

Pancreatic Society of Great Britain and Ireland

The Seventh Annual Meeting of the Pancreatic Society of Great Britain and Ireland was held at Bonham Carter House, London, on 12 November 1982, under the Presidency of Dr Peter Cotton. Abstracts of papers presented at the meeting are printed below.

Pancreatic polypeptide secretion by pancreatic apudomas and its lack of suppression by cholinergic blockade

T E ADRIAN, J YEATS, S M WOOD, J M POLAK, AND S R BLOOM (*Department of Medicine and Histochemistry, Royal Postgraduate Medical School, Hammersmith Hospital, London*) Pancreatic endocrine tumours frequently secrete more than one hormone and in particular high plasma concentrations of pancreatic polypeptide (PP) are often observed. In the course of running a weekly diagnostic screen we have been able to measure PP in more than 200 pancreatic apudomas. Raised plasma PP concentrations (300 pmol/l) were found in 28/97 (29%) gastrinomas, 45/59 (76%) VIPomas, 11/20 (55%) glucagonomas, 7/26 (27%) insulinomas, and seven pancreatic tumours apparently secreting only PP. PP levels were also raised in 16/34 (47%) patients with the carcinoid syndrome, but not in other endocrinopathies including phaeochromocytoma, thyroid medullary carcinoma or pituitary tumours. PP concentrations were normal in 92 patients with adenocarcinoma of various sites including the pancreas.

A common problem encountered is a moderate rise of PP which may be due to an apudoma or alternatively, to a variety of other causes - for example, old age, stress, infections, diabetes, renal impairment or chronic alcohol abuse. Normal PP release is dependent on the cholinergic innervation and it has been suggested that atropinisation should distinguish between autonomous PP secretion by tumours and normal PP release, which is atropine suppressible.

Atropine (1 mg intramuscularly) had no significant effect on circulating PP concentrations in 12 patients with PP secreting pancreatic tumours. In contrast all control subjects showed a fall of at least 50% within the hour.

These results suggest that PP is a frequent component of pancreatic apudomas and that tumour produced PP is unaffected by cholinergic blockade. The

'atropine test' may greatly help in the detection of early, and treatable tumours in patients who have an intermediate rise of plasma PP.

Treatment of pancreatic islet cell carcinoma with streptozotocin - experience in 15 patients

S M WOODS, J YEATS, T E ADRIAN, AND S R BLOOM (*Department of Medicine, Hammersmith Hospital, London*) Streptozotocin has been used since 1968 for the treatment of metastatic islet cell carcinoma not amenable to surgery. We report here our experience with 15 patients treated with intravenous streptozotocin (500 mg/m²) on alternate days for five days. Response to treatment was judged by symptomatic improvement, reduction in plasma peptide concentrations and in some cases regression of tumour. Of the seven patients with VIP secreting tumour, four responded with long term disappearance of symptoms, in three of these plasma VIP returned to normal. One of the asymptomatic patients, however, had persistently raised plasma VIP but this was present in an abnormally large molecular form that was presumably biologically inactive. Two patients had partial symptomatic and biochemical responses and one failed to respond. Reduction in tumour size occurred in only two of the seven.

Four patients with the glucagonoma syndrome were treated. One of these remained in total remission six years after treatment, another partially responded (50% fall in plasma glucagon), two others failed to show any response.

Neither of the two patients with PP secreting tumours responded to treatment. Of the two patients with non-functioning tumours, dramatic tumour regression occurred in one, the other did not respond.

The side effects of treatment included nausea and vomiting in all patients for about six to 12 hours after treatment, mild proteinuria noted in 50% of patients, none

with significant impairment in renal function. Severe thrombocytopenia occurred in one patient preventing further treatment. Transient changes in liver transaminase occurred in 25% of patients.

In our experience streptozotocin is a useful drug in the treatment of metastatic islet tumours. VIP secreting tumours appear the most responsive, occasionally other tumour types show dramatic regression.

Autotransplantation of a collagenase dispersed pancreatic graft in the diabetic dog

D ALDERSON AND J R FARNDON (*Department of Surgery, University of Newcastle upon Tyne*) Free and vascularised pancreatic transplants maintain euglycaemia in experimental diabetic animals. Intermediary metabolism, influenced by insulin, has not been studied in these situations.

This aspect of diabetic control was therefore examined in six dogs receiving intrasplenic autotransplants of collagenase dispersed pancreatic fragments. Three control groups were used: (a) twelve normal dogs, (b) six diabetic dogs (total pancreatectomy) treated with twice daily subcutaneous insulin, (c) six diabetic dogs maintained on insulin as group (b) for two weeks and then studied four days after cessation of all therapy.

Fasting blood concentrations of glucose, lactate, pyruvate, alanine, glycerol, 3-Hydroxybutyrate, cholesterol, and free fatty acids were determined and following an intravenous glucose load of 0.5 g/kg body weight. Glucose clearance (K) was determined in each animal.

Untreated pancreatectomised dogs showed all the metabolic abnormalities seen in human insulin dependent diabetes.

Fasting euglycaemia and normal glucose clearance was achieved with exogenous insulin therapy but plasma lipids remained significantly raised with values similar to those found in untreated diabetic dogs.

Fasting euglycaemia was achieved in transplanted animals, but abnormalities in K values and plasma lipids occurred.

If disordered lipid metabolism is linked to the development of the angiopathic complications of diabetes, the dispersed pancreatic graft may not confer therapeutic advantages over conventional insulin therapy.

Calcitonin and parathyroid hormone (PTH) levels in clinical acute pancreatitis

C W IMRIE, G H BEASTALL, A J MCKAY, F C CAMPBELL, D GORDON, AND J O'NEILL (*Department of Surgery and Radioimmunoassay Laboratory, Royal Infirmary, Glasgow*) Although calcitonin has been used as a possible therapy in patients with acute pancreatitis (AP), the normal levels of this substance in AP are not well documented and have not been correlated with PTH. Furthermore, no definitive role in human calcium homeostasis is accepted for calcitonin, whereas high PTH concentrations have previously been correlated with hypocalcaemia.¹

In 21 patients with AP the mean serum calcitonin on admission was 121 ng/l, and the peak level mean 173 ng/l (upper limit of normal 75 ng/l). Calcitonin concentrations were higher in severe than mild AP, and five of six patients with levels >200 ng/l were objectively graded as severe AP(1). In the three hypocalcaemic patients, with corrected serum calcium <2.0 mmol/l, all recorded calcitonin concentrations >100 ng/l and had raised PTH. Nine of the 21 patients had significantly raised PTH (>700 ng/l) and of these only one did not have an associated rise in calcitonin.

The high calcitonin concentrations in patients with AP suggest that supplementary calcitonin intended to inhibit pancreatic secretion is unnecessary. At present it is merely speculative to suggest a role for calcitonin in AP but intriguing to report a tendency to parallel the rises of PTH.

1. Imrie CW, Beastall GH, Allam BF *et al.* Parathyroid hormone and calcium homeostasis in acute pancreatitis. *Br J Surgery* 1978; 65: 717-20.

The DMO pancreatic function test

N LEUNG, A KAMEYA, T BARTON, AND P R SALMON (*University College Hospital, London*) DMO (5,5-dimethyl-2,4-Oxazolidione) is a demethylated metabolite of the anticonvulsant trimeth-

adione. It is a weak acid (pK' 6.13) with a molecular weight of 129.1. It is excreted by the pancreatic gland.

The pancreatic DMO output was studied in seven control subjects and 10 patients with chronic pancreatic diseases, including two patients with carcinoma. All subjects took trimethadione orally at a dosage of 300 mg four times daily for three days. On the fourth day, a Dreiling tube was passed perorally and positioned under fluoroscopic control. The duodenal aspiration was collected before and after pancreozymin and secretin stimulation (2 chu/kg body weight intravenous bolus). Plasma DMO concentrations were measured.

The total DMO output after secretin stimulation, corrected to a standard plasma concentration of 10 mg/100 ml, was 39.3±10.7 mg/hour in the control group and 27.8±5.4 mg/hour in the patient group (p=0.01), the maximum bicarbonate concentration in these two groups being 113±24 mmol/l and 74±26 mmol/l (p<0.01), the volume excreted was 2.9±0.7 ml/kg body weight and 1.6±1.1 ml/kg body weight respectively (p<0.05).

The results suggest that DMO output in the duodenal aspirate reflects the pancreatic secretory function. It may be a useful test for the diagnosis of early pancreatic diseases.

Aqueous solubilisation of fat in pancreatic steatorrhoea

D FINE, P ZENTLER-MUNRO, AND T C NORTHFIELD (*Department of Medicine, St George's Hospital Medical School, London*) Pancreatic lipolysis is said to be a necessary prerequisite for aqueous solubilisation of lipid. This assumption is based on the finding that jejunal chyme from healthy subjects contains fatty acid and monoglyceride, but virtually no triglyceride or diglyceride.¹ No similar studies have been reported in pancreatic steatorrhoea, but it has been assumed these patients are unable to solubilise dietary fat. We have therefore studied eight patients with steatorrhoea due to adult cystic fibrosis (CF), and eight healthy controls. Jejunal samples obtained after a Lundh meal were ultracentrifuged overnight to separate the aqueous phase. Mean fatty acid and non-fatty acid lipid (mm/l) in aqueous phase were 3.4 and 5.8 respectively in CF, compared with 7.2 and 6.5 in controls (NS). In preliminary studies, CF aqueous phase showed no detectable glyceride in samples, pH <5, but up to 2.6

mm/l at pH >5. Monoglyceride, diglyceride, and triglyceride were present in equal quantities. This pattern is consistent with lingual lipolysis; there was no detectable pancreatic lipase. We conclude that in pancreatic steatorrhoea aqueous solubilisation of lipid is not markedly reduced; that diglyceride and triglyceride can enter the aqueous phase; and that pancreatic lipolysis is not a necessary prerequisite for aqueous solubilisation of fat.

1. Hofmann AF, Borgstrom B. *J Clin Invest* 1964; 43: 247-57.

Has computerised tomography (CT) a role in the early management of acute pancreatitis (AP)?

N W S HARRIS, D H OSBORNE, C W IMRIE, J G DUNCAN, D ANDERSON, I STEWART, AND D C CARTER (*University Department of Surgery and Department of Radiology, Royal Infirmary, Glasgow*) In the last decade, Grey scale ultrasonography (GSU) has been shown to be useful in identifying gall stones in patients with AP but of doubtful value in determining changes in pancreatic morphology. Twenty-five patients with AP (15 men, 10 women) had early CT scan and 22 of these also had GSU performed to assess relative values in detecting changes in pancreatic structure.

Technical failure rate on initial scans were zero for CT and 36% for GSU, while a normal pancreas was 'visualised' in 16% and 18% respectively. Generalised swelling of the gland was the most common finding and was present in 80% on CT and 50% of satisfactory GSU scans.

Localised inflammatory masses were detected in five patients in each group but in only one did this proceed to pseudocyst development. The CT scanner was superior to GSU in identifying the pancreas and its frequent swollen appearance in AP but no better at identifying focal lesions and inferior in gall stone detection. Current expenses of CT scanning make this a 'poor buy' for a nationwide role in the management of AP but in specific centres it has a complementary role to first choice GSU.

Early prediction of severity of acute pancreatitis: the role of prognostic factor analysis

S L BLAMEY, D H OSBORNE, J O'NEILL, C W IMRIE, AND D C CARTER (*Division of Surgery and University Department of Surgery, Royal Infirmary, Glasgow*) Established

methods of prognostic factor analysis are useful in predicting the severity of acute pancreatitis. A prognostic factor scoring system has been used prospectively at this hospital for several years. We report the accuracy of individual factors within the scoring system as well as the scoring system itself in predicting severity.

In a five year period 276 patients with clinical acute pancreatitis and a serum amylase >1200 u/l included 140 associated with gall stones, 104 alcohol abuse, and 32 associated with both alcohol and gall stones or neither. Thirty-eight episodes were clinically severe as defined by death (24) or pseudocyst or abscess proceeding to surgical drainage (14). The degree of severe disease was predicted accurately by LDH >600 u/l, serum calcium <2.0 g/l, serum urea >16 mmol/l, serum glucose >10 μ mol/l, PaO₂ <60 mm Hg, WBC >15 \times 10⁹/l, and serum albumin <32 g/l within 48 hours of admission. AST and ALT >100 u/l and age >55 years were not significant predictors of severity.

Using a scoring system of the seven significant factors, the presence of at least three factors positive identified a high risk group (61% severe) and a low risk group with less than three factors present (6% severe). Better separation of high and low risk groups is possible using a function of LDH and serum calcium alone.

Early detection of late complications of acute pancreatitis

M J MCMAHON, A D MAYER, M BOWEN, AND E H COOPER (*University Department of Surgery, The General Infirmary, Leeds, and the Unit for Cancer Research, University of Leeds*) A recent review of patients with pseudocysts and abscesses of the pancreas who were admitted to the General Infirmary, Leeds, revealed that of 24 patients who developed one of these complications after an attack of acute pancreatitis, 11 (46%) were discharged from hospital with the collection unrecognized.

In this study we have evaluated markers of continuing inflammation for their value in the detection of pancreatic collections.

The study was carried out on 53 patients with acute pancreatitis. Sixteen attacks were classified as severe and a collection developed in 11 of them. Plasma levels of C-reactive protein (CRP), α_1 -protease inhibitor, anti-chymotrypsin, ESR and sublingual temperature were measured during the first 13 days in hospital.

Evidence of continuing inflammation in the severe group began to emerge after five days. Continued rise of WBC and, most prominently, CRP provided good discrimination between severe and mild attacks, but did not differentiate patients with collections from those whose attack was classified as severe for other reasons.

On the basis of these results we suggest that CRP may have a clinical role in the detection of pancreatic collections, enabling high risk patients to be recognised and investigated more fully.

Behaviour of serum α_2 -macroglobulin (A2M) and α_1 -antitrypsin (A1AT) in clinical acute pancreatitis (AP)

C W IMRIE, I D WALKER, A J MCKAY, J O'NEILL, F C CAMPBELL, D A GORDON, AND J G DAVIDSON (*Departments of Surgery and Haematology, Royal Infirmary, Glasgow*) In severe AP it has been postulated that very low serum A2M concentrations would relate to clinical outcome. During a study of 50 patients we found a tendency to low A2M concentrations which in 13 patients were <150 mg% (normal 150–350). These depressed concentrations of A2M, surprisingly, did not correlate with severity of AP, and were not significantly affected by very high dosage Trasylol therapy.

Serum A1AT concentrations tended to be raised >400 mg% (normal 200–400). Sixty-four per cent of patients in the study had raised A1AT and only one of these 32 patients did not have A2M concentrations <200, suggesting a possible inverse correlation between these two substances. The mean A1AT concentration in 13 patients with very low A2M was 600 mg%. While 'consumption' of A2M and A1AT is to be anticipated in the binding of trypsin the raised concentrations of A1AT probably represent the balance of its behaviour as an

anti-protease and an acute phase reactant. Only one death occurred (2%) and in this case neither concentrations of A2M nor A1AT were exceptional. In this study A2M concentrations rarely became critically low even in severe AP, thus possibly indicating why anti-protease therapy is not required in man.

Pancreatectomy for chronic pancreatitis

R C N WILLIAMSON AND M J COOPER (*University Department of Surgery, Royal Infirmary, Bristol*) Since 1978 24 patients with chronic pancreatitis have undergone pancreatic resection in this unit. In 18, severe disease has necessitated a major pancreatectomy: eight extended distal (>50%), two proximal, one progressive (distal followed by total), and seven total. The pylorus was preserved in two recent operations. Mean age was 36 years, and all but three were men. The main aetiological factor was chronic alcoholism (12 patients), previous severe acute pancreatitis (four) or unknown (two). Common features included pancreatic calcification (10) and pseudocyst (six). Of 11 patients with partial pancreatectomy, six have had satisfactory pain relief, one has intermittent pain, three needed coeliac plexus block, and one residual pancreatectomy. Operation precipitated steatorrhoea and diabetes in one patient each; another two became diabetic after six to 12 months. Eight patients with end-stage disease had total excision of the pancreas. There was one postoperative death: a 36 year old man with obstruction of the duodenum and portal vein developed a profuse ascitic leak and venous gangrene of a previous Roux loop. Another man with a tiny coincident carcinoma died from metastases at three months. The six survivors have regained weight and are pain free. Six patients with mild disease have had limited distal pancreatectomy. In five with isolated dorsal pancreas, operation allowed dorsal pancreatography and histological assessment. In the absence of dilated ducts, resection of the affected gland can produce satisfactory results in selected patients with chronic pancreatitis.