representatives even for preliminary discussions with the executors of Alfred Nobel's will until it was evident that the will would become legally recognized. Leading conservative politicians in Sweden declared the will as an infringement of the legal rights of Nobel's heirs.

Meanwhile some of Nobel's heirs in Sweden had brought an action against the executors, claiming that the will should be declared invalid. The executors of the will appointed by Nobel, Mr. Ragnar Sohlman and Civ.eng. Rudolf Lilljequist, would have met an almost insurmountable resistance from the authorities and the heirs had not the nephew of Alfred Nobel, Ludwig's son Emanuel Nobel, in February, 1898, declared that he, although the death of Alfred Nobel had heavily shaken the financial ground of the naphtha enterprises in Russia, was willing to do his best to see that his uncle's will should be respected. The action of Emanuel Nobel on this occasion deserves to be remembered. Such a disregard of what was considered the rights of the heirs as Alfred Nobel had shown was in fact unheard of. Because of the extraordinarily good relations which had always prevailed within the family, Emanuel felt convinced that deeper motives had induced his uncle's decision. He therefore, when the highest representative of the State claimed that Alfred Nobel had been "influenced by peace fanatics and particularly by women" and advised him to act in favour of the heirs' rights, responded: "Your Majesty! It is not my intention to take any action through which members of my family in the future could be blamed by the most highly deserving scientists of the time for having deprived them of something which duly ought to be theirs."

Emanuel Nobel called the executors "solicitors of the soul." He participated in the preliminary discussions between them and the representatives of the Swedish Academy and the Karolinska Institutet. A proposal was made on June 5, 1898, according to which the heirs should be allotted one and a half years' income to the estate, provided they recognized the will and waived any further claims upon the estate. To this they agreed, and thereby the estate was saved for the Nobel Foundation, whose Articles were approved by His Majesty the King in June, 1900. The following year, 1901, the first Nobel Prizes were awarded.

BIBLIOGRAPHY

McClintock, Marshal (1948). Editor of *The Nobel Prize Treasure*. Doubleday, Garden City, N.Y.

Schück, H., Sohlman, R., Österling, A., Liljestrand, G., Westgren, A., Siegbahn, M., Schou, A., and Ståhle, N. K. (1950). *Nobel, the Man and His Prizes*, ed. by the Nobel Foundation. Sohlmans Förlag, Stockholm.

Stevenson, L. G. (1953). *Nobel Prize Winners in Medicine and Physiology, 1901–1950*. Schuman, New York.

The Department of Scientific and Industrial Research will take over part of the former Royal Ordnance Factory at Thorp Arch, near Boston Spa, Yorkshire, for the use of the new National Lending Library for Science and Technology. Present plans are that the library will begin work at Thorp Arch in 1961, becoming fully operational during the following year. The new library—the nucleus of which already exists in the D.S.I.R. Lending Library Unit now at Chester Terrace, Regent's Park, London—will cover all subjects in science and technology, except for some fields of medicine. One important activity will be the expansion of work on the translation of Russian scientific literature, now organized by the Lending Library Unit in collaboration with the National Science Foundation in the United States.

ACUTE PANCREATITIS

ANALYSIS OF 100 PATIENTS

BY

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For a good many years the General Infirmary at Leeds has accepted most of the emergency surgical patients from this city (population 508,000) and the immediately surrounding countryside. The number of acute surgical admissions, excluding head injuries, has been fairly constant over the past six years at 2,300 to 2,600 per annum. During this period 100 patients with acute pancreatitis have been admitted. A further 41 patients have been seen whose serum amylase was raised but in whom the diagnosis of acute pancreatitis was either doubtful or erroneous. It is with this series of 141 patients that the present communication deals.

Aetiology

There are two schools of thought about this unsolved question. The first school is the older, and its two chief exponents have been Opie (1903) and Rich (see Rich and Duff, 1936). At necropsy on a patient who had died of acute pancreatitis Opie found a stone in the ampulla of Vater, blocking the common orifice of biliary and pancreatic ducts and converting them into a continuous channel. He postulated that an increase in biliary pressure would force bile up the pancreatic duct, where it would activate trypsinogen and cause pancreatic necrosis. The second part of this theory he proved by causing acute pancreatitis in dogs by injecting their own bile into their pancreatic ducts. The first postulate, that pressure in the biliary duct must exceed that in the pancreatic duct, has been more difficult to establish. In fact, the most reliable work on biliary and pancreatic duct pressures (Parry, Hallenbeck, and Grindlay, 1955) shows that biliary secretory pressure in dogs almost never exceeds pancreatic secretory pressure. These results may not be applicable in man, however, since the anatomy of the ducts is so different in dogs, the main pancreatic duct opening a centimetre or more below the common bile duct.

It was soon realized that it is unusual to find a stone impacted at the ampulla of Vater in patients with pancreatitis. In the present series 26 patients died. Of these, 22 were examined *post mortem*, and in five a stone was found impacted at the ampulla of Vater. In addition, in one patient operated on during an attack of acute pancreatitis a stone was found at the ampulla and removed. In the remaining cases it has been postulated that the common biliary-pancreatic pathway is established by spasm of the sphincter of Oddi. This is the theoretical background to sphincterotomy in the treatment of chronic relapsing pancreatitis.

In 1936 Rich and Duff published their researches on the pathology of pancreatitis and described a form of pancreatic duct mucosal hyperplasia which they believed could cause obstruction. They postulated that over-secretion by the pancreas against a blocked duct could cause pancreatitis. On the other hand, pancreatography in patients with pancreatitis shows that obstruction to the duct anywhere except at the sphincter of Oddi is exceedingly uncommon (Doubilet, Poppel, and Mulholland, 1957; Pollock, 1958).

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The second school of thought regarding pancreatitis considers that the primary lesion is in the nature of a pancreatic infarct, and that the escape of pancreatic juice is secondary to this. Perhaps the most interesting work along these lines is that of Thal and Brackney (1954), who liken the lesion to a Shwartzman phenomenon and have produced it in rabbits and goats by intraductal, followed 24 hours later by intravenous, injection of meningococcal or *Escherichia coli* endotoxin. The clinical significance of these results is not clear, and one must conclude that ductal obstruction with or without biliary regurgitation plays the major part in causing most cases of human pancreatitis.

Clinically, certain facts about aetiology emerge from a consideration of the present series.

Age and Sex

Of the 100 patients 71 were female and 29 male. There is an extraordinarily wide age variation. The youngest patient was a boy of 6 years:

Case 1.—A boy aged 6 was admitted to hospital as a case of acute appendicitis. Four days before admission he had had abdominal pain and vomiting, which was repeated on the day of admission. The pain did not radiate to the back. There was no history of mumps or any exposure to a case of mumps. No child in the ward subsequently developed that condition. At laparotomy on the day of admission widespread fat necrosis and a grossly oedematous enlarged pancreas were found. The abdomen was closed and the child made a good recovery. The serum amylase was 6,400 units (Somogyi) on the day after operation, and was still raised to 1,800 units four days later. A mumps complement-fixation test was not done. The child was well four years later.

A similar case in a girl of 3 years was reported by Pender (1957). The oldest patient in the present series was aged 83, and the numbers by decades were: first, 1; second, 2; third, 8; fourth, 4; fifth, 11; sixth, 19: seventh, 33; eighth, 19; and ninth, 3.

Association with Gall-bladder Disease

This was less common amongst the men: the gall-bladder was normal in 14, abnormal in 13, and in two there is no information. Of the women, 48 had abnormal and 16 had normal gall-bladders, and in 7 its state was not known. In brief, half the men and three-quarters of the women had abnormal gall-bladders. In most cases the abnormality was the presence of cholecystitis with stones; in some, however, no stones were present (see Fig. 1), but only an acute cholecystitis. In such a case the gall-bladder may fail to concentrate cholecystographic dye during the attack of pancreatitis, only to appear completely normal later.

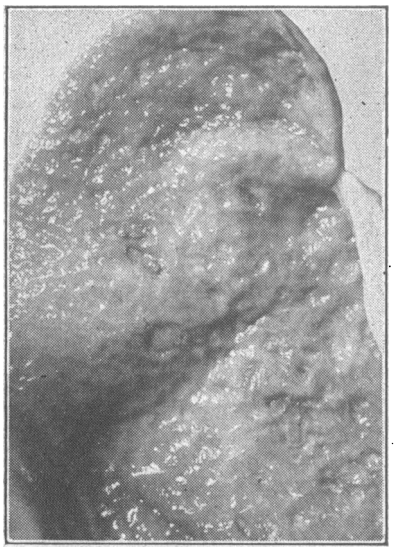

FIG. 1.—Gall-bladder removed *post mortem* from a woman who died of acute haemorrhagic pancreatitis. Note the patchy ulceration of acute non-calculous cholecystitis.

This strong association between disease of the gall-bladder and of the pancreas is difficult to explain on any present theory of the aetiology of pancreatitis, especially as only six patients were shown to have stones impacted at the lower end of the common bile duct. It is possible that the functional removal of the gall-bladder by cholecystitis or cholecystectomy may allow a higher pressure to develop in the common bile duct, and that this pressure, exceeding that in the pancreatic duct, may drive bile up the pancreatic duct to initiate an attack of acute pancreatitis. Menguy, Hallenbeck, Bollman, and Grindlay (1955) have shown in dogs that pressure in the common bile duct rises considerably after cholecystectomy and in one dog it exceeded the pressure in the pancreatic duct.

Other Factors

Alcohol.—In not one single patient in the present series was there any association with alcoholic excess, in contrast to the experience in several American clinics—for example, Puestow and Gillesby (1954).

Food.—No constant time relation was noted between the ingestion of food and the onset of an attack of acute pancreatitis. In a number of patients pre-existing intolerance to certain foods, notably fats, was found.

Operations.—Apart from two patients whose pancreatitis was induced by transduodenal sphincterotomy and pancreatography (this series is to be published elsewhere), there was only one example in the present series of post-operative pancreatitis, such as that of Kirby, Senior, Howard, and Rhoads (1955). We have not found acute pancreatitis as an immediate complication of partial gastrectomy.

Case 2.—A woman of 57 had a right lower parathyroid adenoma excised for classical hyperparathyroidism. She became shocked and anuric the following day, and died nine days later with a serum calcium of 6.2 mg. per 100 ml. At necropsy acute haemorrhagic pancreatitis was found.

Rare Causes

Rare causes of acute pancreatitis include traumatic rupture of the pancreas and pancreatic carcinoma. There was one case of the former and two of the latter association in this series.

Case 3.—A man of 27 was accidentally struck across the upper abdomen by a heavy steel file. This was almost immediately followed by abdominal pain and vomiting. Twelve hours after the injury he was admitted with a diagnosis of a ruptured viscus. At laparotomy much fat necrosis was found, together with a haemorrhagic ascites, and an area of bruising and intense fat necrosis at the upper border of the middle of the pancreas. A drain was led down to this region, and post-operatively he developed jaundice and a pancreatic fistula which discharged for eight weeks and then cleared up. The serum amylase on the day after operation was 3,000 units per 100 ml. (Somogyi). Three years later he is in good health and has had no recurrence of abdominal pain.

Case 4.—Fifteen months after a cholecysto-jejunostomy for obstructive jaundice, a man of 39 developed steatorrhoea, vomiting, and upper abdominal pain. His serum amylase was 1,800 units per 100 ml. He died of gastrointestinal haemorrhage, and necropsy showed a carcinoma of the head of the pancreas, considerable dilatation of the obstructed pancreatic duct, an abscess in the tail of the pancreas, and a large pseudopancreatic cyst.

Case 5.—A woman of 61 had had four attacks of severe upper abdominal pain and vomiting in the five months

preceding her admission. She had a fixed mass in the epigastrium and her serum amylase was 1,160 units per 100 ml. At laparotomy gross enlargement of the head of the pancreas was found. There was a little fat necrosis, and the mass was obstructing the second part of the duodenum. A posterior gastro-jejunostomy was done. She soon became jaundiced, and a cholecysto-jejunostomy was performed. She went rapidly downhill, dying five months after the first operation. Necropsy was not performed and there is no pathological proof of carcinoma in this case, but the clinical course and operation findings are highly suggestive.

Pathology

The differentiation into oedematous and haemorrhagic pancreatitis is arbitrary, and often it is possible, in a pancreas which on the surface shows only oedema, to demonstrate haemorrhage within the substance.

In a few of the patients in this series transduodenal pancreatography has been performed, and has shown that during an attack of acute pancreatitis there is an escape of injected fluid from the ducts, with diffuse opacification of the gland substance. After recovery from an acute attack no entirely characteristic changes have been found, although the pancreatic ducts are usually wider than normal. This method has been abandoned because of its limited value and considerable danger.

In general, especially in the more severe forms of the disease, the onset is explosive and can be likened to a rupture of the pancreas. Activated trypsin, lipase, and amylase are liberated in large quantities into the blood stream, the peritoneal cavity, and the retroperitoneal tissues. Whether the circulation of these enzymes in the blood stream, where their presence can be fairly easily detected by chemical tests, is responsible for any of the general changes of acute pancreatitis is debatable. The evidence points to the conclusion that most of the general effects can be attributed to loss of circulating fluid into the peritoneum and retroperitoneal tissues (Pollock, 1956). There is, however, an isolated case report (Vogel, 1951) of cerebral demyelinization and focal necrosis in organs, particularly the myocardium, in a patient who died of acute haemorrhagic pancreatitis. These lesions probably resulted from the action of circulating trypsin. It is not unlikely (Pollock and Bertrand, 1956) that the electrocardiographic changes which are sometimes found in acute pancreatitis are due to the same cause. The presence of active pancreatic enzymes in the peritoneum and retroperitoneal tissues causes striking effects, notably tissue necrosis and haemorrhage and fat necrosis. Occlusion of the foramen of Winslow may allow the development of a pseudo-pancreatic cyst.

Twenty-five patients with acute pancreatitis were operated on within the first week. In ten of them either a bile-stained ascites or bile staining of the peripancreatic oedema was noted. In the remainder, either the colour of the fluid was not noted or it was said to be haemorrhagic. This observation lends some support to Opie's theory of bile reflux as a cause of the disease.

Occasionally there appears to be an upward extension of pancreatic enzymes, and three patients at necropsy were found to have lesions above the diaphragm which were probably the result of pancreatic enzyme activity. In one there was considerable fat necrosis in the anterior mediastinum, in the second fat necrosis in the posterior mediastinum, and in the third a blood-stained pericardial effusion.

In other cases downward movement of the digestive juices results in necrosis, haemorrhage, and fat necrosis in the right iliac fossa. There were three patients who presented with fixed masses in the right iliac fossa due to the sealing off of such an area.

Case 6.—A woman of 67 was admitted to hospital with a diagnosis of acute appendicitis and a history of severe abdominal pain and vomiting for 24 hours. She was found to be ill, and the right iliac fossa region was tender and rigid. At laparotomy there was a retroperitoneal liquid haematoma in the right iliac fossa, a slightly blood-stained ascites, and a hard enlarged pancreas with some peri-pancreatic fat necrosis. Her recovery was slow but ultimately satisfactory. Three years later she was found to be diabetic. Six years after the operation, she enjoys good health, has a little flatulence, and has to avoid certain foods. Her diabetes is kept under control with insulin.

Case 7.—A man of 70 was admitted to hospital with a diagnosis of strangulated right interstitial inguinal hernia. For nine days he had had some colicky abdominal pain and pain in the back. He had vomited frequently. A large tender mass, which felt fairly superficial, was found above the right inguinal ligament in its lateral half. When the patient was anaesthetized a second fixed mass 3 in. (7.5 cm.) in diameter was felt in the epigastrium. This was thought to be pancreatic. It gradually disappeared over the next four weeks. On incising the mass in the right iliac fossa about 200 ml. of sterile inoffensive clear fluid containing white flecks was liberated, leaving a cavity with shaggy bile-stained walls, in which were spots of fat necrosis. The cavity continued to drain for nearly three months. When seen a year later the patient was in excellent health and had no symptoms of any kind.

Case 8.—A woman of 53 was admitted to hospital with a diagnosis of acute pancreatitis. On the day before admission she had been seized with a violent epigastric pain which lasted nearly two hours and then departed for 16 hours. It then returned, radiated through to the back, and was accompanied by vomiting and mild diarrhoea. She was found to be reasonably well generally, with tenderness and rigidity in the upper abdomen. Her serum amylase was 1,900 units per 100 ml. (Somogyi), blood urea nitrogen 47.2 mg. per 100 ml., and serum bilirubin 1.6 mg. per 100 ml. She made a slow but satisfactory recovery. A week after admission a tender hard fixed mass was felt in the right iliac fossa. This gradually resolved. Five months later her gall-bladder (which contained stones) was removed, and the region of the right iliac fossa was examined. There was still a small partly liquid haematoma present in the retroperitoneal tissues. The pancreas was firm. A year after the operation she was well but had to avoid fatty foods.

So far as the pancreas itself is concerned, the extent of necrosis varies considerably. If it is minimal, in the so-called oedematous type of pancreatitis, resolution may be complete within a short time. More extensive necrosis may heal by fibrosis, and may involve enough islets to lead to diabetes, or may cause obstruction to the common bile duct or the pancreatic duct. Finally, the whole or part of the pancreas may become liquefied, leading to one variety of true pancreatic cyst or abscess.

Symptoms and Signs

Classically, an attack of acute pancreatitis is heralded by the sudden onset of severe constant abdominal pain radiating through to the back and accompanied by frequent vomiting. The vomitus contains bile but rarely frank small-intestinal contents. It is seldom foul-smelling. Only 10 of the 100 patients had no history of vomiting. The nature of the pain was, however, rather more variable. Four patients were comatose on admission and died soon after, and one was anuric

on admission and died soon after; all the remaining 95 patients had abdominal pain. This could be classed as one of three types: sudden onset of pain radiating to the back, 61 patients; sudden onset of pain not radiating to the back, 18 patients; gradual onset of pain with or without radiation, 16 patients.

The exact situation of the abdominal pain also was variable. It might be epigastric, right or left hypochondrial, or lower abdominal. It was usually sharp and severe, though occasionally colicky. It usually responded fairly quickly to bed rest and analgesics unless a pseudo-pancreatic cyst formed, when the pain might be unrelenting and severe.

Physical signs were extremely variable. Most of the patients were well nourished, but obesity was not usually a feature.

The classical picture of acute pancreatitis—the pallor, sweating, cyanosis, low blood pressure, oliguria, and abdominal tenderness and rigidity—was present in about half the patients. Sometimes the general signs of shock due to fluid loss dominated the picture and suggested a diagnosis of myocardial infarction. In four patients the general signs were unassociated with local signs, the patients being comatose and dying within a short time.

The most common erroneous provisional diagnosis was a perforated peptic ulcer, which was made in 29 patients: 16 of these patients were operated on. In the remaining patients both general and local signs were milder and the differential diagnosis lay between cholecystitis, appendicitis, and pancreatitis.

Staining of the flanks was found in only one patient, and this and peri-umbilical staining are regarded as rare and unreliable signs of acute pancreatitis.

Diagnosis

With increasing use of the simple starch-digestion test for amylase in the serum, the accuracy of diagnosis has considerably improved. Of the 100 undoubted cases of pancreatitis, 9 were incorrectly diagnosed until necropsy, 35 were incorrectly diagnosed until laparotomy, and 56 were correctly diagnosed by the clinical picture and estimation of the serum amylase.

The incorrect diagnoses made in patients who came to necropsy were: coma of uncertain origin in four, anuria due to parathyroidectomy in one, myocardial infarction in two, peritonitis of unknown cause in one, and acute cholecystitis in one.

When the correct diagnosis was established by operation a provisional diagnosis of perforated peptic ulcer had usually been made (16 patients). Less common errors were acute cholecystitis (nine patients), acute appendicitis (one patient), and strangulated interstitial hernia (one patient).

Electrocardiographic Changes

It is by no means uncommon to find an abnormal electrocardiogram showing decreased voltage of T waves, sometimes inversion of T, and occasionally depression of ST during the course of acute pancreatitis. Thirty-two patients in the present series have had electrocardiograms taken during their attack. In 19 of these the record was abnormal, in two of them so abnormal as to support a provisional diagnosis of myocardial infarction. One of these patients died.

Case 9.—A woman of 59 was admitted as an emergency case. On the day of admission she had had a sudden attack of severe upper abdominal pain which radiated into the left side of the chest and down the left arm. The left hand became cold and blue. She had vomited many times. A similar attack had occurred 10 months previously. She was found to be shocked and cyanosed, and had some upper abdominal tenderness and rigidity. A diagnosis of myocardial infarction was supported by the electrocardiogram, which showed inversion of T in lead I and slight depression of ST (see Fig. 2). The changes were thought to

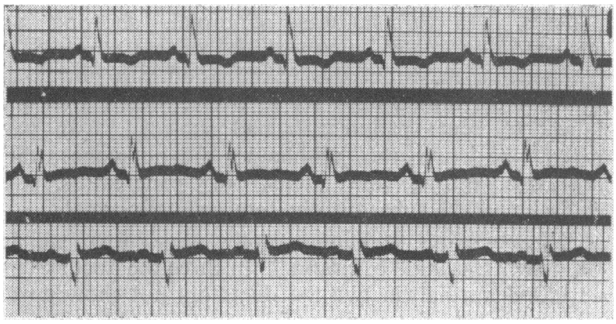

FIG. 2.—Case 9. Electrocardiogram, leads I, II, and III. The inversion of T wave in lead I and the slight ST depression were thought to be in keeping with an antero-septal myocardial infarct. At necropsy the heart was normal and the pancreas was destroyed by acute haemorrhagic pancreatitis.

be in keeping with a recent antero-septal infarct. The patient was treated with heparin and phenindione ("dindevan"), and died a week after admission. At necropsy acute haemorrhagic pancreatic necrosis was found, with extensive fat necrosis in the peritoneal cavity. The gall-bladder contained four small faceted stones. The heart showed no infarction, and the aorta and coronary arteries were practically free from atheroma.

The electrocardiographic changes disappear with recovery of the patient and may return in identical form in subsequent attacks (see Fig. 3).

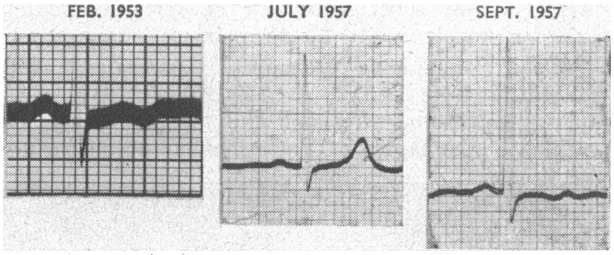

FIG. 3.—Electrocardiogram, lead V4. In February, 1953, this woman of 48 had an attack of acute pancreatitis which produced a biphasic T wave. In July, 1957, she was symptom-free and the T wave had returned to normal. In September, 1957, she had another attack of pancreatitis, which again caused a T-wave change.

The origin of these abnormalities is obscure. They are not specific, as similar changes may be found in the presence of upper abdominal peritonitis from other causes (see Case 12) and may be induced by manipulation of the gall-bladder and bile ducts (Gubner, 1944). Evidence has been presented (Pollock and Bertrand, 1956) that similar changes may be produced by intravenous injection of trypsin or pancreatic juice in dogs. The changes are not due to oligaemia or to hypokalaemia.

Radiological Diagnosis

Sixty-five patients were examined radiographically at some time during the course of their illness.

1. Plain films of the abdomen were taken in the erect and supine positions in 38 patients: in 29 the films were normal; in three the presence of gas and fluid levels in small and large bowels denoted paralytic ileus; in three

there was elevation and poor movement of the right leaf of the diaphragm and in one of the left leaf; in two opaque gall-stones were seen. All films have been reviewed to discover the incidence of the "colon cut-off sign" (Stuart, 1956). In every case in which the films were of adequate quality the sign was negative and it was possible to see gas or faeces in the transverse colon.

2. Oral cholecystography was carried out in 38 patients. In 30 it was abnormal, showing no concentration, poor concentration, or gall-stones. In the patients in whom this examination was normal it was not performed until six to twelve weeks after the attack of acute pancreatitis had subsided. In two patients in whom the gall-bladder did not concentrate the dye during the attack of pancreatitis, the cholecystogram subsequently returned to normal.

3. Intravenous cholangiography was performed in six patients, using "biligrafin." In three the duct system appeared normal, in two the ducts did not show up at all, and in one the common bile duct was dilated.

4. Barium-meal radiography was performed in 26 patients. In 13 it was normal (three of these patients were examined within a week of the onset of pancreatitis). In eight the stomach was grossly displaced forward by a retrogastric mass, which in six patients was a pseudo-pancreatic cyst (see Fig. 4), in the remaining two there was merely a swollen pancreas. In five an abnormality of the mucosal pattern in the stomach or duodenum was found (see Fig. 5). This abnormality was shown in two of the five patients to be due to oedema of the mucosa of the stomach where it was in contact with the inflamed pancreas. The close resemblance to an infiltrating carcinoma of the stomach is obvious and caused great diagnostic difficulty at the time. In one patient an upper jejunal obstruction was found, shown subsequently to be due to multiple adhesions to plaques of fat necrosis.

The radiographic changes associated with pancreatitis have been reviewed by Poppel (1954). That author lays some stress on the "papillary sign"—oedema of the papilla of Vater showing up on barium-meal *x*-ray examination as a filling defect in the second part of the duodenum. It is usually associated with oedema of the surrounding duodenal mucosa and with irritability of the duodenum, stomach, and upper jejunum. This change was found in two of our patients, and it may be more common if the examination is carried out early in the course of the disease.

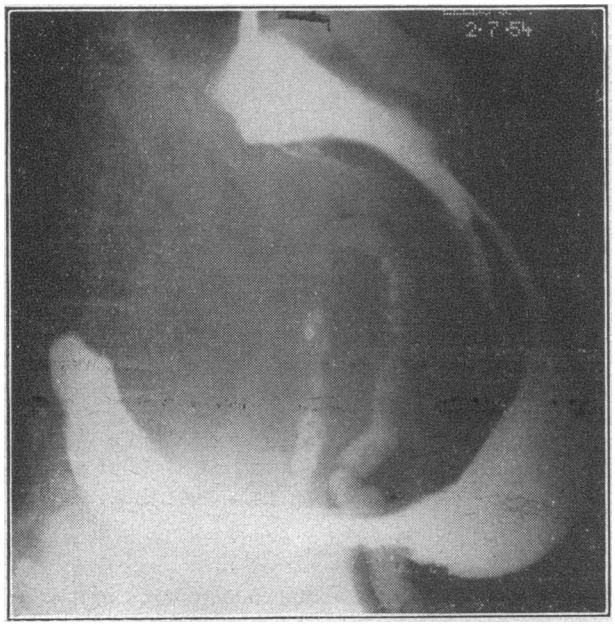

FIG. 4.—A large pseudo-pancreatic cyst displaces the stomach forwards in this barium-meal lateral radiograph. The patient had a fatal cardiac arrest during the performance of cysto-gastrostomy.

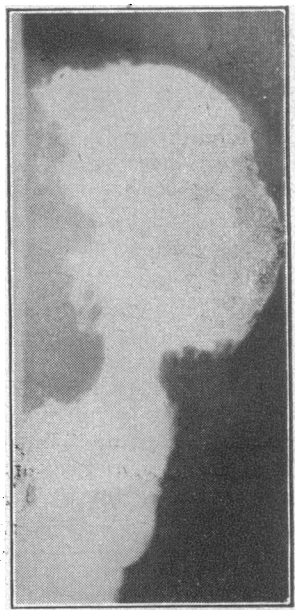

FIG. 5.—Gross irregularity of the gastric mucosal pattern due to oedema of the stomach wall where it was adherent to an acutely inflamed pancreas. The appearance is consistent with carcinomatous infiltration, but it became normal after the attack of pancreatitis had settled down.

Biochemical Diagnosis

Somogyi's method of estimation of the time taken to digest a standard starch solution has been used. In our laboratory the upper limit of normal has been 200 units per 100 ml. of serum.

Serum Amylase between 200 and 600 units per 100 ml.—There were 16 patients with pancreatitis whose serum amylase did not exceed 600 units per 100 ml. In 11 of these the diagnosis was confirmed by operation, in one by necropsy, in one by the development of staining of the flanks (Grey Turner's sign). In the remaining three the clinical picture and course were typical of pancreatitis. During the same period 34 patients have been seen whose serum amylase lay between 200 and 600 units per 100 ml. but in whom the diagnosis of acute pancreatitis was either erroneous or not proved. Seven of these patients had acute cholecystitis with gall-stones. Three had previously had a cholecystectomy, and attacks of upper abdominal pain the cause of which remained obscure. In 12 no satisfactory diagnosis was reached. In the remaining patients the following diagnoses were made: carcinoma of the pancreas (2), cirrhosis of the liver, tuberculous peritonitis, acute appendicitis, ruptured ovarian cyst, aortic aneurysm, myocardial infarct, immediately following gastrectomy, duodenal ulcer, perforated duodenal ulcer (2).

Serum Amylase over 600 units per 100 ml.—This was found in 71 patients with pancreatitis (in the remaining 13 no estimations were done, the diagnosis being made at operation or necropsy). There were in addition eight patients in whom serum amylase estimations lay above 600 units per 100 ml. who were shown not to have pancreatitis. These cases are so important from the point of view of differential diagnosis that each is described below:

Case 10: Perforated Gastric Ulcer.—A man of 60 was admitted to hospital with haematemesis and melaena. A week later he complained of severe upper abdominal pain radiating to the back, with vomiting. His serum amylase was 1,300 units per 100 ml. He was treated conservatively and died the next day. At necropsy a perforated high gastric ulcer and anterior and posterior duodenal ulcers were found. There was no evidence of pancreatitis.

Case 11: Intestinal Obstruction.—A man of 36 had a partial gastrectomy for duodenal ulcer. He was well until

three years later, when he gradually developed abdominal pain and vomited once. He was found to be cyanosed and collapsed, with an unrecordable blood pressure, a haemoglobin of 19.6 g. per 100 ml. (135%), and a serum amylase of 1,600 units per 100 ml. He was treated by aspiration and intravenous fluids on a diagnosis of acute pancreatitis until three days later, when he vomited faeculent fluid. At laparotomy a band obstruction of the lower ileum was found with a non-viable upper constriction ring. This was resected, but he developed septic complications and died two months later.

Case 12: Intestinal Strangulation.—A woman of 68 was admitted to hospital with a strangulated right femoral hernia. This was reduced and repaired. Four days later she collapsed and her serum amylase was 2,000 units per 100 ml. An electrocardiogram showed Q waves in leads III and VF, with some ST elevation in these leads and in lead II. She died next day, and necropsy showed that the reduced loop of bowel had become gangrenous and had perforated. The pancreas and heart were normal.

Case 13: Empyema of Gall-bladder.—A woman of 66 was admitted to hospital with an attack of severe upper abdominal pain and vomiting. Her serum amylase was 750 and 1,070 units per 100 ml. on two separate days, and she was treated conservatively on a diagnosis of acute pancreatitis. By the fourteenth day she had not recovered, and at laparotomy an empyema of the gall-bladder was found. The pancreas felt normal and there was no fat necrosis. Following cholecystectomy she made a good recovery.

Case 14: Stone in Common Bile Duct.—A man of 72 complained of recurrent attacks of severe epigastric pain radiating to the back and associated with vomiting. During the most recent attack he became jaundiced. His serum amylase was 710 units per 100 ml. He made a good recovery and operation was not advised. A year later, however, he had another severe attack of pain, vomiting, and jaundice, and at operation stones were found in the gall-bladder and one in the common duct. The pancreas appeared normal.

Case 15: Myocardial Infarction.—A woman of 64 collapsed with tight precordial pain and vomiting. Her serum amylase was 400 and 650 units per 100 ml. on two separate occasions. Her electrocardiogram showed an inverted T wave and elevated ST in leads V1 to V4, and she was treated for antero-septal myocardial infarct. She made a good recovery, but her subsequent history is not known.

Case 16: Ruptured Ovarian Cyst.—A woman of 28 was admitted to hospital as a case of acute appendicitis with a history of sudden onset of lower abdominal pain, without radiation to the back or vomiting. She was tender in the lower abdomen, and a serum amylase estimation was 1,100 units per 100 ml. She was treated conservatively and made a good recovery. Eleven months later she was readmitted with a similar attack; laparotomy was done, and a ruptured chocolate cyst of the left ovary was found. The right ovary was also affected and both ovaries were removed. Two years later she was well.

Case 17: Myocardial Infarction.—A woman of 86 had had a myocardial infarct diagnosed eight years previously. She made a good recovery and led a moderately active life until four days before her admission as an acute case, when she developed a sudden severe precordial and epigastric pain radiating into both sides of the back. She vomited several times. On examination four days later she was moribund, with a blood pressure of 85/60 mm. Hg, and was tender in the epigastrium. An electrocardiogram showed low voltages but no specific abnormality, and the serum amylase was 800 units per 100 ml. She died next day, and at necropsy the pancreas was normal; the left ventricular myocardium was occupied by an enormous recent infarct 8 cm. in diameter.

Complications

Jaundice.—Thirty-two patients developed clinical or latent jaundice. Recently this has been found much more commonly as a result of estimating the serum bilirubin in all patients with pancreatitis. Only five patients have been found in whom this estimation was within normal limits. In general the jaundice tends to subside with the pancreatitis and it is likely that it is an obstructive phenomenon due to the swelling of the head of the pancreas.

Diabetes.—Three patients were known to be diabetic before the onset of their attack of acute pancreatitis. In one the condition deteriorated after the attack, as judged by the amount of insulin required, and in the other two it remained unchanged. Fourteen patients were discovered to have high fasting blood sugars or diabetic glucose-tolerance tests during or after their attacks of pancreatitis. That it should complicate the more severe forms of the disease is understandable, and is attested by the fact that no fewer than 8 of these 14 patients died. Two of the surviving patients require insulin, one does not, and in three the follow-up period is too short to be sure. It does appear, however, that the diabetes is permanent in each case.

Tetany.—The serum calcium was estimated in 36 patients during their attack of pancreatitis. In 30 the figure lay between 8.5 and 11 mg. per 100 ml. (normal). Four of these patients died. In six patients the serum calcium lay between 5.6 and 8.2 mg. per 100 ml. All these patients developed clinical tetany and they all died, despite massive intravenous administration of calcium in the form of calcium gluconate. The explanation for the low serum calcium which is generally accepted is that the fat in the areas of fat necrosis is hydrolysed by lipase to fatty acids and glycerol. The former combine avidly with ionized calcium to form calcium soaps, and the blood–bone calcium balance is upset. The association between tetany and a fatal outcome is so strong, however (see also Edmondson and Berne, 1944), that this explanation cannot be the whole truth.

Electrolyte Disturbance and Uraemia.—For a variety of reasons, including vomiting, paralytic ileus, ascites, and pancreatic fistula, patients with a severe attack of pancreatitis are liable to disturbances of fluid and electrolyte balance and thence to extrarenal uraemia. There were 17 such patients in the present series, of whom 12 died. The chemical findings showed nothing characteristic, and acidosis was as common as alkalosis. On the whole the response to treatment was poor.

Anaemia and Hypoproteinaemia.—In nine patients a "secondary" type of anaemia became manifest during the course of the illness and responded to blood transfusions. Two of these patients also had hypoproteinaemia, and they both died. It is likely that minor degrees of anaemia were overlooked in many patients.

Gastro-intestinal Haemorrhage.—Three patients had a haematemesis or melaena during the course of acute pancreatitis. Two of these died; in one no lesion was discovered in the stomach or duodenum; in the other no necropsy was allowed, but an ante-mortem barium-meal *x*-ray examination had shown a gastric ulcer. In addition a patient with a pseudo-pancreatic cyst was found to have a gastric ulcer.

Masses and Pseudo-cysts.—Twelve patients developed a clinically palpable mass during their illness. In 10 this was epigastric, in one in the right iliac fossa; and one patient (Case 7) had a mass in both situations. In

two the pancreatitis was secondary to carcinoma of the pancreas and no direct attack on the mass was made. In two it resolved spontaneously. The remaining pseudo-cysts were drained, five into the stomach and four to the exterior. One in each group died—the patient with gastro-cystostomy on the table and the other of prolonged loss of pancreatic juices. The other seven patients recovered.

Prognosis

Twenty-six patients died. The chance of any particular patient dying seemed to depend more on the severity of the attack and the resistance of the patient than on the treatment employed. Some of the factors involved were as follows:

Age.—Of 26 patients below the age of 50, only four died (15%). From 50 to 60 the fatality rate was 22%, from 60 to 70 it was 29%, and over the age of 70 it was 40%.

Sex.—Seven men and nineteen women died.

Severity of Attack.—It is difficult to measure this. The significance of a lowered serum calcium and of the development of diabetes has been mentioned. Apart from these, and the evil significance of uraemia and hypoproteinaemia, it is difficult to prognosticate in the individual patient. Certainly the level of amylase activity in the blood does not reflect the outlook, but a prolongation of the elevation of serum amylase means continued activity of the disease and carries a higher mortality rate. There were 19 patients whose serum amylase was estimated daily and fell to normal within five days. Two of them died (10%). On the other hand, among 30 patients whose serum amylase remained elevated for more than five days, 7 died (23%).

Provided no heroic surgery is undertaken, immediate operation has no deleterious effect on survival. Thirty patients in this series were operated on during the first week of their illness. There were six deaths (20%). Five patients were moribund and died within 24 hours. Of the 65 patients deliberately treated conservatively, 15 died (23%).

A great many patients recover from an attack of acute pancreatitis completely and have had no further trouble, or only mild indigestion, during the one to five years that they have been followed. On the other hand, no fewer than 25 patients gave a history of previous similar attacks, in five of whom a diagnosis of acute pancreatitis was proved at laparotomy. Of the 74 surviving patients, 13 (17%) have had subsequent similar attacks; in 6 of them the diagnosis was proved at laparotomy or by gross elevation of the serum amylase level.

There were thus 11 patients who have had at least two proved attacks of pancreatitis. Of these patients, two died during their second attack, one has recovered from his second attack very recently, four are in good health from one to four years after their second attack, and four have been subjected to transduodenal sphincterotomy, with one death and three satisfactory results up to 18 months.

The high percentage of patients who recover from acute pancreatitis and have no further attacks is striking. It is in line with findings in other published series—for example, Rake and Bartlett (1953). The liability to recurrent attacks does not seem to depend on initial or subsequent treatment.

Treatment

The basic principles of management of patients with acute pancreatitis are well known and are not controversial. They are: resuscitation, control of superadded infection by antibiotics, and control of metabolic and electrolyte disturbances. About other aspects of treatment there is considerably more dispute. These include antispasmodics, antitryptic substances, corticoids, and finally operations.

Resuscitation.—In a severe case of acute pancreatitis the circulating blood volume is suddenly and dramatically reduced and the patient shows clinical signs of shock. Elliot, Zollingen, Moore, and Ellison (1955) have shown a profound fall in circulating blood volume after the experimental induction of pancreatitis in dogs and that the mortality can be reduced by the generous intravenous administration of serum albumin. Fifteen of our patients have been treated by immediate intravenous infusions of 1–3 litres of blood or plasma, and a further 11 by immediate intravenous infusion of electrolyte solutions. Thirteen of these 26 seriously ill patients died, but only three died within five days of the onset of their illness. Shock has given place to later complications as an important cause of death in pancreatitis.

Antibiotics.—It is customary to treat these patients with penicillin or other antibiotics. Seventy patients in the present series have been so treated, with results that are on the whole disappointing. Certainly the incidence of septic complications is less, but many of these patients still die of uncontrollable metabolic and electrolyte disturbances. Comparisons within this series are valueless, since it has been our policy for many years to treat all severe cases of pancreatitis with antibiotics.

Control of Metabolic and Electrolyte Disturbances.—Seventeen patients in the present series either had been or became diabetic. The control of the diabetes with soluble insulin has presented no problems, but one death can possibly be ascribed to untreated diabetic coma. Electrolyte disturbances are common in the more severe forms of the disease, and their correction may prove impossible. Sodium, potassium, and chloride deficiencies have been found, together with acidosis or alkalosis, and correction has been attempted by the usual measures of oral, rectal, and intravenous replacement. It has already been mentioned that tetany may occur, associated with a depression of the serum calcium level. This has been found difficult to correct, and every patient with this complication has died. Hypoproteinaemia and anaemia are commonly found in the later stages of acute pancreatitis and have been treated by blood transfusions.

The main problem with severe cases, however, has been their catastrophic katabolism. In a few patients accurate estimation of the rate of weight loss was possible, and it was found to approach a kilogram a day. This process we have found impossible to control, and most of these patients have died. In the few who have survived, no particular treatment appeared to mark the turning-point. We have had no experience of the use in this condition of androgenic steroid hormones, but have been very disappointed with the results of blood transfusions, high-protein forced feeding, and corticoids.

Antispasmodics.—The assessment of the place of atropine and other drugs with similar action is difficult. In this series atropine or propantheline (pro-banthine) has been used in 12 patients without noticeable effect

on the course of their illness. Theoretically morphine, a potent cause of spasm of the sphincter of Oddi and of the duodenal wall, should not be used in this disease, and in fact most patients who needed analgesics were treated with pethidine.

Antitryptic Substances.—It is likely that some of the general and local effects of acute pancreatitis are due to the liberation of large quantities of active trypsin from the damaged pancreas. There are known to be several substances with high antitryptic potency, and the use of these substances might appear to be indicated in this disease. Evidence from experimental sources (Elliott *et al.*, 1955; Pollock, 1956) indicates that their value is strictly limited. For two years in this hospital it was customary to transfuse large quantities of plasma on account of its albumin content (human serum albumin has been shown *in vitro* to be a potent trypsin inhibitor). No effect has been detected from this treatment, apart, as indicated earlier, from its beneficial effect on shock. Five of the 15 patients so treated died. The most potent trypsin inhibitor has been isolated from soya beans (Kunitz, 1947). This substance has not been tried clinically, but it has been found not to influence the course of experimental pancreatitis (Elliott *et al.*, 1955).

Corticoids.—The first report of the treatment of acute pancreatitis by corticoids seems to be by Stephenson, Pfeffer, and Saypol (1952). Since then isolated cases and small series have been reported, all of which have claimed good recoveries after their use—for example, Rogers, Wilson, Meynell, and Cooke (1956). There has at the same time grown up a volume of experimental and clinical evidence that cortisone may cause pancreatitis. Thus Stumpf, Wilens, and Somoza (1956) found pancreatitis in rabbits treated with cortisone, and Baar and Wolff (1957) reported two fatal cases of acute pancreatitis in children treated with cortisone. In order to elucidate this question, a "double blind" controlled trial of corticotrophin in pancreatitis is at present being conducted. Thirty patients have so far been treated by either corticotrophin or an inert substance resembling corticotrophin in a dose of 40 units twice daily, reducing after 10 days and being stopped after 14 days. The results are being analysed by the restricted sequential procedure of Armitage (see Snell and Armitage, 1957). It is planned to treat 50 patients, but the preliminary results indicate no clear superiority of corticotrophin over placebo.

In one patient laparotomy was performed after the patient had been receiving twice-daily injections of 40 units of corticotrophin for 10 days. Apart from the acute pancreatitis which was confirmed, he was also found to have a recently perforated and sealed acute duodenal ulcer. This may be attributable to the action of the corticotrophin.

Operations

It has become generally accepted that immediate operation in patients with pancreatitis can do no good, and that elective surgery should await the subsidence of the acute attack. On the other hand, diagnostic laparotomy has not been shown to do any harm, and in any doubtful case it is preferable to make sure of the diagnosis by laparotomy rather than miss another condition mimicking it and associated perhaps with an elevated serum amylase level.

When a mass becomes palpable there may be a temptation to explore it with a view to drainage. This should be resisted for two reasons: first, some masses resolve spontaneously; second, external drainage of a recent pseudo-pancreatic cyst invites the occurrence of a pancreatic fistula with its accompanying loss of electrolytes and protein. Provided the patient's general condition is reasonably satisfactory, it is far better to wait for six to eight weeks before operating on a pseudo-pancreatic cyst. By that time it will have become well walled off and may be drained externally or internally with little fear of doing more harm than good. Our own feeling in recent years has been in favour of transgastric anastomosis of the anterior cyst wall to the posterior stomach wall. This simple operation has proved effective in five patients recently. Barium-meal *x*-ray studies have shown no trace of the cysto-gastrostomy after as short a period as one week. Apparently the cyst, having discharged into the stomach, does not fill up again with gastric contents.

The treatment of a diseased gall-bladder after an attack of pancreatitis is more controversial. The traditional view is that the gall-bladder should be removed and that the common duct should be explored if it is dilated. There is, however, a certain amount of theoretical and experimental evidence that after cholecystectomy (or if the gall-bladder is not functioning), the pressure in the common duct may exceed that in the pancreatic duct and result in bile reflux and recurrent attacks of pancreatitis. Certainly in the present series cholecystectomy has not been found to protect the patient against attacks of pancreatitis. Four patients have had recurrent attacks of pancreatitis following cholecystectomy.

In three patients after an attack of pancreatitis the gall-bladder was anastomosed to the stomach. Two of these have had recurrent attacks of pancreatitis, while the third has remained well for five years.

Prolonged T-tube drainage of the common bile duct was used in one patient, who remained well two years later.

Transduodenal Sphincterotomy.—This operation has been used in one patient during her first attack of acute pancreatitis (she suffered a disruption of her duodenal incision and subsequently died of an acute enterocolitis), and in five patients with recurrent acute pancreatitis. One of these five died of a fulminating attack of acute pancreatitis four days later. The remaining four have remained well for 6 to 18 months. The operation is technically easy and theoretically satisfying. It remains to be seen whether the late results justify its continued use. Doubilet and Mulholland (1956) claim that they do.

Finally, it should again be stressed that the great majority of patients who recover from an attack of pancreatitis suffer very few after-effects and that recurrent pancreatitis is a rare disease.

Summary and Conclusions

A series of 100 patients with acute pancreatitis have been studied and reviewed after periods of up to five years.

In half the men and three-quarters of the women in this series the gall-bladder was abnormal. In the presence of a non-functioning gall-bladder the pressure of bile in the common duct may be raised above the pressure in the pancreatic duct. If the ampulla is common to both ducts and if a functional or organic obstruction at the sphincter of Oddi occurs bile may

be forced up the pancreatic duct to initiate an attack of acute pancreatitis.

The general and local effects of pancreatitis are due primarily to the liberation into surrounding tissues and the blood stream of large quantities of active pancreatic enzymes.

Electrocardiographic changes suggestive of myocardial infarction may occur in acute pancreatitis. On the other hand, two patients with myocardial infarction have been seen with grossly elevated serum amylase levels (above 600 units, Somogyi).

Radiographic changes in pancreatitis are discussed. Barium-meal examination early in the course of the disease may prove to be of diagnostic value.

A serum amylase level of over three times the normal (200 units, Somogyi's method) has been found in association with a few cases of perforated gastric ulcer, intestinal obstruction, gall-stones, ruptured ovarian cyst, and myocardial infarction.

Local and general complications are discussed. Six patients developed clinical tetany, and they all died.

One-quarter of all the patients in this series died. Some of the factors influencing prognosis are discussed.

Treatment is discussed in terms of resuscitation, antibiotics, control of electrolyte and metabolic disturbances, antispasmodics, antitryptic substances, corticoids, and operations. A mild case of pancreatitis will recover whatever treatment is given, and for a very severe attack no treatment appears to be of any avail. Most patients who recover from an attack of acute pancreatitis have remained well for one to five years.

I am grateful to all the surgeons, physicians, and pathologists of the General Infirmary at Leeds who have over the past five years allowed me to see their cases. In the present series are patients admitted under the care of Messrs. Armitage, Chamberlain, Latchmore, Oldfield, Shucksmith, and Symons, and of Professors Goligher, Moir, Pyrah, and Tunbridge.

REFERENCES

Baar, H. S., and Wolff, O. H. (1957). *Lancet*, **1**, 812.
Doubilet, H., and Mulholland, J. H. (1956). *J. Amer. med. Ass.*, **160**, 521.
—— Poppel, M. H., and Mulholland, J. H. (1957). Ibid., **163**, 1027.
Edmondson, H. A., and Berne, C. J. (1944). *Surg. Gynec. Obstet.*, **79**, 240.
Elliott, D. W., Zollinger, R. M., Moore, R., and Ellison, E. H. (1955). *Gastroenterology*, **28**, 563.
Gubner, R. S. (1944). *J. Amer. med. Ass.*, **124**, 122.
Kirby, C. K., Senior, J. R., Howard, J. M., and Rhoads, J. E. (1955). *Surg. Gynec. Obstet.*, **100**, 458.
Kunitz, M. (1947). *J. gen. Physiol.*, **30**, 291.
Menguy, R. B., Hallenbeck, G. A., Bollam, J. L., and Grindlay, J. H. (1955). *Surg. Forum*, **6**, 359.
Opie, E. L. (1903). *Disease of the Pancreas: Its Cause and Nature*. Lippincott, Philadelphia.
Parry, E. W., Hallenbeck, G. A., and Grindlay, J. H. (1955). *A.M.A. Arch. Surg.*, **70**, 757.
Pender, B. W. T. (1957). *Lancet*, **1**, 409.
Pollock, A. V. (1956). *Surg. Gynec. Obstet.*, **102**, 483.
—— (1958). Ibid., **107**, 765.
—— and Bertrand, C. A. (1956). *Surgery*, **40**, 951.
Poppel, M. H. (1954). *Radiology*, **62**, 514.
Puestow, C. B., and Gillesby, W. J. (1954). *Amer. Surg.*, **20**, 355.
Raker, J. W., and Bartlett, M. K. (1953). *New Engl. J. Med.*, **249**, 751.
Rich, A. R., and Duff, G. L. (1936). *Bull. Johns Hopk. Hosp.*, **58**, 212.
Rogers, N. C., Wilson, A. O., Meynell, M. J., and Cooke, W. T. (1956). *Lancet*, **2**, 651.
Snell, E. S., and Armitage, P. (1957). Ibid., **1**, 860.
Stephenson, H. E., jun., Pfeffer, R. B., and Saypol, G. M. (1952). *A.M.A. Arch. Surg.*, **65**, 307.
Stuart, C. (1956). *J. Fac. Radiol. (Lond.)*, **8**, 50.
Stumf, H. H., Wilens, S. L., and Somoza, C. (1956). *Lab. Invest.*, **5**, 224.
Thal, A., and Brackney, E. (1954). *J. Amer. med. Ass.*, **155**, 569.
Vogel, F. S. (1951). *A.M.A. Arch. Path.*, **52**, 355.

ELECTROLYTE LOSSES ASSOCIATED WITH THE TAKING OF PURGES INVESTIGATED WITH AID OF SODIUM AND POTASSIUM RADIOISOTOPES*

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It is well known that diarrhoea may result in excessive loss of electrolytes from the bowel, and if the intake is not large enough to keep the patient in balance body depletion will occur.

There are reports that continual purging produces abnormal loss of electrolytes through diarrhoea (Mårtensson, 1953; Schwartz and Relman, 1953; French *et al.*, 1956; Houghton and Pears, 1958; Aitchison, 1958). In this paper three cases are described in which the regular taking of purges was partly or wholly responsible for excessive loss in the stools of sodium or potassium, or both, and for depletion of the body stores of these substances. Electrolyte studies were made in these patients, using chemical balances and radioisotope methods to be described elsewhere (Lubran, 1959).

Case 1

A woman aged 50 was referred in October, 1953, for gastro-intestinal investigation. She had been constipated since early childhood. At 5 years of age rectal prolapse occurred, and from that time she took purges. Without them her bowels did not move and abdominal distension developed. From the age of 20 she had taken the same laxative‡ daily. At 40 years of age diarrhoea with colicky pains began and she passed eight to ten loose stools daily. Even so, she found it impossible to stop taking her customary nine laxative tablets daily, for without them, although continuing to pass about six liquid stools in the day, she was unable to pass sufficient flatus and her abdomen became uncomfortably distended. In November, 1952, ammonium urate stones were removed (by Mr. J. Scholefield) from the left renal pelvis. In March, 1953, she first noticed blood and mucus in the stools.

First Admission (October 23, 1953)

On examination the abdomen was distended, and tender in both iliac fossae. No abnormality was found in any other system.

Investigations.—Stools contained pus and red blood cells but no pathogenic organisms or parasites. Sigmoidoscopy showed a reddened mucosa with superficial ulceration compatible with moderately severe ulcerative colitis. A plain

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‡Composition:

Comp. ext. of colocynth, *B.P.*, 1914	1 gr. (60 mg.)
Ext. of jalap	½ gr. (30 mg.)
Podophyllum resin	¼ gr. (15 mg.)
Green ext. of hyoscyamus, *B.P.*, 1898	¼ gr. (15 mg.)
Menthol	1/20 gr. (3 mg.)