Cystadenoma and Cystadenocarcinoma of the Pancreas *

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IT IS not generally appreciated that at least 10 per cent of pancreatic cysts are actually primary cystic neoplasms. During the 27-year period from 1938 through 1964, 117 patients with proved pancreatic cysts were observed in four New Orleans hospitals. There were 86 pseudocysts, 13 retention cysts, three congenital cysts, and 15 neoplastic cysts (Table 1). Eleven cystadenomas, two cystadenocarcinomas, one cystic leiomyosarcoma, and one cystic rhabdomyosarcoma comprised the neoplastic cysts (Table 2) and accounted for 12.8 per cent of the entire series. This report is concerned with an analysis of our cases of cystadenoma and cystadenocarcinoma and reviews the published experience of others.

Cystadenoma

In 1951, Mozan [36] published an excellent review of the literature of cystadenoma of the pancreas; he discussed 49 firmly documented cases, including one of his own. Since then 104 other cases have been reported,** making a total of 153. With the addition of our 11 cases there are at least 164 recorded cases.

The 11 cases in this series are analyzed in Table 3; these, combined with the 104 cases reported since Mozan's review, comprise a total of 115 cases upon which the ensuing discussion is based. Unfortunately there was great variation in the degree of detail among the various case reports. The per cent of the total number of patients with a given finding, when that information is available, is listed.

Incidence

Cystadenoma is a benign, neoplastic cyst of such rarity that during the past 27 years only seven cases have been recognized among 2,182,427 admissions to Charity Hospital in New Orleans. Frantz [14] reported that among 23,551 surgical specimens at the Presbyterian Hospital in New York there were only ten cystadenomas. Mahorner and Mattson [32] found that there were only two cystadenomas among 108 cases of pancreatic cyst seen at the Mayo Clinic.

Age

These tumors occur at an earlier age than carcinoma of the pancreas, with the highest incidence in the fifth and sixth decades (Fig. 1). One third of the patients were younger than 50 years of age; the youngest was 13 years old and the oldest 83. Almost three fourths of the patients were less than 60 years of age.

Sex

There was a striking predominance of females among the patients with pancreatic

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** 1, 3–6, 8, 9, 12–15, 17, 20–22, 25–28, 30, 34, 38, 40–45, 50, 54–57, 59, 62.

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TABLE 1. *Varieties of Pancreatic Cyst*

	No.	%
Pseudocyst	86	73.4
Retention	13	11.1
Congenital	3	2.7
Neoplastic	15	12.8
Total	117	100.0

TABLE 2. *Neoplastic Cysts of Pancreas*

	No. Cases
Cystadenoma	11
Cystadenocarcinoma	2
Cystic leiomyosarcoma	1
Cystic rhabdomyosarcoma	1
Total	15

cystadenoma (Fig. 2); females outnumbered males by about nine to one.

Pathology

Probably because cystadenomas of the pancreas represent a group of neoplasms of diverse histogenetic origins, gross and microscopic descriptions have been quite varied. Mozan's [36] excellent description of pathologic features includes all types of cystadenomas described; they have varied from very small to huge, filling much of the abdominal cavity. Fibrous or myxoid septa divide these neoplasms into either large- or small-loculated forms. Gross papillary projections may or may not be present. The contents of the cysts may be serous or mucoid. Microscopically the lining epithelium may be flat, cuboidal or tall columnar. Stromal calcification was noted in 18 per cent of Mozan's collected cases but was mentioned in about 10 per cent of more recent cases. Despite the wide variety of gross and histologic appearances, one form of cystadenoma is recognizably distinct; it is multiloculated, without gross papillary formations, usually comprised of a honeycomb of small cysts lined by a very characteristic flat or cuboidal epithelium, and is remarkably similar from patient to patient in published cases and in our series. We believe that it is important to differentiate this group from the remainder of cystadenomas lined by tall columnar epithelium because of very practical considerations regarding malignant potential.

Size of the tumors is listed in Table 4; nearly one half of those recorded were larger than 10 cm.

Cystadenoma may occur anywhere in the pancreas, but there is a striking predominance of distal glandular involvement (Fig. 3). Although the lesion involved the head, to some extent, in one third of 81 cases in which the site of origin was noted, it was confined to the head in only 18 per cent.

Aberrant pancreatic tissue is subject to the same disease processes as is normal pancreas, but we could find no proved case of cystadenoma arising in heterotopic pancreatic tissue.

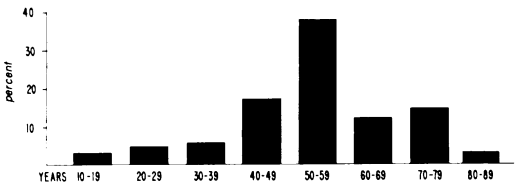

FIG. 1. Age incidence in pancreatic cystadenoma in collected series (not listed in 15 cases).

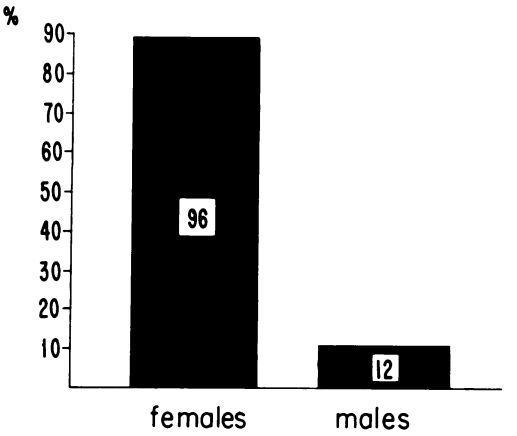

FIG. 2. Sex incidence in pancreatic cystadenoma in collected series (not listed in 7 cases).

TABLE 3. *Analysis of 11 Cases of Cystadenoma of Pancreas (Authors' Series)*

Case	Age, Sex	Clinical Features	X-Ray	Site & Size of Tumor	Operation	Result	Pathology
1	46 F	Abdominal pain, mass—6 yr., L.U.Q. mass	Stomach displaced anteriorly & to left; left kidney pushed superiorly & mesially	Tail 10 cm.	Excision tumor along with tail & spleen	Well 6 yr. later	Tall columnar epithelium of large pancreatic duct type, benign.
2	70 F	Abdominal pain—1 yr., mass in epigastrium	Calcification in L.U.Q.; stomach displaced anteriorly	Body & tail 20 cm.	Distal sub-total pancreatectomy	Did well 14 da., then disrupted wound; died 48 hr. after secondary closure	Low cuboidal to flattened epithelium resembling centroacinar cells, benign.
3	53 F	None related to cystadenoma	Cholelithiasis; stomach displaced superiorly and anteriorly	Body & tail 7 cm.	Distal subtotal pancreatectomy	Reoperation 5 mo. later for pseudocyst; well 10 yrs. later	Low cuboidal to flattened epithelium resembling centroacinar cells, benign.
4	25 F	Nausea, vomiting, indigestion, mass —8 wks., L.U.Q. mass	Mass; distortion superior pole rt. kidney; perirenal air insufflation showed mass, separate from kidney & spleen; stomach had greater curvature filling defect; splenic flexure pushed inferiorly	Head & body 20 cm.	Distal sub-total pancreatectomy, splenectomy	Well 10 yr.	Tall columnar epithelium & gland formation resembling intestinal epithelium, benign.
5	32 F	None related to pancreas; hypertension	Stomach, splenic flexure, left kidney & ureter displaced; diagnosis: renal tumor	Tail 11 cm.	Excision tumor, tail of pancreas & spleen thru flank incision	Well 1 yr.	Tall columnar epithelium resembling large pancreatic duct, benign.
6	43 F	Abdominal pain & mass—3 yr. L.U.Q. mass	Stomach displaced superiorly & anteriorly; transverse colon pushed inferiorly	Body & tail 25 cm.	Marsupialization & partial excision	Well 5 yr.	Tall columnar epithelium resembling large pancreatic duct epithelium, benign.
7	72 F	Epigastric mass	Stomach displaced anteriorly & to left	Head & body 10 cm.	Biopsy tumor head of pancreas & gastroenterostomy 1953 for what was considered inoperable carcinoma head of pancreas; reoperation & & biopsy tumor 1959	Mass persists, but patient asymptomatic 10 yr. after first operation & 4 yr. after second one	Low cuboidal to flattened epithelium resembling centroacinar cells; histological appearance identical 6 yr. later
8	74 F	None	None	Tail 10 cm.	None	Died; cystadenoma was incidental autopsy finding	Low cuboidal to flattened epithelium resembling centroacinar cells, benign.
9	56 F	None	None	Body 10 cm.	None	Died; tumor incidental necropsy finding	Low cuboidal to flattened epithelium resembling centroacinar cells, benign.
10	60 M	None	None	Head 1.5 cm.	None	Died; tumor was incidental autopsy finding	Mixed type of tumor with cysts lined by low cuboidal to flattened epithelium, benign, with mixtures of islet tissue in stroma.
11	67 M	None	None	Body	None	Died; tumor was incidental autopsy finding	Low cuboidal to flattened epithelium resembling centroacinar cells, benign.

TABLE 4. *Pancreatic Cystadenoma: Size of Tumor*

Diameter of Tumor (cm.)	No. Cases	% Cases
0–5	10	12.9
6–10	30	38.9
11–15	21	27.3
16–20	7	9.1
>20	9	11.7
Total	77*	

* Not recorded in 38 cases.

Clinical Features

Clinical manifestations of pancreatic cystadenoma are not sufficiently distinctive to permit a precise preoperative diagnosis or to warrant detailed description; they are essentially those of pancreatic cysts in general. When symptoms occur, they are largely the result of pressure on contiguous structures by the slowly enlarging pancreatic tumor.

The average duration of symptoms was approximately 18 months; more than one third of the patients had symptoms for more than 24 months before diagnosis was established.

Dyspepsia was present in almost three fourths of the patients; pain was the chief complaint in one half. Pain was rarely severe, appearing almost always in the left upper quadrant or epigastrium, with infrequent radiation to the back. The clinical picture was occasionally complicated by evidence of duodenal or gastric ulceration with hematemesis.[9, 45, 54] Splenic vein occlusion with splenomegaly, edema and ascites was an occasional complication of a large, distally-placed mass encroaching upon the splenic pedicle.[3, 30, 56] Associated biliary tract disease was noted in 12 per cent of cases. Jaundice was uncommon because of the infrequency with which the tumor arose from the pancreatic head; it actually was observed in only three [4, 6, 41] of 28 cases of pancreatic head involvement. Diabetes mellitus was present in 8 per cent of cases.

Eighty-five per cent of patients presented with a palpable abdominal mass which apparently had been discovered by the patient in almost half the cases. The mass was almost invariably situated in the left upper quadrant or epigastrium; was apt to be firm, nontender, round, occasionally nodular; and was mobile in more than one half the cases.

Roentgenographic Features

Roentgenography was a particularly useful diagnostic procedure. In conjunction with physical examination, x-rays frequently

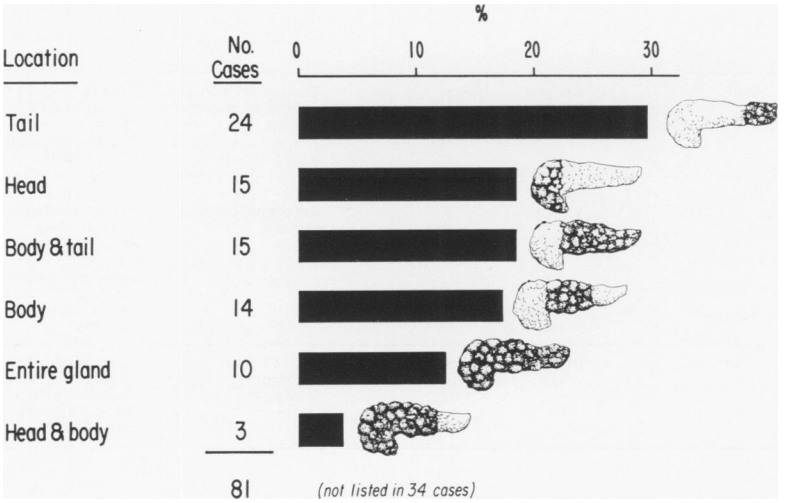

FIG. 3. Pancreatic cystadenoma: location of tumor.

TABLE 5. *Cystadenoma of the Pancreas: Types of Operation Performed in 71 Patients*

Operation	No. Cases	% Cases	Deaths	Residual Tumor
Local excision	25	33.9	0	0
Distal subtotal pancreatectomy	18	24.3	1	0
Pancreatoduodenectomy	10	13.5	1	0
Marsupialization	9	12.2	0	5
Excision tail of pancreas	7	9.4	0	0
Laparotomy and biopsy with or without "by-pass" procedure	5	6.7	0	5
Total	74*	100.0	2	10

* Three patients had two operations for cystadenoma.

prompted the preoperative prediction of pancreatic tumor, but never a precise diagnosis of cystadenoma.

A plain x-ray film of the abdomen disclosed the mass in 11 of the 20 cases in which the examination was done. Either stromal or capsular calcification appeared in about 10 per cent of cases.

Barium x-ray studies of the upper gastrointestinal tract revealed varying degrees of compression or displacement of the stomach in 34 cases (68%) and of the duodenum in 11 (20%). Extrinsic pressure from the cyst resulted in both gastric and duodenal displacement in five of 50 patients examined. Displacement or compression of the colon or both, usually of the splenic flexure, was demonstrated by barium enema x-ray in 16 of 30 patients examined. Because of a tendency to arise from the tail or body of the pancreas, the tumor was prone to displace the left kidney. This was evident in ten of 15 patients having pyelographic studies. Two tumors were removed through a left flank incision by urologic surgeons. Only one instance of distortion of the right kidney was observed (authors' Case 4).

Aortography, splenoportography and radioisotope scanning technics have been utilized in the demonstration of pancreatic neoplasms; specific angiographic features of cystadenoma have been described.[6, 43, 54]

These neoplastic cysts rarely reach sufficient size to elevate the left hemidiaphragm, and no instance of mediastinal extension has come to our attention.

Treatment

Total excision is the ideal treatment for pancreatic cystadenoma because it is a true neoplasm which probably possesses malignant potential. Complete extirpation usually can be accomplished with ease and safety because the tumor is frequently derived from the distal portion of the gland and because of the rarity with which it is bound to adjacent structures by inflammatory and fibrous reaction.

In 16 cases the neoplasm was found after death from other causes. It was recognized and treated surgically in 99 (86%) cases, but only 71 reports (representing 74 operations) included adequate clinical information (Table 5).

Only laparotomy and biopsy were accomplished in three cases[20, 41] in which excision was considered impossible or unwise. A fourth patient,[41] with a large tumor involving the superior mesenteric vessels and obstructing the common bile duct and duodenum, was managed by biopsy, choledochojejunostomy and gastrojejunostomy. These four patients remained in good health for 1, 3, 5 and 15 years, respectively. In our Case 7 laparotomy and an inconclusive biopsy were performed for what was thought to be an inoperable carcinoma of

the head and body of the pancreas. Reoperation and biopsy 6 years later revealed a benign cystadenoma; the patient remains in good health 10 years after the original operation.

Nine patients were treated by marsupialization, with or without partial excision, with early satisfactory results in four. Of the remaining five, one [62] had a persistent fistula 10 years later, one [44] required partial pancreatectomy 6 years later for pancreatic fistula, one [50] experienced a recurrence after 9 months of drainage and was cured by distal pancreatectomy, one [41] had recurrence at last report and one [8] drained for 9 years and finally developed cystadenocarcinoma from which she died. These poor results from marsupialization are not surprising because cystadenoma is composed of many separate cystic spaces which cannot be adequately drained. Also spaces are lined by epithelium capable of continued secretion and perpetuation of the fistula. Although internal drainage would prevent the external pancreatic fistula, it would not solve the problems of inadequate decompression and possible malignant degeneration. We know of no instance in which a cystadenoma has been treated in this manner, but it might be a palliative procedure in the occasional nonresectable lesion which was predominantly cystic.

The most popular operation has been excision of the tumor along with a limited amount of adjacent pancreatic tissue, and recorded results have been excellent. Of 25 patients treated in this manner, none died or had a recurrence. Temporary pancreatic fistula occurred in three [1, 22, 30] and postoperative pancreatitis in one.[17]

In 18 cases the lesion was so situated as to require resection of the body and tail of the pancreas for complete extirpation. One of these patients (authors' Case 3) later developed a pseudocyst requiring operation. Another (authors' Case 2) suffered a wound dehiscence 2 weeks after subtotal pancreatectomy and died following secondary suture of the wound. One patient underwent subtotal distal pancreatectomy for what was histologically considered as benign cystadenoma. However, 8 years later she developed a recurrence which at laparotomy proved to be a huge cystadenocarcinoma, ultimately fatal.[42]

Resection of the tumor along with the tail of the pancreas was the chosen procedure seven times, without recurrence or fatality.

Pancreatoduodenectomy was performed in ten cases in which the lesion involved the head of the pancreas. One patient died of shock 48 hours after operation.[20] In some cases the lesion could be removed only by pancreatoduodenectomy; in others gross characteristics of the tumor led to the belief that the radical procedure was being done for carcinoma, and the true diagnosis was not suspected.

Splenectomy was done in conjunction with varying degrees of pancreatic resection in 13 cases.

Thus, total excision was ultimately accomplished in 60 of 71 patients about whom adequate operative data are available. There were two deaths, a mortality rate of 2.8 per cent. The one patient reported with recurrence 8 years following what was considered to be complete extirpation proved at reoperation to have cystadenocarcinoma from which she ultimately died.[42]

It must be emphasized that follow-up data are lacking in some cases and so meager in others that definite conclusions regarding long-range therapeutic results are impossible.

Cystadenocarcinoma

Cystadenocarcinoma of the pancreas has been the subject of several reviews,[11, 12, 21, 24, 29, 48, 50] one of the most recent by Cullen *et al.*[12] who added 17 cases to 25 previously

TABLE 6. *Cystadenocarcinoma of Pancreas: Analysis of 65 Collected Cases*

Case	Author Year	Age, Sex	Clinical Features	Site & Size of Tumor	Operation	Pathology	Result
1	Kaufmann[23] 1929	42 F		Tail 8 cm.	None	Autopsy: papillary cystadenocarcinoma tail of pancreas with splenic invasion. Hepatic & omental metastases.	Died
2	Lichtenstein[29] 1934	44 F	Splenomegaly 6 yr.; abdominal pain 3 yr; edema of feet; mass left hypochondrium	Tail 10 cm.	None	Autopsy: cystic mass contained 500 cc chocolate fluid. Papillary ingrowths into cyst cavity. Hepatic metastases.	Died 6 yr. after onset of illness
3	Patel[39] 1935	44 M	Epigastric pain, weight loss, indigestion, abdominal distention & mass	15 cm.	Marsupialization	Cyst contained 3,000 cc. fluid. Solid mass in cyst wall. Papillary cystadenocarcinoma.	Died 4th day
4	Baehr & Klemperer[2] 1936	39 F	Abdominal pain for 2 yr.; weight loss, vomiting, fever, mass left hypochondrium	Body 10 cm.	None	Autopsy: cyst contained 750 cc. fluid. Papillary excrescences cyst wall. Multilocular. Papillary cystadenocarcinoma with lymph node metastasis.	Died 2 yr., 10 mo. after onset of symptons
5	Young[61] 1937	39 M	Abdominal swelling & 30 lb. wt. loss—4 yr.; mass L.U.Q.	Body	Marsupialization & partial excision; biopsy sinus tract—7 yr. later	Initial report cystadenocarcinoma. Biopsy sinus tract 7 yr. later shows cystadenocarcinoma.	Died 7 yr. later
6	Kennard[24] 1941	40 F	Swelling lower abdomen 4 yr.; huge mass filling lower 2/3 of abdomen	Body 15 cm.	Local excision	Cyst contained thick, brown fluid. Cystadenocarcinoma.	Well 10 mo. later
7	Hartz & van der Sar[19] 1946	56 F	Pain & weight loss —7 mo.; emaciation; nodular hepatomegaly	Tail 6 cm.	None	Autopsy: cystadenocarcinoma. Lymph node metastasis.	Died 8 mo. after onset of illness
8	Burk & Hill[7] 1952	39 F	Mass & pain—8 mo.; mass L.U.Q.	Body 18 cm.	Local excision	Multiloculated cyst contained 1,000 cc. gray, dark fluid. Papillary excrescences in wall. Columnar cell cystadenocarcinoma.	Well 3 yr. later
9	Sawyer *et al.*[50] 1952	58 F	Pain—abdomen & back, bloating, weakness—2 yr.; mass L.U.Q.	Body 10 cm.	Distal subtotal pancreatectomy & splencectomy	Thick, yellow-brown fluid in cyst. Papillary cystadenocarcinoma.	Reoperation 8 wk. later revealed massive recurrence & metastasis. Died postop.
10	Cattell & Warren[10] 1953	51 F	Epigastric pain—3 yr.; mass L.U.Q. —6 mo.	Body 12 cm.	Biopsy; cyst-jejunostomy	Biopsy inoperable cystic mass showed papillary cystadenocarcinoma.	Alive but deteriorating 2 yr. later
11	Cattell & Warren[10] 1953	38 F	Pain; recurrent mass after previous marsupialization	Body & tail 12 cm.	Distal subtotal pancreatectomy; splenectomy	Papillary cystadenocarcinoma.	Well 2 yr. later
12	Cattell & Warren[10] 1953	48 F	Marsupialization 3 yr. earlier; persistent fistula; L.U.Q. mass	Body & tail 12 cm.	Distal subtotal pancreatectomy	Multiloculated cyst. Polypoid projections into cyst spaces. Cystadenocarcinoma.	Well 6 mos. later
13	Cattell & Warren[10] 1953	49 M	Pain in abdomen & back for 3 mo., wt. loss, diabetes; L.U.Q. mass	Body 14 cm.	Excision	No pathologic report on cyst wall. Adenocarcinoma in biopsy of abdominal wall later.	Returned 4 mo. later with jaundice & adenocarcinoma in scar

TABLE 6.—*Continued*

Case	Author Year	Age, Sex	Clinical Features	Site & Size of Tumor	Operation	Pathology	Result
14	Willis[60] 1953	45 F	L.U.Q. mass—2 yr.	Tail	Aspiration & biopsy	Autopsy: cyst containing turbid brown fluid & papillary growths. Metastasis to regional nodes, kidney, liver, lungs. Papillary cystadenocarcinoma.	Died in postop. period
15	Mahaffey[31] *et al.* 1954	68 M	Nausea, vomiting, pain—R.U.Q.—3 wk.; jaundice & hepatomegaly	Head 8 cm.	Choledochojejunostomy, gastrojejunostomy & marsupialization	Cystadenocarcinoma.	Persistent fistula. Died 6 yr. postop.
16	Mason *et al.*[33] 1954	64 F	Nausea, vomiting, R.U.Q. pain —3 wk.	Body 5 cm.	Excision	Multilocular cyst with papillary excrescences. Cystadenocarcinoma.	Well 1 yr. postop.
17	Sommers & Meissner[53] 1954			Head 1 cm.		Papillary cystadenocarcinoma.	
18	Sommers & Meissner[53] 1954			Tail 5 cm.		Papillary cystadenocarcinoma.	
19	Rowe[47] 1956	47 F	Mobile, nontender mass L.U.Q.—1 mo.	Tail 15 cm.	Distal subtotal pancreatectomy	Multilocular cyst with brown mucoid fluid. Smooth areas & papillary area; cystadenocarcinoma.	Doing well at time of report.
20	Byrd *et al.*[8] 1956	54 F	Draining sinus L.U.Q. since marsupialization cystadenoma 9 yr. ago; bloody drainage & multiple nodules in scar 8 wk.; 12 cm. mass L.U.Q.	Body	Biopsy skin nodule at edge sinus tract	Papillary adenocarcinoma.	Died
21	Gwynne & Wilson[16] 1957	45 F	Progressive ascites for 2 yr.; pain & vomiting; L.U.Q. mass	Body 7 cm.	1) Biopsy 2) Excision 3 wk. later	Papillary cystadenocarcinoma.	Well 3½ yr. postop.
22	Rosman[46] 1958	47 F	Abdominal & back pain—2 mo.; mass for 1 mo.; splenomegaly	Tail 11 cm.	Distal subtotal pancreatectomy	Cyst & large spleen from splenic vein compression. Papillary cystadenocarcinoma.	Well for 9 yr.
23	Rutledge & Lischer[48] 1958	26 F	L.U.Q. nontender abdominal mass—2 yr.	Tail 18 cm.	Distal subtotal pancreatectomy	Mutiloculated cyst with nodule in wall. Papillary cystadenocarcinoma.	Died 1 yr. postop. from cerebral metastasis
24	Mergl & Jiran[35] 1958	49 F	Abdominal swelling —1yr.; hemorrhagic shock following fall on abdomen	Tail 25 cm.	1) Marsupialization 2) Distal subtotal pancreatectomy 3½ mo. later	1,540 Gm. cyst filled with papillary growths & 1,000 cc. dark, bloody fluid.	Well 20 mo. later
25	Cornes & Azzopardi[11] 1959	36 F	Indigestion for 12 yr.; firm mass, L.U.Q.	Body 8 cm.	Distal subtotal pancreatectomy	Multiloculated calcified cyst with papillary projections. Papillary cystadenocarcinoma.	Became jaundiced; re-explored 1 mo. postop; died 36 hr. later

TABLE 6.—*Continued*

Case	Author Year	Age, Sex	Clinical Features	Site & Size of Tumor	Operation	Pathology	Result
26	Cornes & Azzopardi[11] 1959	69 F	Indigestion for 3 mo. with epigastric & back pain; mass, L.U.Q.	Tail 13 cm.	None	Autopsy: unilocular cyst with thick grey mucinous fluid. Papillary adenocarcinoma with metastases to liver, lungs, kidneys, diaphragm, vertebra.	Died 4 wk. after admission.
27	Ducloux & Martinez[13] 1959	30 M	R.U.Q. pain; mass R.U.Q. and flank	Head 12 cm.	Marsupialization	Cyst containing cloudy, purulent fluid. Cystadenocarcinoma	Persistent fistula; developed duodenal obstruction 10 yr. postop.; reop. & well 3 yr. postop.
28	Ducloux & Martinez[13] 1959	70 F	Mass epigastrium—6 yr.	Body & tail	Distal subtotal pancreatectomy & sphincterotomy	Cyst contents: 2½ L. of brown fluid. Papillary cystadenocarcinoma.	Died 18 hr. postop. from hemorrhage
29	Ayella & Howard[1] 1960	53 M	Epigastric discomfort for many years	Head	Biopsy	Cystadenocarcinoma	5 mo. survival
30	Howard & Jordan[21] 1960	69 M	Epigastric pain—9 mo.; melena, hematemesis; large mass, L.U.Q.	Head 12 cm.	Pancreaticoduodenal resection en bloc with transverse colon	Multiloculated cystadenocarcinoma	Died 3 mo. postop.
31	Probstein[42] 1960	32 F	L.U.Q. pain, nausea, vomiting; L.U.Q. mass	Body & tail 25 cm.	1) Local excision 2) Partial excision & marsupialization of recurrence 8 yr. later 3) Biopsy of fistula 4) After irradiation & hemorrhage, radical distal subtotal pancreatectomy	1) Non-papillary cystadenoma 2) Papillary formation, no definite malignancy 3) Adenocarcinoma 4) Cystadenocarcinoma	Died of recurrence several months after radical resection; 10 yr. after 1st operation for cystadenoma
32	Scalvani[51] 1960	62 F	L.U.Q. pain, anorexia, weight loss, fever; L.U.Q. mass	Tail 10 cm.	1) Excision & splenectomy 2) Biopsy 5 mo. later	1) Cyst lined with columnar cells 2) Papillary adenocarcinoma	Recurrent mass 5 mo. after excision; died 7 mo. after initial operation
33	Shulman *et al.*[52] 1961	63 M	R.U.Q. pain, distention, wt. loss; R.U.Q. mass	Head & body 20 cm	Cystojejunostomy	Biopsy of papillary projections: cystadenocarcinoma	Survived 5 yr., 10 mo.
34	Campbell & Cruickshank[9] 1962	48 F	Fistula recurrence, skin metastasis 4 yr. postop.; marsupialization cystadenoma	Tail 9 cm.	Distal subtotal pancreatectomy *en bloc* with fistula	Cystadenocarcinoma	Died from embolus in postop. period.
35	Campbell & Cruickshank[9] 1963	73 F	Mass, L.U.Q. with abcess formation	Tail	Drainage of abcess	Autopsy: cystadenocarcinoma of pancreas invading colon	Died in postop. period from pulmonary embolus
36	Campbell Cruickshank[9] 1962	47 F	Epigastric mass, multiple superficial nodules		Biopsy of skin nodule	Autopsy: areas in cyst wall smooth; others, poorly differentiated and malignant. Cystadenocarcinoma.	Died in hospital

TABLE 6.—*Continued*

Case	Author Year	Age, Sex	Clinical Features	Site & Size of Tumor	Operation	Pathology	Result
37	Mozes & Bogokowsky[37] 1963	15 F	Epigastric pain; L.U.Q. mass for 3 mo.	Tail 14 cm.	Local excision	Blood-filled cyst with red vegetations in lining. Cystadenocarcinoma.	Discharged 12 da. postop.
38 thru 54	Cullen *et al.*[12] 1963	4th:2* 5th:3 6th:3 7th:7 8th:2 F: 13 M:4	Symptomatic (pain, mass): 16 Asymptomatic: 1 Duration symptoms: 1 wk.—15yr. L.U.Q. mass: 8 Epigastric mass: 3 R.U.Q. mass: 2	Body: 4 Head: 3 Tail: 3 H-B-T: 3 B & T: 2 H & B: 1 5–24 cm. Av.: 12 cm.	1) Local excision: 7 3) Marsupialization: 2 4) Biopsy with or without bypass: 2 5) Total pancreatectomy: 1 6) Distal subtotal pancreatectomy: 1 7) Autopsy only: 1	Cystadenocarcinoma	4 patients apparent "5-yr. cures"
55	Vernhet[58] 1963	65 M	Abdominal pain, indigestion, anorexia for 18 mo.	Body & tail 9 cm.	Distal subtotal pancreatectomy, total gastrectomy	Papillary cystadenocarcinoma of pancreas. Adenocarcinoma of stomach, separate lesions.	Well 11 mo. postop.
56 thru 63	Warren *et al.*[59] 1964		(8 cases recorded in addition to those previously reported by Cattell & Warren)		1) Biopsy only: 1 2) Excision: 1 3) Distal subtotal pancreatectomy: 2 4) Whipple: 1 5) Total pancreatectomy: 1 6) External drainage: 2	Cystadenocarcinoma	
64	Becker *et al.* Present series)	23 F	Abdominal swelling for 1 yr., vomiting 6 da.; L.U.Q. mass	Tail 20 cm.	Distal subtotal pancreatectomy; splenectomy	Cystadenocarcinoma	Well 7 yr. later
65	Becker *et al.* (Present series)	53 F	Abdominal pain, wt. loss; mass, L.U.Q.	Body 20 cm.	1) Cystojejunostomy 2) Exploration & biopsy 2 mo. later	1) Cystadenoma (papillary)? 2) Cystadenocarcinoma	1) Febrile course 2) Died after 2nd operation

* First column, decade; second column, no. patients.

reported cases. We found 21 others * and add two of our own, thus making a total of at least 65 cases recorded in the literature (Table 6).

Pancreatic cystadenocarcinoma appears to be about one half as common as benign cystadenoma. Only two cases have been recognized at Charity Hospital among 2,182,427 admissions.

This malignant tumor occurs at an earlier age than the conventional solid pancreatic carcinoma; almost one half the patients were less than 50 years of age; the range was between 18 and 76 years; distribution by decades is indicated in Table 7. About three fourths (76%) of the patients were women.

Grossly, cystadenocarcinomas resemble their benign counterparts; however, visible papillary formations are more commonly found in malignant cysts. In the absence of

* 8, 9, 13, 21, 31, 35, 39, 51, 57, 58, 59.

distant metastasis or obvious invasion of contiguous structures, the lesion can be diagnosed only by histologic examination. It is impressive that in the majority of reported cases and in both our cases, areas of pre-existing benign components lined by a tall columnar epithelium have been recognized, indicative of probable origin from a pre-existing benign cystadenoma of the tall columnar type.

Clinical and roentgenographic manifestations of cystadenocarcinoma (65 cases) are similar to those of cystadenoma (Table 6).

Table 8 records the principal operations employed in 56 surgically treated patients. Of 38 from whom the tumor was removed, 15 were treated by extirpation of the cyst plus a rim of adjacent pancreatic tissue; 16 had distal subtotal pancreatectomy; five had pancreatoduodenal resection; and total pancreatectomy was performed in two. Marsupialization was the procedure in eight cases, and internal drainage in three. In only seven instances biopsy, with or without by-pass procedure, was accomplished.

Although statistically valid data relative to therapeutic results are not available, a sufficient number of patients with cystadenocarcinoma have been followed for impressions to be established. Occasionally the tumor is rapidly fatal; but more often the course is slowly progressive, with a tendency to remain localized for long periods even after attaining a large size. The lesion is more amenable to surgical treatment than is the conventional solid pancreatic carcinoma.

Discussion

The frequency with which pancreatic cysts are actually either cystic primary neoplasms or cysts secondary to a proximal malignant tumor has not received sufficient emphasis. Warren *et al.*[59] recently reported that of 148 pancreatic cysts observed at the Lahey Clinic there were six cystadenomas,

TABLE 7. *Age Distribution by Decades in Collected Cases of Cystadenocarcinoma of Pancreas*

Years	Cases
0–9	0
10–19	1
20–29	2
30–39	9
40–49	16
50–59	9
60–69	14
70–79	4
Total	55*

* Age not listed in ten cases.

12 cystadenocarcinomas and four cysts complicating proximal primary carcinoma. Piper *et al.*[41] indicated that cystadenomas and cystadenocarcinomas comprised 18.9 per cent of the pancreatic cysts encountered at the Mayo Clinic. The choice of operation for any type of pancreatic cyst is dependent upon the specific etiologic or pathologic type of cyst present. Although it is not always possible to differentiate types of pancreatic cysts, cystadenomata or cystadenocarcinomata should be suspected in women with large, nodular, multicystic, movable, relatively nonadherent tumors arising in the body or tail of the pancreas and who have no history of trauma or previous pancreatitis.

Gross and microscopic pathologic features of cystadenomas vary because neoplastic cysts of different histogenetic derivations are lumped into the broad category of cystadenoma. Congenital cysts may not have been differentiated from cystadenomas in some cases in which marsupialization was performed and material was not available for pathologic study. For practical purposes congenital cysts are unilocular and cystadenomas are multilocular, but this generalization does not always apply. A simple gross classification of cystadenomas proposed by Glenner and Mallory[15] divides the tumors into two basic types: simple cystadenoma and papillary cystadenoma. Microscopically the epithelial lining is not

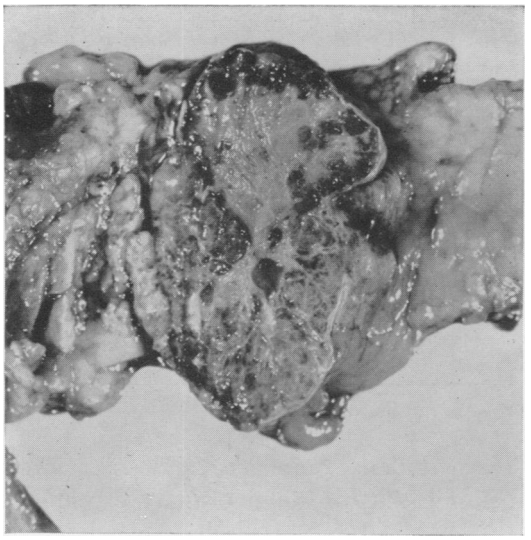

FIG. 4. Cut surface of cystadenoma from Case 9. This is a classical cystadenoma lined by flattened epithelial cells resembling centroacinar cells.

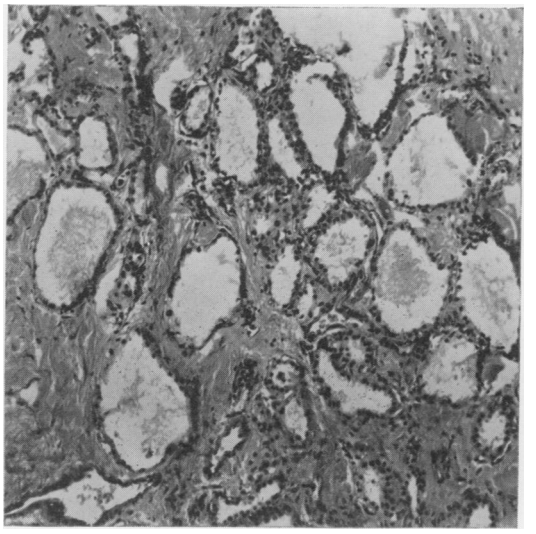

FIG. 5. Microscopic section from Case 9 showing small cystic spaces lined by very flat epithelium, with a moderate fibrous stroma. H & E × 100.

always the same—it may be low, flattened epithelium somewhat resembling centroacinar cells of the pancreas or tall, columnar epithelium resembling large pancreatic duct epithelium; or it may resemble intestinal epithelium or simulate the epithelium of pseudomucinous cystadenomas of the ovary. One form of cystadenoma of the pancreas is recognizably distinct. This tumor we prefer to call the centroacinar cystadenoma (Fig. 4) and is the classical form described in most pathology treatises. Grossly it is a multilobulated tumor which on cut section is a honeycomb of small cysts varying in size from microscopic to several centimeters. The cyst is compartmentalized by fibrous septa of varying thickness, usually quite thin. Microscopically the cysts have a lining of low cuboidal to flattened epithelium; true papillary formations do not appear (Fig. 5). These epithelial cells have

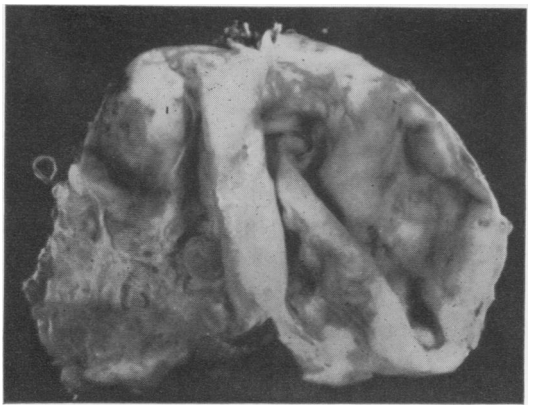

FIG. 6. Opened cyst from Case 5. Cyst is of the large multilocular type.

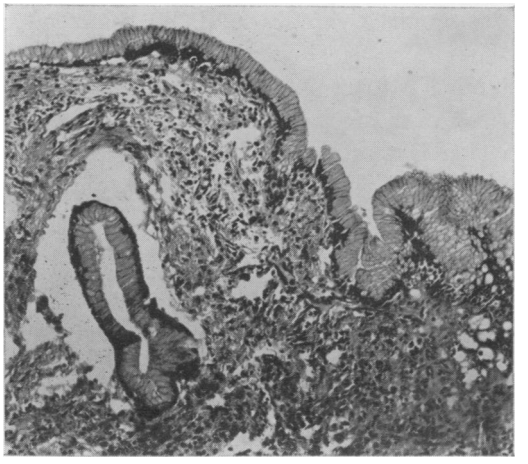

FIG. 7. Microscopic of Case 5. Cyst cavity lined by tall columnar epithelium strongly resembling large pancreatic duct epithelium. H & E × 100.

been likened to the flat cells of the terminal ductules of the pancreas or to centroacinar cells.

It is significant that the centroacinar cystadenoma in our series has not shown malignant potential. One of our patients with centroacinar cystadenoma (Case 7) was biopsied twice, 6 years apart; the histologic picture remained identical, with no progression, papillary formation or anaplasia. It is also significant that cystadenomas lined by large ductal epithelium or intestinal-like epithelium comprise a mixed group and some with intestinal-like epithelium may be related histogenetically to endodermal displacement, although the lesions are undoubtedly neoplastic cysts (Fig. 6–8). Most of these cysts are multiloculated and in our series are the only ones associated with papillary formations.

Both of our two papillary cystadenocarcinomas appear to have arisen from large columnar-cell cystadenomas, with definite residual areas of a benign type of epithelium (Fig. 9–11). On the basis of our experience, and review of reported cases, it appears that the cystadenoma lined by tall columnar cells resembling large pancreatic duct epithelium or intestinal epithelium may undergo malignant change.

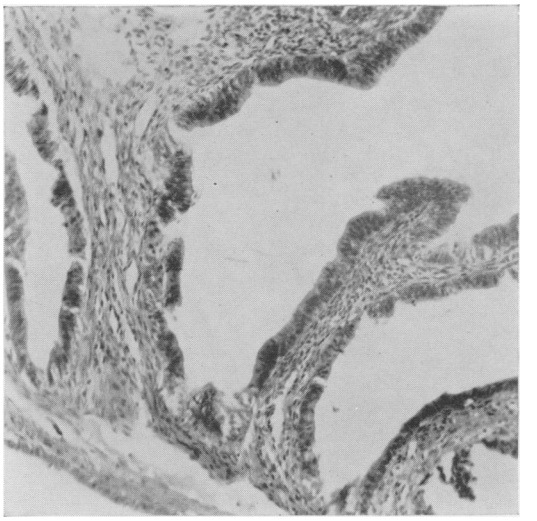

FIG. 9. Case 64 in Table 6. Benign areas of papillary cystadenoma in which the epithelium is hyperplastic and tall columnar. H & E × 100.

The evidence that pancreatic cystadenomas are premalignant will not be reviewed. Majority opinion is that most cystadenocarcinomas probably arise on the basis of a pre-existing benign cystadenoma.

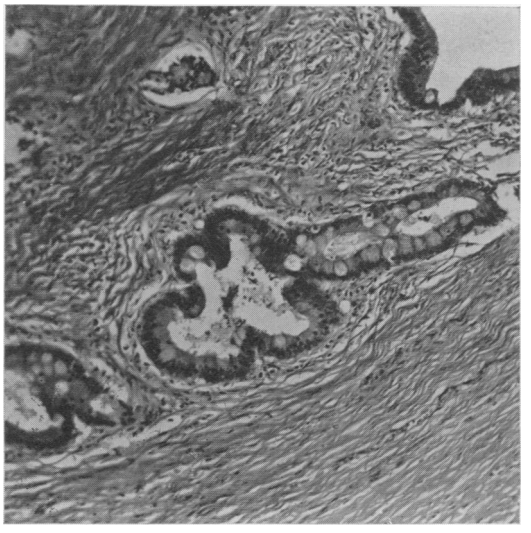

FIG. 8. Case 4. Epithelium and glandular elements strongly resembling intestinal-type epithelium, in which Paneth cells can be identified. H & E × 100.

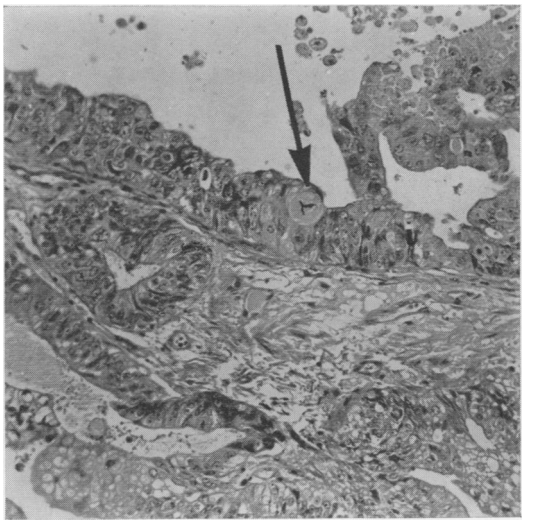

FIG. 10. Case 64 in Table 6. Areas from second biopsy showing definite adenocarcinoma. A "Y"-shaped mitosis is in the center of the field (indicated by arrow). H & E × 100.

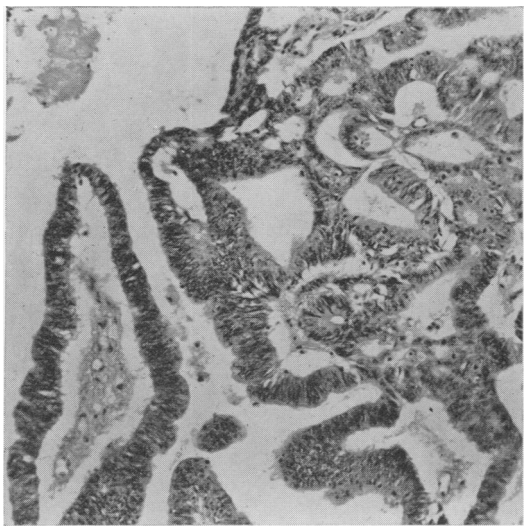

FIG. 11. Case 65 in Table 6. Abnormal gland within gland formation, loss of nuclear polarity and mild anaplasia within papillary processes of cystadenocarcinoma. H & E × 100.

The similarity of age and sex incidence and anatomic site of origin of the two lesions, multiple case reports [8, 42, 61] of repeat fractional biopsies initially benign but later malignant, and the frequent demonstration of areas of transition within the same tumor (Fig. 9, 10) constitute evidence for a direct relationship between cystadenoma and cystadenocarcinoma.

Of importance to the surgeon dealing with malignant neoplastic cysts in the pancreas is the statistical probability that more often the lesion is an ordinary carcinoma of the pancreas associated with a large cyst which, not infrequently, appears to be benign at operation; it is only after biopsy that carcinoma is found to be implanted on the wall of the cyst. Histologically these carcinomas appear as the usual adeno- or undifferentiated carcinoma of the pancreas and should not be confused with carcinoma arising in a pre-existing cystadenoma. The following three pathogenetic mechanisms could explain pancreatic carcinoma associated with a large cyst: 1) carcinoma produced obstruction to a duct with pancreatitis with formation of either a retention cyst or pseudocyst, with subsequent implantation of the cancer in the cyst wall; 2) cancer may have developed in pre-existing chronic pancreatitis with pseudocyst; and 3) a carcinoma may grow so huge that it will undergo massive central necrosis and cyst formation.

TABLE 8. *Cystadenocarcinoma of Pancreas: Types of Operation Performed in 56 Patients*

Operation	No. Patients
Excision	15
Distal subtotal pancreatectomy	16
Pancreatoduodenectomy	5
Total pancreatectomy	2
Marsupialization	8
Internal drainage	3
Biopsy with or without "by-pass" procedure	7
Total:	56

Summary and Conclusions

Ten to 20 percent of pancreatic cysts are primary neoplastic cysts or are cysts secondary to a proximal primary carcinoma.

Eleven cystadenomas and two cystadenocarcinomas comprised 11 per cent of 117 cases of pancreatic cyst observed in four New Orleans hospitals during the 27-year period from 1938 through 1964.

Analysis of a collected series of 115 cases of pancreatic cystadenoma indicates that the lesion is rare, benign, slow-growing, with a tendency to arise in the body or tail of the pancreas of young and middle-aged women. Excellent results follow surgical excision.

Cystadenocarcinoma is even rarer than cystadenoma. The appearance of the two lesions, the similarity in anatomic location, age and sex incidence, and the frequency with which it is possible to demonstrate areas of transition from benign to malignant changes within the same tumor all constitute evidence that cystadenocarcinomas probably develop from pre-existing cystadenomas. Clinical, pathologic and

therapeutic data pertaining to 65 cases of pancreatic cystadenocarcinoma have been summarized. In the absence of local extension to vital contiguous structures or distant metastasis, even bulky cystadenocarcinomas of long duration frequently can be resected with expectation of cure. Decompression by internal drainage will occasionally provide palliation of a large, symptomatic, nonresectable tumor with a cystic component.

Acknowledgments

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Discussion

Dr. Kenneth Warren (Boston): I think Dr. Priestley has pointed out all the important features of the far advanced chronic relapse in pancreatitis, and he has especially emphasized that there is no single operation to accommodate all of these people. Regardless of how you individualize these operations, the long-term results will probably still leave much to be desired.

(Slide) For many years we have been interested in the direct approach, such as Dr. Priestley described, to the treatment of chronic relapse in pancreatitis, believing that all of these patients have partially complete obstruction of the duct of Wirsung. This is the type of procedure which I assume he had in mind. It shows the sacculation. This is a specimen (slide) removed 18 months later from a patient who had a lateral anastamosis and then developed an obstruction in the distal part of the gland with recurrent symptoms.

(Slide) I would like to emphasize that patients may have spontaneous pancreatitis confined to the left segment of the pancreas. Here you see a simple stone to the left of the vertebral column, many satellite stones distal to that, and in the next specimen (slide) you will see the pathology represented by distal pancreatectomy. One might assume from this roentgenogram that this patient has the distal part of the pancreas involved in the far advanced pancreatitis, while the head and neck would be normal.

The cavity you see to your left, near the center of the screen, is the cavity from which the simple stone was removed. There are innumerable stones in the duct beyond that. The duct has been almost destroyed, and there was a spontaneous fistula. This is the type procedure we think indicated in distal pancreatitis of this nature.

We do not believe that internal drainage has a place (and I am sure most of us would agree the same applies to the situation here) in the patient with almost total destruction of the distal part of the pancreas, having had numerous previous attempts to drain the cyst.

(Slide) I put this on the screen to show something Dr. Priestley has not discussed, but it cer-