

# Radical Pancreatoduodenectomy:

## A 22-Year Experience with the Complications, Mortality Rate, and Survival Rate \*

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IN some medical centers, surgeons have become discouraged with the results that follow radical pancreatoduodenectomy (Whipple operation) for malignant disease. The hospital mortality rate, the occasionally prolonged convalescence fraught with multiple major complications, and the relatively low percentage of long-term survivals have led several authorities to question whether the operation might better be abandoned. At the Mayo Clinic, a somewhat more optimistic viewpoint has persisted. The purpose of the present study was to scrutinize objectively the records of a small group of surgeons working under identical circumstances to see whether an alteration in the basic concept was indicated.

### Material

Constituting a 22-year experience, a review of the records of all patients submitted to radical pancreatoduodenal resection for malignant disease from 1941 through 1962 was undertaken. Only those patients undergoing the operation for primary cancer of the general region of the terminal aspects of the bile and pancreatic ducts were included. Therefore, the series totals 239 cases and consists of 119 cases of cancer of the head of the pancreas, 77 of carcinoma of the papilla of Vater, 25 of

cancer of the duodenum, and 18 of carcinoma of the common bile duct.

### Sex and Age Incidence

Of the total group, 159 were men. Males predominated for each tumor site: there were 83 males and 36 females with cancer of the pancreatic head, 45 males and 32 females with cancer of the papilla, 17 males and eight females with cancer of the duodenum, and 14 males and four females with biliary duct carcinoma. The ages ranged from 27 to 80 years and averaged 55.6 years for those with cancer of the pancreas, 58.5 years for those with cancer of the papilla of Vater, 55.7 years for those with cancer of the duodenum, and 58.7 years for those with cancer of the common bile duct. The mean age for the entire group was 56.8 years, and four patients were 30 years or younger.

### Duration of Symptoms

The initial symptom was present an average of 9.3 months for patients with cancer of the pancreas, 8.5 months for patients with cancer of the papilla of Vater, 16.8 months for those with cancer of the duodenum, and 6.2 months for cancer of the common bile duct. Twelve patients had had symptoms for three to four years. This report will not detail the symptoms, physical findings, or laboratory and radiologic data; this information for a portion of the series has been presented in part elsewhere.<sup>4, 5</sup>

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† Mr. Gage died January 13, 1964.

### Technical Features

Whereas 196 patients underwent a one-stage pancreatoduodenal resection, 30 patients had had preliminary surgery to decompress the biliary tract prior to coming to the clinic, and 13 underwent a two-stage procedure at the clinic. A right rectus (paramedian) incision was used for 163, and a right subcostal incision was used for 40 patients. Upper midline, transverse, or oblique incisions were used on occasion. The gallbladder was found to be distended in 127 of the 135 icteric patients who had not had previous gallbladder operations. Operative technic for pancreatoduodenal resection has been described by Waugh and Giberson, and the Waugh modification of the Whipple operation was used most frequently in the series.

Tumors of the region around the papilla of Vater were resected if there was no evidence of distant metastatic lesions and if local invasion was not such as to preclude mobilizing the tumor from retroperitoneal structures. No correlation was found between the presence of pain in the abdomen or the back and the adherence of the tumor to blood vessels. In 50 of the cases (44 of pancreatic carcinoma) resection was well underway before the surgeon discovered that the tumor was adherent to the vessels. Only two of these patients, one with an islet-cell carcinoma and the other with a duodenal carcinoma, have survived five years. Carcinoma has recurred in 46 of the remaining patients already.

In recent years and with increasing frequency, more of the pancreas has been removed than just its head. Hemipancreatectomy was performed in 71 cases; 36 of these cases were of cancers primary in the pancreas. Twelve patients underwent total pancreatectomy: two for functioning islet-cell carcinomas, one for a rhabdomyosarcoma, and nine for multicentric, diffuse, or large carcinomas of the pancreas. The length of common bile duct removed was 3 to 9 cm.

with a mean of 5.3 cm. Generally, the entire duodenum was included in the specimen.

An end-to-end pancreatojejunostomy was constructed for 169 patients and an end-to-side anastomosis, for 21. A polyethylene tube was used in nine cases, and the pancreatic duct was sutured to the jejunal mucosa in three cases. End-to-end pancreatoduodenostomy was performed 17 times and pancreatogastrostomy, once. The pancreatic stump was oversewn in 19 of the early cases.

Choledocho-enterostomy was performed for 224 patients (213 were end-to-side) and choledochogastrostomy, for five patients. The common duct was anastomosed over a T-tube 11 times and over a catheter, brought out as a jejunostomy, 12 times. The bile duct was ligated and the gallbladder was used for biliary anastomosis in ten cases; eight were end-to-side and two were end-to-end. After pancreatoduodenectomy, three patients underwent cholecystectomy for cholecystitis; these three also had benign stricture of the choledochojejunostomy, which required reconstruction at that time.

It is now standard procedure to resect more than the pyloric portion of the stomach. The majority of patients have received retrocolic gastrojejunostomy, and, in recent years, the stoma has been kept narrow by closing the lesser curvature (Hofmeister procedure). End-to-end (Billroth I) gastrojejunostomy was done for only three patients. The end of the jejunum was closed in 36 patients.

### Resectability Rate

The rate of resection was 72 per cent for carcinoma of the papilla of Vater but only 10 per cent for cancer of the head of the pancreas. The rates in the other two categories of cancers were between these two values.

### Early Complications

The median length of hospitalization was 21 days for the patients who survived op-

TABLE 1. *Postoperative Complications in 156 Patients in the Series of 239 Patients\**

Complication	No.	Complication	No.
Postoperative deaths	46	Mesenteric thrombosis (?)	5
Elevation of blood urea	90	Auricular fibrillation	5
Wound infection	21	Coronary thrombosis	3
Pancreatic fistula	21	Pulmonary edema	3
Gastro-intestinal hemorrhage	20	Hepatic insufficiency	3
Biliary fistula	16	Pulmonary embolus	2
Hypotension	14	Wound dehiscence	2
Peritonitis	11	Cerebral vascular accident	2
Biliary and pancreatic fistula	11	Bowel obstruction	1
Pneumonitis	9	Paralytic ileus	1
Sepsis	6	Fecal fistula	1
Gastric retention	5	Gastrojejunal fistula	1

\* 156 patients had significant postoperative complications and certain patients exhibited more than one complication.

eration; when complications occurred, the median length of hospitalization increased to 27 days. A pancreatic fistula or a biliary fistula or both were a significant postoperative complication (Table 1), and at times this led to gastro-intestinal or intra-abdominal hemorrhage or sepsis. Twenty patients experienced gastro-intestinal hemorrhage (11 after a pancreatic fistula), and 18 died. Peritonitis and intraperitoneal abscess occurred in 17 patients, eight of whom had had a fistula; nine succumbed. Wound infection, on occasion a sequel to fistula formation, was noted in 21 cases (8.7%). Hypotension unrelated to blood loss developed in 14 patients and was due to vari-

ous causes—peritonitis with septicemia in four, liver infarction in three, mesenteric thrombosis in three, coronary occlusion in three, and pulmonary embolism in one case. Primary renal insufficiency was a problem for six patients and accounted for five deaths. The other “temporary uremia” states cleared on therapy.

### Hospital Mortality

The overall operative mortality rate was 19.2 per cent: 21.0 per cent for patients with cancer of the head of the pancreas, 15.6 per cent for those with carcinoma of the papilla, 24.0 per cent for those with cancer of the duodenum, and 16.7 per cent

TABLE 2. *Primary Causes of Postoperative Death*

Cause	Location of Malignant Lesion			
	Head of Pancreas (119 Cases), No.	Papilla of Vater (77 Cases), No.	Duodenum (25 Cases), No.	Common Bile Duct (18 Cases), No.
Hemorrhage	3(2)*	6(4)*	4(3)*	1(1)*
Sepsis	7(4)*	0	1(1)*	1
Mesenteric thrombosis	5(3)**	1	0	0
Liver insufficiency	4	0	0	0
Uremia	4	0	0	1
Myocardial infarction	2(1)**	2	0	0
Congestive heart failure	0	1	0	0
Cerebral vascular accident	0	1	1	0
Pulmonary embolism	0	1	0	0
Total	25	12	6	3

\* Number in parentheses indicates number of cases in which a pancreatic or biliary fistula also occurred.

\*\* Number in parentheses indicates number of cases in which gastro-intestinal hemorrhage also occurred.

TABLE 3. *Grade of Malignancy and Incidence of Lymph Node Metastasis*

Grade (Broders')	Location of Malignant Lesion															
	Head of Pancreas				Papilla of Vater				Duodenum				Common Bile Duct			
	No. Patients		With Positive Node		No. Patients		With Positive Node		No. Patients		With Positive Node		No. Patients		With Positive Node	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
1	24	29.2	7	29.2	29	6.9	2	6.9	5	0.0	0	0.0	2	0	0.0	
2	54	63.0	34	63.0	32	34.4	11	34.4	12	33.0	4	33.0	11	3	27.3	
3	34	64.7	22	64.7	14	14.3	2	14.3	6	66.7	4	66.7	5	2	40.0	
4	7	28.6	2	28.6	2	50.0	1	50.0	2	0.0	0	0.0	0	0	0.0	
Totals	119	54.6	65	54.6	77	20.8	16	20.8	25	32.0	8	32.0	18	5	27.8	

for patients with common duct carcinoma. Thirty-four of the patients were examined at necropsy, and four had been reoperated on prior to death. The causes of death are listed in Table 2. Although the patients who received a staged operation included those considered to have a greater surgical risk, the mortality rate for these patients was only 11.6 per cent.

Whereas we have been encouraged by a seven-year hospital mortality rate of approximately 12 per cent,<sup>5</sup> the value of a long-term, all-inclusive study such as this is quite apparent in establishing a factor to reflect the true picture in complete accuracy. This same phenomenon is brought out very clearly in the report by Ross.<sup>8</sup>

### Late Complications

The most frequent late complications were diarrhea (steatorrhea and creatorrhea) and diabetes. Pancreatic exocrine insufficiency was more common in the operative survivors who underwent resection for cancer of the pancreas (47.9%) than in those operated for cancer of the papilla (27.7%). This was also true for diabetes mellitus (22.3 and 9.2%, respectively). Of the 193 patients who survived operation, 75 demonstrated clinical steatorrhea with 25 to 70 per cent fat in the dried stool, and 29 had hyperglycemia; 19 of these were also in the group with steatorrhea. Twenty-four of the patients required insulin in daily doses of 10 to 45 units (14 to 44 units for those with no remaining pancreatic tissue).

Benign stenosis of the biliary-intestinal anastomosis occurred in ten patients, and nine were reoperated on. Reoperation was performed for one pancreatic fistula and for one biliary fistula. Three patients had obstruction of the gastrojejunostomy which necessitated operative relief, whereas 11 patients complained of symptoms of gastric "dumping." Gastrojejunal ulcers developed in only three. The small bowel became obstructed in two patients, and surgical cor-

TABLE 4. Survival Rates After Radical Pancreatoduodenectomy According to Location of Malignant Lesion

Location	Patients		Lived 3 or More Years After Operation		Patients		Lived 5 or More Years After Operation	
	Total	No. Traced	No.	%	Total	No. Traced	No.	%*
Head of pancreas	79	78	19	24.4	68	66	12	18.2
Papilla of Vater	55	53	29	54.7	48	46	18	39.1
Duodenum	16	16	7	43.8	13	13	5	38.5
Common duct	11	10	2	20.0	9	9	1	11.1
Totals	161	157	57	36.3	138	134	36	26.9

\* Based on traced patients. Inquiry as of January 1, 1964. Included in the three-year group are those patients operated on in 1960 or earlier; the five-year group includes those patients operated on in 1958 or earlier. Hospital deaths are excluded in the calculation of the survival rates.

resection was required in both. A ventral hernia developed in one patient.

### Surgical Pathology

The lesions of the pancreas were classified by the surgical pathologists as *type ordinaire* (ductal, scirrhus) in 85 cases, mucous adenocarcinoma in nine, papillary adenocarcinoma in nine, cystadenocarcinoma in four, anaplastic in five, acinar carcinoma in three, and rhabdomyosarcoma in one. There were islet-cell carcinomas in seven cases: four of these tumors were non-functioning; one was associated with hypoglycemia; and two occurred in patients with the Zollinger-Ellison syndrome. Grade 2 (Broders' classification) cancers were most common, and over half of the patients had metastasis to the lymph nodes (Table 3). Perineural lymphatic involvement was recognized on examination of 45 of the lesions.

Carcinomas of the papilla of Vater were classified as papillary carcinoma in 37 cases, adenocarcinoma of intestinal epithelium in 33, scirrhus adenocarcinoma in five, and anaplastic carcinoma in two. Approximately half of the lesions had extended through the duodenal wall, while 16 (20.8%) revealed positive lymph nodes. Seventy-nine per cent of the tumors were Grade 1 or 2 (Broders'). Only four pa-

tients were noted to have perineural lymphatic invasion.

The cancers of the duodenum included 12 adenocarcinomas, five papillary adenocarcinomas, four mucous producing carcinomas (with signet-ring cells), one carcinosarcoma, and three leiomyosarcomas. These tumors were situated in the first part of the duodenum in three cases, papillary in 14, and infrapapillary in eight. About half of the lesions were Grade two. Twelve had infiltrated through the duodenum, and eight had spread to the regional lymph nodes.

There were ten infiltrating adenocarcinomas and eight papillary carcinomas of the common bile duct, and more than half were Grade 2 lesions. Eight of the tumors had extended to the pancreas, and three more involved the duodenum. Five patients had nodal metastasis, and three had perineural involvement.

### Survival Study

Patients operated on prior to January 1, 1959, were considered for the five-year survival study, and those operated on before January 1, 1961, were considered for the three-year survival study. The survival figures are listed according to the site of the primary cancer (Table 4). The post-operative follow-up study was designed also to obtain information as to time of onset of

TABLE 5. *Duration of Palliation in Pancreatoduodenectomy*

Location of Malignant Lesion	No. Patients	Range (mo.)	Average (mo.)
Head of pancreas	66	0-46	9
Papilla of Vater	31	0-46	9
Duodenum	10	2-34	8
Common bile duct	10	3-55	20

recurrence and the duration of comfortable living.

*Cancer of the Pancreas.*—Twelve patients, including the four with islet-cell carcinoma, lived five years or more (18.2%). The five-year survival rate for ductal carcinoma of the pancreas, *type ordinaire*, was 14.3 per cent; five of eight patients who survived had had nodal metastasis, and three had had perineural metastasis. One survivor had had a Grade 3 carcinoma, and another had had a Grade 4 carcinoma resected. The length of time since pancreatoduodenectomy for the 12 patients who were considered five-year survivors ranged from 75 to 230 months. Two have since died, but not from recurrent carcinoma. The other ten patients are living normal lives, nine having gained weight.

Ten patients have been living less than three years. Fourteen have been living less than five years; recurrent carcinoma is evident in three of these patients. The remaining 68 patients died less than five years after resection; carcinoma had recurred in 66 of them.\* The median length of survival for those who died of carcinoma was 12 months. The mean length of palliation was nine months (Table 5), and seven were comfortable for more than two years.\*\*

*Carcinoma of the Papilla of Vater.*—The

\* One patient died 57 months after pancreatoduodenectomy without signs of recurrent carcinoma.

\*\* Palliation was measured from the time of recovery from the operation (usually one month afterward) to the occurrence of symptoms due to recurrent carcinoma.

five-year survival rate for the 46 patients who were eligible for study was 39.1 per cent. Two of these survivors had had high-grade lesions resected, and another two had had lymph node metastasis. Two patients later died of recurrent cancer at 72 and 109 months, whereas five have now lived more than ten years.

One patient died of a myocardial infarction 54 months after resection, with no clinical evidence of cancer. Cancer was the cause of death for 31 patients who lived less than five years, and this group had a median survival time of 15.0 months. Half of these patients were palliated for at least nine months, and four patients had three years or more of palliation before dying of recurrent carcinoma.

Thirteen patients have been living less than five years with no evidence of cancer, and one is alive with recurrent cancer.

*Cancer of the Duodenum.*—Nineteen patients were dismissed from the hospital after resection. Four are alive and free of cancer less than five years later. Five patients, all of whom had Grade 1 tumors that had not metastasized, have already lived five years; one of these was comfortable for more than 12 years before a recurrence became obvious. He died 13 years after pancreatoduodenectomy. A leiomyosarcoma had been resected in one patient who survived five years.

The median length of palliation was eight months for the ten patients who died less than five years after resection (Table 5). The median survival time was ten months.

*Carcinoma of the Common Bile Duct.*—Only one patient has lived more than five years, although three have been living more than two years without signs of malignant lesions. The five-year survivor had had a very low-grade, small papillary carcinoma resected and the lymph nodes were negative. Half of the ten patients who died of recurrent cancer obtained more than 20 months' palliation (Table 5), and they survived for a median time of 22.5 months.

For the entire series of 134 patients who underwent pancreatoduodenectomy, who were eligible for the five-year study, the five-year survival rate was 26.9 per cent (36 patients). Fifteen patients have lived for ten years (ten are still living), and five have been living 15 years after pancreatoduodenal resection. Of those operated on who were not eligible for the five-year study, 31 are living without evidence of cancer.

### Discussion

Carcinoma in the region of the papilla of Vater may occur in the relatively young patient and can be resected successfully even in the elderly. A long duration of symptoms does not necessarily indicate non-resectability since tumors that are favorable for resection are more likely to be slow growing. Although the rate of resection for carcinoma of the head of the pancreas was rather low, in retrospect, more than one third of these lesions were adherent to blood vessels and retroperitoneal tissues and, as a rule, were surgically incurable.

As much as possible of the common bile duct should be resected since carcinoma can infiltrate along the duct or the periductal lymphatic structures. The areolar and lymphatic tissues surrounding the portal structures and the celiac axis should be removed. Tissue infiltrated with cancer is less likely to be severed if hemipancreatectomy is performed.<sup>6</sup> Total pancreatectomy appears to be worthwhile when it is performed for the more differentiated multicentric cancers of the pancreas (two of the four patients survived five years).

The mortality rate for radical pancreatoduodenal resection remains high. Pancreatic fistula has always been a source of great concern and it continues to rank high in the list of causes of death. Cattell and Warren<sup>1</sup> have stressed the technical refinements to reduce this hazard and have noted (as have we) that pancreatic fistula has led directly to serious hemorrhage in cer-

tain cases. Their method of reconstruction has led to an enviably low mortality rate. A pancreatic fistula is a dangerous postoperative complication because of autodigestion of the tissues with subsequent sepsis or hemorrhage. Suturing the jejunal mucosa to the pancreatic duct, whenever this is possible, might reduce the incidence of fistula.<sup>2</sup> Because of the difficult and extensive dissection necessary to remove an adherent carcinoma of the head of the pancreas, mesenteric thrombosis and liver infarction are obvious causes of operative death in this group of patients. Meticulous technic, careful ligation of tributary vessels, and the use of vascular clamps when indicated should result in a higher operative survival rate. None of the patients who received a staged operation had hepatic or renal insufficiency, and the mortality rate for these cases was consequently lower. Perhaps a preliminary cholecystostomy should be used for more of these patients.<sup>12</sup>

Late-developing diarrhea and diabetes mellitus again were shown to be most frequent after resection of a pancreatic cancer. These also were noted more often by patients prior to operation and have been correlated on pathologic study with the more severe degree of chronic pancreatitis present in this group at the time of resection.<sup>5</sup> Although occasionally not needed until several years after operation, oral pancreatic substance<sup>7, 12</sup> will be required in large amounts by many of these patients. On the other hand, insulin requirements, even for patients who have had total pancreatectomy, have not been high.

Recurrent jaundice and cholangitis after resection are now recognized as not necessarily caused by recurrent carcinoma. Such patients deserve reexploration unless there is unmistakable evidence of recurrent cancer.<sup>3</sup> The gastric "dumping syndrome" was not a common aftermath of pancreatoduodenectomy. Adequate gastric resection and distal placement of the gastrojejunostomy could account for the low incidence of

gastrojejunal ulcer. The patient with a known ulcer diathesis will do better nutritionally with a hemigastrectomy and vagotomy than with a high gastric resection.

Careful pathologic study of 112 resected specimens from this series<sup>4, 5</sup> has shown a much higher frequency of perineural lymphatic metastasis than was found on routine examination. The study also demonstrated that half of the carcinomas of the pancreas had infiltrated the posterior margins of the specimens and the retroperitoneal tissues. About half of the carcinomas of the papilla of Vater had penetrated the duodenal wall, but the tumors of the papilla were more differentiated and seldom, if ever, had extended through the pancreas to involve the posterior margin of the resected specimen. Duodenal lesions do, on occasion, extend into the retroperitoneal tissue.

The pathologic type of the cancer as well as the site of its origin must be taken into account. The patients with islet-cell carcinomas have a much better prognosis than do those with ordinary ductal carcinomas of the pancreas, and inclusion of a greater than usual number of patients with such tumors would affect the survival rate. The presence of papillary carcinomas and of sarcomas was also noted.

The five-year survival rate for patients with cancer of the head of the pancreas was lower than that given in previous reports from this clinic. One explanation, borne out by the number of lesions that were adherent to the portal vessels, is that the surgeons have performed resection for a somewhat higher proportion of the patients in recent years. The five year survival rate was almost the same for cancer of the papilla of Vater and for cancer of the duodenum, even though patients with cancer of the duodenum were treated later in the course of their disease. Only one patient with carcinoma of the common bile duct has lived five years, but Warren and associates have reported a more favorable experience with this type of carcinoma.

Although the incidence of long-term survival after resection is decreased if the peripapillary cancer is a more anaplastic tumor or has spread to the lymph nodes, some patients have lived for five years after resection of such cancers. Pancreatoduodenectomy should not be denied to a patient solely on the basis of a high-grade lesion or of local involvement.

On the average, an additional 9 months of comfortable living had been secured for the patients who have died of recurrent cancer of the pancreas, papilla of Vater, or duodenum (Table 5). Seventeen were comfortable for two years (including six patients who had carcinoma of the pancreas), and eight had more than three years' palliation. The average length of palliation was especially satisfying after resection for carcinoma of the common duct. It should be noted that since these patients usually lived less than three months once symptoms of recurrent cancer began, the operation offered relief during most of their remaining life. When careful consideration is given to the selection of cases, radical pancreatoduodenectomy, although it is associated with a higher operative mortality rate than is a biliary-intestinal shunt, can offer palliative benefit<sup>2, 9, 10, 11</sup> to the patient, and a chance of five-year survival.

We continue to be extremely cautious about using radical resection in the obese patient. Difficulty of proper exposure and of accurate anastomoses in such cases may well influence us to accept a purely palliative procedure rather than a radical resection. The serious complications occasionally terminating fatally are definitely more frequent in the obese patient.

### Summary

A 22-year experience, 1941 through 1962, with radical pancreatoduodenectomy for cancer in the region of the papilla of Vater is presented. The 239 cases reviewed consist of 119 cases of cancer of the head of the pancreas, 77 of carcinoma of the papilla



of Vater, 25 of cancer of the duodenum, and 18 of carcinoma of the common bile duct.

The over-all hospital mortality rate was 19.2 per cent.

Operative procedures and methods of reconstruction used are tabulated, and the postoperative course and complications are discussed. Surgical pathology is briefly presented in order that survival data may be evaluated.

Except for the favorable results of resection for islet-cell carcinoma of the pancreas, prognosis could not be related to histologic type. The approximate five-year survival rates were 18 per cent for patients with cancer of the head of the pancreas, 39 per cent for those with cancer of the papilla of Vater or of the duodenum, and 11 per cent for those with carcinoma of the common bile duct. High histologic grade or lymph node or perineural metastasis did not preclude five-year survival.

Palliative benefit of resection to patients eventually succumbing to recurrent cancer is analyzed in terms of comfort rather than of survival.

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### DISCUSSION

DR. CHARLES GARDNER CHILD, III (Ann Arbor, Michigan): I am encouraged to comment upon Dr. Judd's paper by two precedents set at this meeting. These in my experience have been unique. One member admitted to this Society that an operation was difficult, and another presented a case report.

Pancreaticoduodenectomy is a difficult operation, and I wonder if this may not be one of the reasons for the pessimism about it. I am con-

vinced that this very pessimism each year deprives an unknown number of patients of a good but difficult and time-consuming operation, if not for cure of cancer at least for reasonable palliation.

My case report: Mrs. R. B., a housewife, age 41 years, was recently admitted for the first time to the University of Michigan Hospital. She gave a history of having been operated upon two weeks previously at another hospital for abdominal pain and jaundice. A mass in the head of her pancreas was declared inoperable. Her husband was unwilling that so young a woman—and a mother of