

# SURVIVAL FIVE YEARS AFTER RADICAL PANCREATODUODENECTOMY FOR CARCINOMA OF THE HEAD OF THE PANCREAS\*

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FIFTEEN YEARS AGO, Whipple and co-workers established a milestone in the treatment of malignant disease of the gastro-intestinal tract when they described a successful radical operation for carcinoma of the papilla of Vater. Two years later, Brunschwig<sup>2</sup> extended the applicability of extensive pancreatoduodenectomy to carcinoma of the head of the pancreas. These contributions demonstrated the feasibility of radical as opposed to palliative surgery for malignant disease in the region of the papilla of Vater. Recently, there have been encouraging reports<sup>1, 3, 4, 7</sup> of patients who are alive and well five years after radical operations for carcinoma of the papilla of Vater. On the other hand, carcinoma of the head of the pancreas continues to thwart even the boldest attempts at surgical cure. Like Cattell, we have been unable to find in the literature a report of a case of carcinoma of the head of the pancreas in which the patient was alive and apparently free of the disease five years after radical pancreatoduodenectomy for this condition. However, such a case of resected carcinoma of the pancreatic head has been followed at the Mayo Clinic for five years; the patient is alive, working and free of evident recurrence. Because of its singularity, we believe the case warrants a detailed description.

## REPORT OF A CASE

A metal-worker, 41 years of age, was admitted to the clinic on May 15, 1945, with the chief com-

plaint of jaundice of 10 days' duration. His family history was irrelevant. He had contracted malaria in 1923 and had been adequately treated. An 11-year history of alcoholic excess was reported, although the patient stated he had ceased drinking five months before admission. One year prior to his admission the patient had noted the development of easy fatigability, anorexia and loss of weight. Five months before his visit to the clinic, persistent constipation was noted. One month later, he began to experience constant abdominal pain of a crampy nature in the periumbilical region. The distress was increased by intake of food, and frequently relieved by defecation. Three months prior to admission a persistent watery diarrhea began, which occurred as often as 15 times daily and often awakened him at night. No blood, pus, or mucus were noted in the stools, which were not foamy or foul smelling. Two months later, a preparation of belladonna was prescribed by his home physician, and the cramps subsided, but he was left with a gnawing midabdominal pain. The number of stools was reduced to 2 or 3 a day. On May 5 there was a sudden onset of jaundice, clay-colored stools and dark urine, followed a day later by severe generalized pruritus. The dull abdominal discomfort continued, unaccompanied by cramps. He had lost 30 pounds (13.6 Kg.) in 5 months. At no time had there been a history of vomiting, hematemesis, melena, chills and fever, swelling of the abdomen or ankles, transfusion of blood, or exposure to hepatotoxic chemicals.

Physical examination revealed a well-developed and well-nourished white man with moderately icteric skin and sclerae. General physical examination was negative except for the liver, which was palpated 2 to 3 fingerbreadths below the right costal border, and the gallbladder which was questionably palpable. The abdomen was not tender.

Simple roentgenograms of the abdomen and particularly of the region about the gallbladder did not reveal anything remarkable. Roentgenograms of the gastro-intestinal tract were not taken.

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The hemoglobin measured 12.5 Gm. per 100 cc. of blood, and the erythrocyte count was 3,900,000 per cubic millimeter. The sedimentation rate (Westergren) was 34 mm. in the first hour. Urinalysis revealed the following: specific gravity, 1.020; albuminuria, grade 2; biliuria, grade 1; a trace of urobilinogen, and glycosuria, grade 1. The serum bilirubin measured 9.1 mg. per 100 cc. and showed a direct van den Bergh reaction. The prothrombin time (Quick) was 24 seconds, the

On May 22, 1945, surgical exploration was performed by one of us (Clagett). The abdomen was entered through a primary upper right rectus incision. The liver was found to be moderately enlarged without evidence of metastatic involvement. A firm, movable tumor about 4 cm. in diameter was noted in the head of the pancreas. Many inflamed lymph nodes were present around the duodenum and the gastrohepatic ligament but distant metastasis was not apparent. The common

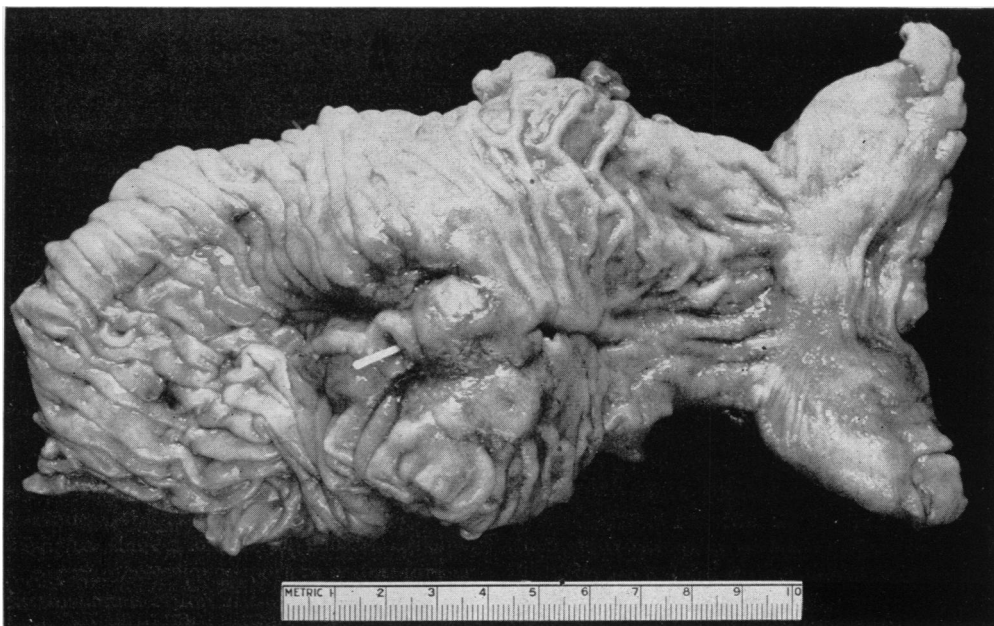


FIG. 1.—Large movable carcinoma of the head of the pancreas which has produced ulceration of the duodenum in the region of the papilla of Vater.

normal time being 17 to 19 seconds. The urea measured 34 mg. per 100 cc. of blood. Because of the low-grade glycosuria, two fasting blood sugar determinations were made, which yielded values of 120 and 139 mg. per 100 cc. respectively. The value for serum amylase was less than 50 units. Schmidt's test for urobilin in the stool showed faintly positive results. Duodenal drainage yielded no bile in the aspirated material; however, gross blood was present in an appreciable quantity.

Preoperatively, the patient was placed on a diet high in calories, in protein, and in carbohydrate. Since glycosuria was not present on further daily examinations of the urine, it was not deemed necessary to administer insulin or control the dietary carbohydrate. Supplements of vitamin B complex were given daily. Daily administration of vitamin K resulted in diminution of the prothrombin time to 20 seconds. Adequate hydration was insured by intravenous infusions.

bile duct measured 2.5 cm. in diameter. The cystic duct paralleled the course of the common duct to the level of the pancreas, so it was necessary to resect the two ducts together, leaving a double-barreled lumen. The gastroduodenal artery was cut and ligated. The pancreas was mobilized from the superior mesenteric and portal vessels. Dissection was difficult in one area where the head of the pancreas was adherent to the inferior vena cava, but was accomplished without perforating the vessel. The pancreas was severed at its neck, where it crossed the superior mesenteric vessels. Next, the lower third of the stomach, the proximal three quarters of the duodenum, the lower ends of the common and cystic ducts and the head of the pancreas were removed *en masse*. The reconstruction was begun by anastomosing the pancreatic duct, which was dilated to about 1 cm., to the distal portion of the duodenum by means of an end-to-end mucosa-to-mucosa approximation

employing silk sutures. The anastomosis was reinforced by invaginating the sectioned end of the pancreas into the duodenal lumen by means of an outer row of silk sutures. An end-to-side antecolic gastrojejunostomy was performed. Distal to this, the common and cystic ducts were anastomosed together to the side of the jejunum. One Penrose drain was placed at the site of the pancreatoduodenostomy and another at the site of the choledochojejunostomy. During the operation, the patient received a transfusion of 1000 cc. of cross-

wound healed by first intention and when the drains were removed, further drainage was not noted. The patient was dismissed from the surgical service on the nineteenth day after operation. He then entered the metabolic unit for study of fecal nitrogen and excretion of fat. It was observed that approximately 50 per cent of the ingested fat and protein were excreted undigested in the stools. The patient was finally discharged on a daily diet of 3000 to 3500 calories which contained 50 Gm. of fat and 100 to 125 Gm. of protein supplemented

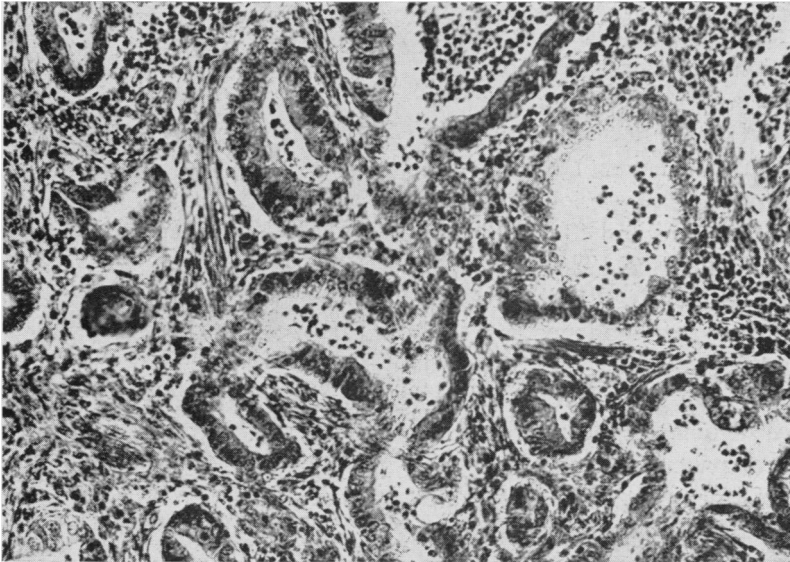


FIG. 2.—Adenocarcinoma, grade 1, of the head of the pancreas showing extensive secondary inflammation (hematoxylin and eosin, x145).

matched blood. At the close of the operation, the patient's condition was satisfactory.

On gross pathologic examination, a neoplasm was found situated in the head of the pancreas close to the termination of the common bile duct (Fig. 1). It measured 5 by 4 by 3 cm. and had produced an ulceration of the duodenum 4 by 3 cm. in size in the region of the papilla of Vater. The common bile duct was dilated to 2.5 cm. and the main pancreatic duct was 1 cm. in diameter.

Microscopic examination of the pancreatic neoplasm revealed that it was an adenocarcinoma, papillary in type (Fig. 2). The lesion was classified as grade 1, according to Broders' method. Several peripancreatic nodes were metastatically involved (Fig. 3). Invasion of the perineural lymphatics or of the blood vessels had not occurred. Inflammation and necrosis were evident in the region of ulceration.

Postoperatively, the patient's course was uneventful. Diabetes was not evident. The operative

by 10 enteric-coated pancreatin tablets with each meal. This regimen reduced the loss of fat by 50 per cent and enabled him to maintain a satisfactory nutritional status. Ten months after operation, the patient returned to the clinic for a check-up. He reported that his health was good and that he had regained his original preoperative weight of 170 pounds (77.1 Kg.).

On August 17, 1950, more than five years after radical pancreatoduodenectomy was performed, the patient reported that his health and strength were excellent. His position as a factory foreman requires that he work 9 hours a day 6 days a week, a routine which he tolerates well. His appetite is excellent and he maintains a weight of 160 to 170 pounds (72.6 to 77.1 Kg.). He avoids diarrhea by taking 3 triple strength pancreatin tablets (Abbott) with each meal and by keeping his diet as fat-free as possible. Both the patient and his wife are satisfied that in every way he is enjoying normally good health and activity.

## COMMENT

Eleven patients with carcinoma of the head of the pancreas underwent radical pancreatoduodenectomy at the Mayo Clinic prior to July, 1945. Of this group, two (18.2 per cent) died in the immediate postoperative period, and six died 12 months or less after the operation. One patient died 22 months after operation and another died 44 months postoperatively. One patient (9 per cent) is alive and well five years after radical resection. Radical resection was performed in seven instances for carcinoma of the papilla of Vater prior to July, 1945. Two patients (28.6 per cent) died in the immediate postoperative period and two patients died 19 months and 48 months, respectively, after operation. Three patients (42.9 per cent) are alive and well five years after radical pancreatoduodenectomy for carcinoma of the papilla of Vater. Cattell reported the following results: of 12 patients with carcinoma of the papilla who survived radical pancreatoduodenal resection, three or 25 per cent were living and well five years after operation and six or 50 per cent had lived three years or more. Of 25 patients with cancer of the head of the pancreas who survived radical operation, 18 died of recurrence with an average postoperative duration of life of 11 months and seven were living at the time of his report. One of these was alive and well more than three years after operation.

It is evident from the figures we have mentioned that radical pancreatoduodenectomy holds promise in the treatment for carcinoma of the papilla of Vater, but that it has not been adequate as a curative procedure for carcinoma of the head of the pancreas. Carcinoma of the pancreatic head is usually more advanced when seen at laparotomy than is carcinoma of the papilla. The latter, because of its location, produces early obstruction of the common bile duct, resulting in the acute onset of icterus. On the other hand, carcinoma of the head of the pancreas is well established at its site of

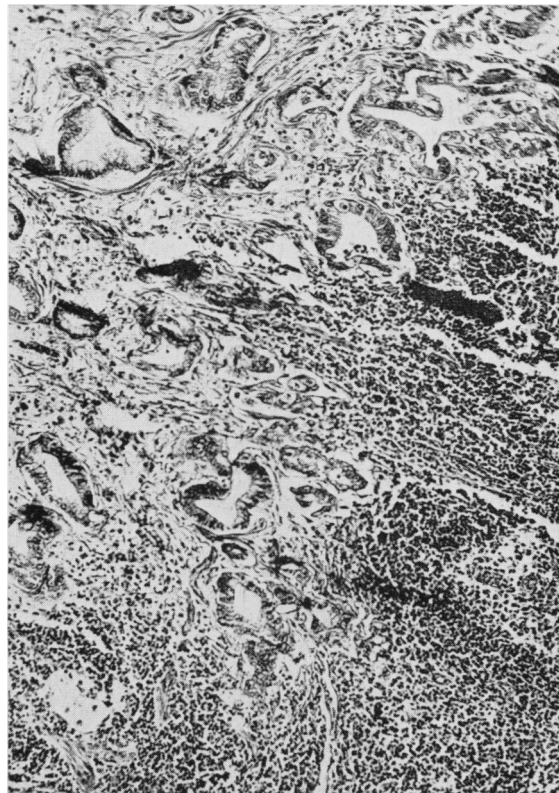


FIG. 3.—Invasion of lymph node by adenocarcinoma, grade 1, of head of the pancreas. This probably represents a direct metastatic process (hematoxylin and eosin, x 90).

origin before it encroaches on the biliary tract. In a review of operative notes, we have found that carcinoma of the pancreatic head was reported as impinging on the major vessels of the portal region in 37 per cent of cases. This factor may account for early metastasis to the liver by way of the blood. Only 6.6 per cent of the lesions of the papilla were adherent to the major portal vessels. Carcinoma of the head of the pancreas metastasizes to the regional lymph nodes in 60 to 75 per cent of instances whereas carcinoma of the papilla exhibits nodal metastasis in 30 per cent. Drapiewski has emphasized the tendency of pancreatic carcinoma toward extensive invasion of the perineural lymphatics of the pancreatoduodenal region. A study<sup>6</sup> at the clinic of radically resected specimens revealed that 60 per cent of pancreatic carcinomas had infil-

trated the perineural lymphatics, usually in cases of patients with the shortest postoperative survival. It is interesting that not one of the lesions of the papilla exhibited the phenomenon of perineural invasion. Lastly, in our study we observed that the transected end of the common bile duct was infiltrated with carcinomatous cells (via the lymphatic sinuses) in 15 per cent of cases of pancreatic malignant disease, but was free of malignant invasion in all cases in which resection had been performed for carcinoma of the papilla.

The factors mentioned help to explain the poorer prognosis associated with carcinoma of the head of the pancreas after radical pancreatoduodenectomy compared with that associated with carcinoma of the papilla of Vater. Whether radical pancreatoduodenectomy should be discarded in the treatment of carcinoma of the pancreatic head is a moot question. An awareness that jaundice is not an early or constant accompaniment of pancreatic carcinoma and a high index of suspicion in all cases of dull epigastric pain with loss of weight will bring patients to laparotomy earlier. In our series<sup>6</sup> of cases in which resection was performed for carcinoma of the pancreas, roentgenograms of the stomach and duodenum yielded positive evidence of the presence of the lesion in a third of the cases. It is likely that emphasis on this diagnostic method will produce an even greater proportion of earlier diagnoses. Cattell suggested that if radical resection is employed, total pancreatectomy should be performed to preclude the dissemination of carcinomatous cells which might occur when the pancreas is cut across during partial pancreatoduodenectomy.

We question whether total pancreatectomy is more radical than partial pancreatoduodenectomy to a degree justifying its crippling after-effects. In all cases in our series, it was noted microscopically that the sectioned end of the pancreas was well beyond the growth. A more likely basis for

recurrence would appear to be the frequent adherence of the neoplasms to the portal vessels. When such a situation obtains, resection should be strictly contraindicated. In every radical pancreatoduodenal resection, the transected end of the common bile duct should be studied by frozen section; if malignant cells are found, more of the duct should be resected if possible. When doubt exists as to the origin of the lesion, as is often the case, we agree with Waugh's contention that radical resection should be performed because of the possibility that the pathologic examination will demonstrate that the carcinoma originated in the papilla. In conclusion, the case herein reported suggests that the occasionally good result for an otherwise doomed patient warrants consideration of the operation in carefully individualized cases of pancreatic carcinoma.

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