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STUDIES ON PANCREATITIS*

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In the same year as von Mering and Minkowski (1889) produced experimental diabetes in dogs by ligating the pancreatic duct, Fitz (1889), of Boston, described a case of "acute catastrophic inflammation of the pancreas." It is a regrettable fact that, 63 years later, the knowledge of exocrine and endocrine physiology of the gland, based on the brilliant work of Pavlov (1902), Bayliss and Starling (1902), and Banting and Best (1921-2), far outstrips the understanding of the clinical entities of pancreatitis. There are several reasons why this should be so: in the first place, pancreatitis is often difficult to diagnose, for the most suggestive symptom—pain—is variable both in site and in intensity, and is closely mimicked by other intra-abdominal conditions; secondly, diagnostic laboratory tests are by no means infallible; and, finally, little is known of the pathology of pancreatitis.

Acute and chronic pancreatitis have long been regarded as separate clinical and pathological entities, the one presenting as an acute abdominal emergency, and the other as a rare cause of abdominal pain, obstructive jaundice, wasting, steatorrhoea, or diabetes mellitus. Comfort *et al.* (1946) have established a link between acute and chronic pancreatitis in their now classical description of "chronic relapsing pancreatitis." Not the least important part of their work was to draw attention to the aetiological significance of alcoholism.

The publication of several reviews on acute pancreatitis (Paxton and Payne, 1948; Warren, 1948; Lipp and Aaron, 1950; Roberts *et al.*, 1950), on subacute pancreatitis (Gray *et al.*, 1938; Macnab, 1949), and on chronic relapsing pancreatitis (Maimon *et al.*, 1948; King, 1949; Gambill, 1949) indicates the amount of contemporary interest in the subject. In Australia, Rose (1951) and Heinz (1952) have reviewed experience in Sydney and Melbourne. While these statistical surveys provide an important overall picture of the incidence and complications of pancreatitis, they are less helpful with regard to information on pathogenesis and individual clinical patterns.

The present work was undertaken, (1) to investigate the clinical features of acute and chronic pancreatitis;

(2) to elucidate some of the aetiological factors involved; (3) to study possible associated disturbances in gastric and hepatic function; (4) to evaluate laboratory tests as aids to diagnosis; and (5) to clarify the position with respect to treatment.

Between October, 1951, and July, 1952, 24 cases of acute and chronic pancreatitis were studied.

Methods of Study

In addition to full clinical examination, diet histories were taken by Miss C. N. Turner (dietitian at the Clinical Research Unit of the Walter and Eliza Hall Institute of Medical Research and Royal Melbourne Hospital). The following investigations were also made:

(1) *Estimation of urinary diastase*, using Dodds's modification of Wohlgemuth's method (Dodds and Dickens, 1925), was carried out during attacks of pain.

(2) *Intravenous Secretin Test*.—The method of Dornberger *et al.* (1948), based on the original studies of Agren *et al.* (1936), was closely followed. A double lumen tube was swallowed by the patient in the fasting state. The progress of the tip of the tube into the duodenum was followed fluoroscopically. Gastric contents were aspirated by Wangenstein suction and the duodenal contents were collected in 30-ml. test-tubes under slight negative pressure (estimated at 20 mm. Hg). After two ten-minute samples of fasting duodenal content had been aspirated, Wyeth's secretin was given intravenously, in a dosage of 1 unit per kg. body weight. The total volume and the bicarbonate content of each sample, estimated by the titrimetric method of Van Slyke, were recorded.

(3) *Gastric Function*.—A histamine test meal was done on most patients, many of whom also had gastric biopsy performed.

(4) *Liver Function*.—Estimation of serum bilirubin, alkaline phosphatase, serum proteins, and the cephalin-flocculation test was performed on most patients. A few also had a liver biopsy done.

(5) *Oral Sugar Tolerance Test*.

(6) *Gelatin Absorption Test*.—This test of protein digestion, based on a technique described by Krauel (1944), was performed on four patients. Gelatin, 50 g., was given orally, and the level of the serum amino-nitrogen was followed at hourly intervals for five hours.

(7) *Radiological Studies*.—Plain x-ray films of the pancreatic area and barium meal x-ray films were taken in most patients, and where cholecystectomy had not previously been performed a cholecystogram was done.

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Acute Pancreatitis

Eleven cases of acute pancreatitis were studied. The age and sex incidence of patients is shown in Fig. 1. In 10 of these cases the diagnosis was made either on clinical grounds or at laparotomy, but in one case severe pancreatitis was an unsuspected and surprising finding at necropsy. Two of these patients died.

Pain and persistent vomiting were the most frequently presenting symptoms. The pain was felt in the epigastrium and radiated to the right and left hypochondrium, and through to the back at the level of the twelfth dorsal to the second lumbar vertebrae. The quality and intensity of the pain were rarely, however, of great diagnostic value: in two patients right-sided localization closely simulated

FIG. 1.—Age and sex distribution of 11 cases of acute pancreatitis. White squares, males; black squares, females.

FIG. 2.—Serial urinary diastase levels in six cases of acute pancreatitis.

pain. Biochemical tests showed this to be of obstructive type. Transient glycosuria was noted in two cases within 48 hours of onset, and in one fatal case acute diabetic coma developed five days after the onset of symptoms.

Estimation of the urinary diastase was of great help in the differential diagnosis of pancreatitis from other acute abdominal conditions. A level of over 100 units is diagnostic of pancreatitis. Although moderate elevation of the urinary diastase has been observed in some cases of perforated peptic ulcer, the significantly high levels, 400–1,000 units, which at times are found in patients with acute pancreatic necrosis should guide the surgeon in this often difficult clinical problem. Serial diastase levels in six cases are shown in Fig. 2. It will be seen that there is a tendency for the diastase to fall to normal levels within two to five days after the onset of pain. Estimation of the urinary diastase test is therefore of real value only if it is done soon after the onset of pain.

Aetiology

Cases fell into three aetiological groups: (1) associated with gall-stones; (2) associated with alcoholism; and (3) apparently due to primary infection.

(1) *Cholelithiasis* (three cases).—Halsted (1901) and Opie (1901) were the first to point out the association of pancreatitis with a calculus obstructing the ampulla of Vater. In

most reviews on acute pancreatitis, gall-stones have been present in 50–80% of patients. In the present limited series of cases the relatively few patients with proved gall-stones is quite a striking feature.

In one patient it was possible to obtain useful correlation between the clinical features and the histological findings in both the liver and the pancreas.

A 73-year-old man with hypertensive vascular disease developed acute abdominal pain and vomiting, and became slightly jaundiced. Laparotomy was performed. The head of the pancreas was swollen and indurated. Material was obtained from this site with a liver biopsy needle; and liver tissue was also taken for section. Cholecystenterostomy was performed. The pancreas showed acute inflammatory changes (Fig. 3), and in the liver severe cholangitis was present.

FIG. 3.—Section of pancreatic tissue obtained by means of an aspiration liver biopsy needle at laparotomy in a man with pancreatitis complicating cholelithiasis, showing acute interstitial inflammatory changes. (Haematoxylin and eosin. $\times 150$.)

Two factors are involved in the production of pancreatitis when calculi obstruct the ampulla: the mechanical reflux of bile into the pancreatic duct causes an acute chemically induced inflammatory reaction; and, as in this patient with obvious cholangitis, bacterial infection undoubtedly plays an important part.

(2) *Alcoholism* (five cases).—Many early writers—for example, Egdaahl (1907)—noted that acute pancreatitis often followed a bout of heavy drinking. Five of the patients under review were exceptionally heavy beer or spirit drinkers, but in none of them was there any evidence of biliary disease. It is of possible significance that all of them had arterial hypertension. In three patients pain followed a bout of heavy drinking.

In February, 1952, a 32-year-old man had severe abdominal pain after a drinking bout. His urinary diastase was 400 units. Five days after admission he lapsed into diabetic coma. He improved with insulin but died two days later from bilateral bronchopneumonia. At necropsy severe pancreatic necrosis was found. The common bile duct and gall-bladder were normal. It is of great interest that an identical twin brother of this patient also had severe pancreatic necrosis, from which he recovered, in 1949.

Two patients had recurring attacks of abdominal pain related to alcoholic episodes. That pancreatitis of this nature is primarily a medical rather than a surgical problem is indicated by the fact that recurrence of pain in these two patients ceased in a period of nine months' observation when they stopped drinking and were able to eat good diets.

FIG. 4.—Section of pancreas showing acute necrosis in a woman dying of acute infectious hepatitis.

(3) *Infection* (two cases).—Certain viruses are known to cause acute pancreatic inflammation. Mumps is the classical example, of which there was one instance in this series. Poppel and Bercow (1949) noted symptoms referable to pancreatitis in no fewer than 17 of a series of 95 cases of mumps. Since both mumps orchitis and meningo-encephalitis without parotitis are known to occur, it is conceivable that occasional obscure cases of pancreatitis may be due to infection with the mumps virus, without demonstrable enlargement of the parotid glands.

Pancreatitis is occasionally an associated condition in severe cases of infectious hepatitis (Lucké, 1944).

A middle-aged woman developed classical signs and symptoms of infectious hepatitis and died in hepatic coma. At necropsy widespread necrosis of the liver cells was found, and the pancreas showed necrotic changes (Fig. 4).

Transient elevation of the urinary diastase has been noted in several cases of acute infectious hepatitis of moderate severity; it is possible that mild pancreatitis may be a common complication of infectious hepatitis.

A strain of Coxsackie virus pathogenic to man is known to cause acute pancreatitis in suckling mice (Pappenheimer *et al.*, 1951), but so far pancreatitis attributable to this virus has not been recognized clinically.

Treatment

The diagnosis of acute pancreatitis may present considerable difficulty, and if an occasional laparotomy is needlessly performed little harm to the patient is likely to follow. Nevertheless, if the diagnosis of acute pancreatitis can be assured conservative treatment is urged.

Pain was satisfactorily controlled with pethidine. Morphine may actually aggravate pancreatic pain.

Continuous *gastric aspiration* was applied until pain and vomiting ceased. Aspiration of gastric juice prevents vomiting and inhibits the hormonal stimulation of the flow of pancreatic juice.

Loss of electrolytes necessitated accurate replacement with intravenous glucose-saline and potassium chloride. Edmondson *et al.* (1952) and Roberts *et al.* (1950) have drawn attention to the dangerous degree of hypochloraemia and hypokalaemia which may occur in pancreatic necrosis; and a factor which the former authors show to have been hitherto neglected is the binding of calcium when fat necrosis is extensive, indicating that intravenous injections of calcium gluconate should be given in severe cases.

Although acute diabetes is a rare complication, the urine and blood sugar should be repeatedly estimated and insulin given when necessary.

Secondary infection is a threat to life in acute pancreatic necrosis. Therefore penicillin (500,000 units six-hourly) and streptomycin (0.5 g. twice daily) were given to all cases.

FIG. 5.—Age and sex distribution of 15 cases of chronic pancreatitis. White squares, males; black squares, females.

In cases in which clinical or radiological evidence pointed to cholelithiasis elective cholecystectomy was performed *after* the attack of pancreatitis had subsided.

Chronic Pancreatitis

Chronic pancreatitis is in some respects a misnomer, for the

natural history of the majority of the 15 patients studied (see Fig. 5) pointed to a relapsing, recrudescing form of disease. The pathology which was observed in patients on whom operation was performed during attacks of pain was that of oedema or haemorrhagic necrosis of the gland. In several patients these repeated attacks had ultimately caused destruction of the acinar and islet tissue, with fibrosis and even calcification, leading to deficiency of both internal and external secretion.

The clinical history of four male patients closely resembled the description of chronic relapsing pancreatitis given by Comfort *et al.* (1946). Another syndrome was that observed in eight female patients who had attacks of pancreatitis following cholecystectomy. The remaining three patients formed a miscellaneous group.

Chronic Relapsing Pancreatitis

All four patients were males. Three of them had essential hypertension; three had been heavy consumers of alcohol. Three patients had a laparotomy performed at one time or another, and, although pancreatitis was noted, there was no evidence of associated biliary disease.

The initial manifestation of the disease was that of recurring attacks of abdominal pain, during which the urinary diastase was raised. In one patient only a few weeks intervened between attacks of pain, but in the remainder several months of freedom from pain were enjoyed. Sometimes a distressing feature was that pain persisted despite a variety of operations undertaken on the biliary tract.

A 51-year-old man, once a heavy beer-drinker, had been admitted to hospital on 16 occasions between 1944 and 1951 with attacks of pancreatic pain. In 1944 his gall-bladder had been removed, but when examined it did not appear to be diseased. Twice the common bile duct was drained during attacks of pain. Ultimately he became a pethidine addict. In one attack of pain relief was obtained by bilateral splanchnic block; a right-sided sympathectomy, removing ganglia from D 8 to L 2, seemed to give more prolonged relief until his death two months later from spontaneous intraperitoneal haemorrhage. Investigations showed impaired fat absorption, a mild diabetic type of sugar-tolerance curve, achlorhydria, and atrophic gastritis. At necropsy the pancreas was shrunken, and histologically showed replacement of much of the pancreatic acinar tissue by fat (Fig. 6). Severe atheroma of the aorta was present.

The disease tends to be progressive, and in less fortunate patients the replacement of acini by fibrotic tissue and deposits of calcium may have profound metabolic effects.

A 49-year-old man had frequent attacks of pancreatic pain and ultimately developed diabetes mellitus. Pain made life

FIG. 6.—Section of pancreas from a case of chronic relapsing pancreatitis. The gland was considerably shrunken. Much of the acinar tissue has been replaced by fat. (Haematoxylin and eosin. $\times 150$.)

FIG. 7.—X-ray film of the pancreatic area in a middle-aged man with relapsing pancreatitis and diabetes mellitus, showing diffuse calcification throughout the gland.

intolerable, and he lost 3 st. (19 kg.) in weight. Investigations showed impaired fat absorption and poor gelatin digestion. An x-ray film of the pancreatic area (Fig. 7) showed diffuse calcification.

The diagnosis of chronic relapsing pancreatitis is based on the history of recurring episodes of upper abdominal pain without other obvious cause, and evidence of deficiency of either internal or external pancreatic secretion, such as glycosuria and hyperglycaemic sugar tolerance (see Fig. 8), frank steatorrhoea, wasting, or a low flat type of gelatin absorption (see Fig. 9). The finding of a raised urinary diastase is of the

FIG. 8.—Oral sugar tolerance curves in seven cases of chronic pancreatitis.

utmost importance in diagnosis in obscure cases. In advanced cases a search should be made radiologically for pancreatic calcification.

In three cases liver biopsy was performed. In one case mild fatty change, presumably of nutritional origin, was found. Gross degrees of fatty change and actual cirrhosis have been noted by other observers (for example, Fiesinger and Olivier, 1933; Snell and Comfort, 1937; Sharp *et al.*, 1952). Whether these cirrhotic changes in the liver develop *pari passu* with pancreatic fibrosis as a result of suboptimal nutrition, or whether they are the result of impaired digestion of fat and protein due to pancreatic insufficiency, is open to debate. In one case gastric biopsy showed severe atrophic gastritis.

The treatment of chronic relapsing pancreatitis is a problem beset with extraordinary difficulties. In the early stages recurrent attacks of pain may be prevented by improving the diet and enforcing strict abstinence from alcohol; but with regard to the more advanced cases there is at present no uniformity of opinion regarding the correct course of action which should be taken. Many American surgeons advise interruption of the afferent nervous pathways, either by limited splanchnic nerve section (de Takats, Walter, and Lasner, 1950) or unilateral sympathectomy

FIG. 9.—Gelatin absorption curve in four cases of chronic pancreatitis. The level of amino-nitrogen is followed at intervals for five hours after the administration of gelatin (50 g.).

(Hurwitz and Gurwitz, 1950), or by the more radical bilateral lumbo-dorsal sympathectomy combined with splanchnicectomy (Connolly and Richards, 1950). However, Cattel and Warren (1952) maintain that these measures offer only temporary relief from pain and advise pancreaticoduodenectomy.

Our own experience is too limited to be of value. In three patients the pain was temporarily abolished by bilateral splanchnic block. In only one patient was a limited sympathectomy performed, and his early death two months after operation prevented adequate assessment of the result.

Relapsing Pancreatitis Following Cholecystectomy

All eight female patients in this group had what might be called the "gall-stone diathesis"—most were obese, most had hypertension, and three were known to have had diabetes mellitus for some time. In all patients calculi were present when the gall-bladder had been removed. Often within a few months of cholecystectomy these patients experienced attacks of upper abdominal pain. Often this was felt below the right costal margin, and led them to believe that their pre-operative biliary colic had returned. Abnormally high levels of urinary diastase were noted during these attacks.

An obese 45-year-old woman with mild diabetes mellitus had her gall-bladder removed for cholelithiasis. Six months later she had a severe attack of abdominal pain lasting two days. The urinary diastase was 1,000 units. Two further attacks occurred and on each occasion the diastase was raised.

In some cases it was noted that pain followed an unusually large fatty meal. Alcoholism and frank dietary deficiency did not seem to be causative factors; in fact, improvement in many cases occurred when measures were taken to reduce weight by advising smaller non-fatty meals.

It seems likely that many patients suffering from the so-called "post-cholecystectomy syndrome" have, in fact, a mild recrudescence of pancreatitis. Doubilet and Mulholland (1949) maintain that spasm of the sphincter of Oddi may cause a rise in pressure in the common bile duct sufficient to lead to regurgitation of bile into the pancreatic duct in patients with a common channel. It is known that bile injected experimentally into the pancreatic duct causes chemical inflammation. They advise section of the sphincter; but we regard the factual basis of their hypothesis as unproved, and none of our patients have been subjected to this operation.

Other Causes of Chronic Pancreatitis

A 23-year-old woman with a long history of ulcerative colitis and a grossly deficient diet had an attack of severe abdominal pain. At laparotomy acute pancreatitis was found, but the organ was also fibrous, indicating chronic pathological change.

Ball *et al.* (1950) described interstitial chronic inflammatory changes in a high proportion of cases of ulcerative colitis examined at necropsy. Since nutritional hepatitis is also common in ulcerative colitis it is reasonable to assume that malnutrition plays an important part in the causation of pancreatitis in this condition.

A 34-year-old woman had infectious hepatitis in 1949. This was followed by frequent attacks of abdominal pain. All investigations were negative except for the finding of high diastase levels up to 152 units during the attacks.

The clinical evidence was in favour of a direct causative relationship between this patient's pancreatitis and the original infection with the virus of infectious hepatitis.

A 26-year-old man had attacks of upper abdominal pain and intermittent jaundice of obstructive type. He also had symptoms of diabetes mellitus. At laparotomy the pancreas was fibrotic and indurated, but the gall-bladder and common duct were normal. The gall-bladder and common duct were drained and the jaundice subsided.

No obvious cause of chronic pancreatitis was found in this case. Obstructive jaundice is not an uncommon manifestation of chronic pancreatitis (Selesnick, 1952), and this case illustrates an important point in the surgical management.

When the gall-bladder is not diseased, under no circumstances should it be removed, for later it may be used with advantage in a short-circuiting operation for the relief of jaundice.

Intravenous Secretin Test

The results of this test in eight normal subjects, five patients recovering from acute pancreatitis, and eleven patients with chronic pancreatitis are shown in Fig. 10. In each group a very wide range of values of both volume and bicarbonate content of the duodenal contents was found.

Although there is an obvious statistical tendency towards lower volumes and bicarbonate content in patients recovering from acute pancreatitis and in patients with chronic pancreatitis, the degree of overlap in values as compared with normal healthy subjects is enough to render the test unsuitable for ordinary diagnostic purposes. Dornberger and his colleagues arrived at a similar conclusion. It would seem that only when parenchymal damage is very severe and extensive is one likely to obtain significantly low values with this test, which also has the disadvantage of being both expensive and time-consuming.

INTRAVENOUS SECRETIN TEST

FIG. 10.—Scatter diagram showing volume and bicarbonate content of duodenal aspirate after the administration of secretin intravenously to eight normal subjects, five patients recuperating from acute pancreatitis, and eleven patients with chronic pancreatitis. + = mean value.

nosed, and chronic pancreatitis may manifest itself under a number of guises which may tax the diagnostic skill of the clinician. Once an increased awareness of this condition becomes prevalent among physicians and surgeons, however, and once the habit of calling for urinary diastase estimations in cases of obscure abdominal pain is acquired, it is likely that more cases will come to light, with opportunities for further study.

One of the difficulties encountered in the diagnosis of milder cases of acute and relapsing pancreatitis is the lack of reliable laboratory tests. The finding of high levels of pancreatic enzymes, either in the serum or in the urine, should suggest pancreatitis, but there is evidence that such elevation is often transient. In our hands the secretin test has been of little practical value. Innerfield *et al.* (1952a, 1952b) have demonstrated a high level of plasma antithrombin activity in both acute and relapsing pancreatitis, and it is possible that this may prove to be a subtle laboratory test of considerable value. In suspected chronic pancreatitis, steatorrhoea (faecal fat content more than 30%), a hyperglycaemic sugar-tolerance curve, and calcification of the pancreas should be looked for.

If these investigations prove negative despite a strong clinical suspicion of pancreatitis, diagnostic laparotomy is justifiable. The pancreas should be carefully inspected and palpated. However, it is believed that closer correlation between naked-eye appearances and actual histology is demanded, and to this end a technique of obtaining biopsy

material is being developed, using a Franseen aspiration liver biopsy needle (the material shown in Fig. 3 was obtained by this means).

In the attempt to elucidate the aetiology of pancreatitis it was apparent that a heterogeneous group of conditions was being grouped under one heading only by virtue of the fact that one organ, the pancreas, was predominantly affected. Now the only things shared in common by infectious hepatitis, Laennec's cirrhosis, infectious cholangitis, and xanthomatous biliary cirrhosis are pathological changes in the liver resulting in jaundice, yet we do not refer to these diseases collectively as "hepatitis." The same reasoning may with justification apply to the pancreas. Chronic pancreatitis complicating ulcerative colitis is a totally different entity from pancreatitis following cholecystectomy; likewise, pancreatitis complicating biliary calculi has an entirely different pathogenesis from that occurring in alcoholic subjects.

What are the factors known and believed to be the cause of pancreatitis? Trauma to the pancreatic ducts, during gastrectomy for example (Millbourn, 1949), causes pancreatic inflammation. Any condition which causes reflux of bile into the pancreatic ducts may also produce pancreatitis. This is presumably the mechanism in those cases of pancreatitis following cholecystectomy in which pressure gradients in the common bile duct are believed to be disturbed. When calculi obstruct the ampulla, in addition to reflux along the "common path," infection is probably an added factor.

There is accumulating clinical and experimental evidence that, as with the liver, certain foodstuffs have a protective action on the pancreas. Fatty changes and fibrosis in the pancreas have been shown to be present (Waterlow, 1948; Davies, 1948) in undernourished native races at necropsy. Necrotic pancreatic lesions have been demonstrated in rats fed on a low-protein diet (Lindsay *et al.*, 1948). It is probable that methionine is an essential protective metabolite, for when the ethyl analogue of methionine, ethionine, which blocks the utilization of methionine, is fed to experimental animals pancreatic necrosis invariably occurs (de Almeida and Grossman, 1952). The clinical counterpart of these experimental findings is the type of pancreatitis which occurs in malnourished alcoholic patients and as a complication in patients suffering from ulcerative colitis. In alcoholic patients there is also the possible additional aetiological factor of the stimulation of excessive quantities of pancreatic juice during a drinking bout. In our studies with the double lumen tube it was noted in control subjects that the rate of flow of duodenal aspirate was trebled when 2 oz. (57 ml.) of brandy was introduced into the stomach.

The presence of arterial hypertension in a high proportion of patients with pancreatitis has been commented upon by Heinz (1952). Care must be taken in interpreting these statistics, for many patients of middle age with cholelithiasis, who comprised a large number of his cases, tend to have the obese hypertensive diathesis. There are a few hints, however, that this correlation may not be entirely coincidental, for there are on record in the literature a number of cases of pancreatitis complicating familial hypercholesterolaemia (Holt *et al.*, 1939; Collett and Kennedy, 1948; Klatskin and Gordon, 1952). There is evidence also that genetic factors may be involved in the causation of chronic relapsing pancreatitis. Comfort and Steinberg (1952) reported on a family in which the condition occurred in four generations; our own observation of acute pancreatic necrosis occurring in identical twins is also of interest. The relationship between hypercholesterolaemia and the development of atherosclerosis is well known, and it is an intriguing possibility that vascular disease may be at least a condition which predisposes to the development of pancreatitis.

Finally, the possibility of a virus infection, either of mumps or of infectious hepatitis, must not be disregarded in obscure cases.

Thus a variety of aetiological factors, acting either alone or in combination, may lead to pathological change in the

pancreas sufficient to cause clinical manifestations. The following entities can be quite sharply differentiated: (1) *Traumatic pancreatitis*, following surgery of the stomach and duodenum; (2) *virus pancreatitis*, complicating mumps and possibly infectious hepatitis; (3) *reflux pancreatitis*, complicating biliary calculi and following cholecystectomy; (4) *chronic nutritional pancreatitis*, or "chronic relapsing pancreatitis," occurring in malnourished alcoholic patients; (5) *metabolic pancreatitis*, complicating hyperlipaemia and hypercholesterolaemia.

The difficult problem of treatment must be approached with this aetiological perspective in view. Surgery plays no part in the immediate management of acute pancreatitis, when electrolyte replacement and the prevention of secondary infection are considerations of life-saving importance. When acute symptoms have subsided an attempt must be made to assess the predominant aetiological factor involved; if radiological studies reveal the presence of biliary calculi cholecystectomy should be performed, but if there is no evidence of gall-bladder disease cholecystectomy is absolutely contraindicated, for it may be necessary to use the gall-bladder later in a short-circuiting operation if further attacks of pancreatitis lead to obstructive jaundice. If the patient is an alcoholic, abstinence must be enforced and a high-protein diet advised. All that can be said at the present time about reflux pancreatitis following cholecystectomy is that control of weight and limitation of fat intake have yielded good results: one waits for further reports from those surgeons who courageously perform ampullary sphincterotomy.

The position with regard to surgery in chronic relapsing (nutritional or metabolic) pancreatitis is still by no means settled. If it is proved that splanchnicectomy and lumbodorsal sympathectomy offer only temporary relief from pain it will be necessary to resort to pancreatico-duodenectomy. This might seem an unwarranted surgical risk, but such is the severity of the pain and the misery of the patient that heroic measures are called for in some cases. Moreover, in competent surgical hands these risks have been greatly reduced, as has been shown by Smith and Brown (1952), in their experience of surgery of carcinoma of the pancreas.

Summary

The clinical features and laboratory investigations in 24 proved cases of acute and chronic pancreatitis have been studied at the Royal Melbourne Hospital, Melbourne, Australia.

It is felt that the confusion of thought which exists on this subject might in part be dispelled if attention was paid to aetiological aspects of the problem. Reasons are presented for considering traumatic pancreatitis, virus pancreatitis (mumps and infectious hepatitis), "reflux" pancreatitis, chronic nutritional pancreatitis, and metabolic pancreatitis as distinct clinical entities.

In acute pancreatic necrosis good results were obtained with conservative treatment—continuous aspiration of the gastric contents, electrolyte replacement, and the administration of antibiotics.

Chronic relapsing (nutritional) pancreatitis is a condition characterized by recurrent attacks of pancreatic oedema and necrosis causing pain; ultimately destruction of the gland and replacement fibrosis lead to wasting, steatorrhoea, and diabetes. Pancreatic calcification is occasionally visible radiologically and induration of the head of the pancreas may cause obstructive jaundice.

In the absence of biliary calculi, cholecystectomy is contraindicated in chronic pancreatitis. When severe and unremitting pain becomes a feature in advanced cases a choice must be made between sympathectomy and pancreatico-duodenectomy.

Relapsing "reflux" pancreatitis was found to occur in female patients following cholecystectomy. Further data on the mechanics of the sphincter of Oddi and the common bile duct are required before agreement on the surgical relief of these patients can be reached.

The diagnosis of mild cases of acute and chronic pancreatitis may be difficult. Although elevation of the urinary diastase level is helpful this may be only transient. Collateral evidence of steatorrhoea, glycosuria, pancreatic calcification, and impaired protein digestion should be sought for in diagnosing chronic pancreatitis of all types.

We wish to thank those members of the honorary medical staff of the Royal Melbourne Hospital who kindly referred patients for investigation. We also wish to acknowledge the help we have received from our colleagues in the Clinical Research Unit.

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In an appeal for funds, signed by Dr. Elliott P. Joslin, the president, the Diabetes Foundation announces that it was incorporated in 1953 with wide powers to include not only activities concerning the support of research and camps for diabetic children, formerly dealt with by separate funds, but also the administration of a new hospital teaching clinic which it is hoped to build as soon as the necessary money is available.