Pancreatic Society of Great Britain and Ireland

The 14th annual meeting of the Pancreatic Society of Great Britain and Ireland was held at the General Infirmary, Leeds on 17 November 1989. The president for the meeting was Mr Michael McMahon and the Lilly guest lecturer was Dr Paul Lankisch from Luneburg, West Germany. The Rodney Smith prize for the best paper went to Mr R Sutton (Oxford) for his work on the function of pancreatic islet autografts. Selected abstracts are published below.

Teenage pancreatitis—Is it a separate entity?
J E TRAPNELL (Royal Victoria Hospital, Boscombe, Bournemouth, Hants) Chronic relapsing pancreatitis in adolescence is a most uncommon clinical problem and has received minimal separate recognition in the literature. It occurs in an age range where the causes of the disease which may operate from birth, overlap with the major aetiological factors in the generality of pancreatitis in adult life. A personal series of 32 patients with pancreatitis aged 11–20 years, seen and treated between 1960 and 1988 is reported. Twenty four of these cases followed a chronic relapsing course. There was therefore a marked reversal of the normal proponentance of acute over chronic relapsing disease. There were four deaths— a mortality of 13%.

The patients divide aetologically into five groups. There were four boys who were alcoholics and two girls who were on longterm steroids. There was one patient with hyperlipaemia and six girls had gall stones—although cholecystectomy did not produce a remission of their disease and five of these required further surgical procedures. Finally in 11 patients, no underlying cause for the pancreatitis could be found and this idiopathic group also ran an unexpectedly severe course.

The reversal of the acute versus chronic disease ratio, together with the troublesome clinical course in the patients with gall stones and in the idiopathic group raises the question as to whether teenage pancreatitis is a distinct entity in the overall spectrum of this disease. It is suggested that a prospective collective study of this subgroup is indicated.

Main pancreatic duct status in pseudocysts complicating acute pancreatitis
N D CARR, S JONES, B A THEIS, W R LEES, R C G RUSSELL (Department of Gastroenterology, The Middlesex Hospital, Mortimer Street, London)
This study evaluates main pancreatic duct status and outcome in 75 patients (57 men, 18 women median age 39 years) who were referred for further management of pancreatic pseudocysts after acute pancreatitis. Investigations included ERCP (58), ultrasound (68), computed tomography scan (17) and percutaneous pancreatography (four). Sixty one patients had pseudocysts which communicated with a completely disrupted (44) or a partially disrupted (17) main pancreatic duct. In the remaining 14 patients the main pancreatic duct was normal.

Forty nine of the 61 patients with complete or partial disruption of the main pancreatic duct underwent partial pancreatectomy. Of 45 patients available for follow up, good results were achieved in 44 (median follow up 62 months) but one required completion pancreatectomy. The other 12 patients were treated conservatively or by drainage. Outcome was satisfactory in seven of these but four died from pancreatic complications and one required resection.

Pseudocysts associated with a normal main pancreatic duct were successfully treated conservatively or by drainage in 10 patients (median follow up 58 months) but four others underwent resection for diagnostic reasons, and also did well.

These results indicate that assessment of main pancreatic duct status is important in deciding on the treatment of pseudocysts caused by acute pancreatitis.

Can Apache-II predict specific complications of acute pancreatitis? A prospective comparison with the Ranson system
M. LARVIN, M J MCMAHON (University Department of Surgery, The General Infirmary at Leeds, Leeds) Death from acute pancreatitis results from early fulminant major organ failure, or more commonly from late septic complications of pancreatic necrosis. Prediction of major organ failure and pancreatic necrosis is important for therapeutic trials, and may aid clinical management. Existing multiple criteria measure only initial severity, and cannot predict pancreatic necrosis. Acute Physiology and Chronic Health Evaluation (APACHE-II) scores provide rapid initial assessment and sequential monitoring of the severity of AP.2 The role of APACHE-II in predicting major organ failure was prospectively evaluated in 290 attacks of acute pancreatitis. By predefined criteria, complications were classified as early major organ failure (within the first week) (21%, 7%), and pancreatic necrosis, proven at autopsy/ laparotomy (15%, 5%). Data were collected to calculate Ranson and daily Apache-II scores.

For the identification of major organ failure, APACHE-II scores at admission provided similar accuracy to Ranson scores 48 hours later. Ranson scores proved poor at predicting pancreatic necrosis compared with APACHE-II.

Circulating concentrations of neutrophil elastase and alpha-1 proteinase inhibitor in acute pancreatitis
R E BANKS, S W EVANS, D ALEXANDER, M J MCMAHON, J T WHICHER (Department of Chemical Pathology and the Department of Surgery, University of Leeds, Leeds) Acute pancreatitis varies in severity from a mild illness with low mortality to a severe form which is frequently fatal. Numerous studies have examined plasma concentrations of pancreatic enzymes, acute phase reactants and proteinase inhibitors in an attempt to predict the severity and outcome of the illness, with variable success. It has been recently proposed that fatal pancreatitis may result as a consequence of excessive leukocyte stimulation.1 We have examined this hypothesis with respect to neutrophil involvement by measuring the concentrations of circulating neutrophil elastase-alpha-1 proteinase inhibitor (E-a1PI) complex serially in 27 patients with acute pancreatitis, using an ELISA method developed in house.

Patients were classified as having severe or mild illness on the basis of Ranson and criteria and clinical outcome. Although plasma E-a1PI concentrations were raised in >90% of the patients on admission compared with control levels, no correlation was seen between E-a1PI concentrations and the severity or outcome of the illness, therefore not supporting a prime role of the neutrophil in determining mortality in pancreatitis. The concentrations of E-a1PI are also examined in relation to CRP and a-2-macroglobulin levels with regard to prognosis.

Trypsinogen activation peptide assay of peri- toneal fluid in acute pancreatitis
D I HEATH, C WILSON, A M GUDGEON, A JEHANLI, G PATEL, C W IMRIE, J HERMON-TAYLOR (Departments of Surgery, Glasgow Royal Infirmary, George and St Georges’ Hospital, London) Trypsinogen activation peptide assay specifically reports trypsinogen activation in vivo by quantifying released activation peptides using C-terminally directed antibodies which do not
bind trypsinogens. Samples of peritoneal fluid were obtained from 20 patients with acute pancreatitis and stored at −20°C without EDTA before assay. Eight patients with proven pancreatic necrosis had peritoneal fluid trypsinogen activation peptide concentrations in the range 0.69–21.0 nmol (mean 5.55); seven patients with complicated pancreatitis, but without proven necrosis, had trypsinogen activation peptide concentrations in the range 0.1–1.68 nmol (mean 0.59); four patients with uncomplicated pancreatitis were trypsinogen activation peptide 0.1–1.11 nmol (mean 0.38).

The data were compared using the Mann-Whitney-U-test. Pancreatic necrosis versus the complicated group p = 0.02; pancreas necrosis versus the uncomplicated group p = 0.05; trypsinogen activation peptide assay of on admission urine samples gives a simple early severity prediction in acute pancreatitis.1

Another study suggests that trypsinogen activation peptide assay applied to peritoneal fluid provides an additional direct assessment of intrapancreatic zymogen activation and may contribute to precise severity assessment of patients with acute pancreatitis.1


Is fatal pancreatitis the consequence of excessive macrophage stimulation?

S W EVANS, R E BANKS, D ALEXANDER, M J MAHER, J T WHISHER (Departments of Chemical Pathology and Surgery, University of Leeds) Acute pancreatitis is usually a relatively mild self limiting disease. In a number of individuals, however, a severe and often fatal form of the disease occurs. It has been suggested recently that severe pancreatitis may be the consequence of excessive leucocyte stimulation.1 One leucocyte which plays an important role in the regulation of inflammation and the acute phase response is the macrophage. Tumor necrosis factor α is a cytokine produced exclusively by macrophages and is a candidate pathological protein in severe necrotising pancreatitis. We have examined the potential role of tumour necrosis factor α in pancreatic necrosis and concentrations of tumour necrosis factor α were measured on samples taken on consecutive days from admission. In many individuals (nine of 22) with acute pancreatitis circulating concentrations of tumour necrosis factor α on the day of admission were increased above normal (15:3 ± 13:5 ng/l, normal values <10 ng/l). There was no correlation between concentrations of tumour necrosis factor α and disease severity. These data suggest that whilst leucocyte activation occurs in individuals with acute pancreatitis there is no evidence that the severe form of this disease is a consequence of excessive activation of macrophages as evidenced by circulating tumour necrosis factor α concentrations.


Encapsulation of porcine islets in alginate/poly-L-lysine/alginate microspheres

R DOWNING, K HEALD, C HAIL (Department of Surgery, University of Birmingham, Birmingham) The complications of longterm immunosuppressive therapy preclude pancreas allo-

transplantation as an acceptable treatment for uncomplicated type I diabetes. Encapsulation of rodent pancreatic islets within biocompatible membranes will, however, prevent their rejection after xenotransplantation.

A simple method for the isolation and encapsulation of islets from the porcine pancreas has been developed. The pancreas was removed from anaesthetised weaning pigs and disrupted by sequential collagenase digestion. Islets were separated from the digested gland by sedimentation through a discontinuous gradient of Percoll at unit gravity. Individual islets were encapsulated within membranes comprised of calcium alginate/poly-L-lysine/calcium alginate.

Glucose evoked insulin secretion by individual islets was assessed in vitro. Eleven of 14 non-encapsulated islets and 14 of 14 encapsulated islets responded to 16 mmol/l glucose: the mean percentage increase in insulin output by non-encapsulated islets was 112% (range 0–1251%) and by encapsulated islets 154% (range 82–1333%).

This study shows that isolated porcine islets withstand encapsulation within alginate microspheres and retain their ability to secrete insulin in response to glucose stimulation.

Simple method for the release of islets by controlled collagenase digestion of the human pancreas

N J M LONDON, P WAKE, C J WILSON, D BASSETT, G M RUMFORD, P TOOMEY, P R F BELL, R F L JAMES (Department of Surgery, Clinical Sciences Building, Leicester Royal Infirmary, PO Box 65, Leicester) We describe a simple technique for the collagenase digestion of the human pancreas based on the principles that the digestion time is tailored to each pancreas and that freed islets are continually removed from the action of collagenase. The pancreas is distended with collagenase, a biopsy taken from the tail and divided into five pieces which are placed in Universals containing MEM and diithiothreitol at 37°C. The pancreas itself is incubated in MEM at 37°C. At five minute intervals a Universal is removed from the water bath, shaken for 30s and the contents examined by microscopy. As soon as free islets are visible the pancreas is placed into one compartment of a kidney bowl divided into two equal halves by a 1 mm mesh. The pancreas is gently teased apart and fluid digest in the empty half of the bowl aspirated and passed through a 500 μm mesh into cold ice storage. This method is repeated until the digestion process has ceased. Using this technique on 20 consecutive pancreata, median wt (range) 53.9 (45.2–72.7) g, we have counted 131672 (43516–400000) islets in the digest, equivalent to 2394 (715–8000) islets/g pancreas. The volume of islet tissue in the digest was 299 (26–1341) mm³ equivalent to 5.81 (0.36–26.81) mm/g pancreas. In conclusion, we have found that this simple technique produces large numbers of viable islets from the human pancreas.

Methods for human pancreatic islet isolation were assessed by application in cynomolgus Macaques after total pancreatectomy. Partially purified islets were prepared by a previously reported method, then autografted. Animals with intraportal grafts (five) displayed mildly impaired glucose handling with qualitatively normal though quantitatively reduced insulin and glucagon responses, whereas animals with intrasplenic grafts (five) had poorer graft function, perhaps because of the smaller venous beds used for grafting within the spleen compared to that within the liver. Animals with intraportal grafts of purified islets prepared by an improved method for human islet isolation (five) displayed slightly stronger insulin responses. Pulsatility of insulin and glucagon release were detected in three of four animals with well maintained graft function, although at a lower frequency than normal. Longterm graft survival correlated with insulin responses to glucose six weeks after transplantation, suggesting that beta cell reserve is a determinant of graft survival; well maintained graft function was observed in two animals for periods of over three months. These results provide further support for the suggestion that isolated islets have the potential of restoring normal or nearly normal pancreatic endocrine function in man.

Comparison of conventional and digital retrograde pancreateography

D J LINTOTT, R C FOWLER, A R COWEN, A G CHALMERS, A T R AXON, P J HARTLEY (Department of Diagnostic Radiology and Gastroenterology Unit, The General Infirmary at Leeds Department of Medical Physics, The University of Leeds, Leeds) Digital fluorography is an image intensifier based technique for general digital radiology. A prototype unit has been used in this department for the past three years, mainly for upper gastrointestinal examinations. Computer enhancement of images has become one of the theoretical limitations of a 512 × 512 matrix.

To test the diagnostic limitations of this matrix, a prospective comparative trial of conventional 105 mm and digital pancreateography was performed. Conventional and digital images were obtained at endoscopic retrograde pancreateography on 20 patients. Comparable images were randomised and assessed blind by three independent clinical observers. Radiographic image quality and diagnostic confidence levels were recorded and compared.

Computer enhanced 512 × 512 mm digital pancreateograms images are of a radiographic quality comparable to conventional 105 mm film. There is good correlation with high diagnostic confidence in 74% of comparable digital and film image pairs. Incidences of poor diagnostic correlation are unrelated to the imaging technique.

Since completion of this study a custom designed digital spot film imager has been installed which provides the facility to obtain on line computer enhanced 1024 × 1024 matrix images.

Longterm function of Macaque pancreatic islet autografts

R SUTTON, D GRAY, P MORRIS (Nuffield Department of Surgery, John Radcliffe Hospital, Headington, Oxford) D MATTHEWS, R TURNER (Diabetes Research Laboratories, Nuffield Department of Clinical Medicine, Radcliffe Infirmary, Woodstock Road, Oxford)

Rapid bolus dynamic computed tomography in acute pancreatitis. What is the significance of computed tomography necrosis?

N J M LONDON, T LEES, J M LAVELLE, K MILES, K WEST D F L WATKINS, D P FOSSARD (Departments of Surgery and Radiology, Clinical Sciences Building, Leicester Royal Infirmary, PO Box 65,
Leicester) Thirty four patients with prognostically severe acute pancreatitis have undergone rapid bolus dynamic computed tomography scanning. Twenty four scans showed computed tomography necrosis which in 13 patients involved less than a third of the pancreas, in four patients one third to two thirds, five patients more than two thirds; two scans showed peripheral necrosis. Cytological examination of fine needle aspirates from computed tomography necrotic areas revealed necrotic amorphous debris. Repeat scans at six weeks in those patients with more than two thirds necrosis showed persisting non-enhancement and ERP in one of these patients failed to show any pancreatic ducts in the computed tomography necrotic area. The 10 patients whose scans did not show computed tomography necrosis had clinically mild attacks. Among the 24 patients whose scans showed necrosis, 10 proved to have mild attacks; 14 had severe attacks. There were six deaths, four from multiorgan failure and two from pancreatic infection. The two patients who died from pancreatic sepsis were the only two with infected fine needle aspirations. Disease severity and the risk of death was unrelated to the computed tomography necrosis. Three patients developed pseudo-cysts in areas of computed tomography necrosis.

We conclude that computed tomography necrosis does represent pancreatic necrosis but that disease severity is unrelated to its site or extent. Infected necrosis carries a high risk of death whilst sterile necrosis may lead to prolonged fistula formation and in a proportion of patients (20%) is associated with death from multiorgan failure.

Effect of cimetidine, glucagon, prophylactic bromide, morphine, pethidin, naloxone, ethyl alcohol on the sphincter of Oddi

N SETAKIS, J ECONOMOU, N RITI, A KONDIS, N GEORGIOUD, G ANDONIOU (Praktovikea, Athens, Greece) The physiology of the sphincter of Oddi is closely related to the pathogenesis of acute pancreatitis. The knowledge of the effect of different drugs on the sphincter of Oddi provides us with more information regarding their effect on pathogenesis or treatment of pancreatitis.

The aim of this study was to determine the effective diameter of the ampulla of Vater before and after administration of 200 mg cimetidine, 2 mg glucagon, 30 mg prophylactic bromide, 5 mg morphine, 50 mg pethidine, 0.4 mg naloxone iv and 10-20 ml ethyl alcohol via nasogastric tube.

The flow rate of normal saline through the human common bile duct into the duodenum was measured on those patients before and after the administration of one of the above substances. From the flow rate/min and based on Poiseille’s law for laminated flow we determined the effective diameter of the ampulla of Vater.

We studied 190 patients. Thirty six patients were given 200 mg cimetidine iv, 62, 2 mg glucagon iv, to 15, 30 mg prophylactic bromide, to 20, 5 mg morphine iv, 36, 0.4 mg naloxone iv, and finally up to 20 patients we administered 20-30 ml ethyl alcohol through a nasogastric tube to the first and second part of duodenum.

The conclusions from our study are as follows: cimetidine produces spasm of the sphincter of Oddi; glucagon relaxes the sphincter of Oddi; prophylactic bromide in the doses that we used has a very small effect of the sphincter; morphine produces very strong spasm, which, however, is reversed by the administration of glucagon; pethidin has no effect on the sphincter of Oddi; naloxone has no effect on the sphincter; ethyl alcohol produces spasm of the sphincter, less than that of morphine, which, however, is not reversed by the effect of glucagon.

Duct drainage procedures in benign pancreatic disease

L C SMITH, T N WALSH, B A THEIS, R C G RUSSELL (Department of Gastroenterology, The Middlesex Hospital, London) The role of drainage procedures in the management of benign pancreatic disease remains controversial, and rarely used. Of 360 procedures performed for benign disease between 1976 and 1989, only 45 were drainage procedures (longitudinal pancreaticojejunostomy 18; accessory sphincteroplasty 20; main duct sphincteroplasty seven). This study evaluates the results of drainage procedures.

The indication for longitudinal pancreaticojejunostomy was pain, previous operation and a duct more than 1 cm diameter, for accessory sphincteroplasty was a pancreas divisum (19) and obstruction of the accessory sphincter by a calculus (one) and for main duct sphincteroplasty was a stricture of the main duct (seven). All patients had an ERP and ultrasound preoperatively and were followed up prospectively in a special clinic. A good result is defined as a patient with minimal or no pain, and leading a normal lifestyle.

After longitudinal pancreaticojejunostomy 13 of 18 had a good outcome, one patient died of haemorrhage at two months, and one patient proceeded to total pancreatectomy, while three patients have symptoms, but are better than preoperatively. After accessory sphincteroplasty, eight patients had a good outcome, seven patients failed and proceeded to resection, while five patients improved but do not require further treatment. After main duct sphincteroplasty, only two patients had a good result, two patients had a resection, and three patients are unchanged.

It is concluded that longitudinal pancreaticojejunostomy is a useful therapeutic procedure with 72% good results, maintained in five patients followed for five years. Accessory sphincteroplasty gives a good result in 40%, and main duct sphincteroplasty is of little value.

Characteristics and management of cystic pancreatic tumours

A C SMITH, V A CHANDRAMANI, C A AINLEY, S J WILLIAMS, B A THEIS, A R W HATFIELD, R C G RUSSELL (Department of Gastroenterology, The Middlesex Hospital, Mortimer Street, London) Cystic pancreatic tumours are said to occur in the distal pancreas, and rarely present with jaundice. In a review of 10 patients (mean age 57 years, range 31-78, F:M 6:4) seen in the last four years, seven occurred in the head of the pancreas and three in the body. The site of pathology determined the clinical presentation which included jaundice (five), abdominal pain (five), abdominal mass (five), weight loss (two), steatorrhoea (two) and fever (one). Ultrasound showed a mean tumour size 7.6 cm (range 4-12). At ERCP two of seven patients had pancreaticoduodenal fistulae. Histological results showed cystadenocarcinoma (five), cystadenoma (three), pseudocyst (one), and one patient had typical ultrasound findings but no histology. In two patients endoscopic stenting was attempted to relieve jaundice but failed because of thick mucus. A pancreaticoduodenal mass, 102 patients who underwent and a distal pancreatectomy in one. Resection was attempted in one but only a choledocho-

Role of resection in the management of pancreatic cancers

V A CHANDRAMANI, B A THEIS, R C G RUSSELL (Department of Gastroenterology, The Middlesex Hospital, Mortimer Street, London) Despite the recent optimism, the outlook for pancreatic cancer patients is dismal. To determine the approach to the patient presenting with a pancreatic mass, 102 patients who underwent resection [adenocarcinoma (PCa) 31, ampullary (ACa) 44, neuroendocrine (NT) 11, miscellaneous (M) 16], 117 patients treated by surgical bypass (SP) and 121 managed by endoprostheses (EP) were reviewed. The diagnosis was confirmed histologically in 69% of the palliative group.

Between group comparisons were made for age, tumour size, hospital stay, lymph node status, resection margins and survival (Table). A log rank analysis showed a significant survival advantage for resection, even after age and tumour size standardisation, but all patients in the PCa group died within three years despite selecting carefully for favourable tumours. In PCa small tumours did better than tumours more than 2 cm, but other factors did not correlate with improved survival.

It is concluded that resection merely delays death by 10 months in PCa. The high incidence of lymph node involvement (36%) and local extension (56%) outside the pancreas in PCa suggests that resection is a last resort procedure, and that the good results of ACa, NT and M demand histological assessment before palliative treatment is advised.

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