

TOTAL PANCREATECTOMY FOR HYPERINSULINISM DUE TO AN ISLET-CELL ADENOMA

SURVIVAL AND CURE AT SIXTEEN MONTHS AFTER OPERATION

PRESENTATION OF METABOLIC STUDIES

JAMES T. PRIESTLEY, M.D.,*

DIVISION OF SURGERY,

MANDRED W. COMFORT, M.D.,

DIVISION OF MEDICINE,

AND

JAMES RADCLIFFE, JR., M.D.,

FIRST ASSISTANT, DIVISION OF MEDICINE, MAYO CLINIC,

ROCHESTER, MINN.

WE WISH TO REPORT A CASE in which complete pancreatectomy was performed for hyperinsulinism due to a small islet-cell adenoma located in the head of the pancreas near the duodenum. The case has several interesting features justifying its report. It is probably the second or third total pancreatectomy, and the first reported case known to us of complete pancreatectomy with survival following operation for more than a few weeks. It is the first total pancreatectomy for a benign lesion of the pancreas. The adenoma discovered in the removed pancreas is one of the smallest functioning islet-cell tumors reported, if not the smallest. Most important is the fact that the patient is living and well at the time that this paper is written, 16 months after the operation. Observations on the resulting diabetes and digestive disturbances are recorded.

CASE REPORT

The patient, a Jewish woman, age 49, registered at the Mayo Clinic July 6, 1942. She complained of fainting spells which had occurred intermittently during the previous three years. There were several different types of attacks, consisting of unconsciousness, dizziness, blank spells and sweating spells, all of which had been relieved by the administration of carbohydrate varying from orange juice to intravenously injected glucose. During one of the patient's unconscious spells, her physician had obtained a concentration of sugar that was less than 30 mg. per 100 cc. of blood. There had been five severe attacks of unconsciousness lasting from one to five hours. The minor attacks were more frequent than those of more severe character, and varied from dizzy or blank spells to attacks of sweating. These lasted from five minutes to one hour. During the blank spells the patient would feel rather foolish and be somewhat confused. Sweating spells would occur almost every day between 10 A.M. and 12 M. They were characterized by drenching perspiration, weakness and slight confusion followed by nausea.

* Since this article was written, Doctor Priestley has been commissioned Lieut. Colonel in the Army of the United States.

They were relieved by orange juice or candy. The patient complained of feeling nervous and depressed, experiencing panicky sensations and feeling disoriented.

General physical examination showed the patient's weight to be 142 pounds (64.4 Kg.). The systolic blood pressure was 140 Mm. of mercury and the diastolic was 80. The results of examination of the heart, lungs and abdomen were essentially negative. Urinalysis, blood counts and serologic tests for syphilis gave negative or normal results. Roentgenograms of the head, thorax and lumbar portion of the spinal column were negative. The hepatic function, as shown by the bromsulfalein test, was normal. An electrocardiogram showed: Rate 93, sinus tachycardia, slurred Q.R.S. complexes in derivations I and III, notched Q.R.S. complexes in derivation II, left axis deviation, notched P waves in derivations II and III, low amplitude T waves in derivation III. Leads IV-R and CR-2 showed positive T waves. The fasting concentration of sugar was 42 mg. per 100 cc. of blood; the concentration of calcium was 9.4 mg. per 100 cc. of serum. A routine 36-hour fast was started, but at 12 hours the concentration of sugar was 52 mg. per 100 cc. of blood, and at 18 hours the patient had a severe hypoglycemic crisis starting with drowsiness and sweating, and merging into stupor and unresponsiveness, and then into complete loss of consciousness, lasting between one and one and a half hours. Her concentration of sugar taken after the onset of this crisis was 29 mg. per 100 cc. of blood. Recovery was slow after intravenous administration of 20 Gm. of glucose, followed by oral administration of 200 cc. of orange juice. Anorexia with severe headache and fatigue followed the crisis but complete recovery was reached in 30 minutes. The concentration of sugar rose to 108 mg. per 100 cc. of blood after the glucose and orange juice had been administered.

A diagnosis of hypoglycemia, probably caused by hyperinsulinism, was made. It was our opinion that a tumor of the islets of Langerhans was present.

Operation.—July 15, 1942: When the abdomen was opened, all of the visible structures, including the liver, appeared normal. There was no evidence of a malignant lesion. The pancreas was exposed by dividing the gastrocolic omentum along the greater curvature of the stomach and reflecting the stomach anteriorly and upward. Prolonged and careful palpation of the pancreas from the tail to the head did not reveal any evidence of tumor. The posterior aspect of the head of the pancreas was exposed by reflecting the duodenum medially but no lesion could be found in this portion of the pancreas. It was felt that there must be an adenoma present which was of the same consistency as the remainder of the pancreas and not situated on the surface of the gland, and that for this reason it could not be detected. At this time the situation was reviewed in consultation with Doctor Wilder, of the Metabolic Service, who was present at the operation, with the hope of determining the best procedure for the patient. It was known that she was incapacitated by her symptoms and it appeared quite certain that these symptoms were caused by hyperinsulinism. If only a portion of the pancreas were removed, it was known from experience that she would not be relieved unless an offending adenoma were present in the resected portion. Accordingly, it was decided to remove the entire pancreas.

The duct of Santorini was isolated approximately 1 cm. proximal to the duodenum and was ligated. The duct of Wirsung entered the common duct about 0.5 cm. proximal to the papilla of Vater, and this duct was ligated. The common duct was severed and ligated proximal to its entrance into the pancreas. The gastroduodenal artery, likewise, was severed and ligated. The head of the pancreas then was dissected free from the duodenum and mobilization of the gland toward the left was continued. Care was observed in order to avoid injury of the superior mesenteric vessels immediately posterior to the pancreas near the head of the gland, and the splenic vessels coursing along the superior border of the body and tail of the pancreas were preserved also. The pancreas then was removed in its entirety. The blood supply of the duodenum was then, of course, inadequate, and, accordingly, partial gastrectomy was performed, approximately

a third of the stomach and the first and second portions of the duodenum being removed and an anterior Pólya-type of anastomosis being made. The duodenal stump at about the level of the superior mesenteric vessels was inverted. The gallbladder then was joined to the posterior wall of the stomach to establish adequate internal biliary drainage by cholecystogastrostomy. The patient was given a transfusion of 1,500 cc. of blood during the operation.

Pathologic Report: The pancreas weighed 80 Gm. Following prolonged search and many transverse incisions into the pancreas, a cellular adenoma of the islands of Langerhans, measuring 8 x 5 x 5 Mm., was found situated in the head of the pancreas. The portions of the stomach and duodenum removed during the course of the operation were normal in appearance.

Postoperative Course.—The postoperative course was uneventful. The patient's weight on admission was 142 pounds (64.4 Kg.). On August 9, the first time after operation that she was weighed, her weight was 132 pounds (59.9 Kg.). This gradually fell and reach 128.5 pounds (58.3 Kg.) at the time of dismissal. The stools varied from two to six a day, usually about two to three after the patient began to take food. They were rather large, light colored and foul in odor at first, with some improvement by the time of dismissal. On August 4, the concentration of hemoglobin was 10.6 Gm. per 100 cc. of blood; erythrocytes 3,370,000, and leukocytes 5,600 in each cubic millimeter of blood. On August 19, the concentration of cholesterol was 216 mg. per 100 cc. of plasma, of cholesterol esters 121, of lecithin 301, of fatty acids 397, and of total lipoids 613. The concentration of calcium was 9.2 mg. per 100 cc. of serum. On August 1, after an Ewald test meal, the total acidity was 60 and the free hydrochloric acid 40; 150 cc. was recovered in an hour and this contained a moderate amount of fine food remnants.

COMMENT.—Reports of total pancreatectomy for benign or malignant disease of the pancreas are exceedingly rare in the literature. In 1908, Sauve¹ presented an extensive study on the subject of pancreatectomy involving the head of the gland. He collected data on 11 cases in which the operation was known to have been performed up to that time. He mentioned a case credited by Mayo-Robson at the Congrès de Paris, in 1900, to Billroth, in 1894, in which entire removal of the pancreas had been performed because of its involvement in a growth and the patient survived. Sauve was unable to find any published account of this case and he felt that there was insufficient evidence of the details to warrant its inclusion in his series. The only case listed in Sauve's series approaching total pancreatectomy was Franke's, in 1900. Here the surgeon attempted total removal because of the apparent involvement of the entire gland by a malignant lesion. He made the following statement: "Under the head of the pancreas, I found a little mass as large as a hazel nut, situated against the duodenum; I thought it was a question of a supernumerary pancreas, and I preserved it." The patient in this case had a good convalescence and showed only mild glycosuria between the fifth and nineteenth postoperative days and no further glycosuria till her death from recurrence of the carcinoma five and a half months later.

The fact that the patient enjoyed "perfect health" without evidence of diabetes until the recurrence of the carcinoma would seem to indicate from numerous reports on partial pancreatectomy on human patients that at least 10 per cent of the gland must have remained, regardless of whether or not

the small mass of tissue represented a supernumerary gland or an unresected portion of the head.

Recently, Rockey² reported a case in which he performed total pancreatectomy for carcinoma of the pancreas, with widespread involvement of the gland. His patient survived for 15 days. Necropsy revealed less than 1 Gm. of pancreatic tissue unresected.

Unless we have overlooked any cases, ours is the second authenticated case of total pancreatectomy for any cause ever reported, and the only case in which there was survival beyond the immediate postoperative period.

In March, 1942, Duff³ presented an extensive *Arbeit* on the "Pathology of Islet-cell Tumors of the Pancreas." From his review of the literature he was able to make the following statement: "The hypoglycemia syndrome has not been observed in association with islet-cell adenomata of a diameter less than 1 cm." The measurements of the adenoma in our case were 8 x 5 x 5 Mm. Smaller adenomas have been reported but they have been found incidentally at necropsy and were not associated with clinical hypoglycemia.

Total pancreatectomy in this case appeared to be justified by the following consideration: Careful examination of the gland at operation did not disclose an adenoma. It was then obvious that the hyperinsulinism was due either to an undiscovered adenoma or to hyperfunctioning of islet cells. Partial pancreatectomy would cure the patient if the resected portion contained an adenoma and might cure the patient if hyperfunctioning islets were the cause of the patient's symptoms, as in the case reported by Graham and Hartman.⁴ However, it has been our experience that partial pancreatectomy in cases in which islet-cell adenomas were not found has been disappointing and has required in some cases repeated resections without favorable results.

Total pancreatectomy, on the other hand, should remove the cause of hyperinsulinism, whether it is due to an adenoma or to hyperfunctioning islet cells, and should not be followed by important disturbance of digestion and nutrition resulting from loss of external pancreatic secretion, as has been shown by the work of Whipple and Bauman⁵ in removing the head of the gland for carcinoma. The decision to remove the entire pancreas and to substitute for the incapacitating illness of hypoglycemia diabetes and external pancreatic insufficiency, which we felt could be controlled fairly well medically, has been a happy one—an adenoma which would have been left behind if partial pancreatectomy had been performed was removed and the patient was cured of hyperinsulinism.

THE EFFECTS OF TOTAL LOSS OF INTERNAL SECRETION OF THE PANCREAS

The metabolic problem resulting from complete pancreatectomy resolves itself into two main considerations: First, a deficiency of the internal secretions of the gland; and, second, a deficiency of the external pancreatic secretions. It has been shown, both experimentally in animals and in cases of partial pancreatectomy performed upon human patients, that more than 80 to 90 per cent of the gland must be resected before diabetes mellitus is

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produced. In 1934, Graham and Hartman reported a case in which they resected 80 to 90 per cent of the gland for hyperinsulinism. The patient was one year old. No adenoma could be found in the resected portion of the pancreas. Complete recovery was attained, and the fasting concentration of sugar nine months after operation was 83 mg. per 100 cc. of blood. Other cases, in which the patients were adults, are reported in the literature in which as much as three-fourths of the gland has been resected and there appears to have been sufficient internal secretory function retained to prevent the occurrence of diabetes.⁵ It was anticipated, of course, in our case that complete pancreatectomy would produce diabetes mellitus but we felt that this could be controlled adequately by diet and insulin. The mild degree of the resulting diabetes was not anticipated.

Our findings in regard to the degree of internal pancreatic insufficiency

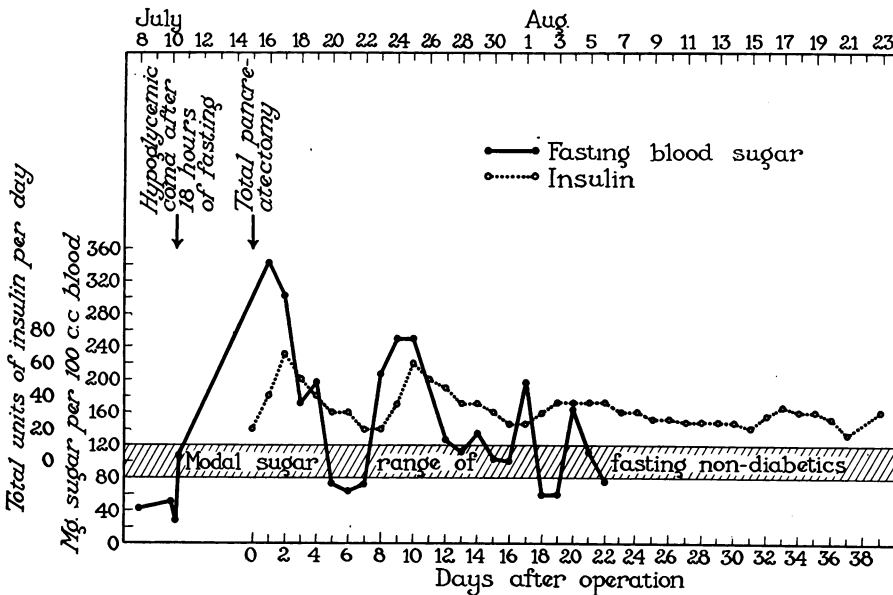


CHART I.—Fasting concentrations of blood sugar and insulin requirements before and after total pancreatectomy.

are in close accord with those of Rockey in his recent report of total pancreatectomy for carcinoma. During the 15 days of postoperative survival of his patient's insulin requirement leveled off at a range of less than 27 units per day.

An interesting point was made in a recent article by Dragstedt⁶ that it is necessary to remove 90 to 95 per cent of the pancreas of a dog to produce diabetes. The resulting diabetes, however, is very severe and, paradoxically, is more severe than if the total gland were removed. There are no published data known to us on man to make a similar comparison. However, in one case (unpublished) at the Mayo Clinic partial pancreatectomy was performed repeatedly for persistent hypoglycemia, and after the final

operation, which left only a small rim of pancreas adjacent to the duodenum, diabetes resulted which required between 60 and 100 units of insulin daily to control nearly one and a half years after operation. When this high insulin requirement is compared with the relatively small amount required to maintain control in Rockey's and in our case, after total pancreatectomy, the same paradox is noted as occurs in dogs.

As shown in Chart I, the fasting daily blood sugar reached a maximal height of 341 mg. per 100 cc. of blood on the morning after operation. The greatest total units of insulin required in any one day were 66. Regular, unmodified insulin was used for about four days after operation to "cover" the intravenous injections of 5 per cent solution of glucose in saline or distilled water. From about the fifth postoperative day the diabetes was controlled by single daily subcutaneous injections of protamine zinc insulin and regular insulin in a single combined dose, administered 20 minutes before breakfast. As will be noted in Chart I, the total daily dose that was required averaged around 30 units a day. The ratio of the two types of insulin varied from one unit of protamine zinc insulin to one to two units of regular insulin. The daily determinations of blood sugar were discontinued on the twenty-second postoperative day and the diabetes was controlled from this point on by testing the urine. Specimens of urine were obtained at 6 and 11 A.M. and at 4 and 9 P.M. The specimens of urine tested were fresh specimens, that is to say, the bladder was emptied by voiding a half hour before each specimen was obtained for testing. By the time of dismissal from the hospital the patient had been taught a system of adjusting her own combined dose of insulin so that the specimens of urine taken before breakfast and before supper showed a trace of sugar. Thus, the occurrence of insulin reactions was avoided but the diabetes was kept in adequate control.

At the time that the patient was dismissed the results of analysis of stools and urine were not available; therefore, the patient was sent home on the diet of 1,965 calories, basal plus 50 per cent, composed of 243 Gm. of carbohydrate, 94 Gm. of protein, and 70 Gm. of fat. No pancreatin was given. Adequate vitamin supplements were added. A letter received from her physician December 14, 1942, four months after her dismissal, stated that the patient was using "anywhere from 10 units of protamine zinc insulin and 10 units of regular insulin to 15 units of each every morning. She controls her dosage very well by checking her own urine. The urine is usually sugar-free. One month ago her fasting blood sugar was 109 mg. per 100 cc. Two days ago her fasting blood sugar was 177 mg. per 100 cc., this being after some holiday dietary indiscretion." Another letter stated that the patient "is doing very well. Her fasting blood sugar, taken two weeks ago, was 134 mg. per 100 cc. She uses just about the same amount of insulin. Her only complaint is severe abdominal cramps each morning." On July 16, 1943, her husband wrote that he was happy to say that "she is doing fine, has gained about three pounds (1.4 Kg.), eats practically everything, and is in fine spirits. She is really enjoying life. She also does

not weigh her food. She still has cramps for two to three hours every morning, but they are not as severe as at first." The latest report we received was in November, 1943. The dose of insulin still varied between 20 to 30 units per day.

As it has been established experimentally that fatty metamorphosis of the liver and hypolipemia usually develop, ultimately, in dogs adequately maintained with insulin unless they are given adequate amounts of raw pancreas, lecithin, choline or the extract of the pancreas or lipocaic,⁶ a diet rich in choline was given to our patient to prevent the development of a fatty liver and hypolipemia. Fifty grams of cottage cheese was a daily constituent of the diet and this, together with a high protein content, was considered adequate to prevent such changes. The excellent health of the patient 16 months after total pancreatectomy is indirect evidence that such developments have not taken place. It has not been possible to obtain studies of function of the liver since dismissal.

EFFECT OF TOTAL LOSS OF EXTERNAL PANCREATIC SECRETION ON DIGESTION AND ABSORPTION

On the twelfth postoperative day the patient was taking a rather liberal solid diet, and the diabetes was under control. At this time, studies were begun to determine the degree of utilization of carbohydrate, protein and fat, and were carried out during two ten-day periods and one five-day period. It is possible that data obtained at a longer interval after operation would reflect the ultimate effect of total pancreatectomy better than those obtained so soon after operation. It is felt, however, that the data obtained are sufficiently interesting to warrant recording them.

The patient's basal caloric utilization was 1,310 calories, as computed by the Boothby nomogram. The three periods were kept essentially isocaloric at basal plus 50 per cent. This equaled approximately 2,000 calories a day. The cooked food was weighed and the content of carbohydrate, protein and fat was estimated according to Sherman's tables. In the first ten-day period the estimated daily intake of carbohydrate, protein and fat was, respectively, 241, 94.5 and 69 Gm.; in the second ten-day period the estimated daily intake of carbohydrate, protein and fat was, respectively, 206, 67.7 and 102.5 Gm. In the third five-day period the estimated daily intake of carbohydrate, protein and fat was, respectively, 222, 70 and 95 Gm. In the second and third periods the intake of protein was decreased approximately 25 per cent below the intake in the first period, while the intake of fat was increased 25 to 30 Gm. over it. The intake of carbohydrate, protein and fat was essentially the same in the third as in the second period. During the third period the patient was given 4.5 ounces (140 Gm.) of powdered pancreatin (Parke-Davis) in gelatin capsules (0.9 ounce [28 Gm.] a day). Data obtained during the third period, which was terminated at the end of five days because of the patient's objection to pancreatin, are not as statistically significant because of shorter duration of the period as those obtained in the

TABLE I
AVERAGE DAILY VALUES FOR FECAL SOLIDS AND CALORIES INGESTED AND LOST

Period	Calories										Fecal Solids						
	Intake					Loss					% Lost		% Total as Fat and Protein				
	Carbohydrate	Protein	Fat	Total	Fecal Nitrogen	Fecal Urinary Sugar	Total Balance	Require-ments	and Urine	Total, Fat, Gm.	Fecal N. Total as Protein, Gm.	% Total as Fat	% Protein				
I—10 days.....	962	378	621	1,961	433.71	207.00	32.64	673.35	1,287.7	1,310	34	131.97	48.19	37	51.75	39	76
II—10 days.....	825	271	923	2,019	326.52	101.64	10.88	439.04	1,580	1,310	22	83.94	36.28	43	25.41	30	73
III—5 days.....	889	280	855	2,024	358.20	73.00	3.36	434.56	1,589	1,310	21	73.4	39.8	54	18.25	25	79

TABLE II
AVERAGE DAILY VALUES FOR INTAKE AND LOSS OF NITROGEN AND FAT

Period	Nitrogen										Fat								
	Intake, Gm.					% Intake Loss in					% Fecal Fat as		% Intake Loss as						
	Urine	Feces	Total	Pancre-atin	Total	Balance, Gm.	Urine	Feces	Neutral	Split	Total	Intake, Balance, Gm.	Fatty Acid	Neutral	Fatty Acid	Total			
I—10 days...	5.27	8.28	13.55	15.12	0	15.12	+1.57	35	55	33.09	15.10	48.19	69	20.81	69	31	48	22	70
II—10 days...	5.88	4.07	9.95	10.83	0	10.83	+0.88	54	38	19.40	16.88	36.28	102.5	66.22	54	46	19	16	35
III—5 days...	5.50	2.92	8.42	11.20	0.66	11.86	+3.44	46	25	22.40	17.40	39.80	95	55.20	56	44	24	18	42

first and second periods. A daily weight was obtained during the last 13 days of the study. This fluctuated within a range of three pounds (1.4 Kg.). The daily average number of stools varied but little from period to period, being 2.4 on the low fat and 2.8 on the high fat diet with pancreatin.

Methods.—The periods were begun and terminated by the use of carmine dye marker technic and feces and urine were collected for five-day periods. The stools were analyzed for total and neutral fat, nitrogen and carbohydrate, the urine for nitrogen and sugar. The total fat was estimated by the method of Saxon,⁷ neutral fat by the method of Saxon, nitrogen was estimated by the method of Kjeldahl, and carbohydrate by the method of Folin and Wu. The results are given in Tables I and II.

Fecal Solids.—The average daily values for fecal solids are shown in Table I. The average daily weight of dried feces was greatest during Period I, when the loss of fat and nitrogen was greatest. The dried weight of the feces was greater than that of normal subjects on the standard Schmidt test diet, as reported by Pratt.⁸ He found that the average daily weight of the dried feces of a series of six normal persons over a period of three days was 54 Gm. and that the maximum was 62 Gm. The average daily values obtained in Period I were comparable to those obtained by Pratt (113 to 154 Gm. a day for a three-day period) in five cases of carcinoma of the pancreas with obstruction to the pancreatic ducts, while the values in Periods II and III were increased only moderately above those in healthy persons.

The fat composed 37 to 54 per cent of the fecal solids (range in normal persons 8.5 to 28.5 per cent; average 18.5 per cent); 54 to 69 per cent of the fecal fat was neutral fat. The daily loss of nitrogen in the stools varied from 2.92 to 8.28 Gm. Computing the fecal nitrogen in terms of protein, average daily fecal protein accounted for from 25 to 39 per cent of the fecal solids. Fat and protein accounted for 73 to 79 per cent of the fecal solids.

Reducing Substances in the Feces and Urine.—Reducing substances in the feces were not measurable in Periods I, II or III. The average daily values for reducing substances in the urine are shown in Table I in terms of calories. These average daily values varied from 0.84 Gm. (3.36 calories) to 8.16 Gm. (32.64 calories).

Nitrogen Balance.—The nitrogen intake and loss are shown in Table II. The greatest nitrogen loss was observed during the period of greatest nitrogen intake (Period I). The nitrogen loss was less during Period III than during Period II, although the intake of both protein and fat was essentially the same during the two periods. Pancreatin was given during Period III and the smaller daily loss of nitrogen during this period appears to have been due to the pancreatin, in spite of the administration of pancreatin in gelatin, not enteric coated, capsules. The effect of this amount of pancreatin in gelatin capsules on the digestion of protein in this case accords with that of one of us (unpublished data of Comfort), and of Beazell, Schmidt and Ivy,⁹ and Rekers, Pack and Rhoads,¹⁰ on the effects of large amounts of

pancreatin given in enteric coated capsules in cases of external pancreatic insufficiency. The daily loss of nitrogen in the urine did not vary greatly in the three periods. The nitrogen balance was positive in Periods I and II despite a small loss of weight, but was more positive in Period I, in which the intake of nitrogen was greater than in Period II. The nitrogen balance was greater in Period III than in Period I, in spite of the greater intake of nitrogen in Period I. This may be due to the smaller daily loss of nitrogen in the stool and greater daily digestion and absorption presumably due to pancreatin.

Fat Values.—The average daily intakes of fat and the total fat in the stool during the three periods are shown in Table II. The proportions of ingested fat that was lost in the stool were, respectively, 70, 35 and 42 per cent in Periods I, II and III. The average daily value for total fat lost was greater on the low fat (69 Gm.) diet than on the high fat (102.5 Gm.) diet. The average daily value for total fecal fat was approximately the same in Period III, when the patient ingested a daily average of 95 Gm. of fat plus powdered pancreatin in gelatin capsules, as in Period II. In short, pancreatin administered in this fashion did not affect the absorption and digestion of fat significantly, contrary to the unpublished data of one of us (Comfort) and published data of Beazell, Schmidt and Ivy and of Rekers, Pack and Rhoads, on the effect of large amounts of pancreatin in enteric coated capsules in cases of external pancreatic insufficiency. The variations of the amount of neutral fat lost in the feces paralleled those of total fat. The percentage of total fat as neutral fat was greatest in Period I (low fat period) while the percentages of total fat as neutral fat were approximately equal in Periods II and III with an equal fat intake, in spite of the administration of pancreatin in Period III. Pancreatin, as given, did not affect the digestion of fat significantly in this case.

The Effect of Loss of Food in the Urine and Feces on Caloric Balance.—The caloric values of the ingested food and of the foods recovered in the urine and feces are given in Table I. The average daily caloric values of the foods ingested varied but little in the three diets. The loss of food in the urine was small; that in the feces was heavy. Metabolic fecal fat and nitrogen have been ignored in computing the balance. The average daily loss of calories was 673, 439 and 435, respectively, during Periods I, II and III, and 34, 22 and 21 per cent of the caloric intake was lost during these same periods. The calories utilized were approximately equal in number to those for basal requirements during Period I and were only slightly in excess of basal requirements in the other two periods. The caloric loss was found to be great enough to affect the estimated necessary caloric intake radically.

SUMMARY AND CONCLUSIONS

A case of hypoglycemia due to hyperinsulinism from a small adenoma of the islets of Langerhans in which a total one-stage pancreatectomy was performed is reported herewith. A less radical procedure would have failed to

cure the patient, since the adenoma was located in the head of the gland, in intimate proximity to the duodenum. We believe that this is the first case of total pancreatectomy for benign or malignant disease in which the patient has survived beyond the immediate postoperative period. Total pancreatectomy was followed by a relatively mild degree of diabetes. Disturbance of carbohydrate digestion was not detected by the methods used, while digestion of protein and fat was definitely diminished. About 35 to 70 per cent of ingested fat and 25 to 55 per cent of ingested nitrogen could be accounted for in the feces. A positive nitrogen balance occurred in spite of the large loss of nitrogen in the feces. Foodstuffs in the urine and feces accounted for 21 to 34 per cent of the calories ingested. The percentage of total fat in the stools as neutral fat varied from 54 to 69 per cent. The dried weight of the stools was greater than values obtained for healthy persons. The patient has remained in excellent health, 16 months after the operation. Evidence of deficiency of lipocaic has not developed.

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