Pancreatic Society of Great Britain and Ireland

The 11th Annual Meeting of the Pancreatic Society of Great Britain and Ireland was held at Guy’s Hospital, London, on 28 November, 1986 under the Presidency of Dr Christopher Mallinson. Guest lectures were presented by Professor Gunter Kloppel of the University of Hamburg and Professor Horst Kern of the University of Marburg. Abstracts of the main papers are printed below.

Specific intraperitoneal antiprotease chemotherapy in acute necrotising pancreatitis (ANP): an experimental study

T J FERRY, D A W GRANT, AND J HERMON-TAYLOR (Department of Surgery, St George’s Hospital, London) Appropriate intraperitoneal antiprotease chemotherapy for ANP may include the use of oligopeptide inhibitors of bacterial origin as these agents are capable of inactivating pancreatic proteases of different specificities in complex with α1-macroglobulin. We have studied the effect of administering these agents, singularly and in combination, in peritoneal lavage (PL) fluid at concentrations of 0.4 μM on the survival times of rats with enterokinase-induced ANP. PL was routinely commenced 12 hours after induction of ANP and consisted of 2×20 ml aliquots of Ringer’s solution at 37°C administered over 20 minutes, and repeated at one and three hours after the first lavage. Rats were randomly allocated into four experimental groups after ANP. Results:

<table>
<thead>
<tr>
<th>Groups</th>
<th>Mortality at 48 hours</th>
<th>Mean survival ± SD (hours)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No PL</td>
<td>12/12</td>
<td>28±3±6±3</td>
</tr>
<tr>
<td>TPL-Ringer’s</td>
<td>9/12</td>
<td>34±2±5±5</td>
</tr>
<tr>
<td>TPL-Enteropept 8X 12</td>
<td>5±4±5±5</td>
<td></td>
</tr>
<tr>
<td>TPL-Enteropept 10X 12</td>
<td>33±3±6±6</td>
<td></td>
</tr>
<tr>
<td>+ Elastatin</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*p<0.05 vs no TPL; p<0.05 vs TPL-Ringer’s

These results show that PL with a balanced physiological salt solution starting 12 hours after ANP significantly reduced mortality and prolonged mean survival of experimental animals. The addition of specific antiproteases to the PL conferred no additional survival benefit. These findings do not support the intraperitoneal administration of antiproteases in the therapy of clinical ANP.

Pharmacokinetic study of intraperitoneal antiprotease therapy

*M LARVIN, *A D MAYER, †W MULLER-ESTERL, AND *M J MCMAHON (*University Department of Surgery, The General Infirmary, Leeds, UK, †Department of Clinical Biochemistry, Surgical Clinic, University of Munich, West Germany) In acute pancreatitis a toxic peritoneal exudate forms, characterised by protease and esterase activity. Peritoneal exudate may be removed by lavage using large volumes of fluid, but this results in heavy albumin loss, respiratory embarrassment, and peritoneal macrophage dysfunction. Reduction in fluid volume might be achieved by adding an antiprotease, although treatment may be compromised by the rate of absorption through the inflamed mesothelium. The effectiveness of bolus instillations of intraperitoneal Trasylol was studied in 15 patients with acute pancreatitis. An 8FG lavage cannula was inserted percutaneously, and lavage performed with 1 litre saline. In 10 cases, 500 ml 0.9% saline containing 5×10⁶ KIU Trasylol was instilled into the peritoneal cavity (Regimen i). In five cases, 1000 ml of 0.9% saline containing 5×10⁶ KIU Trasylol was instilled into the peritoneal cavity, and repeated eight hours later, after draining fluid remaining from the first installation (Regimen ii). Plasma and peritoneal fluid samples were stored at −70°C prior to determination of Trasylol concentrations using an enzyme linked immunosorbent assay.

Intra-peritoneal Trasylol concentrations of 10×10⁶ KIU/litre may be required to inhibit protease activity in the peritoneal exudate from patients with acute pancreatitis. Both regimens provided effective intraperitoneal anti-protease activity, sustained for 20 hours in regime (ii), despite considerable systemic absorption.

Reference

Fresh frozen plasma in the treatment of acute pancreatitis – a multicentre prospective clinical trial

T LEESIDE, M HOLLIDAY, D HEATH, J SCOTT, D WITHERS, T HUNT, M C A BRETT, AND A W HALL (Departments of Surgery and Pathology, University of Leicester, Leicester) An uncontrolled clinical study1 and animal work2 suggest fresh frozen plasma (FFP) reduces mortality in acute pancreatitis, possibly by replenishing the plasma antiprotease system. A prospective controlled randomised clinical trial is underway in Leicester and surrounding hospitals to explore this possibility.

Patients with acute pancreatitis have prognostic markers measured3 and are randomised to receive either FFP (2 U/24 hours for 72 hours) or purified protein fraction (1 bottle per 24 hours for 72 hours) as part of the intravenous fluid therapy. Serum α₁-antiprotease and α₂-macroglobulin levels are measured on days 1, 3, and 7.

To date 128 attacks of acute pancreatitis have been randomised – 64 FFP and 64 colloid control. The two groups are well matched in all clinical criteria including predicted severity of pancreatitis.

No significant difference has yet been shown between the two groups in terms of mortality or other complications. Both show a significant rise in α₁ antiprotease levels after FFP.

Mean FFP concentration (10⁶ KIU/litre) in peritoneal fluid and plasma

<table>
<thead>
<tr>
<th>Regimen</th>
<th>1h</th>
<th>2h</th>
<th>3h</th>
<th>4h</th>
<th>5h</th>
<th>6h</th>
<th>7h</th>
<th>8h</th>
<th>10h</th>
<th>12h</th>
<th>14h</th>
<th>16h</th>
<th>18h</th>
<th>20h</th>
</tr>
</thead>
<tbody>
<tr>
<td>Plasma</td>
<td>0.87</td>
<td>1.44</td>
<td>1.75</td>
<td>1.61</td>
<td>1.44</td>
<td>1.31</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Plasmal</td>
<td>0.48</td>
<td>0.68</td>
<td>0.67</td>
<td>0.62</td>
<td>0.72</td>
<td>0.65</td>
<td>0.67</td>
<td>0.61</td>
<td>1.03</td>
<td>1.07</td>
<td>1.08</td>
<td>1.08</td>
<td>0.87</td>
<td>0.74</td>
</tr>
<tr>
<td>Plasma</td>
<td>0.64</td>
<td>1.37</td>
<td>2.04</td>
<td>1.97</td>
<td>1.64</td>
<td>1.43</td>
<td>1.08</td>
<td>1.10</td>
<td>1.08</td>
<td>1.08</td>
<td>1.08</td>
<td>1.08</td>
<td>0.87</td>
<td>0.74</td>
</tr>
</tbody>
</table>

References
levels from days 1 to 3 and this is not influenced by administration of FFP. α2 macroglobulin levels show a significant fall in the colloid control group from days 1 to 3 (p<0.02) but remain substantially unaltered in patients receiving FFP (p=0.91, two-tailed Mann-Whitney Ranking Test).

Relatively low volumes of FFP have been shown to prevent the usual depletion of serum α2 macroglobulin in acute pancreatitis and this may have therapeutic implications.

References

Experimental pancreatitis: the effect of allopurinol
S W Macgowan, D J Bouchier-Hayes, and P J Broe (Department of Surgery, Royal College of Surgeons in Ireland, St Laurences Hospital, Nth Brunswick St, Dublin) The free oxygen radical scavanger allopurinol has been shown by Sanfey and colleagues to ameliorate the course of acute pancreatitis when administered before induction in an ex vivo, isolated, perfused canine model. We have tested the hypothesis that allopurinol alters the course of acute pancreatitis when administered after initiation in an in vivo model in the rat.

Acute pancreatitis was induced in male Wistar rats by intraductal injection of sodium taurocholate as described by Aho and colleagues. Pancreatitis was confirmed by serum amylase (mean control 8695 IU/l; mean postinduction 19252 IU/l) and also by histology. Allopurinol in a dose of 75 mg/kg was administered intraperitoneally based on dose-response curves. Pancreatitis was induced in 20 animals of which 10 also received 25 mg allopurinol intraperitoneally immediately postoperatively. Five animals died in each group. In a further 10 animals allopurinol was administered before induction of acute pancreatitis. Seven of these survived. These results show that the administration of allopurinol either before or after induction of acute pancreatitis does not alter the mortality in an in vivo model in the rat. The study suggests that further evaluation of the role of oxygen free radicals in acute pancreatitis is required in animal models not involving perfusion techniques.

Follow up of accessory sphincteroplasty for chronic pancreatitis associated with pancreas divisum
I P Linehan and R C G Russell (The Middlesex Hospital, London) The management of patients with pain caused by chronic pancreatitis is difficult, especially in those with associated pancreas divisum and no avoidable aetiological cause. After the failure of endoscopic assessor sphincteroplasty we have used operative accessory sphincteroplasty with cholecystectomy as the first surgical procedure in these patients.

Three men (median age 25 years, range 24–31) and 14 women (median age 38 years, range 18–77) have undergone accessory sphincteroplasty for pain without mortality. Three have been lost to follow up but of the rest median follow up is 24 months (range 9–44). One patient died after a subsequent pancreatoduodenectomy.

The outcome is known in 14; four (29%) are pain free and two (14%) have intermittent periods of pain but have required no treatment other than analgesia. Eight (57%) have required further surgery, six (35% of the whole group) have progressed to total pancreatectomy for endstage disease. Of those who have had no further surgery two (33%) have pancreatic insufficiency and none are diabetic.

We conclude that operative accessory sphincteroplasty combined with cholecystectomy is a beneficial first procedure in the management of patients with pain from chronic pancreatitis associated with pancreas divisum, however, more than 50% will progress and require further surgery.

Long term experience of pancreatic resection using a banding technique
A Cuschieri (Department of Surgery, Ninewells Hospital & Medical School, University of Dundee, Dundee) A technique of pancreatic banding has been used for pancreatic resection (distal hemi- and 3/4 pancreatectomy) during the past 15 years as an alternative to pancreatic parenchymal suture. The method involves tying the pancreatic substance on either side of the proposed transection line sufficiently tightly to ensure haemostasis without cutting into the pancreatic parenchyma using 1/0 double black silk and, more recently, vicryl 4 mm tapes. After banding and pancreatic transection, the pancreatic duct is identified and suture ligated with 4/0 non-absorbable material. The method has been used in 21 patients undergoing resection for pancreatic disease (trauma=three, tumour=two, chronic pancreatitis=16) and in 42 patients undergoing pancreatectomy as part of an R2/3 radical gastrectomy for operable gastric cancer. There was one death in the pancreatic disease group (pulmonary embolism) and four deaths in the gastric cancer group (anastomotic leak=two, pneumonia=one, haemorrhage from the splenic vein=one). Postoperative pancreatic fistula in this series was encountered in two of 21 in the pancreatic group and two of 42 in the gastric cancer group. The overall incidence of pancreatic fistula in this series was 6%. All the pancreatic fistulas healed spontaneously within seven to 12 days. We have found pancreatic banding to be a simple and safe method of effecting pancreatic resection.

Prognostic criteria in acute pancreatitis: a critical evaluation
M Cesur, A Marques, J Deus, M CRAVO, G MeLO, and J Pinto Correia (Department of Medicine 2, University Hospital of Santa Maria, 1699 Lisbon Codex, Portugal)

The prognostic value of different well known severity index in acute pancreatitis (AP) has been examined in 200 patients admitted to the Intensive Care Unit of Gastroenterology between October 1980 and December 1985. These episodes occurred in 184 patients (91 men and 93 women) with mean age of 52 years. Gall stones were presented in 47%, alcoholic habits in 35% and miscellaneous in 10%. Three groups were considered: (i) Non-complicated (63%); (ii) Benign complications (18-5%); (iii) Severe complications (18-5%). General mortality was 5% (all included in group (iii)).

If we considered the prognostic index proposed by Ranson (1982), by Blamey (1984) and by Bank (1983), no severe complications were found in 49% of the patients with less than three criteria of Ranson; in 96% with less than three criteria of Blamey and in 100% with no criteria of Bank. So the false negatives were negligible. However, severe pancreatitis was observed only in 35% of the patients with more than three criteria of Ranson, in 34% with more than three criteria of Blamey, and in 30% with
criteria of Bank. The same results were found with more than five criteria. So there were many false negatives.

In our population, the study of the variables involved showed that only LDH, blood sugar, WBC count, protein, serum calcium, albumin and urca. on admission or at 48 hours, were useful for classification in the three groups. With the discriminative analysis of the three most significant variables (LDH, protein, and calcium) a formula was constructed with the same statistical value: PPV 38%, NPV 95%. With these three variables plus the ratio of 5 mg a prognostic score was elaborated that showed better PPV 44%, and NPV 96%. This prognostic score needs only four laboratory values and gives the same information as the previous more complicated index.

Serial objective measurement of severity in acute pancreatitis

M. Larvin and M. J. Mcmahon (University Department of Surgery, The General Infirmary, Leeds) The severity of acute pancreatitis (AP) is usually classified at admission to hospital – for example, the Ranson and Imrie scores. In the course of the attack – for example, death, major complication etc. There is a need for more precise quantitation of severity, in order to aid clinical management and to enable more accurate evaluation of potential therapies. We examined three objective illness ‘scoring’ systems, the Acute Physiology score (APS-II). Simplified APS (SAPS) and MRC Sepis score (MRC), in a prospective longitudinal study of 63 attacks of AP (17 associated with gallstones, 33 with alcohol). Sixteen attacks were classified as severe according to outcome (six deaths, 10 major complications). The Ranson and Imrie scores were calculated, and the illness scoring systems were evaluated daily throughout the attack.

Identification of Severe Attacks

<table>
<thead>
<tr>
<th>Score</th>
<th>Cut-off level</th>
<th>Sensitivity %</th>
<th>Specificity %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Analysis at 48 hours</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>APS2</td>
<td>11</td>
<td>94</td>
<td>89</td>
</tr>
<tr>
<td>SAPS</td>
<td>&gt;0</td>
<td>88</td>
<td>64</td>
</tr>
<tr>
<td>MRC</td>
<td>&gt;1</td>
<td>68</td>
<td>51</td>
</tr>
<tr>
<td>Ranson</td>
<td>&gt;2</td>
<td>78</td>
<td>65</td>
</tr>
<tr>
<td>Imrie</td>
<td>&gt;2</td>
<td>87</td>
<td>57</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Score</th>
<th>Cut-off level</th>
<th>Sensitivity %</th>
<th>Specificity %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Analysis at 7 days</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>APS2</td>
<td>7</td>
<td>92</td>
<td>86</td>
</tr>
<tr>
<td>SAPS</td>
<td>&gt;7</td>
<td>83</td>
<td>81</td>
</tr>
<tr>
<td>MRC</td>
<td>&gt;1</td>
<td>92</td>
<td>86</td>
</tr>
</tbody>
</table>

APS2 may be superior to other systems for defining severity within 48 hours of admission. At a week after admission, the three illness scoring systems were of similar precision for the identification of patients who developed late complications (three pseudocysts, seven pancreatic abscesses). The conclusion of this study is that illness severity scoring appears to be of potential value for predicting severe pancreatitis, and trends derived from serial analysis may provide advance warning of late complications.

Outcome of patients with acute cholangitis and acute pancreatitis

John Neoptolemos, Trevor Leese, and David Carr-Locke (Departments of Surgery and Gastroenterology, The Leicester Royal Infirmary, Leicester) The association between acute gall stone pancreatitis and acute cholangitis has become increasingly recognised. We have found an incidence of 15% in patients with biliary pancreatitis in the past three years.

The outcome of 29 consecutive patients with this association was reviewed. The median age was 76 years (range 52–87) of whom 23 (79%) were women. Four patients had undergone previous cholecystectomy. Eighteen patients were patients to have a severe attack (Imrie score: 3–6 factors); nine were hypotensive on admission. The median bilirubin was 106 (range 25–231) μmol/L in 28 patients and 8 μmol/L in one patient diagnosed at necropsy (stones passed). Blood cultures were positive in eight of 12 patients. ERCP was successfully performed in 20 of 21 patients and common bile duct (CBD) stones were present in 12 patients who underwent successful endoscopic sphincterotomy (ES) and stone extraction (four with subsequent cholecystectomy). Three of five other patients who underwent surgery were found to have CBD stones. The remaining 13 patients were managed conservatively. Three patients (10.3%) died (all with predicted severe attacks): one following surgical exploration of the CBD and two whilst on conservative treatment.

In conclusion CT scanning was valuable in diagnosing acute pancreatitis and its local complications; but we did not find the admission CT scan to be useful in predicting the severity of the attack.

Lectin histochemistry in pancreatic carcinoma

Chii-Kong Ching, R Black, T Hellier, A Savage, and Jonathan M Rhodes (Departments of Medicine and Histopathology, The University of Liverpool, PO Box 147, Liverpool, and Department of Histopathology, Selly Oak Hospital, Birmingham) It has been reported that lectin histochemistry using the peroxidase labelled lectins Ulex Europaeus agglutinin (UEA-I, fucose specific) and Peanut agglutinin (PNA, Gal-GalNAc specific) selectively detects pancreatic cancer cells in snap-frozen tissue and it has been suggested that this may be useful as an adjunct to pancreatic cytology (Exp Cell Biol 1983; 51: 19–28).

We performed lectin histochemistry on pancreatic biopsies using PNA, UEA, Griffonia Simplicifolia (GS2), soy bean agglutinin (SBA) and wheat germ agglutinin (WGA). Formalin fixed tissue was studied from pancreatic cancer (n=13).
chronic pancreatitis (n=13) and normal pancreas (n=14). PNA positivity was present in 9/14 normals, 11/13 chronic pancreatitis and 11/13 pancreatic cancers and UEA-I positivity in part of all sections. In individual cases PNA showed specificity for malignant tissue and particularly the secreted intraductal mucin but overall specificity was poor. GS2 showed highly selective binding of ductal cells but with no specificity for diseased tissue.

Lectin histochemistry using GS2 may be a useful adjunct to conventional stains for identifying pancreatic ductal tissue. GS2 may prove potentially useful for identifying the cell of origin of experimental pancreatic cancer in hamster. Neither PNA nor UEA-I has been found specific for detecting pancreatic carcinoma on conventionally fixed tissue.

Patients with ampullary carcinoma are prone to other malignant tumours

J F R Robertson, P Boyle, and C W Imrie (Department of Surgery, Royal Infirmary, Glasgow) Carcinoma of the ampulla of Vater, though a well recognised cause of obstructive jaundice is an uncommon neoplasm. One series foundampullary carcinoma in 3% of patients with extrahepatic biliary obstruction and in 0.2% of post mortem examinations. This relative rarity along with its variable clinical presentation often results in delayed diagnosis. In spite of this, carcinoma of the ampulla of Vater carries a reasonable five year survival in the majority of reported series.

It is unusual for any patient to develop more than one malignant tumour during their lifetime although it is certainly documented. We report a consecutive series of 43 patients who underwent surgery for ampullary carcinoma of whom five at some time in life had at least one other malignancy. The primary sites of the other historically distinct tumours were breast (one patient), endometrium (one patient), bronchus (one patient), bladder (two patients) and small bowel (two patients). One patient is still alive. Three died from carcinomas other than their ampullary carcinoma while the remaining patient died from cardiac and renal disease. The occurrence of multiple primary tumours in this selected group is more than three-fold that statistically expected (p<0.003).

Risk of death from acute pancreatitis

I A Goulbourne, J M J Dixon, S Duffy, and G C Davies (Univ Dept of Surgery, Royal Infirmary, Edinburgh) Acute pancreatitis is frequently mild and self limiting. Five to 10% of patients develop severe haemorrhagic disease and die of complications. Prediction of death, using multifactorial assessment is time consuming and accuracy is limited. Two hundred and ninety two consecutively admitted patients have been analysed using 57 separate variables obtainable at or soon after admission. Four independently predictive factors were found by multiple logistic regression to be related to fatal outcome (p<0.0001). These were a reduced total plasma protein <60 g/l (p<0.003), plasma urea in excess of 6 mmol/l (p<0.01), abnormal chest x-ray (effusion, consolidation or collapse) (p=0.001) and the amylase gradient. Amylase gradient was defined as the ratio between initial plasma estimation and the subsequent one the morning after admission. If this ratio was <2 then this constituted a significant risk factor (p<0.005). Seventeen of 20 deaths occurred in patients scoring 2 or more risk factors (Table 1). Ten deaths occurred in an identifiable group of 19 patients who thus exhibited a mortality risk of 56%.

Early diagnosis of biliary aetiology in acute pancreatitis

J Deus, M Cesari, A Marques, M Crawford, and J Pinto Correia (Department of Medicine 2 (UCIGE), University Hospital of Santa Maria, 1699 Lisboa Codex, Portugal) The early diagnosis of gall stones in patients with acute pancreatitis is often difficult, in spite of the new imaging methods. The different management between non-biliary and biliary pancreatitis implies a precise early discrimination.

We have studied prospectively 200 attacks of acute pancreatitis, in 184 patients, admitted in our ICU in the last five years.

Ninety five episodes of biliary pancreatitis were compared with 105 nonbiliary acute pancreatitis episodes.

We have analysed three clinical (age, sex, jaundice) and eight laboratory values (SGOT, SGPT, SGOT/SGPT, serum amylase, bilirubin, alkaline phosphatase, α-GT, leucocyte count). With multivariate analyses, only three (sex, age and SGPT) seem to be of value to discriminate the two groups in the initial 48 hours. These three variables allow reliable identification of gall stone pancreatitis (sensitivity and positive predictive value – 80% and specificity – 81%), and may select early and more accurately patients for different procedures of diagnosis or even treatment, such as endoscopic sphincterotomy.

Serum markers and clinical data in diagnosing pancreatic cancer: a contrastive approach

D Basso, G del Favero, C Fabris, C Angone, A Piccoli, G Dodi, M Lise, and R Naccarato (Istituto di Medicina Interna, Cattedra di Malattie Apparato Digerente, Policlinico Universitario, Padova, Italy) The aim of the present investigation was to assess the role of some serum markers in comparison with simple clinical data in differentiating pancreatic cancer from chronic pancreatitis and other gastrointestinal diseases. In the sera of 32 control subjects (CS), 28 pancreatic cancer (PC), 26 chronic pancreatitis (CP) and 32 extrahepatic cancers (EPD), CA 19-9 (immunoradiometric assay), TPA and CEA (RIA procedures) were determined. Clinical data recorded: sex, age, presenting and onset of pain attacks, pancreatic calcifications, jaundice, alcohol abuse, diabetes mellitus, weight loss. Statistical evaluation, stepwise discriminant analysis (RAO’S V criterion). Serum markers correctly classi-
demonstrates the data related one, operative procedure. High admissions during the pancreatic surgery was initiated in the region during the initial seven year study period.

There were 38 patients – 37 men, one woman – and mean age at presentation was 42.4 years (range 20 to 69 years). At initial presentation 14 patients (37%) were unemployed and 11 (29%) worked as unskilled labourers. Twenty seven patients (71%) required more than one hospital admission. Surgery was indicated in 14 patients (37%) – diagnostic laparotomy (four), cholecystectomy (three), bypass procedures (three), pancreatic resection (four) and drainage of pancreatic pseudocyst (four) and abscess (one). Five patients required more than one operative procedure. Five deaths occurred during the study period – one after total pancreatic resection, one after biliary bypass and three unrelated to pancreatitis. Eight patients (21%) failed to attend for further follow up and attendance rates at one, three, and five years were 76%, 47%, and 34% respectively.

In summary, alcohol induced pancreatitis in this region is primarily a disease of young adult men of lower socio-economic status with a recurring pattern leading to repeated hospital admissions and an unexpectedly high incidence of surgery. Mortality related to the condition, however, is low. The study demonstrates the problem of ascertaining data related to follow up in a condition where, despite intensive efforts, patient compliance is poor.

Variations in the incidence and spatial distribution of patients with primary acute pancreatitis in the Nottingham defined population (1969–85)

BEETINA KATZCHINSKI, J B BOURKE, J A GIGGS, AND D S ERDON (University Departments of Therapeutics, Surgery and Geography, University Hospital and Park, Nottingham) During these 15 years 493 patients were admitted with primary acute pancreatitis. The geographical distribution of the disease within the study area was determined using 62 electoral wards and two patient cohorts namely 214 (1969–76) admissions (1971 Census) and 279 (1977–83) admissions (1971 Census). The incidence of the disease increased from 27 per annum to 40 per annum in the two cohorts. Most of the alcohol associated patients (18 first cohort; 38 second cohort) were young or middle aged men. For gall stone and ‘non gall stone’ associated groups the incidence rose sharply with increasing age for both sexes.

For both cohorts there were large (more than five-fold) statistically significant (p<0.001) variations in the distribution of pancreatitis within the defined population area. Moreover, the spatial distribution was very similar for both cohorts with the highest rate wards clustering in a U-shaped area east of the city centre. Investigation of environmental factors suggested that this coincides with a particular domestic water supply.

This second 1977–83 cohort confirms the previously reported association with the domestic water supply and this observation now applies to a 15 year period. The incidence of the disease has increased during the study period.

Colonic complications of severe acute pancreatitis (AP)

M C ALDREDGE, A G RADCLIFFE, G GLAZER, AND H A F DUDLEY (St Mary’s Hospital, London) Colonic complications of pancreatitis are rare, only 36 cases being recorded in the world literature.

We have managed severe AP by intensive supportive therapy with subtotal pancreatic resection in those failing to improve. Seventeen patients underwent gland resection of whom 10 had colonic complications – seven men and three women (median age 56 years) with a median of 4 Ranson criteria. In six colonic involvement was present at the time of pancreatic resection and in four it presented up to two weeks later as a faecal fistula (n=3) or abdominal sepsis (n=1). The transverse colon was involved in five and the splenic flexure in five. All underwent resection of the involved colon and exteriorisation with either a proximal colostomy (n=9) or ileostomy (n=1) and a distal mucous fistula.

Histology revealed two types of lesion: Type I (n=7) – PERICOLITIS – fat necrosis involving the serosa with congestion of the mucosa and submucosa but no vessel thrombosis. Type II (n=3) – ISCHAEMIC NECROSIS – bowel infarction with thrombosis of vessels in the submucosa and mesentery.

Six patients died (60%) from overwhelming sepsis between one day and four weeks after colonic resection compared with none of the seven without colonic involvement who underwent pancreatic resection. We conclude that colonic complications of severe AP: (a) are commoner than is at present recognised (b) are of two histological types and (c) are associated with a poor prognosis despite surgical intervention.

Autoimmunity and HLA in chronic pancreatitis

ALASTAIR FORBES, GISSELLE SCHWARZ, RITA MIRKIAN, VARINA DRUMMOND, (K CHAN, P B COTTON, AND G F BOTTLA (Department of Gastroenterology, Middlesex Hospital, Mortimer Street, London, Department of Diabetes and Immunogenetics, St Bartholomew’s Hospital, Bartholomew Close, London, and Department of Immunology, Middlesex Hospital Medical School, Toottenham Street, London) Since immunological and hereditary factors may be important in chronic pancreatitis, autoantibodies and histocompatibility antigens of classes I (A, B, & C) and II (DR) were studied in 55 British Caucasian patients (32 men) (median age 42 years; range 18–73 years). Chronic pancreatitis was defined by at least two of ultrasonography, ERP, secretin test, calcification, histology; actiological factors other than alcohol were excluded. In 23 patients (21 men) mean weekly ethanol intake exceeded.
100 g (usually substantially so); the remaining 32 had idiopathic chronic pancreatitis (ICP). Twenty-three patients had autoantibodies, in 13 to gastric parietal cells. Eleven of those with ICP (four men) had parietal cell antibody: more than expected for the age/sex distribution. There were (after exclusion of three insulin-dependent diabetics for whom a DR4 association is recognised) overall excesses of HLA B44, CW5 and DR4 (significant when uncorrected for the number of antigens tested). In ICP there were no HLA associations but in patients with alcohol-related disease the excesses of B44 (54-5%, control 29-4%), CW5 (54-5% v 15-9%) and DR4 (61-1% v 33-6%) were significant (p<0.01, 0.0005, 0.025 respectively) and that for CW5 remained so after correction (p<0.05). An hypothesis that hereditary and possibly immunological factors are important in the aetiology of chronic pancreatitis is supported.

Design of a pancreatic surgery database

I P Linehan and R C G Russell (The Middlesex Hospital, London) The purpose of creating a database is to aid data retrieval; the design, comprising both content and record structure, must be carefully planned. The content must be restricted to the barest minimum avoiding an unacceptably large storage requirement and facilitating data entry and retrieval.

The classic (and simplest) structure is one in which each patient has a single record which contains all the pertinent data. This is not suitable for many patients as they may undergo many operative procedures and have multiple follow up visits. We split each patient record between three separate files; registration details, clinical events – for example, operations or major illness, and clinic visits. Multiple events and visits are allowed for each patient, but indexed in such a way that data for a patient in one file can be related to data for that patient in another.

Each clinical event record starts with an indication code for that event and ends with a closure code which may link into the next event: thus it is possible to trace and analyse the progression of disease of any individual or any group of patients. This aspect is thought to be especially appropriate when studying patients with chronic pancreatitis.

Isolation of purified human islets of Langerhans for transplantation

D Alderson, N M Kneteman, and D W Scharp (St Louis, Mo. Dept of Surgery, Univ. of Newcastle, Newcastle, UK) Islet transplantation is a potential treatment for insulin-dependent diabetes designed to prevent or ameliorate long term complications. Successful application in man has been prevented mainly by an inability to isolate adequate numbers of islets from human pancreas.

A method is described for large scale isolation of human islets based on ductal perfusion at 37°C with purified collagenase (Type X) and mechanical disaggregation followed by purification on a 2-layer Ficoll density gradient. Of 17 consecutive human pancreata from donors aged 8–36 years, 15 were successfully processed, yielding 138000±22000 islets/pancreas (mean±SEM), equivalent to 1858±212 islets/g of gland before purification. Ficoll recovery was 80±7.6% with a purity of 53±5.8% judged by light microscopy following aldehyde fuchsin staining.

After overnight culture at 37°C, islet function and viability were assessed by glucose perfusion and renal subcapsular implantation into nude mice. Typical biphasic insulin responses to glucose were documented with perfusion, peak insulin responses being three to four-fold greater than basal.

Previous reports have indicated yields of 1000 islets/g with purity in the range of 10–40%. This method therefore, represents a considerable advance over earlier techniques, providing sufficient numbers of purified islets to make transplant studies in man feasible.

Identification of a new pancreatic cancer-related glycoprotein in serum by electrophoresis and lectin blotting

Chi-Kong Ching and Jonathan M Rhodes (Department of Medicine, The University of Liverpool, Liverpool, UK) A simple and specific serum test was available for pancreatic cancer it would greatly facilitate diagnosis and allow early screening. Radio-immunoassay of the mucin antigen CA 19-9 (Epithio sialylated factor-NAfucopentose II oligosaccharide) is arguably the best so far but has a considerable false positive rate. In order to detect abnormal glycoproteins shed by pancreatic cancer into serum we have combined electrophoresis with detection of glycoproteins by peroxidase tagged lectin blotting.

SDS-polyacrylamide gel electrophoresis followed by high intensity transfer onto nitrocellulose membrane and incubation with peroxidase tagged peanut lectin (PNA, Gal-Gal NAC specific) and wheat germ agglutinin (WGA, sialic acid specific) was performed on sera from patients with pancreatic cancer (n=17), other cancers (n=14) and normal, jaundiced and pancreatic controls (n=50). At least 10 PNA+ glycoproteins were identified in normal sera. An additional PNA+glycoprotein with a very high mwt (approx. 3.5±10^D) was identified in 8/17 pancreatic cancer sera but not in any of the 64 controls. This high mwt PNA+glycoprotein is WGA negative and is distinct from the CA 19-9 antigen.

It is quite likely that the sensitivity of this test may be improved by using isotypically labelled lectin in which case it should prove very useful as a test for pancreatic cancer.

Collagen quantification in chronic pancreatitis

R I Kennedy and H Saries (Southeast Hospital, Bristol and INSERM U31, Marseille, France) In chronic inflammatory disease either the total amount of collagen rises or the relative proportions of the different collagen types change. Hepatic collagen levels have been extensively studied in cirrhosis but the changes in chronic pancreatitis are unknown.

Normal pancreatic tissue was obtained from organ donors (n=4) and compared with chronic califying pancreatitis (CCP, n=6) and chronic obstructive pancreatitis (COP, n=6). Total collagen measurement by hydroxyproline estimation revealed 45±4.0 mg of collagen/g of dry pancreas (mean±SEM) in normal tissue, 113±30 mg/g in COP and 243±31 mg/g in CCP. Collagen content in chronic pancreatitis was significantly different (p<0.001) to that in normal tissue.

Individual quantification of collagen types I and III was performed by SDS purification, followed by cyanogen bromide digestion. SDS-polyacrylamide gel electrophoresis and densitometric scanning after staining with Coomassie blue. Results are expressed as % type III (type III/type I+type III). Percentage type III was significantly higher in normal tissue 20±2±1% (mean±SEM) and COP: 22±2±1% (p<0.02).

In CCP, increases in total collagen content are comparable to results in hepatic cirrhosis. A decrease in per cent type III collagen is present in other chronic inflammatory conditions, although the significance is unclear.