ACUTE PANCREATITIS

By ROBERT COX, M.B.E., F.R.C.S.

Assistant Surgeon, Westminster Hospital; Surgeon, All Saints' Hospital

Among the many problems presented by the class of patients usually referred to as the acute abdominal emergencies, none is of greater interest than that of acute pancreatitis. Acute pancreatitis is a difficult disease; its incidence is low, so that the average surgeon sees it relatively infrequently. Its aetiology is not known and is the subject of much argument; the pathology is protean and complex; its treatment calls for skill and a well organised clinico-pathological effort; the prognosis is always serious and oft times of the gravest. Nevertheless, all these difficulties have undergone some mitigation in recent years because of an increasing interest in the disease, developments in knowledge of the physiology of the gland, improved diagnostic aids, and better understanding of the principles of treatment, so that the overall picture which this disease presents is not, nowadays perhaps, quite so forbidding.

Incidence

Owing to variations in nomenclature, errors of case recording, etc., it is difficult to arrive at an accurate estimate of the rate at which this disease makes its appearance.

In a five year period at Westminster Hospital however, five undoubted cases of acute pancreatitis were recorded and over the same period 90 cases of perforated peptic ulcer. Enquiries from other London teaching hospitals have elicited comparable figures.

With regard to sex incidence, contradictory statements are to be found in the literature, but most reliable large series show a slight preponderance of male cases. For instance MacKenzie (1954) in his series quotes 56 males to 41 females. This male preponderance is of interest, since biliary disease is undoubtedly more common in the female, and may possibly be due to the greater gusto the male exhibits in his consumption of food and alcohol.

With regard to age incidence, the disease is known to occur through the whole adult range,

and indeed we have in our small series at Westminster Hospital a case of a child, dying with congenital tricuspid atresia, in whom haemorrhagic pancreatitis was a terminal feature seen at post mortem.

The peak incidence is about 50 years of age.

Aetiology

A vast amount of conjectural and controversial literature has been produced on the cause of pancreatitis, but we can sum up by saying that we do not know the cause, and that there are in fact probably several mechanisms by which the pathological processes can be set in train. Among the more popular theories are:

1. *Bile reflux.* Claude Bernard in 1856 produced pancreatitis in animals by injecting bile into the pancreatic duct, but it was Opie, who in describing in 1901 his case of pancreatitis in a patient with a gall stone impacted at the ampulla of Vater, who may be said to have laid the largest foundation stone in the fabric of this theory. But the Opie type of stone, like foundation stones, does not occur very frequently and moreover Hicken and McAllister (1952) using radio opaque injections have shown that fluid can always pass these stones and that obstruction is not complete.

Cattell states that whereas pancreatic enzymes are always found in the gall bladder in acute pancreatitis—which may indicate either intra ductal reflux or vascular blood borne transference of enzymes—bile is only found in the pancreatic ducts in a few cases.

The more of these cases that are seen, the more the literature is studied, the more obvious it becomes that whereas some cases may be due to bile reflux, many cannot be caused in this way.

2. *Infection.* This is a possible cause of acute pancreatitis which has in the past not attracted much favour, possibly because all the inflammatory changes noted at operation or autopsy could be so readily explained by the escape of highly active and damaging enzymes. But Holt, (1954), in an excellent and well balanced review of

this subject, has recently pointed out with much cogency that the pancreas is a compound racemose gland, and does not differ essentially in its subacute inflammations from other analogous glands such as the parotid or submaxillary gland: in these, when some degree of obstruction to the duct system and ascending infection occur together, severe and sudden acute inflammation makes its appearance. Moreover, it is not without interest that an uncommon but well recognized complication of mumps is acute pancreatitis.

3. *Pancreatic duct obstruction.* Many workers have produced acute pancreatitis by ligaturing the main duct of the gland and then stimulating secretion, but Rich and Duff (1936) were probably the first to draw attention to metaplasia in the epithelium lining the ducts which could be an obstructive factor. This obstruction combined with an intra ductal rise of pressure during active secretion could produce rupture with consequent leakage of trypsin into the extra ductal tissues. It is well recognized that there is some connection between heavy intake of alcohol and the onset of acute pancreatitis, and many cases of the subacute relapsing form of the disease can relate their attacks to drinking bouts. Alcohol of course excites a considerable flow of secretin—which activates the pancreas—and has also been accused of causing spasm of the sphincter of Oddi.

4. *Vascular factors.* In the most severe types of acute pancreatitis, haemorrhage and thrombosis are striking features and it is therefore not surprising that a vascular basis has been suggested for the disease, but it is probably only sometimes in action and is not then likely to be so simple as a straightforward embolus or thrombosis. MacKenzie has drawn attention to recent work in America which suggests that the vascular lesions are thrombotic, and occur as a result of sensitization to bacterial toxins.

5. *Trauma.* This is an undoubted factor in certain cases but is an uncommon one. Most frequently the trauma is surgical, but it may be a blunt injury such as a run-over accident. Even in surgical cases injury of the pancreas is only rarely followed by acute inflammation of that organ. Posterior gastric and duodenal ulcers commonly involve the pancreas but no experienced surgeon regards pancreatitis as a practical hazard following gastrectomy for such cases.

The author has seen a case dying of acute pancreatitis after a Polya gastrectomy for anterior duodenal ulcer, but the mechanism on this occasion was an afferent loop obstruction due to rotation, which seems to have caused duodenal contents under high pressure to reflux into the pancreatic ducts and thus activate the enzymes there.

Pathology

Though the aetiological factors are uncertain, once they have set the pathological processes in train the latter are easy to understand.

The pancreatic ferments, trypsin, lipase and diastase are liberated into the tissues outside the ducts. The proteolytic properties of trypsin ensure that the process is for a time a progressive one with digestion of gland substance, and damage to vessels causing both haemorrhage and thrombosis. If the thrombosis is slight or moderate, oedema and blood stained peritoneal exudate may be the only effect, but if it is severe and extensive, the result may be necrosis of large portions of the gland which, should the patient recover, may subsequently be discharged or require removal as pancreatic sequestra.

With so much tissue damage occurring in close proximity to the intestine, and with tissue response impaired by vascular damage, bacterial invasion and suppuration follow very readily, leading to pancreatic abscess which can present anteriorly or in the flank.

Thus the result of the proteolytic enzyme escape may be the production of oedematous, haemorrhagic, suppurative or necrotic pancreatitis, all merely stages in the one process though in years gone by, distinguished by some as separate entities.

Two other aspects of the proteolytic enzyme escape are worthy of notice. Trypsin is clearly most destructive and thus causes much tissue insult with consequent collapse, the latter perhaps being contributed to by the production of proteoses in the circulation.

The other aspect is the development of a spreading upper abdominal peritonitis and a local ileus of the transverse colon and first loop or two of the jejunum, which are the portions of gut closest in contact with the gland. This ileus may give rise to suggestive X-ray findings.

Lipase when free in the tissues attacks the fat depots particularly in the mesocolon, omentum and extra-peritoneal fat, but its effects may be seen even in the limbs. The fat is split, the fatty acids thus released picking up calcium from the tissue fluids to form soaps which give the characteristic appearance to the pearly grey areas of fat necrosis.

Diastase or amylase is important not for any pathology which it causes but because it can be estimated quickly and easily in serum or urine, and this investigation has done a great deal to advance the diagnosis and knowledge of the disease, particularly in its less severe or subacute forms. Serum and urinary amylase tests should be within the capacity of any reasonably set up pathological laboratory and can be performed within 1-2

hours, whereas lipase estimations are not so frequently undertaken, and take 24 hours to carry out.

Before leaving the subject of enzymes, it is necessary to point out that all three are produced in other parts of the alimentary tract, viz. diastase in the parotid and the small intestine, trypsin in the succus entericus, and that in certain circumstances such as acute parotitis or acute upper small intestine obstruction they can be absorbed into the blood stream and give abnormal serum concentrations, but rarely so high as in well developed pancreatitis. Where the damage to the pancreas is severe and widespread the islet cells also suffer so that sugar metabolism is disturbed. Frank glycosuria and diabetes mellitus are most often seen in the relapsing chronic form of pancreatitis, while in acute inflammation a sugar tolerance curve may be required to demonstrate an abnormality. Recovery from islet cell damage after the acute attack always occurs to some extent so that prognosis on this aspect should not be hasty.

When death occurs it may either be within a matter of hours of the onset of the disease from overwhelming toxæmia and hæmorrhage, or more commonly about the 10th to the 14th day, of exhaustion, electrolyte disturbance and possibly peritonitis, a picture which at one time was called pancreatic asthenia.

The Clinical Picture and Diagnosis

From what has been said already about pathology, it is obvious that there can be great variation in the clinical picture presented by the patient suffering from acute pancreatitis. Further, as stated when discussing incidence, most of us see the disease only rarely and regrettably there is thus a tendency to forget it, to omit it from our diagnostic list. Reference to the writings of a previous generation is often surprisingly fruitful and never more than when Moynihan is the author and the subject abdominal surgery. He puts the present matter thus—and I make no excuse for quoting at length from his 'Abdominal Operations' (1926):

'Unless a surgeon has seen previously two or three cases of acute pancreatitis, or unless he keeps the condition constantly in mind, it is seldom that a correct diagnosis is made before opening the abdomen. So many forms of abdominal disaster are seen and among them so few involve the pancreas, that thought of this organ slips from the memory. I have found in not a few instances, that the moment the diagnosis is suggested it meets with eager acquiescence. The first and chiefest symptom is pain; and of all the pains that the human body can suffer, this

is by far the worst. Even the agony caused by perforation of a gastric or duodenal ulcer is less than that in acute pancreatitis. The pain too is remarkable in that it comes so frequently after a good meal and for its area of distribution: it is of fiercest intensity in the epigastrium, but it is felt also in the back and often in both loins.'

Moynihan is of course writing about a severe acute attack. Oftentimes there have been other milder preceding attacks, not recognized, and mistaken for cholecystitis or gall stone colic.

Vomiting follows quickly on the onset of pain and is in most cases persistent; if not, nausea and retching are observed, and these symptoms may cause confusion with high intestinal obstruction though in the latter the nature of the vomit is different and the quantity greater.

Collapse and shock are usually marked. The patient is cold, sweating, pallid with a cyanotic tinge which is said to be characteristic. The pulse is weak and rapid and the blood pressure seriously depressed to high unrecordable levels. Respirations are shallow and rapid. Examination of the abdomen reveals a tense upper abdomen, but not the degree of rigidity seen with a perforation: the lower abdomen may be quite soft. There is exquisite tenderness in the epigastrium and this may also be present in the left costovertebral angle.

After the passage of 24 hours or longer, certain other signs may make their appearance. Discoloration at the umbilicus and in the flanks, due to extravasation of altered blood is associated with the name of Grey Turner. There is often distension limited to the upper abdomen, which was called epigastric peritonitis by Fitz, a Boston physician who gave the first account of acute pancreatitis. It is said that the swollen pancreas can be felt in some cases but it is more likely that the oedematous mesocolon, colon and omentum in fact form most of what is palpable.

A straight X-ray of the abdomen is most helpful, since if gas is not present under the diaphragm, perforation is a less likely diagnosis and sometimes the distended transverse colon and first loop of ileum are clearly seen. In cases with many previous attacks, pancreatic calcification may show, as will opaque gall stones when they are present.

The most important ancillary investigation is the serum diastase estimation, which is normally below 200 units. Between 200 and 500 units the result may be regarded as equivocal, since as already mentioned other conditions can cause a rise, but a figure over 500 units is pathognomonic.

The urinary diastase can also be estimated and has the virtue that an increased figure (normal up to 30 units) may be found hours after the blood

figure has fallen, which it may do rapidly, especially in less severe attacks.

The rise of serum diastase may be so evanescent that it escapes observation, and we have one patient who is proven beyond doubt by laparotomy, who was admitted with a classical clinical picture, a systolic blood pressure of 60 mm. and yet the serum diastase level was but 120 units, nor was any rise observed in the urine diastatic index over the next 24 hours.

Serum and urinary lipase estimations are not in general use and are in any event less reliable than diastase investigations, but have the virtue that they reach their peak about three days after the onset of the attack, thus being of help in the diagnosis of the late case.

From the third day of the disease to about the seventh, the serum calcium level may be depressed and where this occurs it is indicative of much fat necrosis. Occasionally the depression is sufficient to be clinically evidence as tetany.

The electrocardiogram is liable to show changes brought about, it is thought, by electrolyte disturbances, and these changes (inversion of T waves and depression of S—T segments) should not be confused with the changes in acute coronary occlusion (Howat 1952).

Treatment

During the past 25 years there has been a steady trend of opinion towards the non-operative treatment of these patients in the acute stage. Yet there are still those who maintain that surgery plays a part especially in the most serious types, but even in these opinion tends to less extensive procedures within the peritoneum.

In any event, a number of patients do come to laparotomy because the diagnosis is not appreciated and in these it is generally accepted that the minimum of disturbance of the pancreas itself should be the aim. Whether the common bile duct should be drained is less certain, though most writers now advise against such a step, leaving the correction by operation of any biliary pathology to a later date when the pancreas has recovered.

Post-operative burst abdomen is a common complication and the surgeon who has opened the abdomen would do well to pay more than the usual attention to its meticulous closure, and consider also whether in such circumstances it is not wiser to substitute thread or silk for catgut if the latter be the material he routinely uses for suturing.

To say that the treatment is non-operative is not implying that it should be anything less than energetic. Treatment is directed to five main principles:

1. Relief of pain.

2. Correction of shock.
3. Suppression of pancreatic activity.
4. Prevention of ileus.
5. Control of electrolyte and fluid balance.

When first seen the most pressing requirement of the patient is to relieve his agony and morphia will be required in full doses. Theoretically there is an objection to morphia in that it induces a spasm of the sphincter of Oddi, and pethidine or demerol have been recommended as alternatives; these two drugs are in practice found to be less efficient analgesics, and in any event the outlet of the pancreatic ducts is probably compromised by oedema. American writers on this subject recommend such manoeuvres as splanchnic block and even continuous epidural analgesia, but four or six hourly morphia injections is a method which is found to work well in practice.

Shock demands the usual treatment and since intravenous therapy is going to be required for some days a cannula should be introduced into a vein and dextran or plasmosan given in order to correct the fall in blood pressure. Subsequently suitable fluid and electrolyte solutions will be administered as indicated by daily blood chemistry estimations. The serum calcium may be lowered and in these circumstances calcium gluconate is a suitable preparation for intravenous administration.

Atropine should be administered in doses of gr. 1/100 four or six hourly unless cardiac irregularity appears. This drug serves two purposes, it inhibits the neurogenic activity of the pancreas and relaxes, at any rate in theory, the sphincter of Oddi. An intranasal Ryles tube should be introduced into the stomach and the patient put on continuous gastric aspiration, so that acid gastric contents will be prevented from passing into the duodenum and there causing the formation of secretin and pancreozymin, which if liberated, cause further activity of the damaged gland. Some authorities give Alludrox 2 drachms four hourly by mouth in addition.

The use of the Ryles tube, morphia and intravenous fluids together constitute the treatment for, or prophylaxis against, ileus.

Both heparin and the methonium drugs have been suggested in the treatment of this disease, heparin on the basis that much of the pathology is due to spreading thrombosis, the methonium drugs as ganglion blocking agents which will stop the afferent visceral pain impulses and efferent secretomotor impulses. Both in our opinion are dangerous; heparin especially, a dangerous drug at any time, may well in these circumstances determine fatal haemorrhage. The methonium drugs if used in sufficient dosage to have any ganglion blocking effect will produce a low blood

pressure which is clearly undesirable in the presence of thrombotic lesions.

Antibiotics should be used in order to try and prevent bacterial invasion of the damaged tissues adding its quota of trouble to the patient's illness. Despite these aids some patients will develop abscesses and these will have to be dealt with on general principles as they arise. When opened, they frequently contain dark brown or black thick fluid, and sometimes pancreatic sloughs.

The measures outlined above should be continued until the patient's clinical appearance, pulse rate, disappearance of abdominal tenderness, and blood chemistry indicate cessation of activity and a start to healing.

During the convalescent period consideration should be given to two questions. Has the patient developed diabetic tendencies? What is the state of his biliary system? If gall stones are present, plans will need to be laid for appropriate treatment after a suitable interval.

The prognosis in these patients should always

be guarded, both in terms of the short and long term outlook.

As already indicated severe acute pancreatitis is often but one incident in a series of lesser subacute attacks which may continue to occur, and should cause a search to be made for aetiological factors. In some cases the condition progresses to chronic pancreatitis with evidence of increasing fibrosis and failure of both internal and external secretion of the gland.

BIBLIOGRAPHY

- CATTELL, R. B. and WARREN, K. W. (1953), 'Surgery of the Pancreas,' 51.
 FITZ, R. (1899), *Med. Rec.*, 35, 225.
 HICKEN, N. F. and McALLISTER, A. J. (1952), *Amer. J. Surg.*, 83, 781.
 HOLT, R. L. (1954), *Annals of R.C.S.*, 15, 34.
 HOWAT, H. T. (1952), 'Modern Trends in Gastro-Enterology,' 766.
 MacKENZIE, WALTER C. (1954), 'Pancreatitis,' *Annals of R.C.S.*, 15, 220.
 MOYNIHAN, Sir B. (1926), *Abdominal Operations*, 2, 454.
 OPIE, E. L. (1901), *Johns Hopkins Hosp. Bull.*, 12, 182.
 RICH, A. R. and DUFF, G. L. (1936), *Johns Hopkin Hosp. Bull.*, 56, 212.

PULMONARY TUBERCULOSIS

(*Postgraduate Medical Journal*)

Price : 3s. 8d., post free

INTRODUCTORY

Maurice Davidson, D.M., F.R.C.P.

THE GENERAL MANAGEMENT OF THE PHTHISICAL PATIENT FROM THE PHYSICIAN'S STANDPOINT

L. E. Houghton, M.D.

THE PRESENT POSITION OF CHEMOTHERAPY IN TUBERCULOSIS

John C. Roberts, M.D., M.R.C.P.

THE PROBLEM OF TUBERCULOSIS IN CHILDHOOD

A. Margaret Macpherson, M.D., F.R.C.P.

COLLAPSE THERAPY (MEDICAL) IN PULMONARY TUBERCULOSIS

F. H. Scadding, M.D., M.R.C.P.

SURGICAL COLLAPSE THERAPY IN PULMONARY TUBERCULOSIS

J. R. Belcher.

RESECTION FOR PULMONARY TUBERCULOSIS

W. P. Cleland, M.R.C.P., F.R.C.S.

MODERN METHODS OF DIAGNOSIS IN PULMONARY TUBERCULOSIS: CLINICAL, BACTERIOLOGICAL AND RADIOLOGICAL

J. R. Bignall, M.D., M.R.C.P.

Published by

THE FELLOWSHIP OF POSTGRADUATE MEDICINE

60, Portland Place, London, W.1