

ANNALS OF SURGERY

VOL. 124

DECEMBER, 1946

No. 6



RADICAL SURGERY FOR CERTAIN CASES OF PANCREATIC FIBROSIS ASSOCIATED WITH CALCAREOUS DEPOSITS*

ALLEN O. WHIPPLE, M.D.
NEW YORK, N. Y.

FROM THE DEPARTMENT OF SURGERY, COLUMBIA-PRESBYTERIAN MEDICAL CENTER, NEW YORK, N. Y.

PRESENT-DAY ADJUVANTS to the surgeons' armamentarium in the pre-operative, operative, and postoperative periods have made radical operations feasible which ten years ago were considered impossible. In certain fields, such as in primary cancer surgery, these extensive procedures are justified where the wide removal of possible cancer-bearing tissue insures a more certain arrest of the tumor. Or, where with a hazardous operation, technically difficult, a readjustment of the circulation by vascular anastomosis corrects a hopelessly deranged physiology.

The pancreas is one of the organs which in recent years has been dealt with radically in an attempt to cure otherwise hopeless disease and in the past three years total pancreatectomy has been successfully accomplished with surprising results in some instances. Priestley¹ was the first surgeon to achieve this success in a patient with severe hypoglycemia after a thorough exploration of the organ had failed to reveal an islet cell tumor. This patient is cured of her hypoglycemia 36 months after operation, and does not require as much insulin as many a diabetic. To date, 14 total pancreatectomies have been performed, and are recorded in Table I.

The first successful total pancreatectomy for chronic pancreatitis associated with extensive calcareous deposits was performed by Claggett² in November, 1944. This patient was relieved of her unbearable pain. Ten weeks later, while in her home, she developed a severe hypoglycemic reaction which was not recognized, resulting in death. Her diabetes was controlled by a daily dose of eight units of protamin-zinc insulin and 30 units of regular insulin taken in one injection in the morning.

We wish to record two of these total pancreatectomies and three other radical procedures with removal of a large part of the organ for intolerable pain associated with pancreatic fibrosis and calcareous deposits and pancreatic calculi (Table II).

* Read before the American Surgical Association, April 2-4, 1946, Hot Springs, Virginia.

We do not intend to review the subject of pancreatic lithiasis in this paper. The subject has been recently summarized in papers by King and Waghelstein³ in 1942 and by Lionello, Ficcaro and Ryan⁴ in 1944. But we wish to emphasize certain points in the indications for radical resection of the pancreas for this condition.

Extensive calcification of the parenchyma of the organ is rare as compared to the finding of numerous calculi in the ducts. Fibrosis of a part of the organ is frequently associated with either calcification or calculi. Cystic degeneration or dilatation of the obstructed ducts is usually present. Disturbed carbohydrate metabolism in the form of mild diabetes is found in about a third of the cases. The same is true of abnormal fat digestion and

TABLE I

CASES OF TOTAL PANCREATECTOMY PREVIOUSLY REPORTED AND INCLUDING TWO CASES BY THE AUTHOR

Author	Age	Sex	Diagnosis	Survival After Operation	Approximate Insulin Daily Dosage
1. Rockey ⁵ , 1943	51	M	Carcinoma pancreas	15 days—died	27 units
2. Goldner and Clark ⁶ , 1944			Carcinoma pancreas	11 days—died	20 units
Case of Brunschwig					
3. Goldner and Clark ⁶ , 1944	45	M	Carcinoma bile duct	10 days—died	40 units
Case of Clark					
4. McClure ⁷ , 1944 (Case of Fallis)	46	M	Carcinoma pancreas	Alive 9 mos. after operation	26-34 units
5. Brunschwig, <i>et al.</i> ⁸ , 1945	53	M	Carcinoma pancreas	Died 3.5 months after operation	40 units
6. Priestley, ¹ 1942	49	F	Islet cell adenoma	Well after 3 years	18-25 units
7. Waugh, ² 1944	36	F	Islet cell adenoma	Well 8 mos. after operation	32 units
8. Dixon, ² 1944	50	M	Carcinoma of pancreas	15 mos. after operation showed recurrent abdominal mass, anemia and jaundice	40 units
9. Claggett, ² Nov. 1944	37	F	Chronic pancreatitis with calcification	2.5 mos. after operation died in an hypoglycemic attack	38 units
10. Zininger ⁹ , 1945	39	M	Chronic pancreatitis with pancreatic-lithiasis	Died after operation 30 hours	30-50 units
11. Brunschwig, ¹⁰ 1944	67	M	Carcinoma pancreas	3 days—died	} Included in Table II of this paper
12. Brunschwig, ¹¹ 1946			Carcinoma pancreas	14 days—died	
13. Whipple, 1945	26	F	Pancreatic calculi	12 mos. Relieved of pain	
14. Whipple, 1945	46	F	Pancreatic calculi	7 days—died	20-40 units

abnormal stools. Mild pain in the epigastrium or a sense of nagging epigastric distress is present in the majority of the patients. It may appear intermittently with periods of complete freedom or it may be fairly constant. In some patients, however, and not corresponding necessarily with the extent of calcareous deposits in the pancreas, the pain is so severe and constant, frequently radiating through to the back, as to be intolerable and morphinism is a serious threat. A history of a previous acute pancreatitis or of chronic alcoholism is common. The most important laboratory examination is a plain film of the upper abdomen to demonstrate the presence and extent of the calcareous deposits which may appear in the head, the body,

PANCREATIC FIBROSIS WITH CALCULI

TABLE II
RADICAL RESECTIONS OF THE PANCREAS, BY THE AUTHOR, FOR PANCREATIC LITHIASIS

Unit No.	Sex	Age	Duration of Severe Epigastric Pain	Previous Acute Pancreatitis	Deficient Panc. Ferments	Roentgen Ray Evidence of Calculi	Pancreaticoduodenectomy	Total Panc.	Follow-up Result
671642	M	42	9 months	No previous operation	Markedly in all 3 ferments	Positive in head of pancreas	Head and all of duodenum and antrum of stomach		2 yr. F.U. Relieved of pain. Normal digestion working at full capacity.
672681	M	48	6 years	9 mos. previously operation showed edema and large head pancreas	Markedly in all 3 ferments	Positive in head of pancreas	Head, all of duodenum and antrum		3 yr. F.U. Relieved of all former pain. Normal digestion. 98 per cent fat absorption
754745	M	45	5 years	4 mos. previously at operation a large mass was found in head	Markedly in all 3 ferments	Calcium shadows outline shape of pancreas	Total duodenectomy, antrum of stomach. Splenectomy. All of pancreas save a strip over superior mesenteric vessels		Several postoperative visits, last one 20 mos. after operation. Relieved of epigastric pain. Takes capsules of pancreatin to maintain fat digestion
762485	F	26	10 mos.	1 yr. ago in Harlem Hosp. for acute abdomen. Diag.: ptomaine poisoning	Marked deficiency in all 3 ferments	Calcium shadows outline all the pancreas	Total pancreatectomy. Total duodenectomy. Resection of antrum of stomach		5 mos. later developed active pulmonary Tbc. 1 yr. postop. in tuberculosis hosp. Requires 30-80 units of insulin to control her diabetes. Entirely free from pain
784094	F	46	10 weeks	No history of previous pancreatitis, 5 wks. ago. Celiotomy revealed large pancreas that "felt like a bag of shot"	Markedly in all 3 ferments	Calcium shadows outline entire shape of pancreas	Total pancreatectomy. Splenectomy. Total duodenectomy. Resection of antrum of stomach		Patient died on 7th day after operation. Autopsy revealed a localized bile peritonitis and a thrombosis of large branch of portal vein

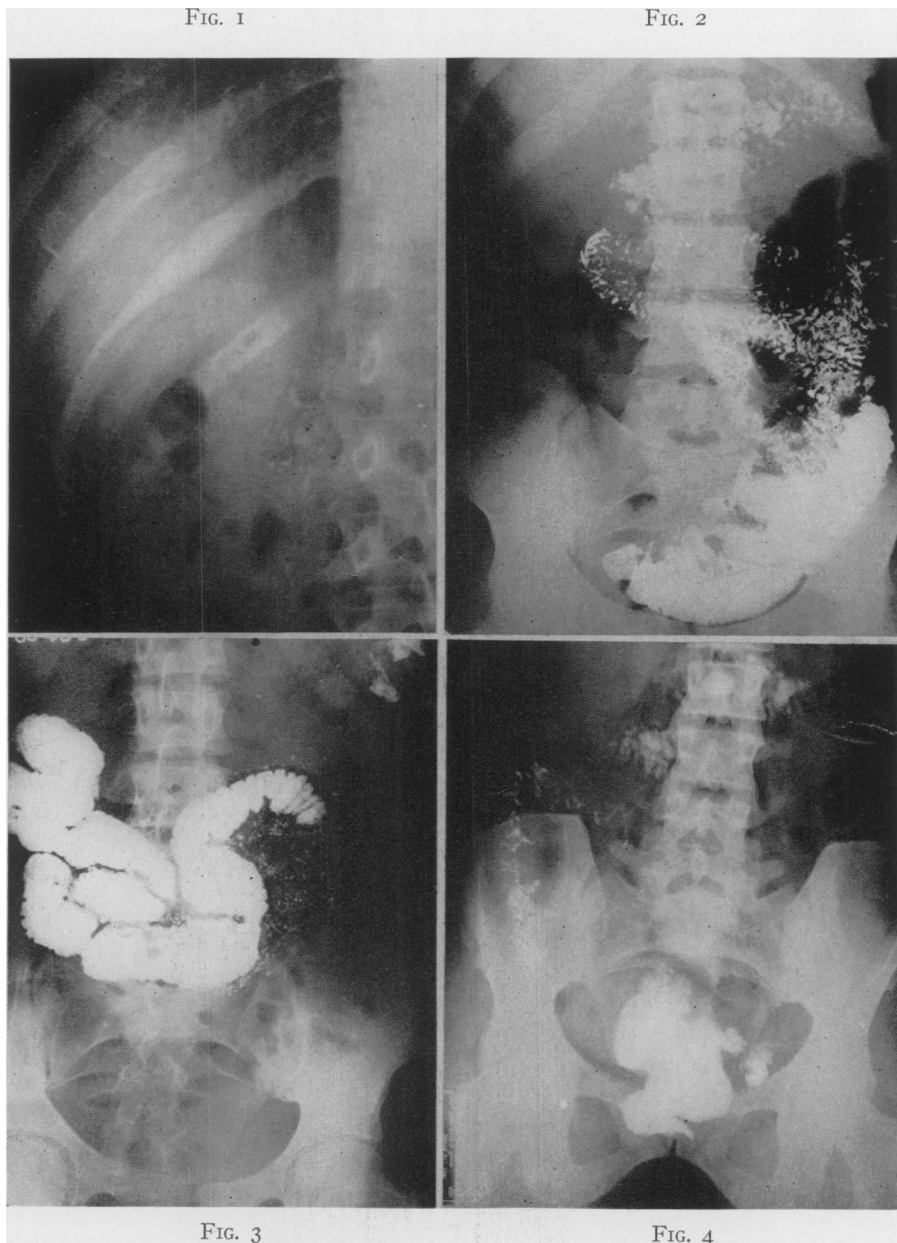


FIG. 1.—C. F. Unit #672681. Case 2. X-Ray film showing calculi in head of the pancreas.
 FIG. 2.—I. S. Unit #762485. Case 4. X-Ray film showing calculi throughout the entire pancreas, before operation.
 FIG. 3.—I. S. Unit #762485. Case 4. X-Ray film of abdomen taken after operation.
 FIG. 4.—B. B. Unit #784094. Case 5. X-ray film of abdomen showing calculi throughout the pancreas, before operation.

PANCREATIC FIBROSIS WITH CALCULI

or the tail of the pancreas, or the entire organ may be outlined by the calcareous material (Figs. 1-6). Next in importance is the finding of a marked deficiency in one or more of the pancreatic ferments, as determined from duodenal aspiration with the administration of metholyl chloride.

Many patients with mild epigastric distress or intermittent pain showing roentgenologic evidence of varying degrees of calcareous deposits are amenable to dietary and medical regimen, and may go for a period of years

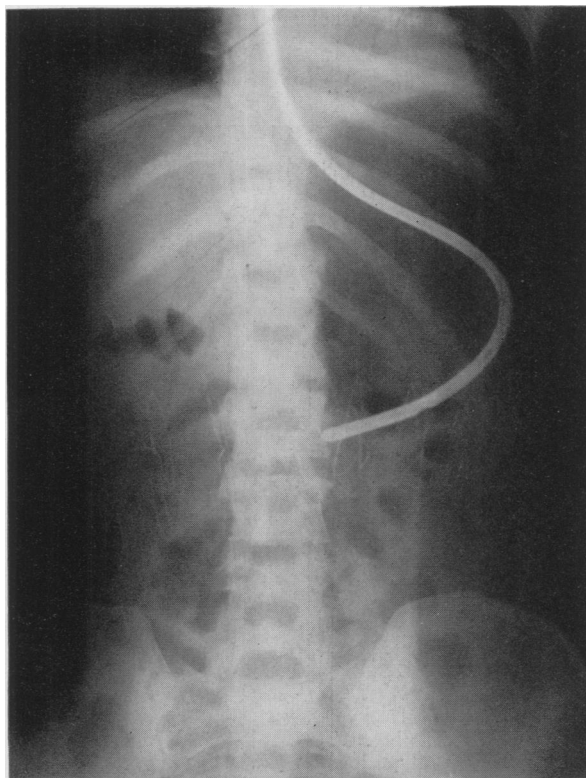


FIG. 5.—B. B. Unit #784094. Case 5. X-Ray of abdomen taken after operation.

with tolerable symptoms. There are a few patients, however, that fail to respond to conservative therapy and develop such severe recurring or constant pain, requiring hypodermic medication, that life becomes intolerable. It is for such patients, in whom the diagnosis of pancreatic calculi and chronic pancreatitis is established roentgenologically and by pancreatic function tests, that radical resection and even total pancreatectomy is indicated and welcomed by the victim of the disease.

In all five of our patients pain was dramatically relieved. Claggett's² patient, in her own words, had been given a new lease on life with the relief of pain. One of our patients had, of necessity, retired from an active busi-

ness and since his operation for the past three years has enjoyed his winters in Florida and his summers in Wisconsin.

The extent of removal of pancreatic tissue in these radical procedures, is determined by the part of the organ showing the calcareous material as seen in the roentgenograms and by the amount of fibrosed tissue. In the cases with the involvement of the head of the organ we have carried out a pancreaticoduodenectomy, as for a carcinoma of the head. In the tail or body we have left the head but have removed the remainder of the organ with the spleen, as the splenic vessels are usually embedded in the fibrosed tissue. In one of our patients we left only a small strip of pancreatic tissue over the superior mesenteric vessels.

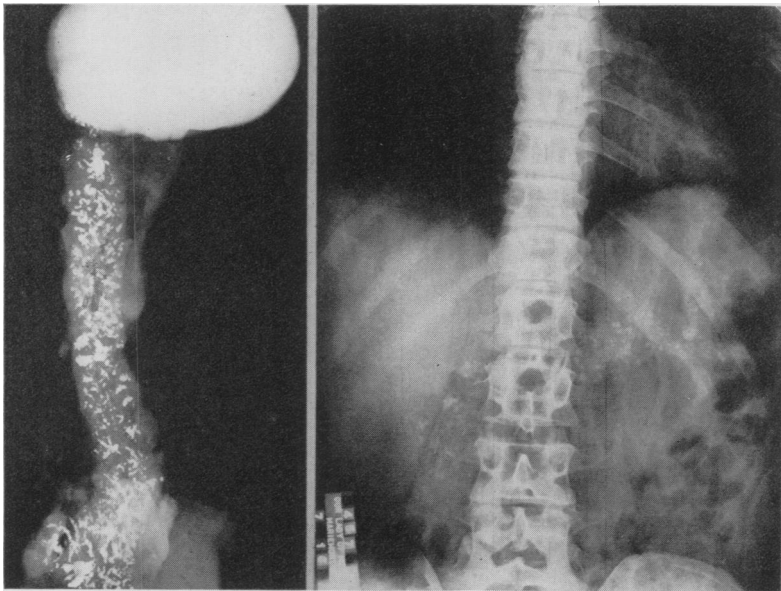


FIG. 6.—Patient of Dr. Zininger, by permission. X-Rays of abdomen before operation. X-Ray of specimen of pancreas removed at operation.

These patients all require transfusion therapy during and after operation. We have used silk technic throughout but have used “near-and-far” steel wire closure of the incision through all the layers because of the possibility of temporary bile and pancreatic ferment leakage and to avoid wound disruption. A small rubber tube within a large rubber tube (Fig. 7) for suction drainage is used to insure dry dressings, to avoid skin irritation and, if necessary, to measure bile or pancreatic juice leakage.

In the patients with total pancreatectomy it is essential to have the close cooperation of an internist experienced in the treatment of diabetes in the pre- and postoperative periods. But it has been astonishing in many of the reported cases to note the relatively small insulin requirements of these patients after a total pancreatectomy. It has caused new theories in the minds of physiologists, internists and surgeons.

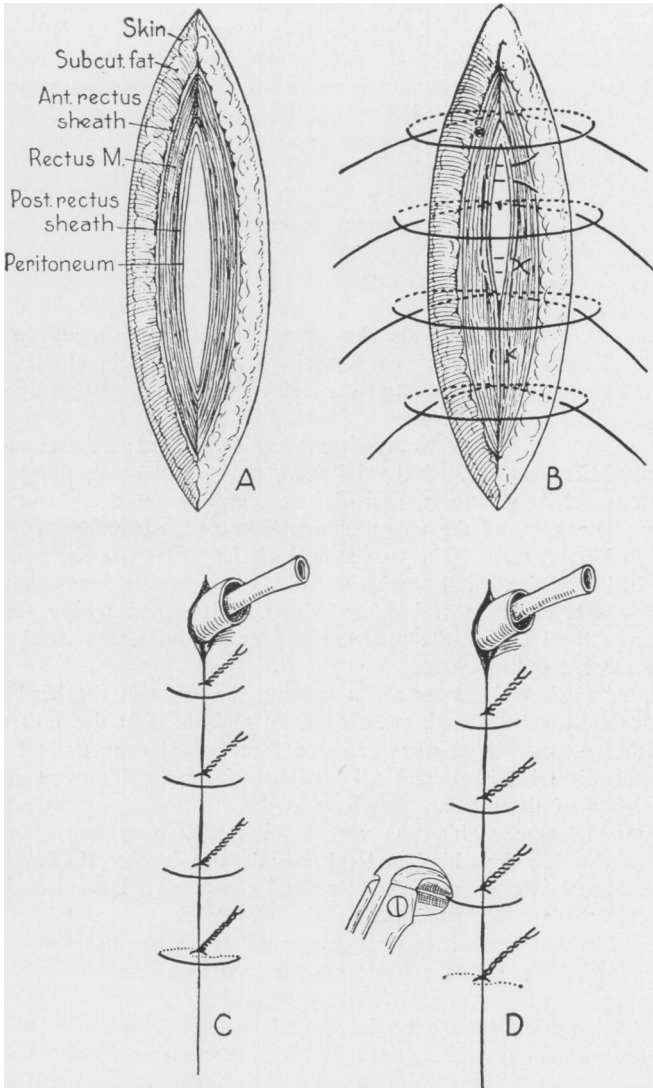


FIG. 7.—“Near and Far, Far and Near” Steel Wire Sutures through all layers for closure of abdominal incision.

Before approximating the wound edges by drawing up and twisting the ends of the steel wires, it is advisable to use interrupted mattress silk or cotton sutures to unite the peritoneum and posterior rectus sheath. No other sutures are necessary for the other layers. The “near and far” wire sutures do not cut the tissues as much as the ordinary retention sutures because the tension is distributed on four rather than on two points. The cross bar of the steel wire is cut at the skin level on the tenth to twelfth day. The next day the twisted ends can be removed.

CASE 1.—Unit No. 671642: F. W., age 42, white, male, salesman. Chief complaint: Attacks of epigastric pain, nine months. F.H. noncontributory. Past: Typhoid at 12. Rheumatic fever at 14. System review irrelevant.

Present: He has had vague indigestion for several years. In July, 1941, he had his first attack of midepigastic pain. Cramp-like, later becoming constant, radiating into the back, so severe as to require morphine hypodermically. In November, 1941, February and March, 1942, he had three similar attacks, pain and marked distention, lasting several days with complete relief with morphine, and no symptoms between attacks. No jaundice. Roentgenologic studies taken in Stamford Hospital were not informative. Was treated for neurosis. Physical examination: T.P.R., B.P. normal. No jaundice. Head, neck, chest, extremities, negative. Abdomen: Tenderness and a vague mass in the epigastrium.

Laboratory Studies: Blood picture and urinalysis are normal. Fasting blood sugar, 95 mg. per cent. Blood amylase, 61 M.K. units definitely elevated. Pancreatic ferment tests with metholyl chloride show marked deficiency in all three ferments. Duodenal bile examination shows no crystals. Roentgenologic studies show some displacement of the duodenum and stomach and vague shadows suggestive of calcified areas in the head of the pancreas.

Operation—5/11/42: Pancreaticoduodenectomy (resection of the antrum of stomach, all of duodenum, 12 cm. of the jejunum, part of common duct) with cholecystectomy, gastrojejunostomy, pancreaticogastrostomy.

Findings: The head of the pancreas was indurated, edematous, so hard that it was thought to be malignant. The true nature of the lesion was not discovered until the pancreas had been divided through the body, where it was found that there were multiple areas of calcification and dilated ducts. Liver and biliary tract appeared normal. Because the lesion in the pancreas was considered malignant the above procedures were carried out.

Summary of Pathologic Report: On opening the ducts in the head of the pancreas numerous calculi are found, some of them embedded in the wall of the duct. These vary from 1-4 mm. Numerous areas of focal necrosis are present which show remnants of calculi and epithelium. All sections show an extreme grade of fibrosis of the parenchyma of the organ.

Postoperative Course: This was very stormy, with a spiking temperature for three weeks. For a few days his blood cultures showed *B. coli*. He developed a pancreatic fistula. Stools were normal in color and consistency, however. He was discharged on his 36th day. Pain had been entirely relieved.

11/24/42: He was readmitted for closure of his pancreatic fistula. This was done by transplanting the fistulous tract into the loop of jejunum distal to his cholecystectomy. Recovery uneventful. No recurrence of pain.

6/14/44: Two years after operation: Feels well, no pain, no indigestion. He has regained normal weight. Stools normal. No recurrence of fistula.

CASE 2.—Unit No. 672681: Admitted 5/25/42. C.F., age 45, white, male, manufacturer. Chief complaint: Epigastric pain, six years. F.H.: Irrelevant. Past: Appendectomy at 21. Influenza at 24. System review negative.

Present: Six years ago he began having intermittent attacks of epigastric pain, colicky in type, at times very severe. Not related to meals. No jaundice until nine months ago when with an acute attack he developed jaundice and signs of acute cholecystitis. Cholecystectomy was performed by Dr. Evans, of Milwaukee, who found an acute gangrenous, noncalculous, cholecystitis together with edema and marked induration and enlargement of the head of his pancreas.

He improved for four months, but in November, 1941, some seven months before admission, he began having very severe epigastric pain radiating to the back, which at times required morphine hypodermically. Roentgenologic studies showed calcified

areas in the head of his pancreas which did not appear before his cholecystectomy. Because of the severe pain and the dread of morphine, he was referred to the Presbyterian Hospital for study and treatment.

Physical Examination: T.P.R. normal. B.P. 150/100. Wt. 130 lbs. A well-developed, well-balanced male. No jaundice. Head, neck, chest and extremities normal. The abdomen shows right rectus R.L.Q. scars, and a questionable mass in the epigastrium.

Laboratory Studies: Blood picture normal. Urinalysis, normal. Pancreatic function test with mecholyl chloride shows very low values for all three ferments. Serum amylase: 30.9 Myer-Killian units (at upper limit of normal).

Glucose tolerance test: Indicates disturbed carbohydrate metabolism as seen in latent diabetes. Roentgenologic studies show a collection of calcium shadows in the head of the pancreas. The study indicates definite pathology in the head of the pancreas.

Operation.—5/26/42: Pancreaticoduodenectomy (resection of the head and part of the body of the pancreas, the pylorus, all of the duodenum, first 10 cm. of the jejunum and part of the common duct). Gastrojejunostomy, choledochojejunostomy, implantation of the pancreatic duct into loop of jejunum.

Findings: The major part of the pathology was found in the head of the pancreas where there were numerous calcified casts of the branches of the pancreatic duct, with marked induration of the head which on biopsy showed no tumor. The pancreatic duct and the common duct were markedly dilated. Gallbladder was absent. Liver appeared normal, showing no evidence of fatty degeneration.

Pathologic Report: Summary, this appears to be very extensive chronic fibrous pancreatitis with pancreatic calculi in dilated obstructed ducts. The common duct showed no stones. There was no evidence of tumor tissue in any of the many sections examined, but all sections of the pancreas showed fibrosis of the parenchyma.

Postoperative Course: Was much smoother than was expected. Wound healed kindly. No fistulae. Pain was entirely relieved. Bowel movements, one a day, appeared normal. Discharged on his 23rd day.

Follow-up.—2/27/45: Two years, nine months, after operation came in for a check-up. He has maintained his weight, has no indigestion, no food intolerance. His former pain has been entirely relieved. Blood studies are normal. Fat absorption study: On a three-day measured fat intake and output test he shows 98 per cent fat digestion.

5/26/45: Three years after operation, letter from patient states he feels well and has had no recurrence of pain.

CASE 3.—Unit No. 754745: Admitted 7/20/44. C. H., age 45, white, male, machinist. Chief complaint: Severe epigastric pain at irregular intervals for five years. F.H. Irrelevant. Past: Typhoid fever and osteomyelitis of tibia 16 years ago.

Present: In 1901, cholecystectomy and appendicectomy were done for lower abdominal pain in another hospital. In 1939 he began having severe, gnawing pain in epigastrium and left upper quadrant, radiating to the back. In 1941, this pain became very severe and during the two weeks of the attack he lost 20 lbs. For three years he improved but pain persisted. In February, 1944, the pain recurred in very severe form, and he developed jaundice. In March, 1944, he was operated upon in Washington, D. C. An orange-sized, hard mass was found in the head of the pancreas which appeared calcified. The common duct was drained by a T-tube. Because of persistent pain requiring morphine he was referred to the Presbyterian Hospital.

Physical Examination: A tall, thin male complaining of pain in L.U.Q. No jaundice. Head and chest and blood pressure are normal. The abdomen reveals two right rectus scars, the mesial one wearing a T-tube. There is tenderness along the epigastrium and L.U.Q.

Laboratory Data: Blood count and blood picture is normal. Urinalysis shows no albumin or sugar. Fasting blood sugar, 97 mg. per cent. Serum amylase 42 Myers-Killian units. Pancreatic function test with 10 mg. mecholyl chloride shows marked deficiency in all three ferments, indicating wide spread disease. Duodenal bile drainage: Light green. No crystals. Roentgenologic studies show a series of calcium shadows occupying the position of the pancreas. These shadows vary in size, some as large as 4 x 7 mm. Some of these in the head of the pancreas suggest the outline of a cyst.

Operation.—7/29/44: Pancreaticoduodenectomy, splenectomy, resection of tail and most of the body of the pancreas (the only part remaining was a narrow strip overlying the superior mesenteric vessels). Choledochojejunostomy. Gastrojejunostomy. Incision: Transverse.

Pathology: The findings in this patient corresponded fairly accurately with those that had been reported in his previous operation by Dr. Anderson. There were very dense adhesions between the colon and omentum, and omentum to anterior abdominal wall, and under surface of the liver and duodenum which required a good hour of careful dissection in order to determine the feasibility of a radical procedure. The pathology in the pancreas was exceedingly interesting. The mass in the head of the pancreas had decreased considerably in size as compared to that noted by Dr. Anderson, at which time it was said to be about the size of an orange. The head of the pancreas was definitely indurated and hard and contained numerous areas of calcification, as shown by his roentgenograms. When the head of the pancreas was cut through at the right hand margin of the portal vein and superior mesenteric vessels there were areas that were almost rock-like in consistency and evidently were the site of calcareous degeneration. The entire body and tail were hard and indurated. No large cyst was encountered. A total pancreatectomy was considered impossible in this case because of the difficulty of dissecting this indurated calcified tissue from the portal vein and superior mesenteric vessels. For this reason a zone about 2 cm. in width was left, covering the portal vein. All of the pancreas to the left of the portal vein, together with the tail of the pancreas and the spleen were removed. The prepyloric part of the stomach, the pylorus and duodenum and head of the pancreas to the right of the portal vein, the duodenojejunal junction and about 6 or 7 cm. of jejunum were removed, making a second specimen.

The T-tube, which had been used at the first operation in March, was still in place. For this reason the common duct was not dilated, but it could be identified by the presence of the T-tube and because it was considered unwise to break up the opening in the common duct by removing the tube at that time it was left in place and was used as a guide in getting through the common duct near its entrance into the posterior wall of the duodenum.

Procedure: The patient had had two previous right rectus vertical incisions and for this reason an oblique transverse incision above the umbilicus was used. This gave very good exposure and made it possible to do the splenectomy and removal of the tail of the pancreas much more readily than if a right rectus incision had been used. A considerable amount of time (almost an hour) was used to dissect the dense adhesions described above, by sharp dissection. The lesser sac was entered after ligating the vessels in the gastrocolic omentum up to the point of the hilus of the spleen. This made it possible to remove the spleen with the tail of the pancreas and because it was essential to control the branches of the splenic vessels to the pancreas the spleen was removed. The pancreas was then dissected to the junction of the splenic and superior mesenteric vessels. The inferior mesenteric joined the splenic near this point. The pancreas was cut through and its stump was covered over by interrupted mattress sutures of No. 1 Deknatel. The duodenojejunal junction was then identified and about 6 or 7 cm. beyond this point an incision in the mesentery of

PANCREATIC FIBROSIS WITH CALCULI

the jejunum was made and the vessels ligated, leaving a good supply to the lower jejunal limb which was made by dividing the jejunum at that point. The proximal part of the jejunum with the duodenojejunal angle was brought up through a rent in the mesocolon and this, together with the duodenum and head of the pancreas, was dissected up to the superior mesenteric vessels and the beginning of the portal vein. The stomach was cut through the prepyloric portion and the distal stump, together with the duodenum and severed head of the pancreas was then removed, after cutting through the common duct below the point where the T-tube was seen. Hemostasis was established. No dilated duct could be made out and the right hand stump of the pancreas was then closed with interrupted No. 1 Deknatel sutures. The distal segment of jejunum was then brought up through the rent in the mesentery. The mesenteric half of the cut end of the jejunum was then closed with an over-and-over stitch of silk and about 1 cm. of the remaining opening of the jejunum was then anastomosed to the cut-end of the common duct after uniting the serous coats with continuous C silk and the two stomas then united with a continuous over-and-over suture of No. 000 chromic on an atraumatic needle. The seroserosal suture was then resumed to the point of beginning and the mesenteric border of the cut-end, which had been closed, was then tacked to the gastrohepatic omentum with interrupted silk sutures. The stump of the stomach was then approximated to the jejunum. The two serous surfaces were united with continuous C silk. An opening in the jejunum corresponding in length to the cut-end of the stomach was made, hemostasis established, and the two openings united by means of No. 00 chromic on two atraumatic needles with an over-and-over stitch, beginning at the center of the two adjacent parallel cut-edges, locked at the angles and carried around to a point opposite the point of beginning. The seroserosal suture was then continued to the point of beginning. This completed the anastomosis.

The peritoneal toilet was completed. A large soft rubber tube, containing a small tube inside of it for suction purposes, was placed in Morrison's pouch for possible leakage and the wound was closed with far-and-near steel wire sutures, steel wire being used because of the possibility of pancreatic or jejunal leakage. The T-tube was left in the original position above this incision.

Postoperative Course: A stormy four days during which time he required plasma and blood transfusions. His temperature ranged from 101°-104°F. for nine days. From then on he improved steadily. Wounds healed well. He was able to overcome his desire for hypodermic medication. He was discharged on his 27th day. Before leaving, a fat tolerance test done for three days on a measured fat intake and output showed that he was digesting 87 per cent of his fat intake. He was relieved of his pain. He was given ten units of insulin a day for an elevated blood sugar.

He has been followed several times by visits to the hospital. Twenty months after operation, he is relieved of his epigastric pain; he has no glycosuria with 10-15 units of insulin. His stools are normal if he takes small doses of pancreatic extract. He is working regularly.

CASE 4.—Unit No. 762485: Admitted 1/26/45. I. S., age 26, colored, married, laundress, separated. Chief complaints: Epigastric pain and voluminous, frequent fatty stools for ten months. F.H. One of 15 children, married, separated. One child eight years old, Husband had chronic cough.

Past: System review negative. One year ago was in Harlem Hospital for severe abdominal pain. Diagnosis: "Ptomaine poisoning." Ten months ago she began to have severe crampy epigastric pain associated with frequent bulky, fatty stools. Has had loss of weight and strength. Recently she has had more severe epigastric pain radiating to her back.

Physical Examination: A thin, unintelligent colored woman. No jaundice. The examination of the lungs reveals no pathology. A soft blowing systolic murmur is heard at the apex, not transmitted. There is some tenderness across the upper abdomen

along the site of the pancreas. Examination of the rest of the abdomen, the pelvis and extremities is negative.

Laboratory Studies: Blood picture is normal. Urinalysis reveals no glucose or albumin. Serology negative for lues. Stools show bundles of fatty acid crystals. Duodenal bile drainage negative. Pancreatic function tests with 10 mg. mecholyl chloride reveal low amylase, very low protease, small amount of lipase. Serum amylase: normal. Glucose tolerance reveals a diabetic curve. Cholecystogram shows no evidence of a gallbladder shadow. Plain films of the abdomen show numerous shadows of varying size and calcium density that almost outline the pancreas. *Diagnosis:* Diffuse pancreatic lithiasis.

Operation.—2/3/45: Total pancreatectomy, pylorotomy, total duodenectomy, choledochojejunostomy, and gastrojejunostomy.

Pathology: The findings in this patient proved to be unusually interesting and corresponded fairly accurately to the roentgenologic studies which had been made, showing extensive calcification of all of the pancreas with areas that might well have been pancreatic calculi. When the abdomen was opened the gallbladder was found to be normal. There were no stones. It was normal in color and it emptied easily. The liver appeared to be normal. There was no evidence whatsoever of fatty degeneration. The pathology was all confined to the pancreas—and there was plenty of it. On exposing the pancreas through the gastrohepatic omentum the body and tail could be seen and palpated. There was an extensive cystic degeneration of the body and tail as well as of the head, and on palpating it there were numerous movable calculi, which gave the feel of a gallbladder containing numerous stones. The body of the pancreas was much larger than normal, probably due to the extensive cystic degeneration. The head was similarly involved; the tail probably less than the body and head. The head of the pancreas, however, showed an unciform process which surrounded the superior mesenteric vessels and made removal of the pancreas difficult. The common duct was not dilated and when it was cut through near the duodenum it was found that the cystic duct ran parallel to it so that, if the duct had been ligated and the gallbladder used as a by-pass, no bile would have been available for emptying into the gallbladder. Because the patient showed all of the evidences of pancreatic deficiency in the presence of fatty stools and because the patient had had fatty stools, it was decided to do a total pancreatectomy. The etiology of the pancreatic calcification seemed to be the result of a previous acute pancreatitis, for there were very numerous filmy adhesions throughout the peritoneum. In places there were sheets of very delicate membrane, resembling fetal membrane. One of these measured in extent the size of the patient's anterior abdominal wall. The lesser sac was obliterated and the only etiology for the calcification seemed to be an acute pancreatitis, the history of which the patient gave in one of her many inaccurate statements that she had been taken to Harlem Hospital a year ago with a diagnosis of acute ptomaine poisoning.

Procedure: A transverse incision was made through both recti and splitting the obliques. The pancreas was approached through the lesser sac where, because of the low position of the stomach, it was possible to free the tail of the pancreas and the body without apparent damage to the splenic artery and vein. After this was done it was decided to remove the duodenum because of the intimate blood supply between the pancreas and the duodenum, and this was carried out by first applying crushing clamps at the duodenojejunal angle, the first portion of the jejunum being drawn up into the right upper quadrant. The duodenum was severed and the distal end was closed with an over-and-over suture of No. 1 silk, followed by a burying suture of No. 1 silk. The duodenum was mobilized with the head of the pancreas, but there the unciform process was found and it was decided to sever the common duct, and after ligating the gastroduodenal vessels the antrum of the stomach was cut through near the pylorus and the body of the pancreas, together with the head, was then dissected away from the superior mesenteric vessels and the portal vein. This was a

difficult and trying dissection because there were numerous tributaries to the portal which had to be carefully ligated, but after the pancreas had been removed with the duodenum the superior mesenteric and the splenic could be easily seen. The inferior mesenteric was not identified. Hemostasis was satisfactory.

A loop of jejunum near the duodenojejunal angle was then brought up anterior to the colon and a choledochojejunostomy was done between the cut-end of the duct and the jejunum by means of a seroserous suture, followed by an over-and-over No. 000 chromic suture of the duct to the small opening in the jejunum. The seroserous suture was then resumed to the point of beginning. About 12 cm. distal to this anastomosis the stomach was anastomosed to the jejunum, end-to-side, using the same technic.

The pancreas having been removed, there was no danger of pancreatic fistula, and a soft rubber tube containing a smaller rubber tube inside of it was placed to Morrison's pouch to take care of leakage. Closure: Steel wire near-and-far sutures.

Pathology Report—Gross: The specimen consists of a small segment of the pyloric end of the stomach and all the duodenum, which, in the fresh state, measure together 10 cm. in length. In the curve of the duodenum and attached to it is a nodular, hard, irregular pancreatic head, measuring 6.5 cm. in greatest dimension. This is attached to the rest of the pancreas and the total length of the organ is 19 cm. Toward the tail there is an irregular thickening and at this site the diameter is 5.5 cm. In the fresh state, particularly in the body of the organ, the tissues feel soft and contain great numbers of calculi.

After fixation and opening the duodenum, it is seen that the pyloric ring is situated about 2 cm. from the inversion. The papilla is not clearly seen, but on opening the common duct along a probe, it appears that in clamping the duodenum the papilla has been included in the clamp. There was apparently a very low point of entry. The opening of the pancreatic duct cannot be made out. The pancreas is, therefore, sectioned. It is an effort to find this opening. The organ is everywhere pitted by large, irregular cavities containing calculi. A greatly dilated pancreatic duct is found which courses irregularly to the head of the organ and is blocked by calculi. These stones are white, heavily calcified, but markedly friable. No normal pancreatic tissue is recognized even in the extreme tip of the tail. Everywhere there are craters surrounded by dense scar tissue. Fixation—formalin.

Microscopic: Section through the head of the pancreas shows ducts with incomplete epithelial lining, greatly distended and containing calculi. Where these have been incompletely decalcified, calcium is seen in section. There is a little granular material about these calculi and occasionally a few polymorphonuclear leukocytes are present. The pancreas is represented outside these ducts by dense cicatricial tissue in which there are widely separated small islets and small ducts. These small ducts are likewise dilated. Remnants of pancreatic acini are seen in a few fibrotic lobules. There is not any significant inflammatory reaction except in the vicinity of the larger ducts, where there are scattered lymphocytes. This same picture is seen in the body of the pancreas and the dilatation of ducts extends to the tip of the tail. The islet tissue is scant throughout. There is no suggestion of carcinoma.

Section taken through the duodenum in the hope of demonstrating a remnant of common duct fails to do so. It shows some cystic dilatation of some of the crypts of the duodenal glands.

Section of the liver biopsy shows no cirrhosis and no cholangitis. Some of the cells are distended by what is probably glycogen.

Section of the peritoneal adhesions shows a membrane composed of an exceedingly thin layer of stroma in which there are only occasional connective cells and no recognizable blood vessels. A single layer of peritoneal cells, flattened, except for their bulging nuclei, constitutes the surface. Unfortunately, this tissue was not impregnated

fresh with silver, so the structure of the surface cells cannot be demonstrated. *Diagnosis*: Chronic pancreatitis. Pancreaticolithiasis. Peritoneal adhesions. Liver.

Postoperative Course: Immediate recovery excellent. Out of bed on fourth day. Sugar in blood and urine was controlled by varying amounts of insulin—30–60 units o.d. The patient was rather ignorant and uncoöperative but before leaving the hospital on the 34th day she had been taught the use of hypodermic for insulin therapy and urinalysis for glucose. The epigastric pain had been entirely relieved. Her stools every day or q. 2 days. Normal in color and amount.

7/24/45: Readmitted for study and because she had developed a cough. Requires now between 30–70 units of globin insulin, on a 300–70–75 diet. Stool studies on a measured fat intake and output over a three-day period show she has 76 per cent absorption. With three tablets of pancreatin after each meal, a later test showed she had absorbed 83 per cent of her fat intake.

Sputum examination reveals tubercle bacilli and roentgenograms of chest shows a cavity in right upper lobe.

The patient was transferred to the Sea View Hospital for tuberculosis. A note from the hospital dated February 20, 1946, one year after pancreatectomy, says: "The right hemithorax is narrowed in volume and suggests the presence of considerable fibrosis in the lung or pleura. The left lung is free of infiltrate. Sputum has been positive. Her diabetic condition is well-controlled by protamin zinc insulin 84 units. Since admission she has presented a personality problem. At times she refused to eat or take her insulin. She has refused to have her temperature taken and at times refused to waken when rounds are made. Her temperature is still fluctuating."

CASE 5.—Unit No. 784094: Admitted 4/21/45. Died 5/7/45. B. B., age 46, white, female, school teacher. Chief complaint: Severe epigastric pain—ten weeks. F.H.—Irrelevant. Past: Influenza 1919. Incision of perirectal abscess in 1940.

Present: She was in relatively good health until 11 weeks ago when she began having voluminous, foul putty-like stools. Ten weeks ago she developed a severe, gnawing epigastric pain radiating to her back, made worse by eating. She was explored in another hospital five weeks later. The surgeon found a remarkable pancreas, having the feel of a "bag of shot," and chocolate cyst of the left ovary. Appendectomy and left salpingo-oophorectomy was done. The epigastric pain persisted, increasing in severity. Nausea and vomiting appeared. She had lost 20 lbs. in two months.

Physical Examination: Temperature, pulse, blood pressure were normal. She appeared to be a thin middle aged woman evidently in severe abdominal pain. No jaundice. Lungs clear. Heart normal. The abdomen showed a midline scar. There was marked epigastric tenderness. No masses or viscera were felt.

Laboratory Findings: Blood count normal. Urinalysis: 1026, acid, albumin 2+. Glucose 4+. No ketone bodies. Blood sugar 106 mg. per cent. Serum amylase 32 units (Myers and Killian). Pancreatic function test (mecholy) shows striking deficiency of all three ferments. Plasma protein 7.1. Urea nitrogen normal. Serum CO₂ 54. vol. per cent. X-ray films of abdomen show extensive calcium shadows in all parts of the pancreas.

Operation.—4/24/45: Total pancreatectomy, total duodenectomy, pylorotomy, splenectomy. Antecolic choledochojejunostomy and gastrojejunostomy. Transverse incision.

Surgical Pathology: The only abnormality was in the pancreas. It was enlarged throughout, was of fibrous consistency except for cystic areas which contained many large and small calculi, giving the "bag of shot" feel noted by the surgeon at the first operation. The liver and gallbladder appeared normal in every respect. The common duct was not dilated.

Pathologic Report: *Gross*: The specimen consists of a large pancreas resected

together with the pylorus of the stomach and all of the duodenum. An additional specimen consists of the spleen, removed separately, and a biopsy of the liver. The pancreas measures 16 cm. in length and 4.5 cm. in width across the body. The head is considerably injected, measuring 8 cm. from above downward and 5.5 cm. from side to side, 3 cm. in thickness. A large portion of this consists of an exaggerated uncinata process in which the groove for the portal vein is found, making it clear that the vein was almost entirely surrounded by pancreas. The segment of stomach and duodenum removed measures approximately 26 cm. in length. The distal portion of the duodenum is hemorrhagic and the serosal surface is torn, apparently from operative trauma. The common duct on the posterior aspect of the head measures about 5 mm. in diameter. There is no suggestion of bile-staining of the tissue. There is a prominent hard lymph node at the lower border of the uncinata process. Palpable through the organ, except at the extreme tip, there are large, grating, irregular calcareous masses. The spleen weighs 80 grams and except for rather deep indentations on the anterior border, is not unusual. The liver biopsy is too small for gross description. The lesion is fixed in Kaiserling before section. After 24 hours fixation the specimen was opened by bisecting the body and tail of the pancreas and making serial sections of the head. The common duct, which was not dilated, was also opened along its length and traced into the ampulla. It was seen that the ducts were blocked by large, irregular calcareous masses with surfaces like fine white coral. The ducts of Wirsung and Santorini enter together and are separated from the common duct. The duct of Wirsung is greatly dilated where it is filled with calculi, measuring as much as 1.5 cm. in diameter. It is dilated throughout the length of the specimen and tortuous. The cut-surface of the pancreas appears as a number of small round openings which are surrounded by dense fibrous tissue. No normal pancreas is recognizable. Fixation—Bouin.

Analysis of the Calculi: The calcareous material was powdered and dried in vacuum and then it dissolved in hydrochloric acid with the evolution of gas. There was some slight organic residue but most of the material went in solution. Analysis showed that there were 42.4 mg. of cholesterol in the 111 mg. of stone. This is practically the theoretic amount to be expected if one assumes that the material is pure calcium carbonate.

Microscopic: Section through the head shows numerous irregularly dilated ducts surrounded by a fairly heavy collar of connective tissue. Peripheral to this collar there are smaller dilated ducts and a considerable number of islets. No recognizable scinar cells are seen. Some of the structures interpreted as ducts might conceivably be atrophic acini. Section through the tail shows a similar picture but here there are a few structures which may be interpreted as pancreatic acini.

I have discussed these findings with Dr. Dorothy Andersen who says that they are, with the exception of the calculus formation, similar to the changes in congenital cystic fibrosis of the pancreas where the obstruction depends on plugging of the ducts with secretion, not calculi. The reason for the calculus formation is obscure. This is not calcification of the pancreas on the basis of the previous inflammation but it is cystic fibrosis following obstruction. *Pathologic Diagnosis:* Pancreaticolithiasis. Fibrosis of pancreas.

Postoperative Course: The temperature rose from normal to 103°F. and remained elevated until a terminal 105°F. On the first day the shock was controlled by parenteral fluids and transfusion. Plasma proteins fell to 4.4, however, in spite of additional plasma and blood. Insulin 50-90 units failed to control the glycosuria. There was no ketonuria. On the fourth day she went into shock again but this was controlled by transfusion. Because of the large amount of gastric Levine tube drainage, a high ileus was suspected. She was reexplored. Some distention of the jejunal loop with edema was found. An anterior gastrojejunostomy was done. The patient went into severe shock, developed a pulmonary edema and died on the seventh day after her pancreatectomy.

Autopsy: The essential findings were a localized fibrinous bile peritonitis about the choledochojejunostomy, with edema of the stoma obstructing the flow of bile into the jejunum. A large branch of the portal vein was filled by an organizing thrombus and there were thrombi in some of the intrahepatic branches. The proximal loop of the jejunum was edematous but not obstructed. Sections of the liver showed areas of central focal necrosis. The gallbladder shows edema and early acute cholecystitis.

REFERENCES

- ¹ Priestley, J. T., Comfort, M. W., and Radcliffe, James Jr.: Total Pancreatectomy for Hyperinsulinism. *ANNALS OF SURGERY*, **119**, 211-221, 1944.
- ² Claggett, O. T., *et al.*: Total Pancreatectomy; A Symposium Presenting Four Successful Cases, with Metabolic Studies. *Proc. Staff Mayo Clinic*, **21**, 25-46, 1946.
- ³ King, A. B., and Waghelstein, J. M.: Calcification of the Pancreas. *Arch. Int. Med.*, **69**, 165-176, 1942.
- ⁴ Lionello, J., Ficarra, B. J., and Ryan, N. H.: Pancreatic Calculi. *Arch. Surg.*, **48**, 137-143, 1944.
- ⁵ Rockey, E. W.: Total Pancreatectomy for Carcinoma. *ANNALS OF SURGERY*, **118**, 603-611, 1943.
- ⁶ Goldner, M. G., and Clark, D. E.: The Insulin Requirement of Man after Total Pancreatectomy. *J. Clin. Endocrin.*, **4**, 194-197, 1944.
- ⁷ Fallis, L. quoted by McClure, R. D.: Discussion. *ANNALS OF SURGERY*, **120**, 416, 1944.
- ⁸ Brunshwig, A., Ricketts, H. T., and Bigelow, R. R.: Total Pancreatectomy with Recovery. *Surg. Gyn. and Obstet.* **80**: 252-256, 1945.
- ⁹ Zinninger, M. M.: Personal communication. 1945.
- ¹⁰ Brunshwig, A.: Surgical Treatment of Carcinoma of the Body of the Pancreas. *ANNALS OF SURGERY*, **120**, 406-416, 1944.
- ¹¹ Brunshwig, A.: Personal communication, 1946.

DISCUSSION.—DR. RICHARD B. CATTELL, Boston, Mass.: We have had three patients with diffuse calculi and calcification of the pancreas, none of whom have been operated upon. I wish to call attention to the probable cause of pain in these cases and a possible means of relief without extensive resections. We have been able to relieve pain in cases of inoperable carcinoma of the pancreas with obstruction of the duct of Wirsung by anastomosing the duct of Wirsung to a defunctionalized loop of jejunum. This is not a difficult technical procedure and we have performed it in nine cases. After division of the gastrocolic omentum, a long antecolic loop of jejunum is brought up and anastomosed to the duct in the midportion of the body of the pancreas over a T-tube. It is quite possible that the same procedure could be utilized in calculous disease of the pancreas, although it would have no effect on the diffuse calcification. I suggest it as a possible means of relieving pain by a less radical procedure than total pancreatectomy.

DR. REGINALD H. SMITHWICK, Boston, Mass.: I hesitate to comment upon Doctor Whipple's presentation because my experience with this problem is confined to one case, because a different form of treatment was employed, and because the follow-up of the case to which I refer is of very short duration, six months.

This patient was a female in her early 50's and for some months she had been suffering from frequent excruciating attacks of deep-seated midepigastric pain, occurring principally at night and requiring large amounts of morphine for relief. She had calcification of the head of the pancreas. She had had a previous cholecystectomy. She was thought to have a duodenal ulcer also. She had severe diabetes and hypertension of moderate severity, associated with considerable evidence of cardiovascular damage.