The management of severe acute pancreatitis

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DURING the past 5 years we have had the unique experience of managing 584 cases of pancreatitis, and this paper is based on a review of 248 of these cases who were seen and treated by us for severe acute attacks during this period (Table 1). *The acute cases are defined as those who presented with severe pain and who were sufficiently ill to require at least gastro-intestinal decompression and intravenous fluid therapy.* In them the initial diagnosis of pancreatitis was made on the clinical picture supported by a serum amylase exceeding 300 Somogyi or Pimstone units (182 cases) and/or clear evidence of acute haemorrhagic or oedematous disease at surgery (112 cases) and/or at autopsy (twenty-one cases). It should be noted that cases classified as mild to moderate or chronic (Table 1) have not been included in this review even though 30% of them gave a history of undoubted acute attacks prior to 1960. During the period 1960-65 the patients in the *mild to moderate* group presented with attacks of pain which often required analgesics and even hospitalization but they were not very ill and did not require intravenous therapy and/or gastro-intestinal decompression while those in the *chronic* group presented with pancreatic dysfunction with or without pain.

We have also classified our cases on an etiological basis because, although *the initial treatment of the acute attack is the same for all etiological types, the*

severity of the attack and the subsequent course and management of the disease depend largely upon the cause (Howard & Ehrlich, 1960; Louw, Marks & Bank, 1963; Marks & Bank, 1963). We have subdivided our cases into four main etiological groups (Table 1) and their distribution in the series as a whole (as well as in the severe acute group) was as follows: alcoholic 59%, biliary 17%, miscellaneous 16% and idiopathic 8%. Our series differs from most others in the preponderance of *alcoholic pancreatitis* which in most parts of the world accounts for only 10-20% of all cases and this is probably due to the ready availability of cheap wines and the drinking habits of our labouring class. Because of the frequency of alcoholic pancreatitis, *biliary pancreatitis* comprised a smaller proportion of the total than the usual 30-60%. It should also be noted that those with acute biliary pancreatitis included thirty-six adults with stones, seven children with ascariasis, one patient with a choledochal cyst and one with a perivaterian diverticulum. The *miscellaneous group* includes a great variety of rarer etiological types and from Table 2, which reflects the various causes of acute attacks only, it should be evident how extensive the search should be to determine the cause of the condition. The *idiopathic group* consists of cases in whom we have been unable to find a cause.

Although the incidence of acute attacks was

TABLE 1
Five hundred and eighty-four cases of pancreatitis, 1960-65

	Severe acute attacks		Mild to moderate attacks	'Chronic'	Total
	Single	Recurrent			
Alcoholic	26	121	83	116	346 (59%)
Biliary					
Gallstones	12	24	4	21	61
No stones	7	2	—	28	37
Total	19	26	4	49	98 (17%)
Miscellaneous	27	9	6	50	92 (16%)
Idiopathic	8	12	10	18	48 (8%)
Total	80	168	103	233	584
	(42%)		(18%)	(40%)	

similar in the various etiological groups, the attacks tended to be milder in the alcoholic group than in the others. This is reflected in Tables 3, 4 and 5. Table 3 shows that the incidence of shock was much less in the alcoholic group (12%) than in the others (22–40%) and Table 4 shows that the mortality of acute alcoholic pancreatitis was 4.7% while that of the others ranged from 8.3% to 20%. On the other hand, gastro-intestinal haemorrhage, acute diabetes and cysts were much more common in the alcoholic group than in the others (Table 3).

Regime of management

During the past 5 years we have followed a policy of 'active conservatism' in the management of acute pancreatitis. The value of such a policy, which has been widely adopted during recent years (Smith, 1962; Elliott, 1965; Menguy, 1965; Welch & Montanez, 1965; Grözinger, 1966), is eloquently supported by our results, viz. a mortality rate of only 8.4%. As indicated in Table 6, however, the conservative approach does not preclude surgical

TABLE 2
Miscellaneous cases of acute pancreatitis

Single attack (27)	
Ascariasis	16
Traumatic	3
Pregnancy	2
Hyperparathyroidism	1
Disseminated lupus erythematosus	1
Postoperative	4
Recurrent attacks (9)	
Ascariasis	2
Traumatic	3
Pregnancy	1
Hyperlipaemia	1
Torsion of spleen	1
Postoperative	1

intervention. Our regime has been based on the following considerations:

(1) In 22% of our patients *shock*, the most serious complication of the condition, dominated the

TABLE 3
Complications of acute pancreatitis

	Alcoholic	Biliary	Miscellaneous	Idiopathic	Total
No. of cases	147	45	36	20	248
No. complicated	73	22	18	14	127
Shock	17 (12%)	18 (40%)	8 (22%)	7 (35%)	50 (22%)
Pleural effusion	3	1	—	1	5
Gastro-intestinal haemorrhage	20	—	—	1	21
Acute diabetes	27	3	—	3	33
Acute steatorrhoea	4	—	—	1	5
Metastatic fat necrosis	5	1	1	—	7
Abscess	3	2	1	1	7
Cyst	26	5	12	5	48
Duodenal obstruction	1	—	1	—	2
Common duct obstruction	1	—	1	—	2
Total No. of complications	107	30	24	19	180

TABLE 4
Mortality and morbidity of acute attacks

	Alcoholic	Biliary	Miscellaneous	Idiopathic	Total
No. of cases	147	45	36	20	248
Deaths					
Primary	4	2	1	2	9
Postoperative	3	5	2	2	12
Complications					
No. of cases	73	22	18	14	127
No. of complications	107	30	24	19	180
Duration more than 1 week	24	23	13	9	69
Jaundice	37	32	10	7	86
Hyperlipaemia	5	—	1	1	7
Raised amylase	93	44	32	13	182

clinical picture and demanded immediate and urgent attention.

(2) All the patients presented as acute abdominal emergencies with *severe pain, fluid and electrolyte imbalance due to vomiting and paralytic ileus* which required treatment from the outset and even before a definite diagnosis of pancreatitis had been made.

(3) Once the diagnosis of pancreatitis had been established—and this required laparotomy in 27%—measures were instituted to *suppress pancreatic secretion and to neutralize proteolytic enzyme activity*.

(4) At the same time steps were taken to *prevent or treat complications*. During the initial stages these

measures were essentially non-operative but operative intervention was occasionally necessary to deal with complications and, in certain carefully selected cases, there was even a place for early definitive surgery.

(5) During the *recovery phase* steps were taken to reduce stimulation of pancreatic secretion and to prevent further attacks. These steps included surgical treatment particularly in patients with biliary pancreatitis.

The problem of shock and its management

In our series severe shock was present in fifty (22%) of the cases. Of these fifty patients, thirteen succumbed, i.e. a mortality of 26%, while among the remaining 198 cases there were only eight deaths, i.e. a mortality of 4% (Table 5). It should be noted, however, that in ten of the thirteen patients who died of shock there was some other complicating factor, viz. haemorrhage, sepsis, acute diabetes, metastatic fat necrosis and hyperlipaemia (Table 5).

The shock in pancreatitis is essentially hypovolaemic and in severe cases the total blood volume may be reduced by 30% or more (Thal, Perry & Egner, 1957; Elliott, 1965; Gray & Rosenman, 1965). The initial volume deficit is due to loss of fluid into the peritoneum and peripancreatic tissues as a result of increased vascular permeability in and around the pancreas (Howard *et al.*, 1963; Gray & Rosenman, 1965). This is probably due to local release of bradykinin and kallikrein which might explain why trasyolol should lessen the severity of the disease (Ryann, Moffat & Thompson, 1965)—see below. A direct effect of the plasma loss is the early development of haemoconcentration and *it is a good rule to regard every case with a raised haematocrit as potentially shocked* (Gray & Rosenman, 1965). However, there is also considerable red cell destruction with the appearance of free haemoglobin in the peritoneal fluid and plasma and therefore haematocrit readings may be misleading.

Other factors which contribute to the shock are

TABLE 5
Causes of death in acute pancreatitis

Primary deaths	No. of cases
Shock	2
Shock and haemorrhage	1
Shock, haemorrhage and acute diabetes	1
Shock and acute diabetes	2
Shock and metastatic fat necrosis	1
Shock and hyperlipaemia	1
Disseminated lupus erythematosus	1
Total	9
Postoperative deaths	No. of cases
Laparotomy	
Shock	1
Shock and hyperlipaemia	1
Drainage of abscess	
Shock, haemorrhage and sepsis	1
Drainage of abscess and cholecystostomy	
Shock and sepsis	1
Shock, haemorrhage and sepsis	1
External drainage of cyst	
Haemorrhage	1
Fistula and sepsis	1
Choledochotomy	
Haemorrhage	3
Sphincterotomy	
Haemorrhage	1
Gastro-enterostomy	
Haemorrhage	1
Total	12

No. of cases = 248, No. of deaths = 21.

TABLE 6
Summary of treatment

Treatment	No. of cases	Early deaths	Later surgery for complications	Late deaths	Total deaths
Conservative only	117	9	30*	6	15 (9%)
Early laparotomy only	50	2	9	—	2 (4%)
Early laparotomy — delayed definitive surgery	1	—	—	—	—
Early laparotomy and definitive surgery	15	3	—	—	3 (20%)
Delayed definitive surgery	5	1	—	—	—
All methods	248	15	39	6	21 (8.4%)

*Thirty-two operations.

myocardial insufficiency and electrolyte and acid-base imbalances which develop in proportion to the severity of the disease. It is, therefore, necessary to take immediate samples of blood for typing, cross-matching and determinations of pH, PCO_2 , CO_2 and serum electrolytes and to set up central venous pressure monitoring.

The first step in the treatment of shock is to commence intravenous fluid therapy. Isotonic salt solution, e.g. Ringer's lactate, may be given rapidly and in uncomplicated hypovolaemic shock as little as 250 ml usually produces significant improvement in blood pressure and pulse quality (Wilson, 1965). At the same time it is essential to correct concurrent metabolic acidosis by infusion of sodium bicarbonate and to provide adequate respiratory support. The airway must be clear and ventilation adequate and in desperately ill cases intermittent positive pressure respiration or the administration of oxygen by an oxygenaire polymask may be required.

The amount of replacement fluid should be regulated according to the patient's needs. If the central venous pressure remains low following rapid administration of volume expanders, more fluid should be run in at a rapid rate, viz. between 1000 and 2000 ml/hr (Shires & Carrico, 1966). The danger of using vasoconstrictors in hypovolaemia deserves emphasis because they may delay proper treatment by masking the true state of affairs and only serve to aggravate tissue hypoxia in a patient whose vasoconstriction is already maximal (Wilson, 1965).

The type of fluid is important. In the less severe cases the blood pressure may return to normal, become stable and remain so after infusion of 1–2 l. of Ringer's lactate only, and if the infusion is given early enough, the need for colloid replacement may be obviated (Gray & Rosenman, 1965; Shires & Carrico, 1966). However, in most cases the response to salt solutions is only transient. Plasma and also whole blood are required and in cases of severe haemorrhagic pancreatitis about half of the replacement fluid should be whole blood. Serum albumen may be of particular value because of its antitryptic activity.

Persistence of hypotension despite an elevated or rising venous pressure indicates that the hypovolaemia is complicated by cardiac insufficiency (Wilson, 1965) and calls for the use of myocardial stimulants. Digitalis preparations are of value particularly for arrhythmias or congestive failure and are given in the form of digoxin 0.5 mg intravenously followed by 0.25 mg 6-hourly until the patient is fully digitalized (Wilson, 1965; du Toit *et al.*, 1966; Shires & Carrico, 1966). If, in spite of digitalization, there is evidence of severe impairment of organ perfusion, e.g. severe oliguria, lethargy and extreme hypoventilation, drugs with positive

inotropic action should be used and we have found isoprenaline particularly useful (du Toit *et al.*, 1966). There is a risk of producing cardiac arrest and therefore all patients on isoprenaline therapy should be monitored cardiographically for signs of ischaemia resulting from tachycardia or arrhythmias. The drug is given as a 1 in 450,000 infusion commencing with a dose rate of 0.5–4.0 $\mu\text{g}/\text{min}$. Prior to the infusion the patient is transfused until the central venous pressure is at least 12 cm water and decrease in central venous pressure below 12 cm water after the isoprenaline has been started is matched with further fluid therapy until urinary excretion commences and/or a systolic blood pressure of 80 mmHg is maintained (du Toit *et al.*, 1966).

The value of adrenal corticosteroids in acute pancreatitis is debatable. During the phase of uncomplicated hypovolaemic shock steroids are best not used unless there is evidence of previous depletion. In cases who present with features resembling endotoxic shock, however, the use of steroids in pharmacological doses is gaining popularity (Shires & Carrico, 1966). The recommended dose is 50 mg hydrocortisone per kilogram given intravenously in the first 24 hr and sometimes repeated over the next 24 hr. We used steroids in more conventional doses in two cases only—one recovered and the other died from haemorrhage from a steroid ulcer.

Vasodilators such as Dibenzyline and Rogitine have also been advocated in recent years. However, we agree with Shires & Carrico (1966) that their use should be confined to experimental work in normovolaemic patients who have prolonged septic shock.

Treatment of pain, electrolyte imbalance and ileus

Relief of pain

Most narcotics in common usage produce some degree of spasm of the sphincter of Oddi which may aggravate the pancreatitis. For this reason morphine is best avoided. Pethidine (Demerol) is the least offender and may be given in doses of 75–100 mg intravenously every 4 hr if necessary (White & Magee, 1961). It has been customary to combine analgesics with antispasmodics to overcome spasm of the sphincter but the only effective antispasmodics are nitroglycerine and amyl nitrite (Efron, 1961; White & Magee, 1961) which, in the presence of shock, should be used with the greatest caution because they potentiate hypotension. Avafortan, which does not produce spasm of the sphincter of Oddi, has been our first choice, but in patients with very severe pain its analgesic effect may not be potent enough (Efron, 1961). The usual dose is 5 ml (40 mg) repeated as required. Continuous epidural anaesthesia, splanchnic block or paravertebral sympathetic block have been reported to

afford relief of pain (White & Magee, 1961), but we have not found it necessary to resort to such drastic measures.

Intravenous fluid and electrolyte therapy

Disturbances of fluid and electrolyte balance are invariably present. Careful monitoring of intake and output, hydration status, urine specific gravity, blood urea nitrogen and serum electrolytes is, therefore, essential (Welch & Montanez, 1965).

In uncomplicated cases one can anticipate the need for approximately 1000–1500 ml of fluid every 8 hr during the first 24–48 hr. When the gastric aspirate is minimal we use 5% invert sugar solutions containing 26 mEq sodium, 26 mEq potassium and 52 mEq chloride per litre provided renal function is good. With large amounts of gastric aspirate, however, the sodium should be increased to approximately 100 mEq/l. It is also wise to give about 500–1000 ml of the total daily fluid in the form of plasma to replace loss of plasma into the retroperitoneal tissues. Hypocalcemia tends to occur in some cases but is usually mild and can be managed with 10–20 ml of 10% calcium gluconate intravenously. A reduction in the serum magnesium level below 1.5 mEq/l may result in neuromuscular excitability and cardiac arrhythmias, which can be corrected by 10 ml of 25% magnesium sulphate given intramuscularly or with the intravenous infusion (Welch & Montanez, 1965). Adequate amounts of vitamins B and C should also be added to the fluids.

In most cases intravenous fluid therapy is required for 3–4 days only but in severe or complicated cases it might have to be continued for longer. In sixty-nine (27%) of our cases intravenous fluids were required for more than a week.

Treatment of ileus

Paralytic ileus should be treated by nasogastric suction and restriction of oral feeding. Suction should be continued until distension has been relieved and active peristalsis has returned. Usually 3–4 days will suffice but in about one-quarter of our cases it had to be continued for more than a week. When there is severe oedema and continuing auto-digestion in the head of the pancreas and when cysts or abscesses complicate the disease the gastric aspirate remains excessive due to localized ileus or mechanical compression of the duodenum. Not infrequently this is misinterpreted as paralytic ileus but a clue to the diagnosis is provided by the character of the aspirate which tends to remain free of bile. In such cases clinical and radiological assessment should allow the correct diagnosis to be made and the proper treatment to be instituted (see below).

Severe and prolonged paralytic ileus with gross abdominal distension is an ominous sign and

carries the added risk of impairing pulmonary ventilation particularly if the patient is obese or has basal atelectasis. In these circumstances gastrostomy may be advisable particularly in patients subjected to diagnostic laparotomy.

Suppression of pancreatic secretion and neutralization of proteolytic activity

Once a definite diagnosis of acute pancreatitis has been made, measures should be instituted to suppress pancreatic secretion and to neutralize proteolytic activity. In 182 of our 246 cases it was possible to make the diagnosis on clear-cut clinical evidence supported by a raised serum amylase but in sixty-six (27%) diagnostic laparotomy was necessary (Table 5). However, all the patients were treated along the following lines:

Restriction of oral feeding and nasogastric suction serve to combat paralytic ileus and also effectively reduce pancreatic enzyme secretion by preventing release of the hormonal stimuli. Starvation, by keeping fats from reaching the upper jejunum, prevents release of pancreozymin while nasogastric suction, by keeping gastric acid from entering the duodenum prevents release of secretin.

Pancreatic secretion may also be reduced by blocking the vagal stimuli by *anticholinergics*, e.g. atropine 0.5 mg subcutaneously every 3–6 hr, propantheline (probanthine) 15 mg intramuscularly every 6–12 hr or pizenzolate bromide (piptal) 5 mg intramuscularly every 6–12 hr. These drugs must be used with caution because they tend to prolong ileus, aggravate hypotension in shocked patients and precipitate urinary retention in the elderly.

Hexamethonium bromide and other ganglion blocking agents have been used in the belief that acute pancreatitis might be due to a vascular catastrophe (Davies, Moore & Wynn-Williams, 1953). Apparent successes have been reported with hexamethonium bromide in doses of 250 mg twice daily for 5–7 days.

Other drugs which have been used include *propylthiouracil* which, in experimental animals at least, reduces pancreatic enzyme secretion by suppressing cellular metabolism (Welch & Montanez, 1965). *Acetazolamide sodium* (Diamox) has been used to inhibit the bicarbonate component of pancreatic secretion (Welch & Montanez, 1965). The drug may be given intravenously in doses of 0.25 mg twice daily for the first 3–5 days. It is also claimed that *methionine* is of value in cases of alcoholic or idiopathic pancreatitis associated with malnutrition. In such cases an acinar cellular membrane block may exist and methionine has been shown to increase permeability of the acinar membrane permitting the passage of trypsinogen into the collecting system (Welch & Montanez, 1965).

Wels & Taheri (1962) have produced experimental evidence that general body *hypothermia* reduces pancreatic secretion and report survival of three out of four patients with fulminating haemorrhagic pancreatitis treated with hypothermia. However, further studies are required to determine enzymatic activity and pancreatic secretion during hypothermia before this method can be recommended.

ACTH and adrenal steroids have been advocated (White & Magee, 1961; Welch & Montanez, 1965) but there is need for caution. Sircus (1961) has shown experimentally that although these hormones reduce bicarbonate secretion they produce an increased output of amylase and trypsin and there are reports of patients in whom acute pancreatitis has apparently been precipitated by long-term steroid therapy. We, therefore, do not recommend steroids in the average acute case although we might use them in severe shock (see previous page).

Trasylol, an inhibitor of trypsin and kallikrein, has been used with varying enthusiasm by many workers over the past few years. Despite the inherent difficulties in conducting a clinical trial in acute pancreatitis, we believe that trasylol is a useful adjunct in the treatment of the condition provided the drug is given early in the attack in the augmented dose of 150,000–300,000 units/day. The importance of this dosage schedule was demonstrated in an *in vitro* study and in a controlled clinical trial carried out in thirty-two of the patients in the present series (Moshal *et al.*, 1963) and may explain the equivocal results obtained in centres in which dosages of 30,000–50,000 units/day were employed (Skyring, Singer & Tornya, 1965). While our data do not permit a definite conclusion to be drawn regarding the efficacy of trasylol in the fulminating and potentially lethal case of acute pancreatitis, there was little doubt regarding its value in reducing the duration of pain and hypertrypsinaemia in the average acute attack. McHardy *et al.* (1963) and Grözinger (1966) have also shown that the drug offers protection when given early. It should be stressed that trasylol therapy always supplements the more conventional methods of treatment. It is our policy to add trasylol to the intravenous fluids in those patients requiring gastric suction and fluid replacement, and to continue with trasylol therapy for as long as the intravenous fluids are considered necessary.

More recently, the administration of trasylol by peritoneal dialysis (Wall, 1965) or by injection into the pancreaticoduodenal artery by the Seldinger technique (Grözinger, 1966) has been claimed to be of value in patients with acute pancreatitis. These alternative routes of administration should be given the benefit of further trial for possible use in the fulminating case, but are unnecessary in the less severe cases of acute pancreatitis.

Prevention and treatment of complications

Secondary infection

Pneumonia, subphrenic and peripancreatic abscesses and parotitis may develop after the first few days. These complications can be minimized by the administration of prophylactic antibiotics especially penicillin and streptomycin which are secreted in high concentrations in pancreatic juice. Tetracyclines, although effective, are not excreted into the pancreatic juice and should be avoided when there is jaundice. Chloramphenicol, on the other hand, has proved to be effective in our cases.

General medical status

Since many of these patients are elderly and obese with associated cardiorespiratory disease, or malnourished and alcoholic, they require more careful attention than the usual acute abdominal emergency. There is an increased tendency to *thrombosis and thrombophlebitis* which demands special care in the form of elastic support and elevation of the lower limbs, active exercises and physiotherapy, but we do not use prophylactic anticoagulants. *Parotitis* is not rare and should be prevented by adequate hydration, mouthwashes and stimulation of salivary secretion.

The *pulmonary status* of patients with acute pancreatitis should be followed attentively (Menguy, 1965). Significant ventilatory impairment may result from pleural effusions associated with elevation and splinting of one or both diaphragms caused by the severe subdiaphragmatic inflammatory process and this may be aggravated by abdominal distension. Pleural effusions, if clinically significant, should be evacuated by needle aspiration and this was necessary in five of our cases. If poor ventilation continues, and particularly if a state of shock is present, tracheostomy should be performed. Indeed, tracheostomy must be considered whenever there is severe atelectasis because it allows frequent tracheobronchial toilet and bronchoscopy without moving the patient from his bed.

Severe mental disturbance

This is seldom a feature of acute pancreatitis and, when present, is usually due to delirium tremens. An acute toxic delirium may rarely occur in the elderly and in the very occasional patient with fulminating pancreatitis. We had one example of the latter who died of shock and who showed metastatic fat necrosis of the femur and evidence of petechial haemorrhages of the brain at autopsy. Schuster & Iber (1965) found that psychotic reactions, particularly hallucinations, were common in alcoholic pancreatitis, but this has not been our experience. It should be stressed that patients with alcoholic pancreatitis are not necessarily chronic

alcoholics and that the characteristic time relationship between the alcoholic bout and onset of the attack—'the afternoon after the day before'—is such that patients are seldom under the influence of alcohol when admitted to hospital (Marks *et al.*, 1965). Delirium tremens is a potentially lethal condition which requires energetic treatment with massive doses of Sparine of the order of 200–600 mg/day. This should be supplemented with large doses of the B complex group of vitamins.

Haemorrhage

There appears to be an increased tendency to haemorrhage in some cases of acute pancreatitis. The haemorrhagic extravasations into the peritoneal cavity and along fascial planes have already been mentioned and the latter sometimes give rise to obvious discoloration of the flanks. When this sign, first described by Grey Turner in 1919, appears it is indicative of very severe disease and a poor prognosis. It was present in two of our patients both of whom died in shock. In addition, the blood may fail to clot at surgery (or even on the autopsy table). These phenomena are possibly due to excessive antithrombin or fibrinolysis (Welch & Montanez, 1965) and may call for the use of whole blood, fresh frozen plasma, vitamin K, fibrinogen, trasylol or epsilon aminocaproic acid (EACA). EACA is given intravenously in doses of 4–8 mg over a 12-hr period, but should be used cautiously because of the risk of generalized thrombosis (Welch & Montanez, 1965).

Patients with acute pancreatitis may also develop haemorrhage from the upper gastro-intestinal tract and our series includes twenty-one such cases (an incidence of 9%). In the majority the bleeding was not excessive and ceased on conservative management but in many the cause remains uncertain. In none was it due to associated chronic peptic ulceration which, in our experience, is not as common as reported by others (Marks *et al.*, 1966). One of our cases, however, was subsequently shown to be suffering from a carcinoma of the stomach. Since twenty of the twenty-one patients belonged to the alcoholic group the possibility of portal hypertension had to be considered but we have found that alcoholic pancreatitis and cirrhosis seldom co-exist (Marks & Bank, 1963) and varices were responsible for the bleeding in only one of the twenty-one cases. Moreover, in this case the varices were due to splenic vein obstruction by the swollen pancreas and not to cirrhosis and he was successfully treated by splenectomy—see below. *In two of the patients massive haemorrhage resulted from intense gastro-duodenal congestion due to the contiguous pancreatic inflammation.* Both of them succumbed without the benefit of surgical intervention but it is problematical whether this would have altered the outcome. In

seventeen of the patients a presumptive diagnosis of acute erosions has been made. Four of them were submitted to diagnostic laparotomy and gastrostomy—see below. The remaining thirteen responded to conservative therapy.

There is also a risk of gastro-intestinal haemorrhage after meddlesome operations performed during the acute attack. This occurred on one of our cases who had a cholecystostomy performed at the time that an abscess was drained, in three patients after choledochotomy (one developed a steroid ulcer), in one after sphincterotomy and in one after gastro-enterostomy for a cyst. All these patients died and, arising from this experience, we believe that it is important to refrain from elective procedures during severe acute attacks—see below.

Acute diabetes

Transient hyperglycaemia and mild glycosuria are very common in acute pancreatitis and do not require any treatment. Acute diabetes, as defined by the presence of a persistently 'brick' urine and hyperglycaemia of more than 3 days duration in a patient without known diabetes, occurred in thirty-three patients in the present series. Twenty-seven of these patients suffered from alcoholic pancreatitis, i.e. an incidence of 18% in this group, but it was distinctly rare in the other etiological groups. The pancreatitis appeared to precipitate diabetic coma in only one of these patients. On the other hand, the diabetic state in known diabetics is always aggravated by an acute attack of pancreatitis and carries a greater risk of precipitating coma. This should always be watched for in patients with gallstone pancreatitis in whom familial diabetes is not uncommon.

Acute diabetes occurring during an attack of acute pancreatitis seldom requires treatment because of the self-limiting nature of the disorder and the extreme rarity of ketosis after adequate rehydration. It is our policy to institute insulin therapy only if the diabetes persists for longer than a week or true diabetic ketosis supervenes (Bank, 1966). In such cases it is important to keep a constant check on the diabetic state because of the tendency for the diabetes to settle at a variable time following the acute attack.

It should be noted that *hyperlipaemia* as defined by the presence of frankly milky serum was present in three of the patients who developed acute diabetes. In all of them it disappeared as soon as the diabetes was controlled. On the other hand, hyperlipaemia unassociated with diabetes appears to be more serious, e.g. we had four such cases of whom three presented problems. Two of the three died in shock and the third suffered from familial hyperlipaemia which required treatment with Atromid.

Metastatic fat necrosis and arthritis

This complication occurred in seven patients (five alcoholic, one biliary and one idiopathic). Two of these showed subcutaneous fat necrosis, two subcutaneous fat necrosis and bone necrosis, one bone necrosis and arthritis, one bone necrosis alone and one bone necrosis, arthritis and subcutaneous fat necrosis. Two of the patients were desperately ill and one died in shock (Immelman *et al.*, 1964).

Subcutaneous fat necrosis usually involved the lower anterior shin and required little more than analgesics. Subcutaneous fat necrosis in other areas may develop into sterile non-inflammatory pseudo-abscesses which should be allowed to settle spontaneously (Bank *et al.*, 1966). The arthritis is rarely severe but usually necessitates analgesic tablets. Osteolytic bone lesions involving weight bearing bones may require prolonged bed rest to ensure satisfactory healing and to protect against the danger of a pathological fracture.

The role of surgery during the acute attack

As indicated above, our policy of active conservative management of acute pancreatitis does not preclude surgical intervention. Indeed, 101 (40%) of the patients in this series were subjected to 113 operations. The indications for surgery were as follows:

1. Diagnostic laparotomy

It is not always possible to have absolute confidence in the accuracy of a clinical diagnosis of acute pancreatitis in a patient who presents with signs and symptoms of an acute abdomen. Also, the serum amylase may not be helpful. In our series of 248 cases of acute pancreatitis the amylase was significantly elevated in 182 (73%) and in general the more severe the disease, the higher was the value, e.g. of fifty patients in this series who were severely shocked the amylase was raised in forty-five (up to 4000 units and over in some of those with biliary disease). However, in five of our patients with severe shock (all in the alcoholic group) the amylase was not raised—and two of them died. Furthermore, the serum amylase may be raised in other acute abdominal emergencies such as perforated peptic ulcer, empyema of the gallbladder, gangrene of the small bowel and afferent loop obstruction complicating gastro-jejunostomy (Foster & Ziffren, 1962). A diagnostic peritoneal tap has been advocated for doubtful cases (Foster & Ziffren, 1962) but it is seldom possible to find fluid at a significant period in the patient's illness (Bernard, 1965) and a high concentration of amylase may also be present with strangulated small bowel. It must be accepted that in some cases of acute pancreatitis it is impossible to rule out one of the surgical conditions listed above and realized that

the consequences of non-intervention in cases of perforated duodenal ulcer, gangrenous gallbladder or strangulated small intestine may be disastrous. On the other hand, a limited laparotomy (which can mean the difference between life and death when dealing with one of the above conditions) *per se* is not detrimental in a case of acute pancreatitis. Therefore, we are convinced that surgical exploration is a justifiable part of the diagnostic work-up when the diagnosis of acute pancreatitis is in any doubt, and in sixty-six (27%) of our cases laparotomy was performed (Table 7). It should be stressed, however, that when acute pancreatitis is discovered during laparotomy intraperitoneal manipulations must be limited to a few useful gestures (Louw *et al.*, 1963; Louw, 1964; Menguy, 1965).

In fifty-one of our cases submitted to laparotomy the abdomen was simply closed following a thorough lavage of the peritoneal cavity with saline to remove

TABLE 7
Early laparotomy for acute pancreatitis (sixty-six cases)

	No. of cases	Deaths
Laparotomy only	51	2
Laparotomy and immediate definitive surgery		
Cholecystostomy	1	—
Cholecystectomy	2	—
Choledochotomy (no stones)	2	2
Sphincterotomy	1	1
Gastrotomy for gastro-intestinal bleeding	4	—
Splenectomy for gastro-intestinal bleeding	1	—
Distal pancreatectomy for trauma	3	—
Pancreatico-gastrotomy for trauma	1	—
Total	66	5

blood, fibrin clots and pancreatic exudate. Two of the patients (one alcoholic and one idiopathic) died in shock but the rest of them entered the recovery room in a better condition than before the operation. Among them there were twelve with gallstones (common duct stones in five) and only one of these, a patient who required a later cholecystostomy (Table 6) failed to recover from the acute attack on conservative management. Of the remaining thirty-seven, complications requiring later surgery developed in nine (seven cysts, one abscess and one choledochal obstruction—all successfully treated) but the rest recovered rapidly from the acute attack.

The above results would appear to support the traditional teaching that during the acute phase the right course to adopt is 'to get out as quickly as possible' (Louw *et al.*, 1963) and 'if gallstones are palpable in the gallbladder they should be left

there and removed later' (Smith, 1962). Recently, however, there has been a trend towards more active intervention especially when biliary tract disease is suspected (Bernard, 1965; Trapnell, 1966), and in this connection it may be argued that our patient who required a later cholecystostomy would have benefited from earlier drainage of the biliary system. We certainly believe that, depending on the severity of the pancreatitis, an acutely inflamed gallbladder should be dealt with by either cholecystostomy or cholecystectomy and three of our patients in whom this was done (one cholecystostomy and two cholecystectomies) all did well (Tables 5, 6 and 7). On the other hand, there does not appear to be any justification for biliary tract surgery in patients who do not have biliary tract disease and in our experience negative exploration of the common duct during the acute attack has been disastrous. In two of our patients in whom the pancreatitis was associated with jaundice the common ducts were explored; neither had stones and both died from postoperative gastro-intestinal haemorrhage (Tables 5, 6 and 7). We cannot agree with Salzman and his associates (Salzman & Bartlett, 1963; Salzman & Nardi, 1965) that the sphincter of Oddi should be explored via a duodenotomy on the assumption that a pancreatic outflow block at the sphincter could be relieved. A procedure of some magnitude under ideal conditions, it might be responsible for a fatality in a patient already desperately ill from pancreatitis (Menguy, 1965) and this, in fact, was the outcome in the single case in our series so treated and who developed postoperative gastro-intestinal haemorrhage (Table 5). Moreover, it is doubtful whether this procedure is of any benefit even in those very rare cases where a stone is impacted in the ampulla of Vater because, should pancreatitis result from pancreatic outflow obstruction most of the damage has been done by the time such an operation could be performed (Menguy, 1965).

When laparotomy is performed for acute pancreatitis associated with gastro-intestinal haemorrhage, the source of bleeding should be found and dealt with if possible. In our experience, however, the bleeding usually occurs from acute erosions and ceases spontaneously. In four of our cases submitted to laparotomy, gastrotomy was performed. No definite lesions could be found but all of them made an uneventful recovery. In a fifth patient the bleeding arose from gastric varices secondary to splenic vein obstruction and was controlled by splenectomy.

Traumatic pancreatitis deserves special attention because it demands *early* definitive surgery (Table 7). It usually follows blunt trauma and the common injury is a 'fracture' of the pancreas. When serious damage is confined to the body or tail of the

pancreas, the accepted treatment is resection of the devitalized fragments of the gland and drainage (Freeark *et al.*, 1965). This was done in three cases with excellent results. Injuries of the head to the right of the superior mesenteric vessels, however, may pose most difficult problems because of bleeding, associated injuries to duodenum and common duct and disruption of the main pancreatic duct. In such cases internal drainage into the stomach or jejunum is the favoured procedure (Freeark *et al.*, 1965). We treated one such case by anastomosis of both ends of the severed duct to the stomach and he had a remarkably smooth convalescence. However, this is not the rule and not infrequently surgical repair of the damage in these very ill patients may become extremely complicated and hazardous.

2. Treatment of complications (Table 8)

Abscesses

This dreaded complication results from bacterial invasion of the haemorrhagic extravasation associated with pancreatitis. Ill-advised attempts at draining the retroperitoneal space during the acute attack no doubt increase the risk of infection and should be avoided. However, once an abscess has formed, surgical drainage offers the only chance of survival. The best drainage is afforded by a left retroperitoneal approach through the bed of the twelfth rib. Pus, necrotic bloodclot and pancreas and pancreatic 'sequestra' are usually found and practically the whole of the pancreas may slough out through the wound. The skin must be protected to prevent excoriation and the depths of the wound irrigated to evacuate sloughs. These patients tend to suffer a prolonged and distressing illness with suppuration and toxæmia which may culminate in secondary haemorrhage and death. Seven of our patients developed abscesses (Table 8). Two of these suffered from gallstone pancreatitis and drainage of the abscesses was combined with cholecystostomy. One died of shock and sepsis and the other died of shock and secondary haemorrhage. In the remaining five the abscesses were simply drained. One developed a lethal secondary haemorrhage and the remaining four had long and complicated 'suppurative' illnesses (with repeated secondary haemorrhages in two of them).

There is a distinct tendency for haemorrhage to occur from drains which have been inserted to deal with pancreatic abscesses (or cysts). This is due to digestion of large vessels and may be massive and exsanguinating. Postoperative haemorrhage occurred in five of our cases treated by external drainage (four abscesses and one cyst). Two of these patients died and another required repeated operations to arrest the bleeding. When bleeding is severe the only way of handling the situation is to re-operate on the patient, find the bleeding point and treat it

TABLE 8
Delayed operations for acute pancreatitis

Indications	Procedure	No. of operations	Deaths
Complications			
Abscesses (7 cases)	Drainage	5	1
	Drainage and cholecystostomy	2	2
Total		7	3
Cysts (32 operations in 30 patients)			
	External drainage	6	2
	Excision of cyst	3	—
	Cyst-gastrostomy	15	—
	Cyst-duodenostomy	3	—
	Cyst-jejunostomy	3	—
	Gastro-enterostomy	1	1
	Cholecyst-enterostomy	1	—
Duodenal obstruction (1 case)	Gastro-enterostomy	1	—
Compression of common duct (1 case)	Choledcho-enterostomy	1	—
Total		34	3
Failure of response to conservative treatment (6 cases)			
	Cholecystostomy	1	—
	Cholecystectomy	2	—
	Cholecystectomy and removal of common bile duct stones	2	—
	Choledochotomy (no stones)	1	1
Total		6	1

by suture and/or proximal ligation. This, however, is seldom possible, and even if bleeding is arrested, there is a grave risk of recurrence.

Cysts

Cysts developed in forty-eight (20%) of our cases but were somewhat rarer in the biliary group (11%). The commonest type of cyst was the classical pseudocyst involving the lesser sac. Less commonly the cyst was within the pancreas (usually the head) between the leaves of the transverse mesocolon near the tail of the pancreas, or above the stomach.

Contrary to popular belief, some cysts may disappear on conservative therapy alone and in our series only thirty patients (62%) required definitive operations for their cysts. On the other hand, there are many arguments in favour of early surgery. Large or expanding cysts require urgent drainage because of the risks of rupture or haemorrhage and of our cases who were not operated upon, one died from rupture of a cyst and another from rupture and haemorrhage. A neglected or unrecognized cyst in the head of the pancreas may lead to persistent duodenal or common duct obstruction and this necessitated gastro-enterostomy in one of our patients and cholecyst-enterostomy in another. Furthermore, although patients may recover completely from the acute attack with apparent disappearance of the cysts, incomplete resolution was responsible for subsequent attacks and/or chronic

pain despite removal of the etiological factor in five of our patients. Finally, it must be remembered that a carcinoma of the pancreas may be responsible for the pseudocyst and in one of our cases biopsy of the cyst wall revealed an unsuspected cancer. This is not only an important consideration in favour of early surgery but also emphasizes the need for careful examination of the pancreas at operation and for biopsy of the cyst wall when possible.

Table 8 reflects the operations performed on thirty of the cysts in this series. It is agreed that internal drainage of the cyst into some part of the gastro-intestinal tract is the treatment of choice (Hoxworth *et al.*, 1963; Menguy, 1965; Parshall & Remine, 1965) and this is supported by our results. However, sometimes external drainage may be required.

External drainage. This should generally be reserved for patients who are desperately ill and for cysts with friable walls which are unsuitable for suture, but may be permissible for small cysts up to 4 in. in diameter (Menguy, 1965). Simple catheter drainage should be used and not marsupialization which is almost always complicated by pancreatic fistulae (Hoxworth *et al.*, 1963).

Six of our patients, all of them very ill with large, friable cysts, were treated by external drainage. Two of these patients died; one from severe haemorrhage and the other from a massive pancreaticobiliary fistula. Two developed chronic fistulae — one was left because of the presence of carcinoma in the

cyst wall and the other was successfully treated by subsequent implantation into a loop of jejunum. One of the cysts became infected and required further drainage and only one patient recovered without complications. These poor results, however, depended on the nature of the cysts rather than on the operative procedure. In the past some good results have been obtained with external drainage, e.g. Waugh & Lynn (1958) reported only one death in forty patients treated between 1948 and 1954. However, persistent fistulae with excoriation of the skin, retroperitoneal abscesses and haemorrhage are well known and common complications of external drainage and the procedure should, therefore, be avoided whenever possible (Hoxworth *et al.*, 1963; Parshall & Remine, 1965).

Excision of the cyst. This is seldom feasible and can be highly dangerous if attempted for cysts of the body or head of the pancreas. For mobile cysts limited to the tail of the pancreas, however, excision of the cyst with the pancreatic tail may be possible and was done in three of our cases with excellent results. The operative site should be drained because there is always some leakage of pancreatic juice.

Internal drainage. In twenty-one of our patients the cysts were treated by internal drainage. There were no deaths and the results have been excellent. These results are in keeping with the experience of others. Various methods of internal drainage are possible. Doubilet & Mulholland (1953) have suggested that since all cysts are connected with the pancreatic ducts adequate drainage can be obtained by sphincterotomy or anastomosis of the duct to stomach or jejunum. However, the size of the communication with the ducts is so small and so variable that decompression via the ducts is usually not practical and even Doubilet & Mulholland also used other drainage procedures in the majority of their cases (Hoxworth *et al.*, 1963). We, therefore, prefer to deal with the problem more expeditiously by cyst-gastrostomy, cyst-duodenostomy or cyst-jejunostomy.

Cyst-gastrostomy may be performed when the cyst forms behind the stomach and obliterates the lesser sac by fusion with the posterior wall of the stomach. The transgastric approach is the best and adequate drainage should be ensured by making a circular opening not less than 2 cm in diameter through the posterior wall of the stomach into the cyst. The procedure was used in fifteen of our patients and the results were highly satisfactory in all but two. One patient developed a recurrence which required later cyst-duodenostomy and the other had persistent duodenal obstruction which necessitated subsequent gastro-enterostomy after which he developed a lethal gastro-intestinal haemorrhage.

Cyst-duodenostomy is suitable for cysts in the

head of the pancreas. When the cyst is situated mainly proximal to the ampulla a formal anastomosis to the first or second parts of the duodenum is preferable because of the risk of injuring the bile duct. When it presents distal to the ampulla transduodenal cyst-gastrostomy is preferred. The latter method was used as a secondary procedure in one of our patients and as a primary procedure in two, one of whom also required cholecyst-enterostomy because of obstruction of the common bile duct by the swollen pancreas. In all of them we have established drainage by puncture through the posterior wall of the duodenum, inserting the cross piece of a T-tube into the cyst cavity and guiding the long limb of the tube along the third and fourth parts of the duodenum into a defunctioned loop of proximal jejunum and then out to the surface. This has enabled us to determine the amount and duration of discharge of pancreatic juice from the cyst without the risk of producing an external fistula. By injecting gastrograffin through the tube into the cyst, we have also been able to assess the size of the cyst and its gradual diminution after drainage. All the cases recovered rapidly without complications.

Cyst-jejunostomy is the form of drainage most widely used (Hoxworth *et al.*, 1963; Parshall & Remine, 1965) but we have reserved it for cysts presenting to the left of the stomach or between the leaves of the mesocolon. A formal anastomosis should be made to a Roux-en-Y segment of jejunum or to a loop of jejunum defunctioned by entero-enterostomy. The procedure was used in three of our cases with excellent results.

Compression of the duodenum and/or common duct

Inflammatory swelling of the head of the pancreas during the acute attack is often responsible for some degree of obstruction of the duodenum and/or common bile duct. Usually, however, this is only transient and does not require surgical treatment. Cysts may also compress these structures but this is almost always relieved by drainage of the cysts. However, in one of our cases duodenal obstruction persisted after drainage and necessitated gastro-enterostomy and in another the common duct was so severely obstructed that cholecyst-enterostomy was combined with cyst-duodenostomy. Very rarely persistent autodigestion with continuing oedema may be responsible for duodenal or common duct obstruction and we have had an example of each. Choledcho-enterostomy was performed in one and gastro-enterostomy in the other with excellent results in both.

3. Failure of response to conservative treatment

While most patients with acute pancreatitis respond rapidly to conservative management, there are some who do not respond well and either succumb at an early stage in a fulminating attack

or pursue a persistent, smouldering course with or without early relapses.

It is generally agreed that surgery has little to offer and is, in fact, hazardous in patients suffering from overwhelming fulminant pancreatitis but Salzman & Nardi (1965) have recently suggested that sphincteroplasty with exploration of the pancreatic duct should be considered in patients who develop postoperative pancreatitis following manipulations in the vicinity of the ampulla. There may be some merit in this suggestion because with the usual conservative measures the mortality remains at 50% (Menguy, 1965). Four of our patients developed acute pancreatitis after such operations. Two of them died and the two who recovered were desperately ill for several weeks. No doubt oedema and haemorrhage in the neighbourhood of the ampulla produced pancreatic duct obstruction and early decompression might have prevented the massive pancreatic necrosis. On the other hand, we agree with Menguy (1965) that 'attempts to explore the pancreas, to debride necrotic tissue in and around the pancreas, or to remove retroperitoneal clots' during the acute attack, 'are reprehensible.' At this stage there is nothing to be drained or evacuated because the process consists of diffuse inflammation with oedema and haemorrhage, spreading more or less widely from the pancreas along retroperitoneal tissue planes. Exploration of the retroperitoneal space serves no useful purpose and, especially if drains are left in place, may introduce infection and lead to the most dreaded complication of pancreatitis, that of peripancreatic abscess.

Watts (1963) has advocated total pancreatectomy in patients not responding to intensive resuscitation. The object is to prevent release of kallikrein from the damaged pancreas and thereby to reduce fluid loss. Although Watts has reported a case successfully treated by this drastic method we feel that further work is needed on the cause of death in these cases before it can be accepted.

Surgical intervention should be more seriously considered in patients who have recovered from the shock phase but in whom the disease continues to smoulder and splutter despite absence of complications. Not infrequently gallstones are responsible and we agree with Bernard (1965) that those who are likely to be suffering from stones should be operated upon forthwith.

The type of surgical procedure will depend upon the operative findings but the decision may be difficult when the pancreatitis is associated with jaundice. As already pointed out, negative exploration of the common duct may be dangerous and this is further emphasized by the result in one of our cases who was operated upon because symptoms and jaundice persisted for a week. The common

duct was explored, no stones were found and he succumbed from postoperative gastro-intestinal haemorrhage. On the other hand, might it not be equally dangerous to leave a stone possibly impacted in the ampulla of Vater, a stone which may be responsible for both the pancreatitis and the jaundice? In coming to a decision it is important to realize that stones in the common duct do not constitute an immediate threat to life and virtually never cause complete obstruction (Menguy, 1965); at least, we have not encountered such a case. Furthermore, the jaundice accompanying pancreatitis is more often due to compression of the bile duct by pancreatic oedema or to focal liver injury by proteolytic enzymes. In the present series no less than eighty-six (34%) of the patients were jaundiced but of these only twenty-four had gallstones and among them only seven had stones in the common bile duct. (Of the latter, four recovered from the acute attack on conservative therapy after initial diagnostic laparotomy.)

In view of the above we consider it unwise to interfere with the common bile duct in gravely ill patients with haemorrhagic pancreatitis. In such cases it is wiser to perform cholecystostomy if common duct stones are suspected. This was done in one of our cases (a week after diagnostic laparotomy). He then recovered from the acute attack and stones were subsequently retrieved from his common duct. If the pancreatitis is not too severe and stones are palpable in the gallbladder but common duct stones are not suspected, cholecystectomy should be performed. This was done in two of our patients, both of whom did very well. In similar cases with jaundice it is our policy to explore the common bile duct only when stones are palpable in the duct or visible on the operative cholangiogram and in two of our cases cholecystectomy and choledochostomy were performed with excellent results. Salzman & Nardi (1965) have made a plea for sphincteroplasty and exploration of the pancreatic duct in such cases, but we have not yet encountered a case where such drastic surgery during the acute attack has appeared to be justified.

The recovery phase and prevention of further attacks

General measures

The phase of clinical recovery usually begins between the 4th and the 6th day in the average case. At this stage nasogastric suction and intravenous fluids are discontinued and oral feeding with the traditional bland, low-fat diet commenced. This diet is particularly important in patients with suspected gallstone pancreatitis. Since clinical improvement does not necessarily imply complete pathological resolution, treatment with antibiotics and intensive anticholinergic and antacid therapy should

be continued for a further week or two. In uncomplicated cases a normal diet may be resumed and all treatment discontinued by about the 14th day.

Persistent diabetes necessitating continued therapy may occasionally follow an acute attack, but this is unusual. For the majority of patients insulin or oral therapy requirements decrease either rapidly or progressively over a number of weeks and, in these, the danger of hypoglycaemic attacks from unnecessary medication must be recognized. In this connection it should be stressed that the finding of an abnormal and, indeed, diabetic glucose tolerance curve does not warrant continued treatment in an asymptomatic patient once the acute attack has subsided. Patients with diabetes due to alcohol-induced pancreatitis should be warned that continued alcohol intake carries with it the hazard of deterioration in their diabetic state due to further pancreatic damage and a liability to severe and possibly lethal episodes of alcohol-induced hypoglycaemia while on insulin or oral therapy (Marks & Bank, 1965a).

Acute steatorrhoea is seldom a problem in patients with non-calcific pancreatitis, and when it occurs it tends to settle spontaneously over a period of 2–3 months. This was the case in three of our patients (two alcoholic and one idiopathic) who developed this complication. On the other hand, steatorrhoea which developed during an acute attack in two patients with calcific (alcoholic) pancreatitis persisted for a long period of time and the effects were more pronounced. Pancreatic replacement therapy in adequate dosage usually improved the diarrhoea, the character of the stools and fat absorption (Marks & Bank, 1965b). Good results have been obtained with Viokase, a whole pancreas extract, given in a dose schedule of two tablets every 2 hr during the day but other preparations such as Cotazyme or Pancrex may be effective if given in equivalent doses.

Investigations during recovery phase

After the acute attack has completely subsided the case should be thoroughly investigated to assess the condition of the pancreas and to determine the cause of the pancreatitis. Pancreatic function may be assessed by means of the pancreatic function test, glucose tolerance test and faecal fat excretion and information regarding the head of the pancreas or presence of a pancreatic cyst obtained by intravenous cholangiography and barium studies in selected cases. In determining the cause of the pancreatitis no effort should be spared to exclude cholelithiasis, particularly in those patients in whom the attacks do not appear to be related to the intake of alcohol. It should be stressed that evidence of gallstones may be obtained only after

repeated cholecystography and examination of the post-pancreozymin duodenal aspirate for cholesterol crystals. Hyperparathyroidism, hyperlipaemia and ascariasis, although rare causes, should be excluded in every case and the problem of an underlying carcinoma presenting as an acute attack borne in mind. Pancreatic arteriography may be considered in the latter.

Prevention of further attacks

This depends mainly on removal of the cause. In alcoholic pancreatitis further attacks can be prevented by total abstinence from alcohol in the vast majority of cases. In our experience, all other measures, medical or surgical, are doomed to failure if alcohol is not abandoned. In biliary pancreatitis associated with gallstones further attacks are almost invariably prevented by removal of the stones and diseased gallbladder but alcohol has no effect on the progress of the disease. Elective operation for proved gallstones may be carried out as early as 2–3 weeks after the acute attack in selected patients (Bernard, 1965; Elliott, 1965) but we have preferred to wait for 6–8 weeks. If there should be any evidence of a relapse, however, early laparotomy should be performed. In biliary pancreatitis associated with ascariasis, however, surgery is not indicated because further attacks can be effectively prevented by the use of anthelmintics. Other causes (Table 2) may require specific surgical or medical therapy, e.g. one of our patients who suffered from hyperparathyroidism has had no further attacks of pancreatitis since removal of his adenoma, and another who has familial hyperlipaemia was treated with Atromid for 3 months and has remained well in the 2-year follow-up. The most difficult group to treat is the idiopathic. Factors known to precipitate acute attacks, e.g. rich, fatty foods, large meals, starvation, alcohol, steroids, chlorthiazides and ferrous salts should be avoided, but only too frequently these patients, like those in the alcoholic group, eventually require surgical treatment to prevent relapses or alleviate chronic pain (Smith, 1962; Menguy, 1965; Sarles *et al.*, 1965; White, 1965).

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