

Some Current Views on Pancreatitis

I. N. MARKS, B.SC., M.B., CH.B., F.R.C.P. (EDIN.), S. BANK, M.B., CH.B., M.R.C.P. (LOND.), AND J. H. LOUW, CH.M., F.R.C.S. (ENG.), *Gastro-intestinal Service and Department of Surgery, Groote Schuur Hospital, Cape Town*

SUMMARY

Current views on the pathogenesis, classification, diagnostic criteria, natural history and surgical treatment of pancreatitis are reviewed.

S. Afr. Med. J., **45**, 1138 (1971).

The past decade has seen few dramatic advances in the diagnosis and treatment of pancreatitis. The aetiopathogenesis remains uncertain, the diagnosis is still difficult and the management is seldom straightforward. But there has been a broadening in the understanding of the classification, diagnostic features, natural history and surgical management of the disease.

PATHOGENESIS

The cause of acute pancreatitis remains elusive, and the aetiology and pathogenesis of the disease is almost as controversial now as it was some 50 years ago.

McCutcheon,¹ in an attempt to unify the various aetiological factors, has reviewed the evidence for reflux of duodenal contents into the pancreatic duct as the mechanism responsible for initiating the disease and concludes that reflux pancreatitis is the common denominator in all cases of pancreatitis. This would appear to be an over-simplification of the problem, particularly in alcohol-induced pancreatitis, since many patients do not give a history of nausea or vomiting before the onset of pain. Furthermore, the elegant experimental studies of Davis² suggest that alcohol-induced pancreatitis is due to factors other than duodenal reflux into the pancreatic duct.

The pathological changes in acute pancreatitis range from slight oedema to extensive haemorrhagic infarction. A vicious circle of increasing vascular damage occurs in acute pancreatitis, and experimental studies by Goodhead³ support the view that these changes in pancreatic blood flow are crucial in determining the outcome of an attack. A decreased blood flow favours the development of acute haemorrhagic pancreatitis. Low-molecular-weight dextran has been shown to exert a protective effect in maintaining a normal perfusion rate and has been used, with good results, in patients with severe acute pancreatitis. Another aspect of the pathogenesis which has a therapeutic bearing has been recently reviewed by Creutzfeld and Schmidt.⁴

These workers have stressed that the morphology of pancreatitis can best be explained by the intrapancreatic effect of phospholipase A and elastase, and that only small amounts of trypsin are required for activation of these enzymes. It will be interesting to note whether this de-emphasis of the dominant role of trypsin in the pathogenesis of pancreatitis will herald a decline in the vogue of the antitryptic preparation Trasylol in this disease.

A challenging breakthrough in the pathogenesis of alcohol-induced pancreatitis has recently been made by Sarles *et al.*⁵ These workers were able to reproduce the histological lesions of calcific pancreatitis in man by means of a two-year period of ethanol intoxication in the rat. The changes in the affected lobules in the experimental animal comprised protein plugs, some of which were calcified, in the ducts; acinar cell replacement by dilated ducts; and sclerosis. Sarles *et al.*⁵ believe that the primary disturbance in calcific pancreatitis is protein precipitation in the ducts leading to duct obstruction and, subsequently, to duct dilatation, acinar cell atrophy and fibrosis.

CLASSIFICATION

The conventional clinical classification has given way to the aetiological and, more recently, the clinico-pathological classification.

The aetiological approach has the great advantage of affording an insight into the natural history of the disease and of providing a guide as to the advisability or surgery in a particular patient. Alcohol-induced pancreatitis account for 62% of pancreatitis in the Cape Peninsula, and biliary disease, miscellaneous and unknown causes for the remainder.⁶

The clinico-pathological classification recognizes acute, acute relapsing, chronic relapsing and chronic varieties.⁷ In the acute varieties, clinical and pathological restitution takes place following the attack, whereas the chronic varieties show permanent residual pancreatic damage. The main shortcoming of this classification is that it is largely dependent on histological confirmation, a problem in centres such as ours where laparotomy is not readily undertaken and where pancreatic biopsy is viewed with disfavour. Furthermore, the clinico-pathological classification is a pathological rather than a clinical classification and does not allow separation of those patients in the chronic groups

who have had clinically acute attacks. In general, gallstone pancreatitis tends to be acute and alcohol-induced to the chronic varieties of the disease.

DIAGNOSTIC CRITERIA

There has been a trend toward stricter diagnostic criteria in recent years, and many workers insist on one or more of the following for diagnosis: laparotomy evidence showing haemorrhagic pancreatitis, fat necrosis or histological evidence of chronic pancreatitis, a serum amylase in excess of 1 000 Somogyi units, radiological calcification of the pancreas or autopsy evidence of the disease. To these may be added a grossly abnormal pancreatic function test.

The serum amylase values in 32 consecutive patients with laparotomy evidence of acute pancreatitis show that the amylase level is not necessarily greater than 1 000 units and may indeed be normal in a small proportion of those with alcohol-induced acute pancreatitis. In addition, the serum amylase level is of no value in distinguishing haemorrhagic from oedematous pancreatitis.

We believe that a definite, let alone a gross abnormality in the pancreatic function test offers adequate biochemical support for pancreatic disease. Only 75% of patients with calcific pancreatitis, the most advanced form of the disease, have grossly abnormal pancreatic function; a definite abnormality is present in a further 20% and the test in the remaining 5% is normal or borderline.

Recognition of these factors have led to consideration of criteria other than those outlined above. A suggestive history coupled with an abnormal pancreatic function test and a serum amylase value in excess of 300 U is sufficient to warrant a diagnosis of pancreatitis. An abnormal provocative enzyme test, glucose tolerance test or barium meal suggestive of pancreatic compression is of limited diagnostic value, but the combination of one of these abnormalities with a suggestive history and disturbed pancreatic function or a raised serum amylase level may be regarded as being in favour of the diagnosis. Pancreatic scanning with ^{75}Se has been claimed by some enthusiasts as one of the more important diagnostic aids in pancreatic disease, but our experience with this technique has not been particularly rewarding. It may have a limited place as a screening procedure for carcinoma or pancreatitis in centres which do not have facilities for the pancreatic function test.

Radiology

The radiological features of pancreatitis are well known but there are 4 radiological signs that merit attention. The first is the 'target deformity' of the duodenal cap on barium meal examination which simulates an active ulcer crater surrounded by a 'halo' of oedema, and the second is the characteristic tapering of the lower third of the common bile duct on cholangiography. The presence of reflex ileus or the colon cut-off sign on straight X-ray of the abdomen is a recognized feature of acute pancreatitis, but the finding of multiple fluid levels in patients with an acute abdomen should direct attention to the probability of an intestinal obstruction requiring urgent surgery. Hypotonic duodenography is sometimes of value in demonstrating

inflammatory or malignant disease of the head of the pancreas. With regard to the latter it should be stressed that painless pancreatic steatorrhoea unassociated with overt diabetes in the elderly should be regarded as being due to carcinoma of the pancreas until proved otherwise.

Other Clinical Features

Consideration should also be given to the diagnostic value of other clinical features of pancreatitis. It is now appreciated that the Cullen's and Grey Turner's signs may occur not only with acute haemorrhagic pancreatitis but in other conditions associated with retroperitoneal and indeed intraperitoneal haemorrhage. The latter conditions may also cause methaemoglobinaemia, a sign hailed initially as diagnostic of acute pancreatitis.⁸ Hyperlipaemia or subcutaneous metastatic fat necrosis in patients with abdominal pain may alert one to the diagnosis of pancreatitis.

Diagnostic labels applied to patients before recognition of the true nature of their disease are legion and underline the importance of an awareness of the possibility of pancreatitis in all cases of abdominal pain. A word of caution is necessary, however, regarding the possible over-diagnosis of pancreatitis. This is particularly important in patients presenting with an 'acute abdomen' in whom there is any doubt about the diagnosis. Confirmation of the diagnosis by laparotomy is far safer than temporizing with a possible perforation or bowel strangulation.

NATURAL HISTORY

Differences between the natural histories of alcohol-induced and gallstone pancreatitis have been studied in some detail during the past decade and most workers are now agreed to their being separate and distinct disease entities.

Alcohol-Induced Pancreatitis

Essentially a disease of the young or middle-aged males, it tends to develop some 5-15 years after the commencement of alcohol overindulgence. The majority of our patients are moderately heavy drinkers rather than 'chronic alcoholics' in the accepted sense of the term, and the clue to the alcohol aetiology is provided mainly by the characteristic time relationship between a night's overindulgence and the onset of pain some 24 to 48 hours later. Typically, the attack starts on the 'afternoon after the night before'. The pain is frequently gradual in onset and mild to moderate in severity, and the attack usually settles within 4-5 days; acute, fulminating attacks occur in less than 10% of patients. An elevated ESR and white blood count, transient glycosuria and slight jaundice are useful diagnostic leads but the serum amylase is usually slightly rather than markedly raised. There is a marked tendency to recurrent attacks and, not infrequently, progression to diabetes, pancreatic calcification and steatorrhoea some years after the first attack. Complete alcohol withdrawal is the only effective measure in reducing the liability to further attacks and progressive pancreatic damage, and surgery is of value only in the management of complications such as cyst and abscess formation and common-duct obstruction.

Gallstone Pancreatitis

This tends to occur in middle-aged or elderly patients and is usually a more severe disease than the alcohol-induced variety. It often presents as an acute abdominal emergency but less severe attacks sometimes manifest as acute cholecystitis associated with a raised serum amylase level or laparotomy evidence of an oedematous pancreas. Despite the relapsing nature of the untreated disease, pancreatic insufficiency is rare and cyst formation unusual. The diagnosis of acute pancreatitis is readily established by serum amylase determinations or laparotomy findings but the gallstone aetiology is not always apparent. The latter was overlooked in a number of patients subjected to emergency laparotomy and subsequent cholecystography and the diagnosis was sometimes made only after repeated oral and intravenous cholecystography and biliary drainage and microscopy. Further attacks are almost invariably prevented by removal of the stones and diseased gall-bladder, preferably as an elective procedure.

SURGICAL TREATMENT

The role of surgery in pancreatitis has become more clearly defined. In general, surgeons have become more aggressive with regard to laparotomy in establishing a diagnosis of pancreatitis in patients in whom doubt exists regarding the nature of an acute abdomen⁹ and rather more cautious with regard to the surgery of chronic pancreatitis. Surgical intervention is, of course, indicated in gallstone pancreatitis and in the management of local complications such as persistent obstructive jaundice, cyst formation, duodenal stenosis, and segmental portal hypertension due to splenic vein compression.

Surgery in Chronic Pancreatitis

Recurrent attacks of pain, lasting a few days at a time, are usually due to acute exacerbations of the pancreatitis and are treated in much the same way as attacks of acute pancreatitis. The prognosis of these exacerbations is always good, and the attacks tend to become milder with progressive destruction of the pancreatic parenchyma. Surgeons have been tempted in the past to perform a variety of procedures on such patients in the hope of reducing the frequency and severity of attacks—to no avail. Sphincterotomy, biliary surgery and distal pancreatectomy with pancreaticogastrostomy, despite certain theoretical advantages, have failed to stand the test of time and are now regarded as being little better than the outlawed vagotomy for the control of recurrent attacks.

Persistent pain. Surgical exploration is important in patients with persistent pain following an acute or sub-acute attack, in patients with persistent pain despite medical treatment and alcohol withdrawal and in patients with a complication such as a cyst or persistent obstructive jaundice with or without common bile-duct stones.⁶ The operation is undertaken to exclude a cyst or intrapancreatic abscess, pancreatic or bile duct obstruction, pancreatic carcinoma or incidental disease. A cyst should be treated by means of a suitable internal drainage procedure, but further investigative procedures are usually indicated if no cyst is apparent. An operative cholangiogram and trans-

duodenal and, if necessary, transpancreatic or retrograde pancreatogram should be carried out to allow selection of an operative procedure on the basis of the character and site of the obstructing lesion or lesions.

Cholecystenterostomy or choledochenterostomy may be adequate in patients with a dilated duct with symptoms compatible with cholangitis rather than pancreatitis. There is little indication for a definitive procedure if the pancreatic duct is normal, but retrograde pancreaticogastrostomy or pancreaticojejunostomy should be carried out if single or multiple areas of obstruction are demonstrated. If the pancreatic duct is palpably dilated and filled with stones, it may be opened directly and anastomosed to a loop of jejunum (Puestow's operation). The problem, however, is complicated by the fact that these seemingly rational decompressing procedures yield rather disappointing long-term results. This has led to the wider use of ablative procedures, at least in patients with advanced pancreatic insufficiency. Intractable pain in patients with the latter may warrant subtotal pancreatectomy, and the 95% distal pancreatectomy recommended by Fry and Child¹⁰ is the current favourite.

However, the possible advantages of ablative procedures and, in particular, radical pancreatectomy should be weighed against the risk of further deterioration in steatorrhoea and diabetes. Patients with adequate pancreatic function should not be subjected to radical pancreatectomy and in them one of the drainage procedures should be adopted as a primary operation. Persistent pain in patients without evidence of duct dilatation and with adequate pancreatic function poses a real problem in management, and in such cases one may be tempted to consider sympathectomy or coeliac ganglionectomy.¹¹ Not all workers would agree with this, however, and some other ill-advised procedure would probably be carried out. The decision is easier in patients with calcific disease and advanced pancreatic insufficiency, but it should be mentioned that a few workers remain enthusiastic about the Puestow operation carried out with a generous pancreaticojejunostomy of 10 cm or longer¹² or with a mucosa-to-mucosa type anastomosis.¹³

Persistent pain of relatively short duration. The finding of a hard and indurated pancreas in elderly patients with a short history raises the possibility of cancer. Opinions differ as to the advisability of pancreatic biopsy but most workers are loath to carry it out because of the high diagnostic error and appreciable morbidity of the procedure.

REFERENCES

1. McCutcheon, A. D. (1968): *Gut*, **9**, 296.
2. Davis, A. E. (1971): Paper presented at the Pancreatic Symposium, Canberra, 1970.
3. Goodhead, B. (1969): *Ann. Roy. Coll. Surg. Engl.*, **45**, 80.
4. Creutzfeld, W. and Schmidt, H. (1970): *Scand. J. Gastroent.*, **5**, suppl. 6, 47.
5. Sarles, H., Lebreuil, G., Tasso, F., Figarella, C., Clemente, F., Deraux, M. A., Fagonde, B. and Payan, H. (1971): *Gut*, **12**, 377.
6. Marks, I. N., Banks, S. and Louw, J. H. (1968): *Progr. Gastroent.*, **1**, 412.
7. Sarles, H., Sarles, J.-C., Camatte, R., Muratore, R., Giani, M., Guien, C., Pastor, J. and Le Roy, F. (1965): *Gut*, **6**, 545.
8. Bank, S., Barbezat, G. O., Marks, I. N. and Silber, W. (1968): *Brit. Med. J.*, **2**, 86.
9. Trapnell, J. E. (1966): *Ann. Roy. Coll. Surg. Engl.*, **38**, 765.
10. Fry, W. J. and Child, C. G., (1965): *Ann. Surg.*, **162**, 543.
11. White, T. T. (1966): *Pancreatitis*, p. 201. London: Edward Arnold.
12. *Idem in Riis, Anthonisen and Baden, eds. (1970): Advance Abstracts: 4th World Congress of Gastroenterology, Copenhagen 12-18 July 1970*, p. 218. Copenhagen: Danish Gastroenterological Association.
13. Silen, W. (1971): Paper presented at the Pancreatic Symposium, Canberra, 1970.