

# Evaluation of Pancreatic Biopsy \*

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## Introduction

THE DIAGNOSIS of lesions of the pancreas at the time of operation continues to present a difficult problem. Should a biopsy specimen be taken? How accurate is the diagnosis made by biopsy? What is the risk of excising a pancreatic biopsy specimen?

Many prominent surgeons believe that pancreatic biopsy should always be done prior to embarking upon radical operative procedures.<sup>6, 8, 12, 13, 15, 16</sup> Other surgeons believe that pancreatic biopsy does not give enough information to warrant the risk of specimen removal involved.<sup>3, 4, 5, 7, 14</sup> They, therefore, advocate pancreatic resection on clinical findings alone, without biopsy.

The fears of resection of a specimen for pancreatic biopsy expressed in the literature have been primarily based upon clinical experience with operations on and about the pancreas. Few reports have actually dealt with the risks and complications of the technical aspects of specimen removal alone. The present study was undertaken for this reason.

## Material and Methods

The records of 159 patients from whom pancreatic biopsy specimens were taken between 1948 and 1961 in several Denver hos-

pitals were reviewed. In most of the patients, additional procedures were performed in other areas of the gastro-intestinal tract (Table 1). Care was taken, however, to exclude all cases in which other operative procedures were performed directly on the pancreas. The cases were treated by a large number of different physicians whose experiences are fairly representative of the surgical practice of this community.

The major pancreatic ductal systems in five cadavers were injected with methylene blue through a polyethylene catheter inserted into the distal end of the duct. The ampulla of Vater was left open so that the dye would not be injected under pressure. Biopsy specimens were then taken with a Vim-Silverman needle in ten different sites of the head and body of the pancreas. This was done to demonstrate the ease with which the pancreatic ductal system could be entered. The lesions created were considered positive when methylene blue was found in the specimen core.

## Results

There were 26 deaths (16.4%) in this group of 159 patients (Table 2). In 20, the cause of death was probably not related to the pancreatic procedure. In six, complications of the pancreatic incision were considered the major factor leading to death. These six cases are summarized in Table 3. In five patients, autopsy findings clearly indicated that pancreatic leakage, or pan-

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TABLE 1. *Other Surgical Procedures—  
159 Patients*

Cholecystojejunostomy, or other bypass procedures	57
Cholecystectomy	31
Choledochotomy and exploration	25
Sphincterotomy and exploration	5
Partial gastrectomy	5
Liver biopsy	16
Gastro-enterostomy	10
Others	34
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creatitis at the operative site were the cause of death. In the sixth (Case 5), the technic was presumably the cause of death. This patient had a wedge of a pancreatic mass removed. The procedure was difficult because of poor exposure and considerable bleeding ensued. When suture ligatures failed to control bleeding, the area was packed with oxycel and the abdomen was closed with drainage. Postoperatively the clinical course was typical of acute pancreatitis, characterized by abdominal pain, vomiting, distention, and spiking fever. He succumbed on the fourth postoperative day. Unfortunately, permission for

TABLE 2. *Total Deaths in Study—  
159 Patients*

	No.	%
No. patients	159	100
No. deaths	26	16.4
Deaths from biopsy	6	3.8
Deaths from other causes	20	12.6

autopsy was not granted, so that the clinical diagnosis could not be confirmed. In view of the technical difficulties with the biopsy, the fact that no other abdominal procedure was performed, and the striking postoperative course, the procedure would appear to be the primary factor leading to death.

Two methods of obtaining biopsy specimens were used. Three deaths resulted among the 25 patients in whom Vim-Silverman needles were utilized (12%); two deaths occurred in the 130 patients who had wedges of tissue removed (1.5%); and one death occurred in four patients in whom both technics were used (Table 4).

Nine nonfatal complications occurred. There were six pancreatic fistulas; four

TABLE 3. *Details of the 6 Deaths due to Pancreatic Biopsy*

Case Age Sex	Preop. Dx.	Biopsy Dx.	Pathological Dx. at Autopsy	Cause of Death	Postop. Day of Death	Other Opera- tions	Type Biopsy
1. 62 F	Obstructive jaundice	Chronic pancreatitis	Carcinoma of common duct	Subphrenic abscess, pan- creatitis & peritonitis	20	Cholecysto- jejunostomy	Wedge
2. 69 F	Duodenal ulcer	Normal pancreas	Acute hemor- rhagic pan- creatitis	Acute hemor- rhagic pan- creatitis	1	Vagotomy & pyloroplasty	Needle (trans- duodenal)
3. 70 F	Obstructive jaundice	Severe pan- creatic fibrosis	Carcinoma of head of pan- creas	Leakage of biopsy site, peritonitis & pancreatitis	14	Cholecysto- jejunostomy	Needle
4. 28 M	Abdominal pain	Normal pancreas	Retroperitoneal abscess of pancreas	Pancreatic abscess	137	None	Needle (trans- duodenal)
5. 52 M	Perforated ulcer	Fatty infil- tration of pancreas	No autopsy	Acute pancrea- titis and hemorrhage	4	None	Wedge
6. 69 M	Obstructive jaundice	Normal pancreas	Acute pan- creatitis & fat necrosis	Acute pan- creatitis & peritonitis	5	Choledoch- jejunostomy	Wedge & Needle

closed spontaneously without further treatment; one required x-ray therapy; and one developed a pseudocyst which required a second operation. Five of these were wedge specimens, the sixth a needle specimen. The other three complications included one patient with severe hemorrhage from a wedge site which required several transfusions; one patient with peritonitis, presumably from a leak through the needle site; and one patient with acute pancreatitis whose serum amylase was over 1,000 units on the first postoperative day following wedge excision. Her pancreatitis subsided over the next few days (Table 5).

Needle samples from injected specimens demonstrated methylene blue staining in 80 per cent of random cores (Table 6). This is explained by the many ramifications of the pancreatic ductal system which extend to all portions of the pancreas. It thus becomes apparent that a needle placed anywhere in the pancreas has an excellent chance of entering the ductal system at some point.

Discussion

There are many disadvantages to the technical steps in pancreatic biopsy. In this study there were 15 complications (9.5%) with six proving fatal (3.8%). Particularly distressing was that four of the six deaths occurred in patients with benign disease, and the diagnosis was missed on biopsy in the remaining two patients who had carcinoma.

Equally important is the accuracy of such biopsies. When representative tissue is ob-

TABLE 4. *Types of Biopsy*

Type Biopsy	No. Patients	No. Deaths	%
Vim-Silverman needle	25	3	12
Wedge	130	2	1.5
Combined needle & wedge	4	1	
Totals	159	6	3.8

TABLE 5. *Nonfatal Complications in 159 Pancreatic Biopsies*

Type of Biopsy	No. Patients	No. Complications
Fistula		6
Closed spontaneously	4	
Required 2nd operation	1	
Required x-ray treatment	1	
Hemorrhage		1
Peritonitis		1
Pancreatitis		1
		9 (5.7%)
		No. Complications
		9 (5.7%)
Needle	25	2 (8%)
Wedge	130	7 (5.4%)
Combined	4	0
	159	9 (5.7%)

tained, frozen sections have been reported to be over 90 per cent accurate.<sup>15</sup> However, obtaining representative tissue is a major problem in pancreatic lesions. Pancreatic carcinoma is frequently surrounded by a zone of chronic pancreatitis, which may be more extensive than the actual neoplasm.<sup>3</sup> When the biopsy reveals carcinoma, it can usually be relied upon, although there have been occasional reports of false positives.<sup>10</sup> When the biopsy reveals chronic pancreatitis, the diagnosis of carcinoma has not been ruled out. The incidence of false negative diagnoses varies from 12 to 54 per cent, averaging 35 per cent (Table 7). But, as Warren and Cattell<sup>17</sup> have pointed

TABLE 6. *Needle Biopsies in Injected Specimens\**

Cadaver No.	No. Positive Biopsies	% Positive Biopsies
1	6	60
2	9	90
3	9	90
4	7	70
5	9	90
Average	8	80

\* Ten needle specimens were taken from each of five fresh human pancreases whose major duct was injected with methylene blue.

TABLE 7. *Pancreatic Carcinoma—Missed on Biopsy*

Author	No. Cases of Carcinoma	No. Cases Not Diagnosed	% Error
Cote <sup>6</sup>	53	Needle—17	32
Cote <sup>6</sup>	56	Wedge—30	54
Spjut & Ramos <sup>15</sup>	52	Wedge—6	12
Probstein <sup>14</sup>	21	11	52
	182	64	35

out, most of these reports include large numbers of patients whose lesions were clinically unresectable due to extension. If only small, resectable lesions were considered, the incidence of false negative biopsies would probably be higher.

When Kirtland<sup>9</sup> described the Vim-Silverman needle for pancreatic biopsy specimens in 1951, it was hoped that this would provide more representative samples, and decrease the incidence of false negatives. Although this has helped in a few cases, it has not lived up to expectations. Cote,<sup>6</sup> comparing the needle and wedge technic in patients with pancreatic carcinoma, found the wedges failed to reveal the carcinoma in 54 per cent, while the Vim-Silverman needle missed the diagnosis in 32 per cent (Table 6).

Other theoretical advantages of needle over wedge specimens include less chance of pancreatic fistula and pancreatitis, since the needle tract is small, and should seal over. Our experiences, however, do not bear this out. There were at least three deaths in 25 patients thought to be directly related to the needle technic and two more patients with serious complications. As experiments in the injected pancreases showed, the pancreatic duct system is usually entered with a needle. If the pancreatic duct is obstructed, there is a pathway through which pancreatic juice may escape. If it goes through the pancreas, a fistula will develop. However, it is also pos-

sible for juice to leak into gland substance without reaching the free peritoneal cavity. In this case, diffuse pancreatitis can develop. It is this complication which makes transduodenal needle aspiration risky. Although a fistulous tract would empty into the duodenum, and present few difficulties, diffuse pancreatitis cannot be prevented. Indeed, this was probably the mechanism of death in Cases 2 and 4, in both of which the transduodenal technic was used. Case 2 died 24 hours later of acute necrotizing pancreatitis; Case 4 died four months later, with pancreatitis and pancreatic abscesses.

With these shortcomings in mind, what then are the indications and contra-indications for pancreatic biopsy?

No specimen should be removed from patients with an obvious explanation for pancreatic masses, such as an associated duodenal ulcer. Biopsy is contra-indicated in patients with unresectable lesions. Although it is of some value to be able to make a definitive diagnosis, the complication and mortality rates are too high to justify biopsy for diagnostic purposes only. Frequently a liver nodule, or common duct lymph node can be removed instead to provide the same information.

Biopsy is not necessary in resectable lesions that clinically appear to be carcinoma. The clinical characteristics of peri-ampullary carcinoma are a dilated common bile duct, a firm, hard, discrete mass in the head of the pancreas in the region of the common bile duct, and a palpable, dilated pancreatic duct. When these clinical features are present, one is justified in proceeding with pancreaticoduodenectomy without removing a biopsy specimen. In such a lesion the incidence of false negative biopsies is so high (over 35%) that many surgeons believe a negative biopsy is valueless. Therefore, if a resection is to be done regardless of the biopsy report, one only wastes time and perhaps spreads the neoplasm. Using these criteria without the aid

of biopsy, Warren and Cattell<sup>17</sup> did pancreaticoduodenectomies for benign disease in six of a series of 218 patients. Thus, clinical judgment was in error in less than 3 per cent of cases.

The only time biopsy is indicated is in the case of a clinically resectable lesion which does not have the malignant characteristics of a dilated common bile duct or pancreatic duct.

The technic of specimen removal is also important. The duodenum or common bile duct should be opened first. If an obvious tumor is present, a wedge can be removed. If no tumor is seen in the ampullary region, scrapings of the common duct, with a scoop, may yield positive tissue. If these have failed, one is then justified in either excising a wedge, or a needle core of tissue directly from the mass.

### Summary

A review of 159 patients undergoing removal of a pancreatic biopsy specimen revealed a complication rate of 9.5 per cent with a mortality rate of 3.8 per cent.

There were three deaths in 25 needle procedures, two deaths in 130 wedge procedures, and one death in four combined needle and wedge procedures.

The accuracy of pancreatic biopsy is poor (averaging about 65%), because it is difficult to obtain representative tissue.

For these reasons, pancreatic biopsy specimens should not be removed indiscriminately. Biopsy specimens should not be taken for unresectable lesions, nor for resectable lesions which clinically appear to be carcinoma. Biopsy of the pancreas should be reserved for those resectable lesions which do not have the obvious features of neoplasm.

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