Pancreatic Exocrine and Endocrine Function After Operations for Chronic Pancreatitis

ROBERT P. JALLEH, F.R.C.S., and ROBIN C. N. WILLIAMSON, M.D., F.R.C.S.

Exocrine and endocrine function of the pancreas was assessed in the early postoperative period (≤2 months) and subsequently (mean, 25 months; range, 3 to 120) in 103 patients (69 men, 34 women; mean age, 42.4 ± 11.6 years) undergoing operation for chronic pancreatitis. Alcohol was the main causative agent (69%) and pain the most frequent indication (87%) for operation. Drainage procedures (n = 23) did not alter pancreatic function either initially or on long-term follow-up. In the early postoperative period, distal pancreatectomy (n = 42) often impaired endocrine function without affecting exocrine function; seven patients (17%) became diabetic, and results of oral glucose tolerance test showed deterioration in 23 of 28 patients (82%, $p < 0.05$). On subsequent follow-up, 11 patients developed exocrine failure ($p < 0.01$) and 10 patients endocrine ($p < 0.01$) failure. Proximal pancreatectomy (n = 38) precipitated clinical exocrine failure in 14 patients (37%, $p < 0.01$), yet pancreolauryl tests in 18 patients showed little objective change in exocrine status ($0.50 > p > 0.10$). Endocrine function was initially spared after proximal pancreatectomy, but six additional patients (16%, $p < 0.05$) required treatment for diabetes at a mean of 19 months (range, 3 to 34). Deterioration in pancreatic function is thus not an invariable immediate consequence of pancreatic drainage procedures or partial pancreatectomy for chronic pancreatitis. Progression of disease must account, in part, for failure of both exocrine and endocrine function on long-term follow-up. Drainage operations appear to delay this progressive decline in pancreatic function.

From the Department of Surgery, Royal Postgraduate Medical School, Hammersmith Hospital, London, United Kingdom

OPERATIONS FOR CHRONIC pancreatitis are performed to relieve severe intractable pain and to deal with complications such as pseudocyst, biliary obstruction, and bleeding. Although success is generally judged on the extent of pain relief, the choice of operative procedure is influenced by consideration of pancreatic exocrine and endocrine function. In patients with pancreatic duct dilatation or pseudocyst, for example, a decompressive (drainage) operation can relieve pain without sacrificing function.[1] Preservation of endocrine function is also the object of newer operations such as pancreatic autotransplantation (segmental or islet cell) after massive pancreatic resection.[2,3]

Preoperative tests of pancreatic function help to assess the severity of disease[4] and to guide perioperative metabolic requirements. After operation, impaired exocrine and endocrine function can lead to malnutrition and other risks, including death.[5] Pancreatic function testing is thus important for proper patient management. Although most surgical series include some description of pancreatic function, full analysis and comparison between different reports is a difficult exercise. Often, only a single type of operation is performed in a particular series, yet considerable variation exists in surgical procedures recommended for chronic pancreatitis.[6,7] Compounding factors include unspecified definitions of normal and abnormal pancreatic function and differences in investigations employed, data interpretation, and duration of follow-up. To our knowledge, no report has yet focused solely on the effect of operations on pancreatic exocrine and endocrine function in chronic pancreatitis. Changes in the immediate postoperative period are especially neglected.

We present a survey of pancreatic function in a personal series of 103 patients undergoing operation for severe chronic pancreatitis. This report is aimed at providing a descriptive analysis of both the early and long-term metabolic sequelae of partial pancreatectomy and drainage procedures, together with implications for patient management. It is based on clinical review and the use of simple but informative investigations that are easily performed in most hospitals.

Address reprint requests to Robin C. N. Williamson, M.D., F.R.C.S., Department of Surgery, Royal Postgraduate Medical School, Hammersmith Hospital, DuCane Road, London W12 ONN, United Kingdom.

Accepted for publication February 4, 1992.

Materials and Methods

Patients

A personal series was reviewed of 119 patients undergoing partial pancreatectomy or drainage procedures for chronic pancreatitis between February 1978 and September 1991 at Bristol Royal Infirmary or the Hammersmith Hospital, London. The diagnosis was confirmed histologically or on radiologic and operative findings. Our policy throughout this period was to evaluate both exocrine and endocrine function before and after operation, although in some cases emergency presentation or early discharge precluded full documentation. We found sufficient information to allow analysis of pancreatic function in 103 patients, who form the basis of this study. Patient characteristics are outlined in Table 1. There were 69 men and boys and 34 women and girls (male:female = 2:1), with a mean age of 42.4 years (range, 7 to 70 years). Seventy-two patients (69%) gave a strong history of alcohol abuse (estimated consumption = 202 ± 212 g/day, mean ± standard deviation) over an estimated 13.8 ± 9.3 years. Severe abdominal pain, either of a constant or recurrent, episodic nature, was a feature in 90 (87%) patients. At least 60 of these had a history of opiate intake, and eight had failed fluoroscopy-guided percutaneous celiac plexus blocks.

Operations

Operative procedures were classified into three groups: pancreatic drainage, distal pancreatectomy, and proximal pancreatectomy. Twenty-three patients underwent drainage operations. These consisted of longitudinal pancreaticojejunostomy, with at least an 8- to 10-cm pancreaticoenteric anastomosis, in 11 patients and a pseudocyst-jejunostomy Roux-en-Y in eight patients.[8] Four patients had combined pseudocyst and pancreatic duct drainage, and six had concomitant biliary drainage procedures. Distal pancreatectomy involved a 40% to 70% resection, and in 13 of 42 patients the spleen was conserved.[9] Definitions of the estimated amount of pancreatic tissue excised are detailed elsewhere.[10] Pylorus-preserving pancreatoduodenectomy was performed in 33 of the 38 patients undergoing proximal pancreatic resection and involved loss of approximately half the gland.[5] In our current practice, a conventional Whipple's operation is performed only in cases with duodenal scarring or where invasive carcinoma is suspected.

Assessment of Pancreatic Function

Pancreatic function was assessed shortly before and after operation. Assessment was based on clinical criteria and on exocrine and endocrine function tests undertaken in the early postoperative period (defined as within 2 months of operation). Only clinical information was used for long-term assessment, because most of these patients were not readmitted for investigations unless symptomatically indicated. Duration of follow-up was taken as the interval between operation and the last verified record of the patient's condition. In nine patients, six undergoing distal and three proximal pancreatectomy, the duration of follow-up for purposes of this study was limited by completion total pancreatectomy.

Exocrine function. Diarrhea, steatorrhea, and the need for enzyme replacement therapy were clinical criteria for abnormal exocrine function. Objectively, this was measured using one of the following: 3-day collection of feces for estimation of fat content (normal < 7, intermediate 7 to 15, abnormal > 15 mmol/day), duodenal intubation

TABLE 1. *Patient Characteristics*

	Drainage Procedures n = 23	Distal Pancreatectomy n = 42	Proximal Pancreatectomy n = 38	Total n = 103
Sex				
M	13	27	29	69
F	10	15	9	34
Age				
Mean (yr)	43.9	40.5	44.4	42.4
Range (yr)	7–68	20–67	25–70	7–70
Etiology				
Alcohol	15	28	28	71
PAP	1	3	3	7
Congenital	—	—	1	1
Gallstones	1	—	—	1
Idiopathic	6	11	6	23
Duration of follow-up				
Mean (mo)	38	20	24	25
Range (mo)	5–77	3–120	3–120	3–120

PAP, previous attacks of idiopathic acute pancreatitis.

TABLE 2. *Diagnostic Venous Blood Glucose Values for Oral Glucose Tolerance Test*

	Fasting (mmol/L)		2 hr After Glucose (mmol/L)
Diabetes mellitus	≥6.7	and/or	≥10.0
Impaired glucose tolerance	<6.7	and	≥6.7–<10.0
Normal	<6.7	and	<6.7

Adapted from the Report of the WHO Study Group on Diabetes Mellitus 1985.

studies with pancreatic stimulation, and the Pancreolauryl test[11] (normal > 30%, intermediate 20% to 30%, abnormal < 20%). The first two methods were employed in a few patients during the early years of this study and have since been discontinued. Although semiquantitative and an indirect measure of exocrine function, the convenience of the Pancreolauryl test (Charwell Pharmaceuticals, Ltd., Alton, Hampshire, UK) makes this our current investigation of choice.

Endocrine function. Clinically, a diagnosis of abnormal endocrine function was made based on the need to treat diabetes mellitus with diet modification, oral hypoglycemic agents, or insulin. Oral glucose tolerance test (GTT), measuring venous whole blood glucose levels, was used for objective assessment. Blood samples were taken before a 75-g glucose loading dose, and at 30-minute intervals thereafter up to 120 minutes. Patients were classified into diabetes mellitus, impaired GTT, or normal groups according to criteria set by the 1985 WHO Study Group on diabetes mellitus (Table 2).[12]

Statistical Analysis

Chi square and two-tailed paired t tests were used.

Results

Exocrine Function

Drainage operations (n = 23). Using clinical criteria, drainage procedures did not affect pancreatic exocrine function in the early postoperative period (Fig. 1). In six patients in whom data from exocrine function tests were available, three showed worsening of function, and three showed some improvement. These changes were minimal and confined to the intermediate and abnormal ranges. There was also no alteration in exocrine function profile of these patients during long-term follow-up.

Distal pancreatectomy (n = 42). Exocrine function was not altered in the early postoperative period after distal pancreatic resection. Of 11 patients (27%) who had evidence of exocrine insufficiency before operation, nine continued to require enzyme replacement after resection. Treatment was stopped in two patients without side effects, whereas another two needed enzymes for steatorrhea developing after operation. Our clinical assessment was supported by analysis of the pancreolauryl ratio in 17 patients (Fig. 2). A 31-year-old man, who had pancreatic and biliary sphincteroplasty in addition to 50% distal pancreatectomy, showed a marked improvement of pancreolauryl ratio from 11% to 81% after operation. In this particular instance, histologically proven papillary fibrosis probably contributed to the gross preoperative exocrine dysfunction. On long-term follow-up, 11 additional patients developed symptoms of malabsorption and were placed on enzyme replacement at a mean of 13 (range, 3 to 38) months after operation. One patient had apparent improvement in exocrine function and was able to discontinue enzyme therapy without developing symptoms.

Proximal pancreatectomy (n = 38). In contrast to drainage procedures and distal resections, there was substantial deterioration in exocrine function in patients un-

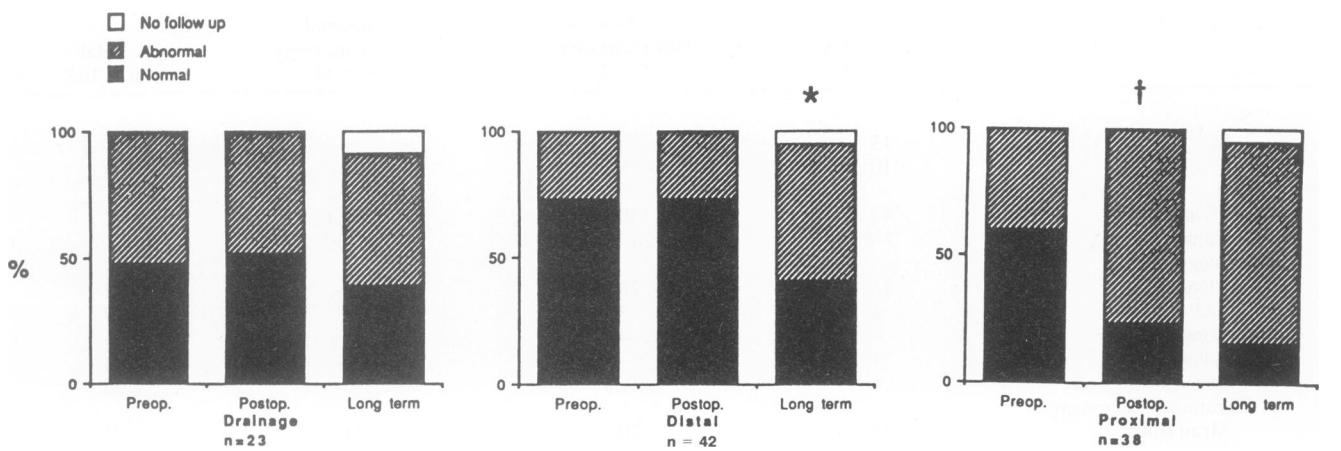

FIG. 1. Clinical assessment of exocrine function. Statistical significance (chi square test): *p < 0.01 *versus* postoperative value, †p < 0.01 *versus* preoperative value.

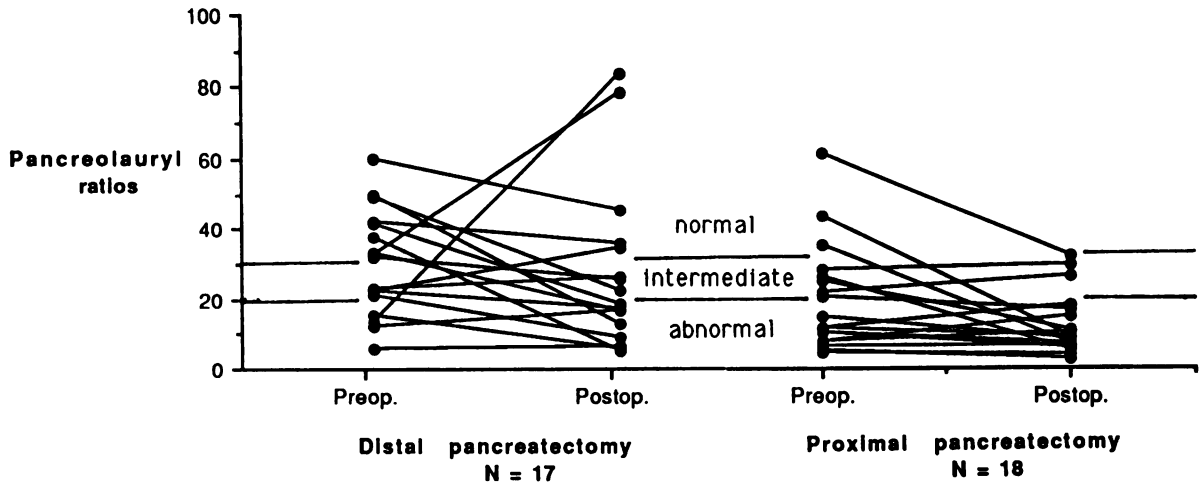

FIG. 2. Pancreolauryl ratios in patients undergoing partial pancreatectomy. There was no significant difference between preoperative and postoperative profiles in either group.

dergoing proximal pancreatectomy. No patient showed an improvement in function. Fourteen patients (37%) were started on enzyme replacement as a direct consequence of operation. Pancreolauryl ratios before and after operation in 18 patients, however, did not reflect our clinical findings (Fig. 2). Long-term follow-up showed that only one further patient went into exocrine failure, 51 months after resection. No difference in exocrine function profiles was observed between those undergoing pylorus-preserving pancreatoduodenectomy and Whipple's operation ($0.50 > p > 0.10$).

Endocrine Function

Drainage operations. There was no change in the incidence of diabetes mellitus during the postoperative period (Fig. 3), and GTT was likewise unaltered (Fig 4). On subsequent follow-up, only two patients required insulin therapy, at 54 and 77 months after operation.

Distal pancreatectomy. Only one of 42 patients was on insulin at presentation. Seven patients were rendered diabetic after operation, all but one of whom had at least a 60% distal resection. Five of these were treated with insulin, with a mean dose of 24 (range, 12 to 56) U/day. One patient was started on glibenclamide, and the other was advised on diet modification. Figure 4 highlights the significant impairment of postoperative GTT profiles in 28 patients, compared with preoperative data. On subsequent follow-up, a further 10 patients were diagnosed as diabetics at a mean of 14 (range, 5 to 24) months after operation. Eight of these, plus the patient initially on glibenclamide, required insulin at a mean daily dose of 25 (range, 6 to 28) units for adequate control of blood sugar levels. Two other patients were treated with oral hypo-

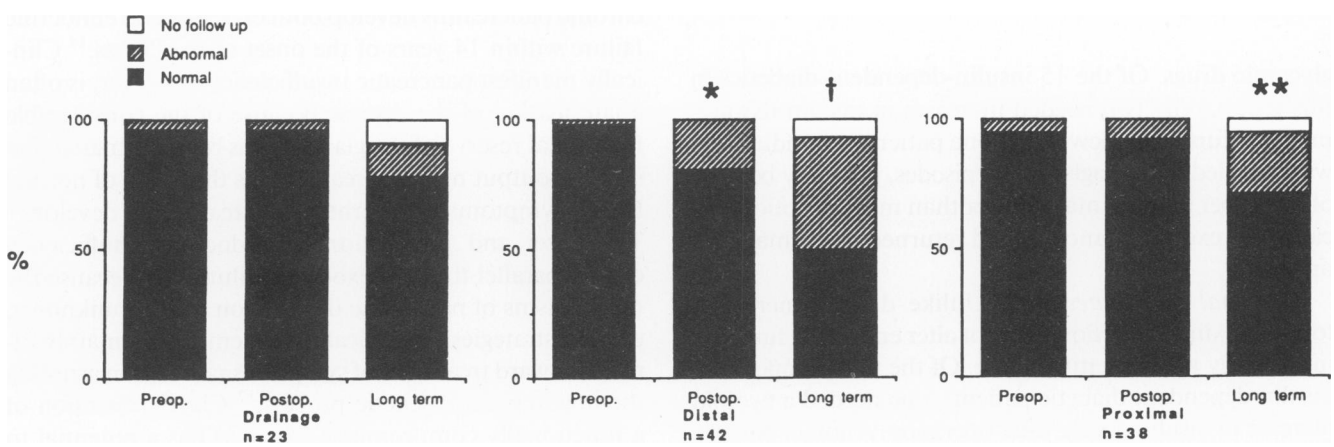

FIG. 3. Clinical assessment of endocrine function. Statistical significance (chi square test): *$p < 0.02$ *versus* preoperative value; †$p < 0.01$, **$p < 0.05$ *versus* postoperative value.

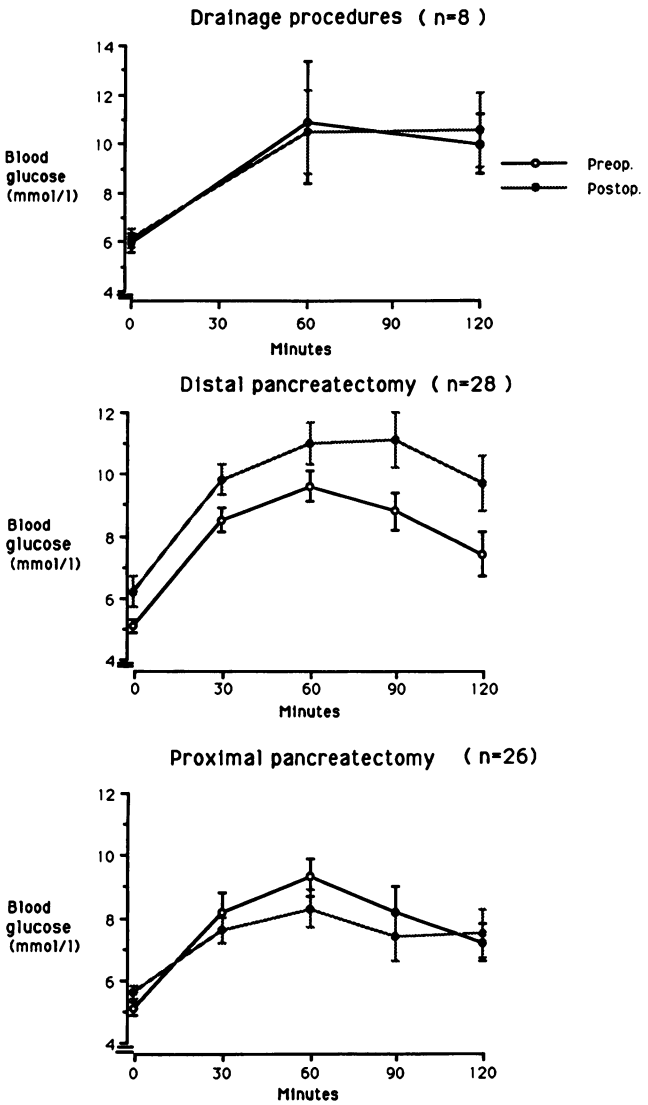

FIG. 4. Results of oral glucose tolerance tests before and after operation. Values represent mean ± SEM. In the distal pancreatectomy group (only), differences between pre- and postoperative mean values were significant at every point except at 30 minutes ($p < 0.05$).

glycemic drugs. Of the 15 insulin-dependent diabetics in this group, only two needed increases in insulin requirement on further review. Only one patient, a nondiabetic, was troubled by hypoglycemic episodes, probably because of improper dietary intake rather than malabsorption, because her exocrine function had returned to normal after operation.

Proximal pancreatectomy. Unlike distal pancreatectomy, proximal resections did not alter endocrine function in the early postoperative phase. Of the two preoperative insulin-dependent diabetic patients, one needed a twofold increase in insulin dosage after operation. Another patient, with a preoperative diabetic GTT but not on any treatment, was started on insulin (24 units) after postoperative GTT showed a deterioration of function. Glucose tolerance test findings in 26 of our 38 patients support this clinical assessment (Fig. 4). On long-term follow-up, six patients were diagnosed as diabetics at a mean of 19 (range, 3 to 41) months after operation, but only two of them needed insulin treatment.

Combination of Exocrine and Endocrine Function

Before operation, only two patients were assessed as having both exocrine and endocrine failure. After operation, six additional patients were diagnosed as such, four after distal pancreatectomy and two after proximal pancreatectomy. On long-term follow-up, however, a total of 22 patients (21%) needed treatment for diabetes as well as malabsorption. Although five late deaths were recorded in these 103 patients, none were related to pancreatic insufficiency or complications of chronic pancreatitis.

Discussion

This study indicates that an appropriate operation does not affect pancreatic function in many patients with chronic pancreatitis, even if half the gland is resected and even though most patients were left with residual disease. Drainage procedures do not alter pancreatic function either in the immediate postoperative period or on subsequent follow-up. Distal pancreatectomy compromises endocrine function without affecting exocrine function at an early stage, and proximal pancreatectomy precipitates exocrine but not endocrine insufficiency. The difference is attributable in part to the relative preponderance of islet cells in the body and tail of the pancreas.[13]

The natural history of chronic pancreatitis involves progressive deterioration of both exocrine and endocrine function, presumably related to progressive destruction of the gland. Ammann et al.[14] have shown that even without an operation, all patients with alcoholic (calcific) chronic pancreatitis develop both exocrine and endocrine failure within 14 years of the onset of the illness.[14] Clinically manifest pancreatic insufficiency, however, is often a late feature of the disease because of the considerable functional reserve of the gland. It has been estimated that enzyme output must decrease to less than 10% of normal before symptoms of diarrhea and steatorrhea develop.[15] The onset and progression of endocrine insufficiency closely parallel those of exocrine failure.[14,16] Because the mechanisms of pancreatic destruction remain unknown, current strategies in surgical management are mainly directed toward treatment of symptoms rather than arresting the ongoing pathogenetic process.[17] Clearly resection of a functionally compromised pancreas has a potential to adversely affect pancreatic function. The finding that it often does not do so presumably reflects the fact that in

many cases the resected tissue has already been functionally destroyed.

Various investigations are currently employed to estimate pancreatic function. Tests of exocrine function may be classified into two groups, those quantifying pancreatic enzyme secretion after pancreatic stimulation and indirect measures of the digestive action of enzymes such as fecal fat estimation and various tubeless chemical tests.[18] Developed more than 20 years ago,[19] the Pancreolauryl test has now been shown to have a specificity of up to 97% and a sensitivity of up to 93%.[18] Further, Lankisch and co-workers[20] have shown that, as an indicator of pancreatic steatorrhea, the test has a positive predictive value of 76%.[20] Investigations of endocrine function involve identification of impaired insulin secretion and glucose metabolism. These include measurements of serum insulin and C peptide levels and 24-hour urinary C peptide estimation.[21] Abnormal intravenous and oral GTTs are indicators of impaired glucose metabolism. In this study, we have employed investigations that were noninvasive, inexpensive, and convenient to perform. We found that these tests adequately reflected the clinical status of our patients.

The theoretical advantage of a drainage operation is that it preserves remaining functional pancreatic tissue. Initial optimism, based on an experimental dog model,[22] that such operations may improve pancreatic function has not been supported by long-term clinical results despite radiologic evidence of anastomotic patency.[1,23] Reflecting our earlier experience,[8] both exocrine and endocrine function remained unchanged by drainage procedures, there being neither improvement nor deterioration. These observations suggest that pathologic changes in the diseased pancreatic parenchyma play a more important role in exocrine insufficiency than ductal strictures preventing flow of pancreatic enzymes to the duodenum. In line with findings from some earlier series[1,24] (but not others[23]), the long-term stability in both exocrine and endocrine function in our patients may indicate a beneficial effect of drainage procedures on the progression of pancreatitis. It is conceivable that this stabilization of disease is related to a reduction in the high parenchymal pressure that we and others have found in chronic pancreatitis[25,26] as a consequence of "filleting" the gland.

There was no appreciable change in exocrine function immediately after distal pancreatectomy. On long-term follow-up, however, 28% of patients developed symptoms of malabsorption. This deterioration in function was most likely due to continuing pancreatitis in the remaining proximal pancreas. The incidence of long-term exocrine failure in this study (56%) was comparable to that of earlier reports.[2,27] In the absence of data from the immediate postoperative period, it is impossible to determine whether exocrine failure in these series developed early or late. By contrast, distal pancreatectomy directly precipitated the need for insulin in 17% of patients, and this was accompanied by a significant deterioration in measured glucose tolerance. On long-term follow-up, the percentage of patients with diabetes increased to 46%, a figure similar to that previously reported for a 40% to 80% distal resection.[2,27,28] Although almost all our diabetic patients needed insulin, control was not difficult. It has been shown that the incidence of diabetes is directly related to the extent of resection.[27] In support, 75% of patients who developed postoperative diabetes underwent a 60% or greater distal resection.

The situation with proximal pancreatectomy is quite the reverse. The immediate effect of operation is a sharp decline in clinical exocrine function. Although 39% of patients were in exocrine failure before operation, 76% needed enzyme replacement after operation ($p < 0.01$). Clearly, in most patients, enzyme production in the remaining distal pancreas was unable to meet requirements for normal digestion. In addition, edema of the end-to-end pancreaticojejunostomy anastomosis could have caused temporary obstruction to the flow of pancreatic juice into the gut. The adverse effect of this "nondelivery" of pancreatic juice is highlighted by the Erlangen/Nurnberg experience, in which there was a distinct decline in exocrine function after use of an occlusive gel to obstruct the pancreatic duct after proximal pancreatectomy.[7] Pancreolauryl values remained unchanged after operation, however. It may be that as patients began to eat better with pain relief, pre-existing enzyme insufficiency (hidden by poor food intake) was unmasked. This probably accounts, in part, for the discrepancy between preoperative clinical and biochemical assessment of exocrine status. Exocrine function remained poor on long-term follow-up. Although generally not tested in our patients, anastomotic stricture and occlusion has been observed at autopsy after pancreatoduodenectomy.[29] Unlike exocrine function, endocrine function was preserved after proximal resection both clinically and on testing. Our experience parallels that of Beger et al.,[6] who studied endocrine function in patients 10 days after a modified operation to excise the diseased pancreatic head. Deterioration of glucose homeostasis in the long term is probably related to disease progression. Observed in 25% of patients, this prevalence is in keeping with more favorable reports in the literature.[6,30]

Assessment of exocrine and endocrine function has obvious therapeutic implications. In the immediate postoperative period, these data are used to identify early changes in function so as to either initiate new or modify existing treatment regimens. It also provides baseline values enabling subsequent comparison. Close scrutiny on continued follow-up of all patients forms an essential part in the total management of this disease.

References

1. Prinz RA, Greenlee HB. Pancreatic duct drainage in chronic pancreatitis. Hepatogastroenterology 1990; 37:295–300.
2. Morrow CE, Cohen J, Sutherland DER, Najarian JS. Chronic pancreatitis: long-term surgical results of pancreatic duct drainage, pancreatic resection and near-total pancreatic and islet autotransplantation. Surgery 1984; 96:608–615.
3. Rossi RL, Soeldner JS, Braasch JW, et al. Long-term results of pancreatic resection and segmental pancreatic autotransplantation for chronic pancreatitis. Am J Surg 1990; 159:51–58.
4. Latifi R, McIntosh JK, Dudrick SJ. Nutritional management of acute and chronic pancreatitis. Surg Clin North Am 1991; 71:579–595.
5. Williamson RCN, Cooper MJ. Resection in chronic pancreatitis. Br J Surg 1987; 74:807–812.
6. Beger HG, Buchler M, Bittner R. The duodenum preserving resection of the head of the pancreas (DPRHP) in patients with chronic pancreatitis and an inflammatory mass in the head. Acta Chir Scand 1990; 156:309–315.
7. Gebhardt C. Surgical treatment of pain in chronic pancreatitis. Acta Chir Scand 1990; 156:303–307.
8. Cooper MJ, Williamson RCN. Drainage operations in chronic pancreatitis. Br J Surg 1984; 71:761–766.
9. Aldridge MC, Williamson RCN. Distal pancreatectomy with and without splenectomy. Br J Surg 1991; 78:976–979.
10. Aldridge MC, Williamson RCN. Distal pancreatectomy in chronic pancreatitis. *In* Johnson CD, Imrie CW, eds. Pancreatic Disease: Progress and Prospects. London: Springer-Verlag, 1991, pp 127–135.
11. Barry RE, Barry R, Ene MD, Parker G. Fluorescein dilaurate—tubeless test for pancreatic exocrine failure. Lancet 1982; ii:742–744.
12. Alberti KGMM, Hockaday TAR. Diabetes mellitus. *In* Weatherall DJ, Ledingham JGG, Warrell DA, eds. Oxford Textbook of Medicine, 2nd Edition. New York: Oxford Medical Publications, 1987, pp 9.51–9.101.
13. Wittingen J, Frey CF. Islet concentration in the head, body, tail and uncinate process of the pancreas. Ann Surg 1974; 179:412–414.
14. Ammann RW, Akovbiantz A, Largiadier F, Schueler G. Course and outcome of chronic pancreatitis: longitudinal study of a mixed medical-surgical series of 245 patients. Gastroenterology 1984; 86:820–828.
15. DiMagno EP, Go VLW, Summerskill WHJ. Relations between pancreatic enzyme outputs and malabsorption in severe pancreatic insufficiency. N Engl J Med 1973; 288:813–815.
16. Doty JE, Fink AS, Meyer JH. Alterations in digestive function caused by pancreatic disease. Surg Clin North Am 1989; 69:447–465.
17. Rossi RL. Pancreatic resections for chronic pancreatitis. Hepatogastroenterology 1990; 37:277–282.
18. Li Y, Chiverton SG, Hunt RH. Exocrine pancreatic function tests. J Clin Gastroenterol 1989; 11:376–378.
19. Kaffarnik H, Meyer-Bertenrath JG. Zur Methodik und Klinischen Bedeutung eines neuen Pankreas-lipase-Tests mit Fluoresceindilaurinsaureester. Klin Wochenschr 1969; 47:221–223.
20. Lankisch PG, Otto J, Brauneis J, et al. Detection of pancreatic steatorrhea by oral pancreatic function tests. Dig Dis Sci 1988; 33: 1233–1236.
21. Kendall DM, Sutherland DER, Najarian JS, et al. Effects of hemipancreactomy on insulin secretion and glucose tolerance in healthy humans. N Engl J Med 1990; 322:898–903.
22. Carnevali JF, ReMine WH, Dockerty MB, et al. An experimental study of side-to-side pancreaticojejunostomy after ductal obstruction. Arch Surg 1960; 80:774–787.
23. Warshaw AL, Popp JW Jr, Schapiro RH. Long-term patency, pancreatic function and pain relief after lateral pancreaticojejunostomy for chronic pancreatitis. Gastroenterology 1980; 79:287–293.
24. Nealon WH, Townsend CM, Thompson JC. Operative drainage of the pancreatic duct delays functional impairment in patients with chronic pancreatitis. Ann Surg 1988; 208:321–329.
25. Jalleh RP, Aslam M, Williamson RCN. Pancreatic tissue and ductal pressures in chronic pancreatitis. Br J Surg 1991; 78:1235–1237.
26. Ebbehoj N, Borly L, Madsen, Svendsen LB. Pancreatic tissue pressure and pain in chronic pancreatitis. Pancreas 1986; 1:556–558.
27. Frey CF, Child CG III, Fry W. Pancreatectomy for chronic pancreatitis. Ann Surg 1976; 184:403–414.
28. Warshaw AL. Conservation of pancreatic tissue by combined gastric, biliary and pancreatic duct drainage for pain in chronic pancreatitis. Am J Surg 1985; 149:563–569.
29. Tashio S, Murata E, Hiraoka T, et al. New technique for pancreaticojejunostomy using a biological adhesive. Br J Surg 1987; 74: 292–294.
30. Rossi RL, Rothschild J, Braasch JW, et al. Pancreatoduodenectomy in the management of chronic pancreatitis. Arch Surg 1987; 122: 416–420.