23-37 | 4-24 | 9:30 A.M. | 320 |
| | 1-20 | 9:25 " | 210 | 3:50 P.M. | | | |
| | 1-21 | 9:30 " | 156 | | | | |
| | 1-22 | 10:00 " | 266 | No. 9 | 7-28 | 11:00 A.M. | 160 |
| | | 5:50 P.M. | 338 | 7-28-37 | | 4:30 P.M. | 110 |
| | | | | 10:30 A.M. | | 9:00 " | 90 |
| No. 2 | 1-29 | 6:00 " | 133 | | 7-29 | 10:30 A.M. | 105 |
| 1-29-37 | | 11:00 " | 185 | | | 2:40 P.M. | 120 |
| 5:45 P.M. | 1-30 | 9:00 A.M. | 190 | | 7-30 | 9:30 A.M. | 133 |
| | | 1:50 P.M. | 312 | | | 4:40 P.M. | 222 |
| | | | | | 7-31 | 12:30 " | 280 |
| No. 3 | 2-12 | 9:40 " | 245 | | 8- 1 | 10:10 A.M. | 300 |
| 2-12-37 | 2-13 | 9:00 A.M. | 138 | | 8- 4 | 9:00 " | 440 |
| 3:00 P.M. | | 7:15 P.M. | 384 | | | | |
| | | | | No. 10 | 8-24 | 3:30 P.M. | 137 |
| No. 4 | 3-10 | 9:00 A.M. | 80 | 8-24-37 | 8-25 | 9:30 A.M. | 200 |
| 3-9-37 | | 5:00 P.M. | 133 | 11:30 A.M. | 8-26 | 3:30 P.M. | 400 |
| 4:00 P.M. | | 10:00 " | 250 | | | | |
| | 3-11 | 9:00 A.M. | 308 | No. 11 | 8-27 | 11:35 A.M. | 172 |
| | | 1:30 P.M. | 396 | 8-27-37 | | 2:00 P.M. | 182 |
| | | 4:30 " | 440 | 11:30 A.M. | | 4:00 " | 200 |
| | | | | | 8-28 | 9:00 A.M. | 200 |
| No. 5 | 4-15 | 9:00 A.M. | 141 | | 8-29 | 9:30 " | 334 |
| 4-14-37 | 4-16 | 9:30 " | 280 | | 8-30 | 10:30 " | 400 |
| | | 9:00 " | 360 | | 9- 1 | 9:00 " | 572 |
| No. 6 | 4-22 | 12:05 P.M. | 141 | No. 12 | 8-30 | 3:40 P.M. | 200 |
| 4-22-37 | | 5:00 " | 172 | 8-30-37 | 8-31 | 10:00 " | 308 |
| 11:30 A.M. | 4-23 | 9:30 A.M. | 262 | 3:30 P.M. | 9- 1 | 9:00 A.M. | 400 |
| | 4-24 | 9:30 " | 286 | | | | |

on No. 1, 40 days after pancreatectomy, a piece of abnormal pancreatic tissue was found on the dorsal side of the portal vein. It measured approximately 16 mm. long, 7 mm. wide, and 2 mm. thick, and consisted of a wild proliferation of ducts imbedded in fibrous tissue with an occasional group of cells identified as islets. This rabbit, however, put out as high as 50 gm. of sugar daily.

[2] Shapiro, R., and Pincus, G., PROC. SOC. EXP. BIOL. AND MED., 1936, **34**, 416.

Four of the rabbits presented in Table I lived for extended periods —rabbit 1, 40 days; rabbit 4, 4 months; rabbits 9 and 10 survived for 82 days and 38 days respectively. The other rabbits died in about 3 days from a severe diarrhea or peritonitis.

Blood sugars in the depancreatized fed rabbits without insulin injections remained around 400-500 mg. % as determined by the micro-method of Folin-Wu. The highest amount of sugar excreted in 24 hours occurred in rabbit 4, which put out 54.35 gm. in 1000 cc. of urine. Rabbits 4 and 10 excreted about 5 gm. of sugar daily or were negative with the subcutaneous injection of 6 units of protamine zinc insulin each morning. Rabbit 9 excreted about 1 gm. of sugar daily with 4 units of protamine zinc insulin. The food intake determined the amount of insulin it was possible to give. For example, at one time rabbit 4 received 12 units of protamine zinc insulin daily and still excreted 5 gm. of sugar daily. Good gains in weight were made in each case during the insulin administration.

No acetonuria has been demonstrated by the qualitative test during prolonged periods without insulin.

Pancreatectomy in the rabbit should be as complete as that which is possible in the dog, if each stage of the removal is carefully done. Microscopic examinations of suspected tissue have always been made at autopsy and no pancreas was found except that noted above in rabbit 1. However, rabbits surviving the operation were able to live for long periods without insulin. Rabbit 1 received no insulin for 31 days and maintained a constant weight. A constant weight was also maintained by rabbit 4 for 16 days without insulin. Rabbit 9, however, was kept 34 days without insulin and lost 490 gm. in weight, excreting daily an average of 24 gm. of sugar in the urine. The continued loss of weight despite a high food intake, the high blood sugar level and the enormous sugar excretion indicate a very definite diabetes. The successful production of pancreatic diabetes in the rabbit opens a new field in the study of carbohydrate metabolism since hypophysectomy, hepatectomy, etc., are readily carried out in this excellent laboratory animal.