

Pancreatic Society of Great Britain and Ireland

The 15th annual meeting of the Pancreatic Society of Great Britain and Ireland was held at the Armitage Centre, University of Manchester on 15 and 16 November 1990. The president for the meeting was Dr Joan Braganza. A full day meeting on the pathogenesis of acute pancreatitis was followed by free papers on the second day. The Rodney Smith prize for the best paper went to Mr M Aldridge (London) and the travelling fellowship was awarded to Mr R Kennedy (Bristol). Selected abstracts are published below.

Correlation between zymogen activation and tissue damage in acute pancreatitis

D I HEALTH, C W IMRIE (*Glasgow Royal Infirmary*) It is widely assumed, although unproved, that the pivotal event in the production of an attack of acute pancreatitis is the inappropriate intraglandular activation of zymogens. Our recent finding that urinary concentrations of trypsinogen activation peptide (TAP) differ significantly between mild and severe attacks agree with this hypothesis. In this study we have examined the relation between zymogen activation (through measurement of urinary TAP and phospholipase A₂ (PLAP) concentrations and markers of tissue injury (through measurement of serum interleukin 6 (IL6) and C reactive protein (CRP) concentrations).

Twenty four patients with acute pancreatitis were studied (10 severe and 14 mild). Serum and urinary samples were taken six hourly for 48 hours and 12 hourly for a further three days. Specimens were centrifuged, aliquoted, and stored at 20°C until analysis. Comparison of the areas under the curve has shown a good correlation between IL6 and CRP concentrations ($r=0.86$, Spearman rank correlation). However, the correlations of IL6 with TAP and PLAP were only 0.57 and 0.65 respectively. The results suggest a complex relation between the markers of the inflammatory response (IL6 and CRP) and the markers of zymogen activation.

Prognostic value of serum tumour necrosis factor alpha in severe acute pancreatitis and the effects of plasma infusion

A R EXLEY,* M HOLLIDAY,† T LEESE,‡ J COHEN* (**Infectious Diseases Unit, Hammersmith Hospital, †Department of Chemical Pathology, Leicester Royal Infirmary, ‡Department of Surgery, University of Leicester*) To investigate the association between circulating tumour necrosis factor alpha (TNF α) and morbidity in systemic inflammatory disorders, we have studied 38 consecutive patients from a prospective randomised trial of high dose fresh frozen plasma (FFP) versus colloid plasma protein factor (PPF) in severe acute pancreatitis (AP). Serum TNF α , by specific ELISA, was detectable in 47 of 110 (48%) samples, median 35 pg/ml (range 5–943). Pretreatment TNF α correlated with severity of AP, $r=0.36$ $p=0.027$ (all patients), $r=0.58$ $p=0.005$ AP (gall stones). TNF α in patients with a modified Glasgow prognostic score of IV was 194 pg/ml (16–260) v 44 pg/ml (8–86) for patients with a score of III, $p=0.015$. Pretreatment, 6 of 26 (23%) survivors were TNF α positive, median 19 pg/ml (8–48) v 5 of 11 (45%) of those who died, 86 pg/ml (17–260) $p=0.077$ (two tailed). Following therapy with FFP or PPF serum, TNF α showed no correlation with AP score or mortality but was significantly associated with FFP, $p<0.0001$ (day 3) and $p=0.001$ day 7.

FFP therapy can increase serum protein values and may affect TNF α values indirectly via increased TNF α binding proteins or directly by stimulating TNF α release.

Complicated pancreatitis results in disease specific impairment of clearance of protease-antiprotease complexes

D ALEXANDER, M MADAN, J HODGSON, M J McMAHON (*University Department of Surgery, The General Infirmary, Leeds*) Severe pancreatitis results in impairment of receptor mediated phagocytosis by the reticuloendothelial system (RES), both at the onset of the attack and later, at the time of complications. But is this a consequence of a 'septic' like illness or a disease specific phenomena?

We investigated the phagocytic activity of the RES by measuring the half-life ($t_{1/2}$) of ¹⁴C radioactivity in plasma after an injection of ¹⁴C methyl trypsin (1 mg: 10 μ Ci). Eleven patients with acute pancreatitis (severe or complicated) were compared with seven patients with severe sepsis from other causes and six normal controls. The degree of sepsis was quantified using the APACHE II score. In each group separation using sephadex G 200 showed that at least 95% of radioactivity eluted with α_2 macroglobulin trypsin complexes.

The results show that the median $t_{1/2}$ of ¹⁴C trypsin in plasma of patients with severe acute pancreatitis was 25 minutes and the median APACHE II score was 4. The median APACHE II score of the septic patients was 13 ($p=0.05$ cf acute pancreatitis), but the median $t_{1/2}$ of ¹⁴C trypsin was 15 minutes. The median $t_{1/2}$ of normal controls was 11 minutes and this was not significantly different from the septic patients. These results suggest that impaired phagocytosis in the RES in patients with severe acute pancreatitis is not due solely to the magnitude of the septic illness and may be disease specific.

Oxygen free radicals do not activate zymogens of rat pancreatic juice

D SCHOFIELD,* H HADLEY,† T NEVALAINEN,‡ R M CASE,† J BUTLER,‡ J M BRAGANZA* (**Royal Infirmary, †Medical School, ‡Paterson Laboratories, Manchester*) Oxygen free radicals seem to play a pivotal role in experimental pancreatitis. An excess of these species tends to destroy proteins, eg α_1 , protease inhibitor, but occasionally enzyme activity is enhanced (eg guanylate cyclase). We therefore investigated the effect of superoxide and hydroxyl free radicals on zymogens of rat pancreatic juice. The radicals were generated by a linear accelerator using a caesium source. Activities of trypsin and phospholipase A₂ in juice were measured by sensitive methods. Aliquots of juices from 10 rats were analysed before and

after irradiation, and after incubation with enterokinase or trypsin. In nine juices, <10% of potential trypsin and phospholipase A₂ activity was in the active form: ionising irradiation did not change these values (102%, range 84–109% for trypsin, 110%, range 62–142% for phospholipase A₂). In the sample that happened to contain all its trypsin as active enzyme, irradiation did not reduce activity; and neither did it reduce phospholipase A₂ activity of a solution of purified porcine enzyme. We conclude that if oxidative stress is involved in pancreatitis, it acts in ways that do not directly influence (activate or inactivate) pancreatic zymogens.

No ascorbic acid in acute pancreatitis patients' sera

C BRUCE, P D SCOTT, A RICKERS, D SCHOFIELD, R F McCLOY, J M BRAGANZA (*Royal Infirmary, Manchester*) Ascorbic acid (AA) is a key natural resource in combating oxidative stress. Mounting evidence of free radical involvement in experimental and human pancreatitis led us to measure, using HPLC, the vitamin and its reversible oxidised product (DHAA) in admission serum samples from consecutive patients with acute pancreatitis. In 17 non-smoking controls, values ranged from 5.3 to 16.7 μ g/ml, median 10.0 μ g/ml; with no DHAA. Admission sera from the pancreatitis group gave AA values of <0.5 to 4.3 μ g/ml, median <0.5 μ g/ml ($p<0.001$); with no DHAA. The possibility that the absence of AA in pancreatitis sera may have been due to sequestration of AA into blood cells and tissues seems unlikely because serial samples, taken up to 12 months later in individual cases, showed no change. Provided that the same holds true for total vitamin C, ie including the irreversibly oxidised product (DKA), then our data may indicate that: (a) dietary deficiency of vitamin C facilitates acute pancreatitis in patients with predisposing factors and (b) that parental supplements of AA may help to abort progression of the disease.

Phase one study on the use and tolerance of somatostatin analogue RC-160 in the treatment of patients with advanced exocrine pancreatic cancer

G J POSTON, A V SCHALLY,* A M SCHALLY,* P J GUILLOU (*Academic Surgical Unit, St Mary's Hospital, London, and *Department of Medicine, Tulane University and VA Medical Center, New Orleans, USA*) We have recently shown the efficacy of various analogues of somatostatin in inhibiting the growth of experimental pancreatic cancers both in vitro and in vivo. The purpose of this study was to determine the tolerance of somatostatin analogue RC-160 given in high dose to patients with pancreatic

cancer, and to evaluate any possible evidence of tumour regression. All patients had Karnofsky scores >60% and life expectancy >4 weeks at entry. Twenty patients with biopsy proved disease have been treated. These patients have been followed monthly with repeat haematology, biochemistry, and Karnofsky scores and three monthly CT scans of marker lesions. Twelve patients have died and two patients have been withdrawn due to failure to administer the treatment (500 µg three times daily by self administered subcutaneous injection), and delayed gastric emptying. Median survival is currently 16 weeks and one patient is alive 11 months after starting therapy. Ten patients have improved their Karnofsky scores one month after starting treatment. Side effects have been otherwise minimal and controlled by regular medication. One patient has CT evidence of static disease at both three and six months after starting therapy. In conclusion, long term treatment of patients with pancreatic cancer using RC-160 is safe and well tolerated. RC-160 may offer some therapeutic benefit to a number of patients with pancreatic cancer.

Human reconstituted (SCID-hu) severe combined immunodeficient (SCID) mouse: a model for isogeneic and allogeneic human islet transplantation

N J M LONDON, S M THIRDBOROUGH, S M SWIFT, R F L JAMES, P R F BELL (*Department of Surgery, Leicester Royal Infirmary*) The purpose of this study was to develop an in vivo model system for assessing human islet allograft survival. SCID mice were reconstituted with a human immune system by the intraperitoneal injection of 5×10^7 splenocytes (prepared from organ donor spleens). Ten days after reconstitution the mice had high human immunoglobulin values in their sera and responded to a tetanus toxoid injection with the production of human antitetanus toxoid IgG. Analysis of the reconstituted SCID spleens showed numerous T cell areas (CD3 +ve) and follicles containing B cells (CD19 +ve). The model of isogeneic transplantation was provided by reconstituting with splenocytes from an organ donor and transplanting islets from the same donor to the renal subcapsular space. The model of allogeneic human islet transplantation was provided by splenic reconstitution followed by transplantation with islets from an unrelated donor.

We found that isogeneic transplants were accepted with no evidence of rejection. Allogeneic transplants, however, were rejected and immunohistology showed that the infiltrating cells were of human lymphoid origin. Most of these cells were T cells (CD3 +ve) of which 80% were cytotoxic effector cells (CD8 +ve) and the remainder CD4 +ve helper T cells. In conclusion, the SCID-hu provides an excellent model system in which to study human islet immunogenicity.

Effect of capsule composition on the in vivo response to alginate/poly-l-lysine capsules

H A CLAYTON, N J M LONDON, P S COLLOBY, P R F BELL, R F L JAMES (*Departments of Surgery and Pathology, University of Leicester, Leicester Royal Infirmary*) Encapsulation of transplanted islets in alginate/poly-l-lysine has been proposed as a method to prevent rejection and autoimmune damage. The effect of capsule composition on the foreign body reaction has not previously been studied. Empty capsules

were prepared from high mannuronic acid alginate (M-alginate) and coated with: (1) poly-l-lysine (PLL) alone, (2) PLL+high guluronic acid alginate, and (3) PLL+M-alginate. Capsules were placed in the renal subcapsular space, or intraperitoneally, and retrieved for histology after three weeks. Recipients were WAG, diabetic BB, non-diabetes prone BB, and nude rats. The severity of reaction to the capsules was determined by measurement of the infiltrate thickness or by a scoring system. Renal subcapsular capsules provoked a strain dependent reaction which was most severe in the BB and nude rats, although independent of capsule composition. Intraperitoneal samples also displayed a strain dependent reaction which was more severe than the corresponding renal subcapsular samples. However, capsule composition did affect the severity of reaction in the peritoneal cavity, the weakest reaction being provoked by PLL+M-alginate capsules. The infiltrating cells were predominantly macrophages and fibroblasts. We conclude that capsules coated with M-alginate are the most biocompatible for the future transplantation of encapsulated islets.

Pancreatitis: a late manifestation of inborn errors of metabolism

C J TAYLOR, J R BONHAM (*Departments of Paediatrics and Clinical Chemistry, Children's Hospital, Sheffield*) A child with isovaleric acidemia is described. He presented with pancreatitis complicating severe metabolic acidosis. This is one of eight similar patients recently reported associated with disorders of the catabolic pathways of branched chain amino acids.

AB, a six year old Pakistani child, presented with fever, abdominal pain, and vomiting. He was ill on admission with 15% dehydration, severe acidosis (pH 7.18), and clouding of consciousness. His parents, who were first cousins, had lost five previous children. The most recent, a sister, presented with a similar vomiting illness and died aged 4 years from pancreatitis. There was no significant perinatal history but questioning showed evidence of global development delay and examination revealed microcephaly. Investigations excluded Reye's syndrome, although the EEG suggested an encephalitic process. An exploratory laparotomy was performed following an abdominal ultrasound scan which revealed fluid around the head of the pancreas associated with a dilated duodenal loop. Operative findings included a haemorrhagic and oedematous pancreas. Fluid obtained by peritoneal drainage and biopsy of retroperitoneal tissue showed elevated amylase values (1214 and 1500 IU/l respectively), yet serum estimations had been within the normal range (103 IU/l, normal range 40–150 IU/l). Urine obtained for organic acids showed marked excretion of 3-hydroxy isovalerate and isovaleryl glycine. Enzyme assay on cultured fibroblasts disclosed 10–15% normal activity of incorporation of isovaleric acid into protein. A protein restricted diet was introduced with glycine (5 g/day) supplements. Dietary protein has been increased to 8 g/day and supplemented with 140 g/day of a low branch chain amino acid formula (Maximaid MSUD, Scientific Hospital Supplies). Subsequent progress has been satisfactory with serial urines ketone free and urinary aminograms demonstrating good control with the disappearance of 3-hydroxy isovalerate and greatly reduced values of isovaleryl glycine.

Pancreatitis seems to be a late manifestation

of inborn errors of branch chain amino acid metabolism.

Percutaneous pancreatic biopsy – a sensitive and efficient diagnostic measure

M J KERIN, D WAI, J MACFIE, C J MITCHELL (*Scarborough Hospital, North Yorkshire*) The complications associated with blind pancreatic biopsy are well recognised. The aim of this study was to evaluate the use of an ultrasound guided biopsy technique in the diagnosis of pancreatic disease. All biopsies were performed with an 18 G Tru-cut biopsy needle using an automatic firing device (Biopsy-Radiplast Sweden). We present results from a consecutive series of 67 patients. Pancreatic biopsy was successfully performed in 60 (90%), failed in 2 (3%), and abandoned in 5 (7%) because hepatomegaly obscured the pancreas. The indications for biopsy were mass lesions on clinical investigation (47), clinical suspicion of pancreatic disease with equivocal results (10), and unusual appearance of the pancreas on CT or ultrasound (5). Percutaneous biopsy confirmed the clinical diagnosis of pancreatic carcinoma in 31 patients with mass lesions. In 11 patients percutaneous biopsy altered clinical management by diagnosing unexpected neoplasms (2), unexpected benign lesions (3), chronic pancreatitis (2), and an altered primary tumour (4). There were four minor complications and one false positive result. Ultrasound guided biopsy using the Biopsy gun is a safe and efficient means of establishing the histological diagnosis and significantly influences clinical management of patients with pancreatic disease.

Natural history of acute peripancreatic fluid collections

M C ALDRIDGE, R HITTINGER, P RUTTER, G GLAZER (*St Mary's Hospital Multicentre Acute Pancreatitis Study, St Mary's Hospital, London*) Fluid collections may be detected by ultrasound (US) or computed tomography (CT) during an episode of acute pancreatitis, but their significance is unclear. The relation of early US or CT evidence of a peripancreatic fluid collection to late outcome has been evaluated in 42 patients. In a prospective study of 309 patients with acute pancreatitis, 42 (13%) had a peripancreatic fluid collection on US or CT. They comprised 30 men and 12 women of median age 51 years (range 29–80). In 35% of patients the attack was graded severe (3 or more Ranson criteria).

Collections were classified as either pancreatic or extrapancreatic by imaging. Pancreatic collections (n=23) were either intrapancreatic (12) or peripancreatic (11), typically on the anterolateral surface of the gland. Extrapancreatic collections (n=19) were within the lesser sac (n=7), in the anterior pararenal space (n=9), or beneath the left lobe of the liver (n=3). In 22 patients (52%) (12 pancreatic, 10 extrapancreatic) the collection resolved spontaneously (median hospital stay=12 days). In nine patients (21%) (three pancreatic, six extrapancreatic) the collection was drained radiologically with resolution in one, recurrence in four (one underwent cystgastrostomy; three were discharged for future 'cyst' management), progression to surgical debridement of infected necrosis in two (one died), and death in two patients from necrosis and sepsis. In seven patients (17%) (six pancreatic, one extrapan-

creatic) surgery was employed without prior radiological drainage and comprised pancreatic abscess drainage in one (died), cystjejunostomy in two, cystgastrostomy in one, debridement of infected necrosis in two (both died), and lavage in one. In four patients (10%) neither radiological nor surgical treatment was employed, the collection remained and they were discharged for future 'cyst' management.

While over half of 'acute' fluid collections resolve spontaneously, they carry a one in three chance of a severe attack, a one in six chance of coexisting necrosis or abscess and a one in seven chance of death. Percutaneous drainage probably has little place in the acute phase and may even be disadvantageous if necrosis coexists.

Can the outcome of pancreatic pseudocysts (PC) be predicted?

M G SHEARER, C W IMRIE (*Department of Surgery, Glasgow Royal Infirmary*) Thirty patients with a PC after acute pancreatitis have been studied to develop an assessment system to select those in whom a PC is more likely to resolve.

A PC resolved spontaneously in 15 patients and was drained surgically in 11; two patients died and two survived with a PC still present.

The features of an abdominal mass, abdominal distension, hyperamylasaemia, and leukocytosis occurred more frequently in those undergoing surgery. The mean maximum PC diameter (by ultrasound) was 3 cm greater in those treated surgically compared with those with resolving PCs.

Considering these findings, an assessment system based on five criteria: (1) US diameter of ≥ 6 cm; (2) abdominal mass; (3) abdominal distension; (4) serum amylase ≥ 450 IU/l; (5) leukocytosis $\geq 12 \times 10^9$ cells/l, has been applied to the data, three or more criteria positive implying that the PC will require drainage. The results are summarised in the Table:

Criteria	<3	3+
PC resolved	11	4
PC drained	1	10

With the use of percutaneous drainage of PCs increasing, it will be of value to detect patients whose PC has a high chance of resolving spontaneously. Refinement of the system suggested here could provide the basis of such assessment.

Enteric coated microspheres of pancreatin (creon) in the treatment of pain associated with chronic pancreatitis: a double blind randomised placebo controlled crossover study

M J McMAHON, W F G THOMAS, M C A PUNTIS (*University Department of Surgery, The General Infirmary, Leeds, Royal Hallamshire Hospital, Sheffield, and University Department of Surgery, Cardiff*) Seventy eight patients with confirmed chronic pancreatitis but without steatorrhoea were entered into the study. They received four weeks each of creon and placebo at a dosage of 12 capsules daily. A rescue analgesic (dihydrocodeine) was supplied. Sixty five patients completed the study; there were 40 men (62%; mean age 46.7 years) and 25 women (38%; mean age 52.8 years). Alcohol abuse was considered to be the cause of the pancreatitis in 29 men and seven women. Mean pain severity scores (measured on a scale of 0-5) were

placebo 2.05, creon 1.92 ($p=0.34$). In the patients with alcohol related pancreatitis the scores were placebo 2.03, creon 1.78 ($p=0.12$) with men exhibiting the most noticeable response. Scores of overall wellbeing and patient preference also affected this trend. The alcohol related subgroup demonstrated the strongest preference for creon ($p=0.077$). Mean daily dihydrocodeine use was similar for both groups; placebo 51 mg, creon 45 mg. Bowel habit was similar for both treatments (placebo 1.7, creon 1.5) and body weight was not changed by either treatment. These results suggest that a symptomatic response to pancreatin is most likely in patients with chronic pancreatitis associated with alcohol abuse, and indicate the need for careful stratification by cause in therapeutic trials on chronic pancreatitis.

Spleen preserving distal pancreatectomy for pancreatic disease

M C ALDRIDGE, M J COOPER, R C N WILLIAMSON (*Departments of Surgery, Royal Postgraduate Medical School and Royal Devon and Exeter Hospital*) The intimate relation of the splenic artery and vein to the body of the pancreas makes splenectomy a routine part of distal pancreatectomy. Yet splenic conservation is both desirable for immunological reasons and sometimes feasible. A personal series of 95 distal pancreatectomies undertaken between 1978-90 included 37 women and 58 men with a median age of 43 years (range 17-78). Conventional resection, including splenectomy, was performed in 59 patients for chronic pancreatitis ($n=46$), pancreatic carcinoma ($n=7$), other neoplasms ($n=5$), or pancreatic trauma ($n=1$). Conservative resection with splenic preservation was performed in 36 patients (38%) for chronic pancreatitis ($n=15$), suspected pancreatitis ($n=11$, including eight with pancreas divisum), neoplasia ($n=5$), recurrent acute pancreatitis ($n=2$), pancreatic trauma ($n=2$), or pancreatic duct stricture ($n=1$). Distal resection was a part of total pancreatectomy in 22 patients, including four reoperated for the postoperative complications of proximal pancreatectomy. There were six deaths in this group. Among the 73 patients undergoing distal resection only, there were no postoperative deaths. Complications of conventional resection were reactive haemorrhage ($n=3$), gastrointestinal fistula ($n=2$), and a peripancreatic collection requiring percutaneous drainage ($n=4$). Complications of the conservative approach were adhesion obstruction ($n=2$), peripancreatic collection ($n=1$), and delayed wound infection ($n=1$). One patient had a persistent pancreatic fistula and rupture of a false aneurysm of the splenic artery requiring emergency splenectomy. The splenic vessels were ligated (away from the splenic hilum) in five patients, but subsequent isotope scans and haematological indices did not indicate hyposplenism.

The spleen can safely be preserved in many distal pancreatectomies including those for inflammatory disease.

Outcome of surgical management of patients with benign pancreatic disease

R C G RUSSELL, B A THEIS (*The Middlesex Hospital, London*) The concept of surgical management has been criticised because the disease is self limiting and the outcome poor. To refute these criticisms, 480 patients referred for surgery between 1976 and 1989 have been

followed and their status, as assessed by wellbeing, pain, analgesic requirement, bowel control and activity, expressed as a percentage according to Visick grading.

Seventy three patients had a drainage procedure (cystgastrostomy (CG) 22; pancreaticojejunostomy (PJ) 20; accessory sphincteroplasty (AS) 24; main duct sphincteroplasty (MS) 7) and 250, 15 of whom had failed drainage, had a resection (pancreatoduodenectomy (PD) 104; distal pancreatectomy (DP) 137; and total pancreatectomy (TP) 9). Of these resections, 43 were failures and progressed to a TP, resulting in a total of 282 resections (11 DP operated elsewhere) in 250 patients. A total of 172 patients were managed non-operatively.

In 355 operations there were nine deaths (2.5%) (CG 1, PD 2, DP 3, TP 3). Late deaths occurred in 24 patients (PD 8, DP 10, TP 6), and were alcohol related in 10. Failure of the primary operation with further operative intervention took place in 54 patients (CG 2, PJ 2, AS 8, MS 3, PD 12, DP 31), of whom four had an AS to PD to TP. Failure occurred by a median of 14 months. Twenty patients have been lost to follow up. Visick I and II status by final operation (CG 20, PJ 18, AS 16, MS 4, PD 92, DP 106, TP 52) is shown in the Table.

Years	%						
	CG	PJ	AS	MS	PD	DP	TP
1	83	88	67	75	86	80	52
3	90	85	55	-	73	82	41
5	78	83	57	-	64	82	41
7	100	-	-	-	80	77	-

After surgery failures occur early; outcome remains stable over a period of years; alcoholism takes its toll and accounts for poor results. Improved results will follow better selection of patient and operation. It is concluded that surgery offers a better prospect than continued medical management.

Isogeneic islet transplantation - the effect of gamma irradiation

I M LOFTUS, N J M LONDON, S THIRDBOROUGH, P R F BELL, R F L JAMES (*Department of Surgery, Leicester University, Leicester Royal Infirmary*) Islet pretreatment with gamma irradiation (2.5 Gy) has been shown to prolong allograft survival. The purpose of this investigation was to study the effect of irradiation (40, 20, 10, and 5 Gy) on islet viability. Rat islets were isolated and cultured for 48 hours before irradiation. After 96 hours' further culture, 750 islets, found to be the minimum required to successfully reverse diabetes (blood glucose < 10 mmol/l by day 7), were transplanted to the renal subcapsular space of isogeneic streptozotocin induced diabetic (blood glucose > 20 mmol/l) recipients. Animals whose diabetes was reversed had an IVGTT at day 14 and the area under the IVGTT curve (AUC) computed. In the 40 Gy group a reversal rate of 1/6 was observed. This was significantly lower than that of the control group (8/8; $p<0.002$), and 20, 10, and 5 Gy groups (6/6; $p<0.008$). However, the AUC of the 20 Gy group was significantly higher than that of the control and 10 Gy groups ($p<0.002$ in both). There was no significant difference between the AUC of the control and 10 Gy group. Therefore, the maximum dose of gamma irradiation to which islets can be exposed without affecting viability is 10 Gy. This has important implications for human islet immunomodulation.