SURGICAL RESEARCH

ABSTRACTS FROM THE ANNUAL MEETING OF THE SURGICAL RESEARCH SOCIETY OF AUSTRALASIA, HELD IN WESTMEAD, SYDNEY, NSW, 15–17 SEPTEMBER 1988

Systemic and tissue fibrinolysis in cutaneous ulcers

M. C. STACEY*, K. G. BURNAND, M. MAHMOUD-ALEXANDRONI AND P. J. GAFFNEY

*Department of Surgery, St Thomas' Hospital, London, England, *Present address: University Department of Surgery, Fremantle Hospital, Fremantle, Western Australia*

(Introduced by W. M. Castleden)

Enhancement of impaired systemic fibrinolysis has been advocated for the treatment of lipodermatosclerotic skin[1], and has been employed recently in the treatment of venous ulcers. This study assesses tissue fibrinolysis in cutaneous ulcers, and its relation to systemic fibrinolysis.

Twenty Wistar rats were studied. Systemic fibrinolysis was reduced in 10 by giving intraperitoneal tranexamic acid. Ulcers were made in the skin of the back by excision and by intradermal sodium tetradecyl sulphate (STD), and a skin incision was made on the abdomen. Tissue fibrinolysis was measured in the ulcers at days 1, 3, 5, 7 and 10, and wound tensile strength was measured in the abdominal incision at day 10.

Systemic fribrinolysis was reduced significantly in the tranexamic acid treated group ($P < 0.05$, Wilcoxon's rank sum test). Comparing the two groups there was no significant difference in wound tensile strength ($P > 0.10$), or tissue fibrinolysis in the ulcers or normal skin. Tissue fibrinolysis in ulcers was greater than that in normal skin, from day 1 in STD ulcers ($P < 0.05$), and from day 5 in excised ulcers ($P < 0.05$), until completion of the study at day 10.

Systemic fibrinolysis did not influence tissue fibrinolysis or wound tensile strength. Tissue fibrinolysis was greater in ulcers than in normal skin. Enhancement of systemic fibrinolysis may have little influence on cutaneous ulcer healing.

REFERENCE

1. BURNAND K. G., CLEMESON G., MORLAND M., JARRETT P. E. M. & BROWSE N. L. (1980) *Brit. Med. J.* **280**, 7–11.

Effect of SMS 201–995 on the growth and development of hepatic metastases

J. N. BAXTER, D. NOTT, S. A. JENKINS, S. GRIME, J. YATES AND T. G. COOKE

University Department of Surgery, Royal Liverpool Hospital, Liverpool, England

As reticulo-endothelial system (RES) inhibitors promote tumour growth the present study was carried out to establish whether an RES stimulant, SMS 201–995, had any effect on the growth and development of liver metastases. Hepatic metastases were induced in Fisher rats by intraportal injection of 4×10^7 Walker cells. An experimental group ($n = 20$) received 2 μg SMS subcutaneously, twice daily, commencing on the day of inoculation. Control animals ($n = 20$) were dosed similarly with isotonic saline. All rats were killed 3 weeks later and the extent of liver replacement by tumour assessed. Hepatic and splenic RES activity was determined by the uptake of ^{99}Technetium sulphur colloid and the effects of SMS on Walker cell growth measured both *in vitro* and *in vivo*. SMS significantly inhibited the growth and development of hepatic metastases ($P < 0.05$). Thus, in two animals, there was no tumour and, in a further 12, solitary metastases (1–2 cm diameter) were present. In four rats treated with SMS, 25% of the liver was replaced by tumour. In contrast, in control rats, the degree of liver replacement by tumour varied 60–90%. SMS stimulated the growth of Walker cells *in vitro* but had no effect *in vivo*. RES activity was stimulated by SMS, this effect being particularly marked in the liver ($P < 0.02$). These results indicate that SMS significantly inhibits the growth and development of experimentally derived hepatic metastases, possibly through RES stimulation.

A prospective randomized controlled clinical trial comparing somatostatin and injection sclerotherapy in the control of acute variceal haemorrhage: A preliminary report

J. N. BAXTER, S. A. JENKINS, S. ELLENBOGEN AND R. SHIELDS

University Department of Surgery, Royal Liverpool Hospital, Liverpool, England

Recent studies have suggested that somatostatin (SRIF) may be of value in the control of bleeding oesophageal varices. However, in view of the efficacy of injection sclerotherapy in controlling variceal bleeding, it has been suggested that this treatment should be the gold standard against which new therapies are evaluated. Therefore, the aim of this study was to compare the efficacy of SRIF with emergency injection sclerotherapy in the control of acute variceal haemorrhage.

Forty-three consecutive patients admitted with endoscopically proven, severe bleeding oesophageal varices were randomized to either emergency injection sclerotherapy or SRIF (bolus dose of 250μg followed by a continuous infusion of 250μg/h) for 5 days. The aetiology of the portal hypertension was similar in the two groups, as was the distribution of the patients among the categories of the Child's classification. Twenty-two patients received SRIF and 21 received injection sclerotherapy. The initial variceal haemorrhage was controlled in all 22 patients receiving SRIF but three rebled during the 5 day trial period. Overall, control of bleeding was achieved in 19 of the 21 patients randomized to injection sclerotherapy. There was no significant difference ($P = 0.52$ Fisher's exact test) between the two forms of treatment.

The initial results of this trial suggest that SRIF is as effective as injection sclerotherapy in controlling acute variceal haemorrhage.

Effects of extrinsic denervation on the histochemistry of the gall-bladder

R. PADBURY, J. TOOULI AND J. FURNESS

Departments of Surgery and Anatomy, Flinders University, Adelaide, South Australia

This study was undertaken to determine the short-term effects of extrinsic denervation on chemically defined nerve fibres in the wall of the gall-bladder of the Australian possum. Specimens were taken at 3 weeks from two animals after truncal vagotomy (TV) and two animals after coeliac-superior mesenteric denervation (CSM) and were compared with preparations from non-lesioned animals. Sections from the gall-bladder were studied by immunofluoresence histochemistry after labelling with antisera specific for the peptides vasoactive intestinal peptide (VIP), galanin (GAL) and enkephalin (ENK) and anti-tyrosine hydroxylase (TH) for noradrenergic nerves. A visual assessment of fibre distribution and frequency was tabulated according to whether there was no change, a definite decrease, a definite increase or complete disappearance of fibre types in the subepithelial plexus (SE), muscle (M) or blood vessels (BV) (Table 1).

Table 1. Visual assessment of fibre distribution and frequency

	TV			CSM		
	BV	M	SE	BV	M	SE
VIP	N	N	↓	N	N	↓
GAL	N	N	N	↓	↓	↓
SP	N	↓	↓	N	↓	↓
GRP	N	N	↓	N	N	↓
TH	N	N	N	D	↓D	D
ENK	N	↑↓	↓	N	↓	↓D

N; no change; ↓: definite decrease; ↑: definite increase; D: complete disappearance of fibres.

Most pronounced was the loss of GAL, ENK and TH in all layers after CSM. Effects on other peptidergic nerves were commonly observed in the SE after both TV and CSM.

These results indicate that a significant proportion of chemically defined nerve fibres in the gall-bladder wall have an extrinsic origin.

Histochemistry of gall-bladder innervation

R. PADBURY, J. TOOULI AND J. FURNESS

Departments of Surgery and Anatomy, Flinders University, Adelaide, South Australia

The aim of this study was to determine the distribution and chemistry of neural elements within the gall-bladder wall. Sections and wholemount slides were prepared from gall-bladders of the Australian brush tail possum, *Trichosurus vulpeculus*. The specimens were labelled with antisera specific for the peptides vasoactive intestinal peptide (VIP), substance P (SP), enkephalin (ENK), galanin (GAL), somatostatin (SOM) and gastrin-releasing peptide (GRP) and anti-tyrosine hydroxylase for noradrenergic nerves. Two ganglionated plexuses were found: an outer subserosal plexus containing larger ganglia and an inner plexus containing smaller ganglia, situated deep in the lamina propria (LP) but adjacent to the muscle. There was a dense subepithelial plexus of fine varicose fibres which received projections from the ganglionated plexus in the LP. The outer ganglia communicated with large nerve trunks and both the trunks and ganglia gave rise to finer fibres distributed to the muscular wall. Relative frequencies of fibre types are shown (Table 1).

Two ganglionated plexuses and innervation of both the muscle and mucosa have been described. Their role in gall-bladder motility and mucosal transport remains to be elucidated.

Table 1. Relative frequencies of fibre types

	Most	Intermediate	Least
Subepithelial	VIP GAL	SP ENK GRP	SOM TH
LP	VIP GAL	SP GRP	SOM TB ENK
Muscle	VIP GAL SP	GRP TH	
Outer plexus	VIP GAL TH	GRP SP	
Blood vessels	VIP GAL TH	GRP	SP

In conclusion, SO and DUO contractions are independent, but have similar IDC lengths. The SO contracts throughout the IDC and the onset of the SO AF precedes that of the DUO. After food, SO amplitude and duration and basal pressure decreases, facilitating passive flow of bile through the SO.

Table 1. Contraction of SO throughout the IDC

SO	DUO phases of contraction I, II, IV	III (AF)
f (waves/min)	3 ± 1.3	10.4 ± 1.4*
wave amplitude (A) (mmHg)	79 ± 35	101 ± 35*
basal pressure (mmHg)	8 ± 6	13 ± 6*

*$P < 0.05$.

Human sphincter of Oddi and duodenal manometric activity: Fasting and postprandial

C. S. WORTHLEY, R. A. BAKER, J. IANNOS, G. T. P. SACCONE AND J. TOOULI

Gastrointestinal Surgical Unit, Flinders University, Adelaide, South Australia

The interrelationship between sphincter of Oddi (SO) and duodenal (DUO) motility was studied in 13 patients 2–3 weeks after cholecystectomy and choledochotomy for stones. SO and DUO manometry were performed after a 12 h fast. A triple lumen catheter was positioned via the T-tube, two lumens recording SO and one the adjacent DUO activity.

Fasting activity A complete interdigestive cycle (IDC) was observed in six patients (duration (D) = 100 ± 33 min ($\bar{x}$ ± s.d)). The DUO IDC revealed four phases: I — quiescent; II — irregular wave frequency (f); III — maximal f (the activity front (AF)) and IV — irregular f. The SO contracted throughout the IDC (Table 1).

The SO and DUO AF coincided, but the SO AF onset preceded the DUO. The D of the SO AF was significantly longer than that of the DUO (4.5 ± 2.4 vs 3.9 ± 2.2 min). The DUO AF f (11.9 ± 1.9 waves/min) was significantly greater and A less (30 ± 7 mmHg) than in the SO, where statistical significance was indicated by $P < 0.05$ using Student's *t*-test.

Postprandial activity In eight, a composite liquid meal was ingested 40 min after an AF. In the 20 min post-ingestion period (compared with a 10 min pre-ingestion period), there was a significant reduction in SO A (70 ± 26 vs 40 ± 16 mmHg), wave D (5.8 ± 1.4 vs 4.2 ± 0.9 S) and BP (7 ± 4 vs 5 ± 4 mmHg). SO f was unchanged, but DUO f was significantly increased.

Antibody responses following splenectomy

M. CLAYER, P. A. DREW, A. S-Y. LEONG AND G. G. JAMIESON

Department of Surgery, Royal Adelaide Hospital, Adelaide, South Australia

It has been shown that antibody response to immunization following splenectomy is reduced. Vaccination against pneumococci (and more recently meningococci and haemophilus) has been advocated to protect the splenectomized patient against overwhelming post-splenectomy infection (OPSI). The timing of vaccination to produce the optimal antibody response is unknown. This study investigated the effects of splenectomy and timing of vaccination after splenectomy on the antibody response to a peritoneal antigenic challenge.

Rats were either immunized with sheep red blood cells (SRBC) prior to operation or not immunized. The rats either underwent splenectomy, sham splenectomy, anaesthesia alone or no operation. The day following operation, all rats were injected with 1 ml of SRBC, i.p. In another group, rats were splenectomized and the timing of the SRBC challenge was varied up to 1 year after operation. The antibody response was measured 5 and 14 days after SRBC challenge.

In all groups, the immunized rats produced more antibody than their non-immunized counterparts. The unoperated and anaesthetized rats produced a fourfold higher response than sham or splenectomized rats. The response to SRBC remained depressed in rats up to 1 year after splenectomy.

It is concluded that splenectomy results in long-term depression of antibody formation and, therefore, there appears to be no advantage in delaying vaccination.

Phagocytic function of regenerated splenic tissue

M. CLAYER, P. A. DREW, A. S-Y. LEONG AND G. G. JAMIESON

Department of Surgery, Royal Adelaide Hospital, Adelaide, South Australia

Spleen autotransplantation or ligation of the splenic artery have been suggested as strategies to retain functional splenic tissue in patients who require splenectomy. It is not known, however, if such tissue retains phagocytic capacity. These operative techniques were used in a rat model to study the ability of regenerated splenic tissue to remove colloid or opsonized red blood cells from the blood.

Rats underwent either splenectomy, splenectomy with autotransplantation, hemisplenectomy or splenic artery ligation, or remained as unoperated controls. Technetium–stannous colloid or chromium-labelled, IgG-coated red cells were injected i.v. in rats, 2 weeks to 15 months after operation. The results at 6 months were as follows (results are reported as medians).

Red cell clearance There were 15 rats in each group. Unoperated and hemisplenectomized controls cleared 71% and 70%, respectively. Autotransplants cleared 54%, devascularized spleens cleared 52% and splenectomized rats cleared 41%, and these clearances were significantly less than controls.

Colloidal studies In unoperated controls, splenic uptake of colloid was 4.9%, devascularized spleens removed 0.4% and autotransplants 0.2%.

It is concluded that regenerated splenic tissue has significantly reduced phagocytic activity compared with normal spleens and may not protect against septicaemia.

Interaction between colon cancer cells and fibroblasts in collagen matrices

M. V. AGREZ

Discipline of Surgical Science, University of Newcastle, Newcastle, New South Wales

Interactions between tumour cells, mesenchymal cells and the extracellular matrix (ECM) are thought to be important in regulating tumour cell growth and invasion of tissues. The purpose of the present study was to examine this concept for colon cancer in an *in vitro* collagen matrix culture model. Cell growth, morphology and matrix-binding forces of two well-characterized human colon cell lines designated SW480 (adenocarcinoma) and CCD-18 (normal fibroblasts) were studied in serum-free conditions.

Increased cell spreading and elongation of CCD-18 fibroblasts seeded in collagen gels were observed on exposure to tumour-conditioned medium (TCM) from SW480 cells. This was linked to increased cell–matrix attachment forces reflected in the ability of the fibroblasts to induce a greater degree of collagen lattice contraction. TCM from SW480 cells appeared to contain factor(s) capable either of acting directly as attachment factors between fibroblasts and collagen fibrils or of stimulating synthesis of matrix attachment molecules by the fibroblasts. This stimulated effect was not related to a mitogenic response by the fibroblasts to TCM. DNA synthesis by SW480 cells was significantly enhanced in cocultures with CCD-18 within the matrix in contrast to growth of tumour cells alone or when fibroblasts were seeded as a separate layer not in contact with tumour cells.

The *in vitro* findings suggest that modulation of the ECM by colon cancer cells may play a role in fibroblast spreading and collagen reorganization *in vivo*. This could provide a more favourable environment for colon cancer cell contact with fibroblasts, thereby facilitating transfer of nutrients or growth factors which promote tumour growth.

Nature of neurotensin-like peptides in tumours

A. SHULKES, M. KAPUSCINSKI, D. READ AND K. HARDY

Department of Surgery, University of Melbourne, Austin Hospital, Melbourne, Victoria

Neurotensin (NT) is a 13 amino-acid brain–gut peptide. NT-producing tumours are rare but provide a convenient source for examining the control of synthesis and processing of NT and NT-related peptides. The biosynthesis (mRNA), storage (tissue concentrations) and secretion (plasma levels) in four NT-producing tumours have been compared. NT-like immunoreactivity was characterized in the tumours and plasma by high performance liquid chromatography together with radio-immunoassay (RIA) with both *N*- and *C*-terminal directed antisera (Table 1).

Table 1. NT-like immunoreactivity in tumours and plasma characterized by HPLC and RIA

Tumour	Tissue conc. (pmol/g)		Plasma conc. (pmol/l)	
	N	*C*	*N*	*C*
Pancreatic	1330	330	1050	225
Prostatic	2700	1700	1300	378
Carcinoid	15	3	198	88
Fibrolamellar	30	145	324	1005
Normal ileum	60	59	32	15

Pancreatic, prostatic and carcinoid tumours had an excess of *N*-terminal fragments, mainly NT(1–8) and NT(1–11). The only *C*-terminal immunoreactivity (C-IR) was NT(1–13): no *C*-terminal fragments were detected. The presence of *N*-terminal fragments in the circulation of the patients with pancreatic, prostatic and carcinoid tumours is similar to normal, suggesting a comparable metabolic pathway. However, with the fibrolamellar hepatoma, C-IR predominated in both the tumour and plasma. This previously unidentified peptide is probably a member of the family of NT-related peptides. Northern gel analysis showed that the NT mRNA were similar in the tumours and normal ileum with two major species of NT mRNA, 1.4 and 1 kb in length. The results suggest that the major reason for the heterogeneity of tumour NT is variations in post-translational processing of a common precursor.

Computer image processing as an aid in the interpretation of mammograms

D. INGRAM, P. SMITH AND P. DAVISON

University Department of Surgery, Queen Elizabeth II Medical Centre and Remote Sensing Application Centre, Department of Land Administration, Perth, Western Australia

Evidence that metabolites of anaerobic bacteria may cause ulcerative colitis

W. E. W. ROEDIGER, E. ARNOLD, A. DUNCAN, A. Y. YOUNG AND S. H. NANCE

Department of Surgery, The Queen Elizabeth Hospital, Woodville, and Adelaide University, Adelaide, South Australia

Genesis of active ulcerative colitis correlates with inhibition of fatty acid oxidation (FAO) in colonic epithelial cells:[1] inhibition of FAO with L-bromo-octanoate produces experimental colitis similar to the human disease.[2] Agents, likely to be found in the human colon and likely to inhibit FAO, were assessed for their capacity to alter oxidative metabolism of fatty acid (*n*-butyrate) in isolated colonocytes of rat and man.

Cell suspensions were prepared by disaggregation of colonic mucosa after exposure to chelating agents. Cells were then incubated with [1-^{14}C]-butyrate and with 2-mercapto-acetate, 3-mercapto-propionate, 4-mercapto-butyrate, dichloroacetate, butyrate sulphate, sodium sulphite and sodium nitrite. Maximal inhibition of FAO occurred with 3-mercapto-propionate and sodium sulphite ($P < 0.02$); sodium nitrite enhanced the inhibitory effect of these two agents. Sodium nitrite is a product of inflammatory cells and 3-mercapto-propionate/sulphite is most likely a metabolite of anaerobic sulphate-reducing bacteria of the colon. Further investigations should assess whether these organisms, in conjunction with other factors, may be the cause of ulcerative colitis.

REFERENCES

1. ROEDIGER W. E. W. (1980) *Lancet* **ii**, 712.
2. ROEDIGER W. E. W. & NANCE S. H. (1986) *Brit. J. Exp. Pathol.* **67**, 773.

Benefit of the omental pedicle on compromised intestinal anastomoses

W. ADAMS, G. CTERCTEKO AND M. BILLOUS

Department of Surgery, Westmead Hospital, Westmead, New South Wales

(Introduced by R. Allen)

An experimental model using Wistar rats was designed to investigate the ability of the omental pedicle to limit leakage from compromised intestinal anastomoses and to reduce adhesions.

Under ketamine anaesthesia, a section of small bowel was divided, then re-anastomosed using one of five techniques: a 'control' anastomosis using a continuous Connell suture; a 'deficient' anastomosis using only three interrupted sutures; and an 'ischaemic' anastomosis in a 2 cm segment of devascularized bowel. The 'deficient' and 'ischaemic' techniques were repeated with the addition of a wrap of omental pedicle. Ten rats were randomly assigned to each group. All rats underwent post-mortem examination on the day of death or when sacrificed at 6 weeks.

Nine of the control rats survived with intact anastomoses to 6 weeks. Nine of the 10 'deficient', and all of the 'ischaemic' models died from anastomotic leaks. When protected by omentum, the 'deficient' group had nine intact survivors at 6 weeks and the 'ischaemic' group had six.

All anastomoses, including controls, not protected by omentum developed intraperitoneal adhesions involving 50–100% of the circumference of the anastomosis. Thirteen of 20 anastomoses protected by omentum developed no adhesions.

The study has demonstrated a significant benefit from the use of the omental pedicle in limiting leakage from an anastomosis and adhesions to it. This finding has stimulated a further study into the microvascular and histological changes that occur during the healing of these anastomoses.

Histological events in a healing anastomosis protected by an omental pedicle

W. ADAMS, G. CTERCTEKO AND M. BILLOUS

Department of Surgery, Westmead Hospital, Westmead, New South Wales

(Introduced by R. Allen)

The histological stages of healing were examined in a series of intestinal anastomoses performed on 98 Wistar rats.

Five anastomotic techniques were utilized. There were two compromised anastomoses, performed both with and without a protective wrap of omentum, and a control. On postoperative days 1–7, 10, 14, 21 and 42, a sample of rats from each group were sacrificed. The abdomen was re-explored and the anastomotic segment of bowel was disconnected from the rest of the gut and its mesentery, leaving attached the omentum or adhesions. The aorta was then cannulated and a dye injected before the bowel was removed and examined histologically. This technique demonstrated the vascular contribution from the pedicle (or adhesions) to the bowel wall.

The control group healed by primary intention. The compromised anastomoses healed by secondary intention. On days 1 and 2, the omentum acted as a seal to anastomotic defects. By day 3, the omentum was the major source of granulation tissue. By days 10–14, the omentum had formed a mature fibrous plug over which the new mucosa would later grow. Anastomosis between omental and bowel wall vessels could first be demonstrated by day 3, but occurred too late to limit the extent of the original ischaemic insult. Random adhesions were unreliable as a circumferential seal, but provided a source of neovasculature to survivors by day 3.

It is concluded from this study that the omental pedicle is protective to a compromised anastomosis by providing a biologically viable plug to prevent early leakage and a source of granuation tissue and neovasculature for wound repair.

Lipid peroxidation and cross-linking of collagen in diabetic complications

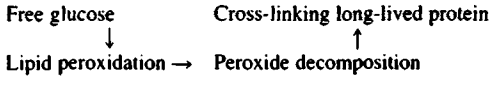
M. HICKS, L. DELBRIDGE AND T. S. REEVE

Sydney University Department of Surgery, Royal North Shore Hospital, St Leonards, New South Wales

During diabetes mellitus, highly cross-linked, fluorescent derivatives of long-lived proteins such as collagen are formed by a process known as non-enzymic glycosylation. Aspects of this mechanism have recently been brought into question. Similar peptide cross-linking is associated with lipid peroxidation and subsequent peroxide decomposition. This study examines the ability of glucose and glycosylated collagen to initiate lipid peroxidation and the potential for peroxide decomposition to induce collagen cross-links.

Rat tail tendons (some after non-enzymatic glycosylation *in vitro*) were used as a source of collagen and polyunsaturated fatty acid vesicles as a source of lipid. Free glucose in concentrations similar to those of uncontrolled diabetics initiated peroxidation in fresh unperoxidized vesicles. Glycosylated collagen also hastened the onset of peroxidative damage.

The extent of cross-linking was assessed physically by thermal rupture time (TRT). After glycosylation, TRT increased from 5.12 to 26.38 min. After these glycosylated tendons were incubated in decomposing lipid peroxide, for 21 h, TRT increased to 3360 min. TRT for control tendons after identical treatment in peroxidized lipid increased from 5.12 to 210 min. Thus, an alternative cross-linking mechanism may be described as follows:



A model of tracheomalacia and its repair using periosteum

R. C. COHEN

Department of Paediatrics, Paediatric Surgical Unit, Westmead Hospital, Westmead, New South Wales

Tracheomalacia which causes collapse of the airway and involves a long segment of trachea and/or bronchi cannot presently be treated satisfactorily.[1] Recent experiments have demonstrated that free tibial periosteal grafts (FPG) can be used to repair tracheal defects successfully.[2]

A model of tracheomalacia was created in the cervical trachea of 13 lambs by performing a submucosal resection of 10 cervical tracheal cartilagenous rings (6–7 cm) over 30% of its circumference. A silastic endotracheal tube was inserted to support the airway for 10 days. In four lambs, after endoscopic removal of the stent, the trachea collapsed and airway obstruction followed. These results indicated that this was a suitable model of tracheomalacia. In a further nine lambs, tracheomalacia was created as described in the untreated controls and repaired immediately by applying a strip of FPG on either side of the cartilagenous defect throughout its entire length.

Results indicate that the FPG ossifies, reduces the degree of airway collapse and prevents signs of airway obstruction over a period of 3 months.

REFERENCES

1. Blair G. K., Cohen R. C. & Filler R. M. (1986) *J. Pediatr. Surg.* **21**, 781–5.
2. Cohen R. C. & Filler R. M. (1986) *J. Thoracic. Cardiovasc. Surg.* **92**, 296–304.

Circulatory decompensation in acute hypovolaemia is due to a CNS endogenous opiate mechanism

J. Ludbrook, R. G. Evans, S. J. Potocnik and A. Van Leeuwen

Baker Medical Research Institute, Prahran, Victoria

Acute blood loss is at first compensated for by reflexly mediated systemic vasoconstriction. However, when approximately 30% of blood volume (BV) is lost, there is abrupt failure of vasoconstriction, and blood pressure (BP) plummets. This sudden decompensation is due to activation of an endogenous opiate mechanism, but it is not known whether it resides in the CNS or peripherally.[1]

In five conscious rabbits, haemorrhage at a rate of about 6% BV/min was simulated by controlled restriction of venous return. This was done after intravenous naloxone (0–8.0 mg/kg), or naloxone injected into the fourth ventricle (0–68 μg kg).

After sham treatment, or subthreshold doses of naloxone, simulated haemorrhage evoked a biphasic response. At first, systemic vascular conductance (SVC) fell steadily, and BP fell only slightly.

When cardiac output (CO) had fallen by about 45%, SVC rose abruptly, and BP plummeted. After a critical dose of naloxone, SVC continued to fall throughout simulated haemorrhage, and BP was maintained well even when CO had fallen by about 65%. The critical dose of intraventricular naloxone was 90–100 times less than when it was given intravenously.

It is concluded that the endogenous opiate mechanism responsible for the failure of reflex vasoconstriction is located in the CNS. The class of opiate receptor that is responsible is currently being determined in order to see if there are therapeutic prospects for a specific opiate antagonist.

REFERENCE

1. Ludbrook J. & Rutter P. C. (1987) *Proc. Aust. Physiol. Pharmacol. Soc.* **18**, 68.

Metabolic manifestations of Crohn's disease

J. M. Church and G. L. Hill

University Department of Surgery, Auckland Hospital, Auckland, New Zealand

Patients hospitalized with Crohn's disease have usually lost weight, are often septic, and frequently require intravenous nutrition (IVN). The aims of this study were to measure prospectively the severity of the metabolic and nutritional abnormalities to be found in such patients, to relate them to clinical presentation and to assess their effect on the efficacy of IVN.

In vivo neutron activation analysis and indirect calorimetry were used to measure body composition and energy expenditure respectively before and after 2 weeks of IVN (Table 1). Results are expressed as mean and s.e.m. Patients were categorized into those with active disease (AD — Crohn's disease activity index (CDAI) > 150), inactive disease (ID — CDAI < 150), or postoperative disease (PO). All groups had lost weight (AD = 16.5 ± 1.4% well weight; ID = 14.0 ± 1.6%; PO = 13.9 ± 2.5%), all had lost more than 30% of their normal body protein, and the active and postoperative groups showed significantly raised levels of energy expenditure (AD = 117 ± 4% of predicted; ID = 105 ± 6%; PO = 128 ± 6%).

Crohn's disease might result in marked protein malnutrition, and, when active, causes a significant metabolic stress. This stress blocks restoration of body protein by IVN, overriding the anabolic effect of extreme protein depletion. Active Crohn's disease needs to settle before nutritional repletion can occur.

Table 1. Change in body compartments with 2 weeks IVN

	ΔWeight (kg)	*P*	ΔProtein (kg)	*P*	ΔWater (kg)	*P*	ΔFat (kg)	*P*
Active (n = 22)	0.6 ± 0.6	NS	−0.4 ± 0.2	0.05	0.2 ± 0.3	NS	0.7 ± 0.3	0.05
Inactive (n = 14)	2.6 ± 0.6	0.01	0.6 ± 0.2	0.01	1.2 ± 0.8	NS	0.8 ± 0.6	NS
Postoperative (n = 15)	− 0.8 ± 0.5	NS	−0.3 ± 0.2	NS	−1.4 ± 0.7	NS	1.0 ± 0.5	NS

NS: not statistically significant.

Metabolism of body water and electrolytes after surgery for ulcerative colitis: Brooke ileostomy versus J pouch

P. M. CHRISTIE, G. S. KNIGHT AND G. L. HILL

University Department of Surgery, Auckland Hospital, Auckland, New Zealand

Some authorities believe that patients with Brooke ileostomies (BI) are chronically water- and salt-depleted[1,2] but there are no data on the metabolism of body water and electrolytes in J pouch patients (JP). To clarify the situation the body composition of 13 patients with well functioning BI (eight females, age = 44 ± 14 years) and 13 patients with well functioning JP (six females, age = 32 ± 10 years, with an output of 4.3 ± 1.4 stools/24 h) was studied. Both groups were compared with two closely matched control groups of 13 subjects each. Bodyweight (BWT), total body fat (TBF), fat-free mass (FFM), total body water (TBW) and extracellular water (ECW) were measured by neutron activation analysis, tritiated water and bromine dilution. Twenty-four hour collections of urine and stool were analysed for sodium and potassium content (Table 1).

The results show that the body content of water and extracellular fluid in BI patients and JP patients is normal. The stool volume and chemistry is similar in both groups resulting in a similar and significant decrease in urine volume, and sodium retention.

REFERENCES

1. CLARKE A. M. *et al.* (1967) *Lancet* **ii**, 740–3.
2. COOPER J. C. *et al.* (1986) *Gut* **27**, 680–5.

Restoration of normal body composition in the months following J pouch for ulcerative colitis

P. M. CHRISTIE AND G. L. HILL

University Department of Surgery, Auckland Hospital, Auckland, New Zealand

It has been suggested that patients having proctocolectomy and ileostomy for ulcerative colitis may never return to normal body composition.[1] Little is known of the body composition changes following J pouch (JP). To clarify the situation, body composition was studied longitudinally in 20 patients (eight females, age = 31 ± 11 years) having J pouches performed for ulcerative colitis with 4.4 ± 1.5 stools/24 h. Bodyweight (BWT), total body protein (TBP), total body fat (TBF), fat-free mass (FFM), and total body water (TBW) were measured by neutron activation analysis and tritiated water dilution (Table 1).

The results confirm that these patients have significant depletion of body protein stores when presenting for JP surgery, consistent with major surgical stress and steroids. Repletion of protein stores, normalization of hydration status and increased fat storage have been demonstrated, but these body compositional changes occur late in the convalescent period after the defunctioning ileostomy is closed.[2]

REFERENCES

1. COOPER J. C. *et al.* (1986) *Gut* **27**, 680–5.
2. MAX E. *et al.* (1987) *Dis. Col. Rect.* **30**, 508–12.

Table 1. Metabolism of body water and electrolytes in Brooke ileostomy and J pouch patients

	Control	BI	Control	JP
TBF* (% BWT)	24.5 ± 1.8	27.4 ± 2.7	20.3 ± 1.4	27.1 ± 2.1
FFM (kg)	51.2 ± 1.8	45.8 ± 2.6	58.2 ± 3.5	50.2 ± 3.4
TBW/FFM	0.733 ± 0.005	0.730 ± 0.006	0.733 ± 0.006	0.730 ± 0.006
ECW/FFM	0.320 ± 0.010	0.310 ± 0.010	0.310 ± 0.010	0.310 ± 0.008
Stool 24 h				
Weight (g)	—	569 ± 4.6		495 ± 6.4
Na (mmol)	—	75 ± 10		58 ± 10
K (mmol)	—	14 ± 5		8 ± 1
Urine 24 h				
Volume (ml)†	1554 ± 153	1221 ± 154		983 ± 112
Na : K‡	2.1 ± 0.03	0.9 ± 0.2		1.3 ± 0.1

*Controls vs JP: $P < 0.05$; †Control vs JP: $P < 0.005$; ‡Control vs BI: $P < 0.005$, Control vs JP : $P < 0.01$; BI vs JP: $P < 0.05$

Table 1. Restoration of normal body composition in the months following J pouch for ulcerative colitis

Parameter	Predicted well value	Day 0	Day 14	Day 90	Day 360
BWT (kg)	71.2 ± 3.1	65.9 ± 2.9	64.0 ± 3.7	64.4 ± 3.5	69.1 ± 3.9*
TBF (kg)	15.5 ± 0.8	16.09 ± 1.4	13.3 ± 2.0	15.0 ± 1.3*	17.5 ± 2.0
TBP (kg)	11.1 ± 0.6	9.1 ± 0.6**	9.1 ± 0.9	8.7 ± 0.8	10.3 ± 0.6***
TBW/FFM	0.728 ± 0.002	0.752 ± 0.006***	0.747 ± 0.110	0.762 ± 0.010	0.735 ± 0.010

Results are shown as mean and s.e.m., using unpaired *t*-test. *$P < 0.05$; **$P < 0.025$; ***$P < 0.005$.

What proportion of body protein can be lost before physiologic impairment occurs in pre-operative patients?

J. A. WINDSOR AND G. L. HILL

University Department of Surgery, Auckland Hospital, Auckland, New Zealand

Protein-depleted patients have been shown to have an increased incidence of postoperative complications, especially when there is an associated impairment of important physiologic functions.[1] It is not known how much protein must be lost before such an impairment occurs. In 101 pre-operative patients (male 51, female 50, median age = 64 years, range: 15–91 years), the following variables have been measured: protein loss (by *in vivo* neutron activation analysis), voluntary hand grip strength (by dynamometry), respiratory muscle strength (as the average of the percentage of predicted maximum inspiratory and expiratory pressures), and plasma albumin, pre-albumin and transferrin concentration. The patients were ranked by protein loss and the mean (and s.e.m.) value for each test of function was calculated and expressed as the percentage of a predicted value for each successive group of 10 patients. One-way analysis of variance revealed a significant relationship between protein loss and all the functions except albumin concentration. In addition, it was possible to demonstrate that a 20% loss of body protein was required before there was a significant reduction in pre-albumin concentration, and a 25% loss for respiratory muscle strength and transferrin concentration. There was no critical protein loss for grip strength which decreased in a linear relationship with protein loss.

These preliminary results show that surgical patients must lose 20–25% of body protein before there is impairment of some important physiologic functions.

REFERENCE

1. WINDSOR J. A. & HILL G. L. (1988) *Ann. Surg.* **207**, 290–6.

Doctor, how long will it take to get over my operation? A study of postoperative fatigue

D. SCHROEDER AND G. L. HILL

University Department of Surgery, Auckland Hospital, Auckland, New Zealand

Surgeons are well aware of postoperative fatigue, yet it is difficult to predict who will suffer, and for how long. Twenty-six patients undergoing surgery for benign and malignant intra-abdominal disease were studied pre-operatively and at days 7, 14, 28 and 90 postoperatively. Fatigue was measured by Christiansen's fatigue score (FS);[1] total body protein by *in vivo* neutron activation analysis; voluntary muscle function by grip strength (GS); involuntary muscle function by ulnar nerve stimulation at 50 Hz (F_{50}).

Prior to operation, patients fell into two distinct groups, depending on whether they were tired (FS ≥ 4; seven females, eight males) or fit (FS = 1–3; five females, six males; Table 1).

Table 1. Pre-operative and postoperative FS for tired and fit patients undergoing surgery for intra-abdominal disease

	Tired	Fit	*P*
Age (years)	54 ± 4	45 ± 6	NS
PI	0.933 ± 1.08	1.005 ± 0.06	NS
GS ($_0$)	28 ± 3	37 ± 4	< 0.05
F_{50} ($_0$)	3.87 ± 0.06	5.36 ± 1.4	NS
FS			
Day 0	4.93 ± 0.33	1.9 ± 0.3	
Day 7	6.9 ± 0.6*	4.3 ± 0.7*	
Day 14	6.6 ± 0.6*	4.2 ± 0.8*	
Day 28	4.73 ± 42	2.9 ± 0.5*	
Day 90	3.7 ± 0.5*	1.9 ± 0.4	

*Significantly different from values at day 0.

Data are expressed as mean and s.e.m. PI: protein index = measured total body protein/predicted total body protein. NS: not statistically significantly different.

The results show that fit patients can expect to be back to a similar status after 1 month. Patients who

are tired, with actual muscle weakness, will be just as tired 1 month after operation, with only one-half attaining fitness after 3 months.

REFERENCE

1. Christiansen J., Benedix T. & Kehlet H. (1982) *Brit. J. Surg.* **69**, 417–9.

Ileus after operation is a preventable complication

D. Schroeder and G. L. Hill

University of Auckland Department of Surgery, Auckland Hospital, Auckland, New Zealand

Patients undergoing gastrointestinal surgery usually have a variable time of postoperative starvation due to ileus, with an 'obligatory' lag phase of negative nitrogen balance. Moss claims that continuous naso-oesophageal aspiration prevents ileus, allowing immediate nasojejunal feeding, with rapid restoration of normal gut activity, decreased postoperative complications, and earlier discharge from hospital.[1]

Twenty patients undergoing excisional gastrointestinal surgery were randomized to receive either the usual postoperative regimen, or oesophagogastric suction through a modified Levin tube and feeding of full strength osmolyte (via a nasojejunal tube placed at surgery) on return to the ward. Suction and feeding were discontinued on day 3 and full diet was allowed. Pre-operatively and at day 14 total body protein was measured by *in vivo* neutron activation analysis and total body water by tritium dilution. The clinical progress was observed and any complications noted (Table 1).

Table 1. Significance of postoperative naso-oesophagogastric suction

Results	Controls	Tube-fed
Sex (M:F)	6:4	5:5
Age (years)	57.7 ± 24	48.2 ± 17
Length of operation (min)†	210 ± 87	208 ± 108
Time to flatus (h)†	58 ± 11.08	82 ± 9.3
Time to bm (h)†	73.2 ± 12.3	112 ± 32.1*
Days to possible discharge‡	8.5 ± 12.3	14 ± 2.8*
Days to actual discharge‡	15.1 ± 1.5	15.3 ± 2.9
Complications		
Minor	0	2
Major	4	1
Loss of protein‡	0.394 ± 0.373	0.708 ± 0.194

*$P < 0.01$. †Data are expressed as mean and s.d. ‡Data are expressed as mean and s.e.m.

Naso-oesophagogastric suction does prevent ileus and allow immediate naso-enteral feeding and earlier return of gastrointestinal activity, but offers no significant advantage in protein preservation, and, in the New Zealand setting, no real decrease in hospital stay.

REFERENCE

1. Moss G. & Nassif A. C. (1986) Preserved postoperative GI function and full enteral nutrition. *Surg. Rounds.*

Total body water and fat-free mass in surgical patients in 10 minutes — useful tool or toy?

D. Schroeder, P. Christie and G. L. Hill

University Department of Surgery, Auckland Hospital, Auckland, New Zealand

Knowledge of a surgical patient's fat-free mass is invaluable as an aid to administration of certain drugs and calories, and as an assessment of adequacy of ongoing nutrition. Bioelectrical impedance analysis (BIA) offers a rapid, painless, non-invasive method of determining total body water (TBW), from which fat-free mass (FFM) can be derived, either by density, or by assuming a constant hydration index of FFM of 0.73.

Nine normal volunteers and 71 surgical patients underwent 107 measurements. TBW and FFM were derived from a supplied computer program utilizing age, sex, weight, height and total body impedance as measured by a BIA device (RJL Systems), following exactly the manufacturer's instruction. TBW was also measured by tritium dilution (TBW(Au)) and FFM by the Auckland method (FFM(Au)) (that is, adding to TBW the measured total body protein (by *in vivo* neutron activation analysis) plus total body minerals and glycogen based on regressions relating to height, biacromial diameter and mediastinal thickness). FFM was also derived from TBW (BIA) assuming a constant hydration of FFM of 0.73 (FFM(H)) (Table 1).

Table 1. FFM and TBW using BIA

	Weight (kg)		Error cf. Auckland method (%)
TBW			
Au	36.2 ± 0.87	0.963	4.6 ± 0.4
BIA	36.44 ± 0.84		
FFM			
Au	48.9 ± 1.1	0.953	7.0 ± 0.5
BIA	46.5 ± 1.0		
H	50.2 ± 1.1	0.966	5.3 ± 0.3

Correlation and error of methods with Auckland method. Au: Auckland; H: using hydration constant at 0.73. Data for weight and error expressed as mean ± s.e.m.

The results show that bioelectrical impedance is a useful clinical tool in the rapid measurement of TBW and FFM in both normal and surgical patients. However, accuracy is not sufficiently good to recommend its use as a precise research tool.

Delay in gastric emptying of solids in patients with gastro-oesophageal reflux disease

G. G. JAMIESON, J. C. MYERS, P. J. COLLINS, T. C. B. DEHN, G. J. MADDERN AND M. HOROWITZ

Departments of Surgery, Medicine and Nuclear Medicine, Royal Adelaide Hospital, Adelaide, South Australia

It has been shown previously that gastric emptying of a digestible solid is delayed in a significant proportion of patients with gastro-oesophageal reflux disease (GORD).[1] A new technique has been developed to quantify emptying from proximal, distal and total stomach[2] and applied in 22 patients with GORD (14 males, eight females, age range: 21–66 years). Based on previously documented normal ranges for gastric emptying from the whole stomach,[1] these patients were divided into two groups: normal emptying (NGORD, $n = 11$) and delayed emptying (DGORD, $n = 11$).

The following parameters were measured. For total stomach emptying: the lag period before food left the stomach (LP), the percentage retention of food in the stomach at 100 min (TR100) and the rate of emptying (LER). For the proximal stomach: the percentage retention of food at 55 min (PR55). For the distal stomach: the time taken to reach 90% of maximum content (DT90), and a parameter LP-DT90. This latter parameter is a measure of retention time in the distal stomach. The results (median and interquartile range) are shown (Table 1). Significance was tested by the Mann-Whitney U Test.

Table 1. Gastric emptying of a digestible solid for NGORD and DGORD patients

Parameter	NGORD	DGORD	*P*
LP (min)	30 (24–39)	63 (54–67)	0.0001
TR100 (%)	37 (36–50)	66 (61–71)	0.0001
LER (%/min)	0.88 (0.74–0.94)	0.80 (0.66–1.1)	NS
PR55 (%)	33 (23–53)	56 (41–73)	0.028
DT90 (min)	33 (26–40)	53 (47–65)	0.0047
LP-DT90 (min)	−7.0 (−11.0–5.0)	5.0 (0.0–7.0)	NS

It is concluded that, in patients with GORD and delayed solid emptying, the delay is due to slow transit of solid from proximal to distal stomach. Once solid reaches the distal stomach, normal emptying appears to occur.

REFERENCES

1. JAMIESON G. G., MYERS J. C., COLLINS P. J. *et al.* (1985) *Brit. J. Surg.* **72**, 344–7.
2. JAMIESON G. G., MYERS J. C., COLLINS P. J. *et al.* (1988) *Brit. J. Radiol.* **61**, 12–8.

Cyclosporine immunosuppression in canine pancreas transplantation

T. WILSON, H. EKBERG, W. HAWTHORNE, P. WILLIAMSON, S. DEANE, G. STEWART, J. GRIERSON AND J. M. LITTLE

Departments of Surgery, Immunology and Histopathology, Westmead Hospital, Westmead, New South Wales

Cyclosporine (CsA) immunosuppression in the transplantation of pancreatic tissue in large animal models has resulted in only marginal prolongation of graft survival. Earlier work has suggested that this is due to poor absorption of CsA in pancreatectomized models. The use of a bladder-drained whole pancreas transplant model (WPT) without host pancreatectomy using oral CsA as the sole immunosuppressive agent is reported.

Animals were divided into two groups: WPT, no immunosuppression ($n = 7$) and WPT, with CsA (25 mg/kg per day) ($n = 21$). Animals lost during the first week due to technical complications were excluded. Post-transplant trough and peak levels of CsA were measured. Graft survival is indicated in Table 1.

Table 1. Comparison of graft survival in animals transplanted with and without immunosuppression

Group	Survival (days)	Median survival
1 (no CsA)	7, 7, 9, 10, 12, 12	9.5
2 (CsA)	7, 8, 9, 10, 11, 15, 15, 20, 23, 32, 33, 33, 46, 46, 89, 109, 159	23

In group 2, loss of graft function, as determined by urinary amylase concentration < 5000 U/l, occurred in eight of 17 dogs. In seven of these, despite adequate serum levels of CsA, this was related to rejection changes in the pancreas on histopathology. Up to 20 days, failure was unlikely to be related to rejection but after 30 days, rejection changes had occurred in more than 40% of failures.

These results show that although CsA can significantly prolong graft survival in WPT dogs, a high proportion of late failures are related to rejection. Further studies are indicated to determine if combination immunosuppression or rescue therapy can diminish late failure due to rejection.

Tumour-induced vessels within experimental colon carcinomas display altered permeability characteristics

C. THIEN AND P. E. O'BRIEN

Monash University Department of Surgery, Alfred Hospital, Prahran, Victoria

Tumour-induced angiogenesis has been the subject of much research interest because of the dependence of tumour cells on the microcirculation for the expression of their malignant phenotype. The present study aims to define the permeability characteristics of the microvessels within 1,2-dimethylhydrazine-induced colonic carcinomas in Sprague-Dawley rats.

Macromolecular substances such as albumin (effective diam. = 5.6 Å) are generally impermeable to the capillaries of normal tissues. In this study FITC-labelled albumin was used as a macromolecular tracer. A computer video image analysis system was used to measure the degree of interstitial fluorescence (which was expressed as optical density per pixel) after i.v. administration of the labelled albumin.

Twenty-eight carcinomas were studied ranging 2–10 mm in diameter with a median size of 5 mm. They varied from nodules to pedunculated polyps and plaques. Histologically they were either early invasive, well-differentiated adenocarcinomas showing localized invasion into and just beyond the muscularis mucosae, or they were frankly invasive with invasion into and beyond the muscularis propria and were well to moderately well differentiated.

The distribution and density of fluorescence are indicated in Table 1. Colon from normal rats showed no evidence of fluorescence within the interstitium. All fluorescence was confined to the intravascular compartment indicating that the normal colonic microvessels are essentially impermeable to albumin. In all tumours there was marked fluorescence throughout the interstitium. The degree of interstitial fluorescence was greater at the peripheral margins of each tumour ($D = 0.25 \pm 0.081$) than at the central zone ($D = 16 \pm 0.049$). The degree of interstitial fluorescence was not different between the early invasive and frankly invasive groups. No evidence was found to suggest that microvascular permeability varied with the size of the tumours.

Table 1. Comparison of intravascular and interstitial volume density between normal rats and those with carcinoma

	Intravascular vol. density (%)	Interstitial vol. density (%)	Interstitial *D*
Normal ($n = 6$)	4.47 ± 2.06	37.4 ± 4.3	0
Carcinoma ($n = 28$)	5.95 ± 6.51	32.3 ± 13.7	0.21 ± 0.07

The enhanced permeability of a macromolecule may be due to immature or abnormal intercellular junctions. Surprisingly, this increased permeability did not cause an increase in the interstitial space of the tumours and this may be explained by either loss of interstitial fluid onto the surface of the tumour or an increased flux of interstitial fluid into the intravascular compartment that is nearly equal to the leakage of fluid from the intravascular compartment.

Microvascular changes following ethanol and aspirin administration in the rat stomach

G. M. FRYDMAN AND P. E. O'BRIEN

Monash University Department of Surgery, Alfred Hospital, Prahran, Victoria

Changes of the gastric microcirculation have been implicated as part of the mechanism of gastric injury following ethanol (EtOH) and acidified acetyl salicylic acid (ASA) ingestion. The microvascular changes following injury of the gastric mucosa were investigated.

Microvascular casts of the rat gastric mucosa were prepared 7 and 15 min following damage by EtOH and ASA and studied by scanning electron microscopy. Seven minutes after 100% EtOH instillation, patchy superficial damage with multiple extravasations was seen. At 15 min, however, there was gross disruption of the normal structure, with loss of patency of large foci of the capillary network, extending frequently to the submucosal vessels but with preservation of the venules. Patches of extravasation were seen at the interface of the damaged areas with areas of normal microvessels. With 50% EtOH, similar types of changes were seen but with greater extravasation and fewer areas of loss of patency of the mucosal microvessels. After 15 min exposure to 25% EtOH, areas showed early signs of disruption of the superficial capillary network. Extravasations were noted in these and normal areas. No areas of deep damage were seen. After both 7 and 15 min of exposure to ASA, a homogenous and confluent picture of loss of patency of the superficial micro-

vessels was observed. No areas of intact surface vascular pattern were present. However, in contrast to EtOH, no extravasation was noted in any of these specimens.

Thus specific patterns of microvascular change are seen for EtOH and for ASA. The extent of the change after EtOH is dependent upon concentration. Extravasation of casting medium occurs as an early event, apparently prior to vessel occlusion, suggesting that a change in the microvascular permeability is an early component in damage following EtOH. Extravasation does not occur after ASA damage.

Microvascular architecture of experimental colonic tumours

S. A. SKINNER AND P. E. O'BRIEN

Monash University Department of Surgery, Alfred Hospital, Prahran, Victoria

Tumour cell proliferation within solid tumours is strongly dependent upon concurrent growth of a supporting vasculature. This study aimed to characterize the microvessels as a central component of the malignant potential of the tumour. Twenty-two colonic tumours were induced in 16 Sprague-Dawley rats by repeated subcutaneous administration of dimethylhydrazine. A cast of the microvessels was prepared by intra-arterial administration of an acrylic resin (Mercox). After corrosion of the tissue, the cast was examined by scanning electron microscopy.

Tumours ranging in size from 2.6 mm to 12.0 mm diameter were examined. In polypoid carcinomas, two distinct vascular zones can be seen in most tumours: a peripheral vascular zone is continuous with the vasculature of the normal mucosa, and a central zone of major vessels is continuous with the normal submucosa/muscularis propria vessels. Within the peripheral vascular zone of the tumour, microvessels are arranged in a similar fashion to that seen in normal colonic mucosa.

In the smallest tumours, the organization of microvessels had the same general pattern as the vasculature of normal colon, but there was elongation of individual vessels, and dilatation of capillaries (5–50 μm) and venules (50–100 μm). In larger tumours, an irregular vasculature with a greater density was seen. Individual microvessels had abnormal morphological characteristics which consisted of large diameter microvessels with frequent, irregular, saccular dilatations. Networks of frequently anastomosing microvessels were formed in some areas. Extravasation of resin occurred from some microvessels into the interstitium of the tumour and onto its surface. Elongated vessels of uniform diameter which travel distances up to 2 mm without branching were seen and were probably arterial vessels.

These appearances indicate that there are two distinct phases of development of the vasculature in these tumours. In the early phase of growth, the tumour is supplied by pre-existing host microvessels which retain a similar organization to normal colon. However, with growth, proliferation of new vessels with abnormal morphologic characteristics are induced by the tumour. The morphological changes seen within tumours would be expected to result in an inefficient vasculature. Elongated and irregular microvessels would result in an increased vascular resistance and poor blood flow. Large diameter vessels are inefficient for nutrient exchange because of their low surface area : volume ratios.

Quantitative histological evaluation of the cytoprotective properties of anti-ulcer therapies

P. O'BRIEN, R. HOLMES, C. MALCONTENTI, D. PHELAN AND G. FRYDMAN

Monash University Department of Surgery, Alfred Hospital, Prahran, Victoria

The capacity for cytoprotection has been claimed for a number of drugs which may have a place in the treatment of peptic ulcer disease. This study used quantitative histological criteria to evaluate the ability of these drugs to be cytoprotective, and compared their effect with that of natural prostaglandin E_2 (PG). The standard rat model, with injury by instillation of 1 ml of absolute ethanol (EtOH), was used. Putative protective agents were administered 15 min after EtOH. Each animal was sacrificed 15 min after EtOH. The stomach was removed and studied using quantitative histological techniques described previously.[1] The technique provides a measure of both the surface area and volume of mucosa damaged.

Table 1 shows the results for agents which are protective. These include PG, enprostil (ENP), bismuth subsitrate (BIS), and sucralfate (SUC).

Table 1. Cytoprotectiveness for agents PG, ENP, BIS and SUC compared with natural PGE_2

	Dose	*n*	Area damaged (%)	Volume damaged (%)
EtOH alone	1 ml	20	76 ± 19	14.0 ± 9
PG	25 μg/ml	6	45 ± 26*	2.2 ± 2*
ENP	1 μg/ml	12	47 ± 33*	3.1 ± 5*
BIS	10 mg/kg	5	93 ± 18	2.7 ± 3*
SUC	25 mg/kg	6	64 ± 38	6.5 ± 6*

*Significant difference from EtOH alone. Data are expressed as mean ± s.d.

Cimetidine, ranitidine, omeprazole and pirenzipine did not exhibit cytoprotection. Indomethacin pretreatment did not alter the protective effect of BIS but abolished the effect of SUC, suggesting that this latter agent acts, at least in part, by stimulating endogenous PG synthesis.

REFERENCE

1. O'Brien P., Schultz C. & Gannon B. (1987) *J. Gastroenterol. Hepatol.* **2**, 113–21.

'Adjuvant' chemotherapy in experimental colonic carcinoma

S. G. Archer and B. N. Gray

University Department of Surgery, Royal Perth Hospital, Perth, Western Australia

Recent clinical trials have shown a significant survival advantage for patients with stage B and C colonic carcinoma receiving portal vein 5-fluorouracil (5-FU) infusion. However, the role of the portal vein in the perfusion of early metastatic liver disease remains controversial. A two part study was conducted in order to quantify the contribution of the portal vein and hepatic artery to the internal vascularity of small liver metastases and to assess the response to adjuvant 5-FU infused via each route. Liver metastases were generated in Wistar-Wag rats by the intraportal injection of cultured colonic carcinoma spheroids.

The first part of the study examined 633 tumours ranging 0.5–6.0 mm in diameter in 18 animals using radio-isotopically labelled microspheres. The ratio of radioactivity in tumour compared with normal tissue was determined after simultaneously injecting microspheres into the portal and arterial circulation of each animal. The average hepatic artery T/N ratio was significantly greater than the portal vein for all tumour sizes studied ($P < 0.005$). Nodules that were 0.5 mm diameter had a mean hepatic artery T/N ratio of 1.52 (s.d. = 1.04) in contrast to mean portal vein ratios of 0.13 (s.d. = 0.34). Thirty-two animals were then infused with 5-FU into the portal vein and hepatic artery for a period of 7 days commencing 0, 2, 4 and 6 days from tumour inoculation. Comparison of liver tumour growth at 1 month with that in 11 controls showed a 91% reduction in liver metastases when portal vein 5-FU was commenced on the same day as tumour inoculation. Infusions commenced at 6 days, when tumours were $< 300\,\mu m$ in diameter, produced no tumour response. In contrast, hepatic artery infusion from day 0 produced a 66% response which improved as the commencement of the infusion was delayed.

It is concluded that the portal vein contributes significantly to the internal circulation of small hepatic metastases and that portal vein chemotherapy is only effective in treating lesions $< 300\,\mu m$ in diameter. This has significant implications for adjuvant chemotherapy in gastrointestinal cancer.

Hormone stimulated pancreatic exocrine secretion: Influence of endogenous prostaglandins

D. G. MacLellan, J. R. Upp and J. C. Thompson

Department of Surgery, University of Melbourne, Austin Hospital, Prahran, Victoria and UTMB, Galveston, Texas, USA

Exogenous prostaglandins are well recognized as inhibitors of pancreatic exocrine secretion, but the influence of endogenous prostaglandins on pancreatic exocrine secretion is unclear. Endogenous prostaglandin generation can be blocked by indomethacin (IDN), a cyclo-oxygenase inhibitor. The aim of this study was to determine whether prostaglandin synthesis blockade by IDN affected secretin (S) and cholecystokinin (CCK) stimulated pancreatic exocrine secretion.

Six dogs prepared with chronic Herrera fistulae were studied following an 18 h fast. On non-consecutive days, dogs were infused with graded doses of S (30, 60 and 120 ng/kg per h) or CCK (40, 80 and 160 ng/kg per h) plus either saline or IND (2 mg/kg bolus, then 0.5 mg/kg per h infusion i.v.). Samples of pancreatic secretion were collected every 15 min for volume, bicarbonate and protein assay, and the results are shown in Table 1.

It can be seen that IND abolished S but not CCK stimulated pancreatic exocrine secretion.

In conclusion, S-stimulated pancreatic exocrine secretion is dependent on intact endogenous prostaglandin synthesis. Since S, but not CCK, acts through cAMP in pancreatic acinar cells, this study suggests that endogenous prostaglandins are an important component in the adenylate cyclase pathway.

Table 1. Integrated outputs, mean and s.e.m.

	Volume (ml [0–30]/min)		Protein (mg [0–30]/min)	
	Control	IND	Control	IND
S (60 ng/kg per h)	24.5 ± 2.6	2.1 ± 1.2*	102 ± 38	91 ± 41
CCK (80 ng/kg per h)	8.3 ± 1.1	8.0 ± 0.9	256 ± 48	284 ± 32

*$P < 0.05$ (Mann-Whitney) compared with control.

Endogenous prostaglandins as mediators of secretin inhibition of gastric acid output

J. A. MARTIN, D. G. MACLELLAN, A. SHULKES AND K. J. HARDY

Department of Surgery, University of Melbourne, Austin Hospital, Melbourne, Victoria

Prostaglandins (PG) are members of the eicosanoid family, derived from arachidonic acid. They are not stored, but must be synthesized as needed from cell membrane phospholipids. The actions of endogenous PG include inhibition of gastric acid secretion. Secretin (S) also inhibits gastric acid secretion. However, the relationship between endogenous PG and secretin in gastric secretion has not been elucidated. The aim of this study was to examine the role of endogenous PG on secretin-mediated inhibition of gastric acid output in the rat.

Groups of six male Sprague-Dawley rats were prepared with tracheostomy, gastric fistula and venous access under general anaesthesia. Gastric acid secretion was stimulated by i.v. infusion of bethanechol (B) (100 μg/kg per h) for 120 min. In a second group of six rats, secretin (1.3 μg/kg per h) was also infused from 30 to 90 min. Gastric acid output (GAO) was measured every 10 min. All of the experiments were repeated after pretreatment with a PG synthesis inhibitor, indomethacin (IND), 10 mg/kg, i.p., 1 h prior to infusion (Table 1).

Secretin inhibition of gastric acid output is abolished by pre-treatment with IND. Thus, in conclusion, secretin inhibition of gastric acid output is prostaglandin-dependent.

Table 1. Influence of IND on GAO

	GAO (mEq/10 min)
Without IND	
B	+ 3.0
B + S	− 0.4*
With IND	
B	+ 2.8
B + S	+ 4.2

*$P < 0.05$ (Mann-Whitney).

Quality of life assessment in advanced cancer: A study of attitudes of doctors and nurses

I. R. GOUGH

University Department of Surgery, Clinical Sciences Building, Royal Brisbane Hospital, Brisbane, Queensland

The assessment of quality of life (QL) has received increasing attention in recent years, but the subject remains complex and controversial.[1] A study was designed to obtain information on the importance of QL assessment during palliative chemotherapy. A questionnaire was completed by 542 health professionals (392 general practitioners (GP), 20 specialist oncologists, and 130 oncological nurses).

In both a simulated patient situation and multiple choice questions, GP and nurses rated QL higher than other standard methods of assessment (for tumour response, toxicity, performance status, analysis by Chi-square tests gave $P < 0.001$). Oncologists ranked QL highest in the multiple choice questions but gave it less importance than tumour response in the simulated patient situtation. QL was considered more important than length of survival by all groups. QL is perceived to be an independent entity and is the most important objective of palliative chemotherapy for advanced cancer.

REFERENCE

1. GOUGH I. R., FURNIVAL C. M., SCHILDER L. *et al.* (1983) *Eur. J. Cancer Clin. Oncol.* **19**, 1161–5.

Surgery in Perth 80 years ago

B. N. CATCHPOLE

University Department of Surgery, Queen Elizabeth II Medical Centre, Nedlands, Western Australia

The casenotes of a consultant general surgeon practising in Perth during 1909–12 have come into the care of the Department of Surgery. Entries were all written with pen and ink and diagnosis was not usually added. However, likely diagnoses can be assumed from many of the case histories. In 1911, the population of Western Australia was 282,000 and of Australia about 4.4 million.

The surgeon saw 45 men and 53 women in 6 months, most of whom were between 30 and 50 years of age. There were 17 gynaecological consultations in this period, and children were occasionally seen. Six patients with tuberculosis and patients with gonorrhoea featured in his case book.

Quoted fees for various operations and prescriptions for patients being treated conservatively were highlights of his record. These will be presented.

Use of chemo/radiotherapy in adenocarcinoma involving the oesophagus: An advance in treatment?

P. G. GILL, G. G. JAMIESON, P. G. DEVITT, R. BRITTEN-JONES AND E. YEOH

Department of Surgery, Royal Adelaide Hospital, Adelaide, South Australia

Survival following potentially curative resection for adenocarcinoma involving the oesophagus is < 5% after 5 years. The palliative treatments available for the condition also are far from ideal. Neither radiotherapy nor chemotherapy as sole adjuvant therapy

has improved results. Indeed, adenocarcinoma has been regarded conventionally as a resistant tumour to both radiotherapy and cytotoxics. The effect of radiotherapy and synchronously administered chemotherapy has been assessed in 24 patients with adenocarcinoma involving the distal oesophagus. The patients have received 30 Gy or 36 Gy preoperatively in 15 or 18 fractions respectively and synchronous 5- fluorouracil by continuous infusion on days 1–5 and 22–26 inclusive of the radiotherapy schedule. Cisplatin (80 mg/m^2) was given on days 1 and 22. Patients were reassessed by endoscopy and biopsy, and by computerized tomography scan 4 weeks after completion of therapy. Tumour resection was undertaken in 12 patients, two awaiting surgery. The responses to chemo/radiotherapy in this group were as follows: seven complete responses; two partial responses; and three without response. The complete regression of disease was confirmed by histological examination of the resected specimens. Two anastomotic leaks occurred but both patients survived. One operative death occurred. Ten patients who were unsuitable for surgery were also treated with chemo/radiotherapy and six obtained complete endoscopic and radiological regression of their primary tumours with relief of dysphagia. It is concluded adenocarcinoma of the oesophagus is responsive to synchronous chemo/radiation therapy.

Human growth hormone reduces protein catabolism in severely ill surgical patients

R. G. Douglas, D. A. Humberstone, and J. H. F. Shaw

University Department of Surgery, Auckland Hospital, Auckland, New Zealand

Severely ill surgical patients remain in net negative nitrogen balance despite the provision of adequate protein and calories.[1] This protein catabolism may be ameliorated by administration of human growth hormone (HGH), which is an anabolic agent.

Isotopic tracer methodology, hormonal assays and indirect calorimetry have been used to investigate protein, fat and glucose metabolism in eight patients receiving total parenteral nutrition (TPN) and eight patients recovering from major trauma. In four of the TPN patients and in all eight trauma patients, a single daily dose of HGH (20 iu, s.c.) was administered. The patients were studied both before and after 3 days of therapy with HGH. Four of the TPN patients were studied twice but no HGH was given.

In the TPN patients, there was a 40% reduction in net protein catabolism with no such change in the control group. In the trauma patients, there was a 26% increase in fat oxidation whereas glucose oxidation was unaffected.

It is concluded that HGH conserves lean body mass in severely ill surgical patients by reducing protein oxidation while encouraging fat oxidation. On this basis HGH treatment may prove to be a useful therapeutic intervention in such patients.

REFERENCE

1. Shaw J. H. F. & Wolfe R. R. (1987) *Aust. N.Z. J. Surg.* 57, 41.

Deranged tissue metabolism as the basis for cancer cachexia

D A. Humberstone, R. G. Douglas and J. H. F. Shaw

University Department of Surgery, Auckland Hospital, Auckland, New Zealand

It was hypothesised that cancer patients lose weight due to parasitization of essential nutrients by the cancer with subsequent changes in healthy tissue. The aim of the present study was to identify and quantify abnormalities of protein metabolism in patients undergoing surgical resections, both in the cancer and in normal tissue.

Intra-operative isotopic infusions of [^{14}C]-leucine were performed with measurements of protein dynamics in the cancer, normal tissue and the whole body in 40 patients; nine normals (NORM), 16 with non weight-losing cancer (NWLC), and 15 with cancer cachexia (CC). Fractional synthesis rates of protein (FSR) at different tissue sites were quantified and whole body protein synthesis (WBPS), whole body protein catabolism (WBPC) and net protein catabolism (NPC) at the whole body level were measured. Results are shown in Table 1.

Table 1. Protein synthesis rates at different tissue sites

	WBPC (g/kg per day)	FSRM (%/day)	FSRL (%/day)	FSRCa (%/day)	FSRH (%/day)
NORM	3.1	5.1			
NWLC	2.9	3.7	13.8	19.2	7.5
CC	4.9*	5.6	34*	20.4	7.8

*Significantly different from NORM and NWLC. FSRM: synthesis in muscle; FSRL: synthesis in liver; FSRCa: synthesis in cancer; FSRH: synthesis in host tissue.

There were marked increases in WBPC in cachectic patients coupled with increases in hepatic protein synthesis.

In conclusion, cancer cachexia is associated with increases in whole body protein catabolism with associated compensatory increases in visceral protein synthesis. The use of anabolic agents is suggested in the treatment of this lethal condition.

Demonstration of cytogenetic changes in breast cancer

P. J. HAINSWORTH, K. L. RAPHAEL, O. M. GARSON AND R. C. BENNETT

University Departments of Surgery and Medicine, St Vincent's Hospital, Melbourne, Victoria

The demonstration and analysis of the karyotype is of proven value in the haematogenous malignancies. According to the somatic mutation theory of cancer, genetic changes are also central to the neoplastic transformation of solid tissues. It is probable that the study of genetic rearrangements in solid tumours such as breast cancer will assume biological and clinical importance.

The aim of this project was to demonstrate the feasibility of obtaining karyotypes in breast cancer and to study their characteristics. Eighty-eight specimens of fresh breast carcinoma from 87 patients were studied. Cytogenetic analyses were performed using direct, short-term culture and synchronized culture techniques. Greatest success was achieved using a direct technique, which closely represents the *in vivo* situation.

Analysable karyotypes were obtained in 24 (27%) of the 88 specimens. This is a much higher success rate than is generally reported. Forty-four of the 88 specimens were obtained from 44 patients treated at St Vincent's Hospital who had not received prior radiotherapy or chemotherapy: 16 (36%) provided analysable karyotypes. Analyses were successful in six (21%) of the 28 tumours from other hospitals. Many and varied structural chromosomal abnormalities were identified and the following chromosomes implicated in descending order of frequency: # 1, 11, 17, 3, 16 and 7.

It is concluded that the karyotyping of breast cancer is feasible and is best demonstrated in fresh tumours using the direct technique and, also, that the importance of the chromosomal abnormalities seen is currently being assessed, but is limited by numbers.

Localization of the gastric trigger zone that induces transient lower oesophageal sphincter relaxations in the dog

S. J. FRANZI, C. J. MARTIN, J. DENT AND M. R. COX

Department of Surgery, St Vincent's Hospital, Melbourne, Victoria

The aim of this study was to localize the region of the stomach responsible for triggering distension induced transient lower oesophageal sphincter relaxations (TLOSR). In two groups, each of four dogs, the stomach was partitioned into two innervated regions by a linear, loosely sutured felt buttress. This separated either the fundus from the lesser curve, or the antrum from the proximal stomach. A further four dogs with intact stomachs served as controls. Each region was distended at a constant rate with a thin-walled, plastic bag, while monitoring oesophageal body and lower oesophageal sphincter (LOS) motor events with a sleeve catheter. At the time of the first TLOSR, gastric wall tension was estimated from the bag pressure and volume, and the recordings were analysed for changes in background LOS pressure.

Distension of the intact stomach, lesser curve, or proximal region alone, produced a progressive increase in LOS pressure, and triggered TLOSR at low tension thresholds (31, 35, and 40 mmHg/cm, respectively). Distension of the antrum produced a progressive fall in background LOS pressure, while distension of the fundus alone had little effect. Both the fundus and the antrum had significantly higher thresholds for triggering TLOSR than the other three regions (105 and 96 mmHg/cm, $P < 0.01$).

It is concluded that the subcardiac region of the stomach is primarily responsible for triggering TLOSR induced by distension, and that there are regional differences in the gastrosphincteric reflexes controlling basal LOS pressure. These findings are relevant to the understanding of the genesis and therapy of gastro-oesophageal reflux.

Response of oesophageal propulsive force to bethanechol

C. RUSSELL, G. BUTHPITIYA, G. WHELAN AND N. BRIGHT

Departments of Surgery and Medicine, Prince Henry's Hospital and St Vincent's Hospital, Melbourne, Victoria

Normal oesophageal function as measured by standard manometry can be altered by a variety of pharmacological agents. Bethanechol has been shown to slow oesophageal peristalsis and transit velocity while increasing peristaltic amplitude. The aim of this study was to assess the effect of bethanechol on oesophageal peristaltic force.

Ten normal volunteers swallowed a capsule incorporating a linear strain gauge transducer and a side-hole for standard manometry with a low compliance perfusion system. The gauge was calibrated at 37°C to measure force in g. Measurements were made in the supine position before and after 0.07 mg/kg s.c. bethanechol at 5, 10 and 15 cm above the lower oesophageal sphincter in response to dry and wet (5 and 10 ml) swallows.

Analysis of variance, sign rank and linear regression (with t-test for significance) were used to analyse data.

Manometric pressure for dry swallows was increased after bethanechol ($P < 0.01$) but not for wet swallows. There was no change in propulsive force.

In conclusion, oesophageal propulsive force was not altered by the administration of bethanechol, despite a rise in manometric pressure.

Aetiology of post-parotidectomy gustatory sweating

G. M. Otto, W. D. Proudman and W. E. Roediger

Department of Surgery, Queen Elizabeth Hospital, Adelaide, South Australia

Gustatory sweating (GS) is a common complication of parotid surgery due either to direct skin re-innervation from the parotid surface, or to auriculotemporal nerve injury and aberrant regeneration. The purpose of this study was to test these hypotheses of development of GS in the rat.

In 30 rats, the fluorescent dye Fast Blue (FB) was injected into both parotids. Half of the rats were subjected to superficial parotidectomy (SP) and the remainder to auriculotemporal nerve crush (ATNC). Sham operation was performed on the contralateral side. Prior to sacrifice intracutaneous Diamidino Yellow (DY) was administered. The otic and superior cervical ganglia were removed and examined. The rates of single dye neuronal labelling (FB or DY) and double neuronal labelling (FB + DY) were estimated.

At 10 days survival, there were no differences in otic ganglion labelling rates between the SP group and the ATNC group. No double-labelled cells were observed. Otic ganglia were labelled with DY (5.5%) and FB + DY (1.9%) 56 and 84 days after ATNC, but not after SP ($P < 0.001$).

In conclusion, in the rat there was re-innervation of the skin by otic ganglion neurones after ANTC but not after SP.

Calcitonin gene-related peptide: Potent vasodilator in hepatic and renal vasculature

K. G. Braslis, D. R. Fletcher, A. Shulkes and K. J. Hardy

Department of Surgery, University of Melbourne, Austin Hospital, Melbourne, Victoria

Calcitonin gene-related peptide (CGRP) is a product of alternate splicing of the calcitonin gene. It is found in nerves in the vasculature and is known from *in vitro* studies to be a potent vasodilator. It is found abnormally in the circulation of patients with medullary thyroid carcinoma and has been proposed to be a cause of symptoms. This study was designed to determine the dose-response effects of CGRP infusion in the intact sheep on blood flow to liver and kidney, organs that are known to be innervated richly by CGRP containing nerves. Blood flow was measured by an indicator dilution technique using [^{131} I]-labelled iodohippurate. CGRP infusion at both 1 and 5 pmol/kg per min produced significant ($P < 0.05$) increases in both renal and hepatic blood flow (Table 1). This increase in flow occurred despite a significant fall in perfusion pressure ($P < 0.05$) at the higher infusion rate. At the highest infusion rate of 10 pmol/kg per min, when fall in perfusion pressure was even more marked, renal and hepatic blood flow was maintained.

It is concluded that the renal and hepatic vasculature are particularly responsive to the vasodilatory effects of CGRP and it is proposed that CGRP containing nerves in those vessels have a major role in maintaining blood flow to those organs.

Table 1. Dose–response effects of CGRP infusion on hepatic and renal blood flow measured by heart rate and arterial pressure

CGRP (pmol/kg per min)	Blood flow (ml/min)				Heart rate (beats/min)		Mean arterial pressure (mmHg)	
	Hepatic		Renal					
	Before	During	Before	During	Before	During	Before	During
1	1705 ± 53	2167 ± 279	804 ± 36	885 ± 35	77 ± 9	77 ± 9	70 ± 6	71 ± 5
5	1407 ± 152	2091 ± 261	797 ± 60	876 ± 72	78 ± 5	114 ± 7	75 ± 5	66 ± 6
10	1694 ± 195	2006 ± 223	816 ± 51	867 ± 53	71 ± 3	127 ± 12	71 ± 5	61 ± 4

Duodenal intramural nerves are major controllers of pyloric motility and gastric emptying

P. J. TREACY, G. G. JAMIESON AND J. DENT

Department of Surgery and Gastroenterology Unit, Royal Adelaide Hospital, Adelaide, South Australia

Localized or isolated pyloric pressure waves (IPPW) have been shown to be associated with a retardation of gastric emptying. The role of ascending duodenal intramural nerves has been investigated in the stimulation of IPPW and the slowing of gastric emptying.

In five pigs, duodenal intramural nerves were interrupted by duodenal transection. Another six pigs without transection acted as controls. After 4 weeks' recovery from surgery, a manometric assembly was positioned with a sleeve sensor astride the pylorus and nine side-holes spaced across the antropyloroduodenal segment. Gastric emptying of an ingested 1000 ml of radiolabelled 5% dextrose was measured by drainage of the proximal duodenum via a cannula. Test isosmolar 3.1% dextrose/saline and control normal saline solutions were infused intraduodenally at 20 ml per min.

The stimulation of IPPW, inhibition of antropyloric pressure waves (APW), and retardation of gastric emptying seen in control pigs during intraduodenal dextrose infusion, were reduced in pigs with duodenal transection (Table 1).

These studies show that the stimulation of IPPW and inhibition of APW by intraduodenal dextrose depends in part upon feedback via ascending intramural nerves. Reduction of these motor effects is associated with impaired retardation of gastric emptying.

Effect of pylorus excision on gastric emptying of a digestible solid in the pig

P. J. TREACY, G. G. JAMIESON AND J. DENT

Department of Surgery and Gastroenterology Unit, Royal Adelaide Hospital, Adelaide, South Australia

The trituration and emptying of digestible solids from the stomach have been ascribed to peristaltic contractions of the pylorus and antrum. These two functions were investigated in six conscious pigs with pylorus excision and in six pigs with pylorus intact.

The rate of gastric emptying of a 400 g meal of 1 cm^3 radiolabelled liver was determined over 2 h by drainage of the proximal duodenum via a cannula. The particle sizes of the liver emptied were determined by sieving. For logistic reasons, it was not possible to perform sieving and manometry simultaneously, so a second set of studies was performed, to record antropyloric motility with emptying: a manometric assembly was positioned with a sleeve sensor astride the gastroduodenal junction and six side-holes in the antrum and duodenum. Manometric recordings were continued for 2 h following ingestion of 400 g of radiolabelled hamburger.

The hamburger emptied at a constant rate of 55 g/10 min interval, during which time antropyloric pressure waves occurred at a rate of 1.69/min. Following pylorus excision, the hamburger emptied at a constant rate of 97 g/10 min interval ($P < 0.05$), during which time antropyloric pressure waves occurred at a rate of 1.80/min (not significantly different). The liver also emptied at a faster rate following pylorus excision, but the proportion of particle sizes did not change substantially (Table 1).

It is concluded that following pylorus excision, adequate trituration is maintained, but emptying of the triturated meal is more rapid. These findings suggest differential functions of the antrum for trituration and of the pylorus for control of transpyloric emptying of the triturated meal.

Table 1. Trituration following pylorus excision

Particle size	Control pigs	Pylorus excision
Total liver	100 g	153 g*
< 0.15 mm	42 g (42%)	74 g (48%)
> 1.0 mm	30 g (30%)	49 g (32%)

*$P < 0.05$.

Table 1. Intraduodenal infusion measured by stimulation of IPPW, APW and gastric emptying

Infusate (surgery)	IPPW (/min)	APW (/min)	Gastric emptying (ml/30 min)
Saline (duod. intact)	0.39	0.71	739
Dextrose (duod. intact)	2.61*	0.00*	107*
Dextrose (duod. transect)	1.03†	0.77†	266†

*$P < 0.05$, versus saline; †$P < 0.05$ versus duod. transect.

Ceftriaxone versus other regimens in preventing postoperative infection: A controlled trial

W. T. MORRIS

University Department of Surgery, Auckland Hospital, Auckland, New Zealand

Postoperative infection of wound, chest and urinary tract is expensive in terms of morbidity and money. More than 40% of patients in the Auckland Surgical Unit suffer postoperative chest infections following major alimentary tract abdominal operations and 16% wound infections despite rational antibiotic prophylactic regimens. The antibiotics used in these regimens have short-lived effective serum levels. It was decided to try ceftriaxone whose effective serum level after one dose lasts for at least 24 h against the standard regimens in the prevention of infections of chest, wound and urine in patients undergoing operation on the abdominal alimentary tract. The standard regimens for gastroduodenal and biliary surgery are 1 g cefoxitin at induction of anaesthesia repeated after 8 and 16 h. The regimen for large and small bowel is 2 mg/kg gentamicin and 500 mg metronidazole, i.v. The ceftriaxone regimen was 1 g at induction. For inflammatory bowel disease prophylaxis was continued for 5 days. The research nurse saw the patients each day and documented clinical wound infection, clinical and radiological chest complications and bacteriologically shown urinary infection. Patients were all seen 2–3 weeks after discharge for observation of late complications (Table 1).

Of 182 patients who were randomized, 37 were excluded for various reasons. Chest complications were significantly fewer in the ceftriaxone group ($\chi^2 = 5.6$; $P < 0.25$). There were significantly fewer infective combinations in those having ceftriaxone ($\chi^2 = 10.34$; $P < 0.01$).

Experimental renal transplantation using total lymphoid irradiation and antithymocyte globulin

P. WILLIAMSON, H. EKBERG, R. ALLEN, G. J. STEWART, K. W. TIVER, S. A. DEANE, J. CARTER, W. HAWTHORNE AND J. M. LITTLE

Departments of Surgery, Immunology, Radiation Oncology, and Histopathology, Westmead Hospital, Westmead, New South Wales

Total lymphoid irradiation (TLI) has attracted attention as a general immunosuppressant and for its potential to produce transplantation tolerance in experimental animals. This study compared the effects of a standard TLI protocol with a low-dose regimen, with and without additional antithymocyte globulin (ATG). Renal transplants were performed in MLR mismatched, outbred mongrel dogs following 18 Gy or 8 Gy of TLI alone or in combination with ATG. Animals were divided into 6 groups: (i) no immunosuppression ($n = 5$); (ii) ATG alone ($n = 5$); (iii) 8 Gy TLI ($n = 5$); (iv) 8 Gy TLI and ATG ($n = 4$); (v) 18 Gy TLI ($n = 4$) and (vi) 18 Gy TLI and ATG ($n = 4$). Irradiation was delivered in 1 Gy fractions over a 4–5 week period while ATG (10 mg/kg per day) was administered intravenously on days 0,2,4,6,8 and 10 post-transplant.

Both regimens of TLI produced a marked lymphopenia but graft survival time was not significantly prolonged in any of the treatment groups. Median graft survival times were as follows: (i) 7 days; (ii) 6 days; (iii) 9 days; (iv) 9 days; (v) 9.5 days; and (vi) 10 days.

In conclusion, these results conflict with some other large animal studies and highlight the variability associated with this treatment.

Measurement of muscle tension and blood flow in the fore-arms of pianists: Piano Performance Analysis Unit

M. G. HAYES, G. G. JAMIESON, J. VEALE AND J. W. WHITE

Department of Surgery, Royal Adelaide Hospital, Adelaide, South Australia

Donor strain blood transfusion accelerates the rate of rejection of rodent fetal pancreas allografts

A. D. HIBBERD AND K. M. BOWEN

Discipline of Surgical Science, Faculty of Medicine, Universtity of Newcastle, New South Wales

Although pre-graft blood transfusion (PBT) prolongs survival of primarily vascularized allografts,

Table 1. Postoperative infection measured against antibiotic treatment

Regimen	No. patients	No. chest complications (%)	No. wound infections (%)	No. urinary infections	No. intra-abdominal sepsis	Mean postoperative hospitalization (days)
Ceftriaxone	65	13 (20)	4 (6)	1	0	9.8
Other treatment	80	34 (42)	10 (12.5)	5	3	11.2

its effect upon secondarily vascularized fetal pancreas allograft rejection is unknown.

PVG ($RT1^c$) fetal pancreas allografts were cultured in 95% O_2 and 5% CO_2 for 14 days before transplantation beneath the renal capsule of Wistar Furth ($RT1^u$) recipients pre-treated with PVG blood (containing 8×10^9 red blood cells, i.v., weekly for 4 weeks) or heated blood (56 °C for 1 h) with and without cyclosporin A (CsA) (30 mg/kg, s.c., for 4 days after the transfusion). Graft rejection and viability were scored histologically on a scale of 0–7 on grafts retrieved 7 days after transplantation. Statistical comparisons were done by Wilcoxon rank sum test.

Donor strain blood accelerates the rate of rejection of the allografts (blood: median = 6.0, range: 6.0–6.3; untreated control: median = 5.0, range: 5.0–5.0, $P < 0.05$). The accelerated rate of rejection was reduced in order to control levels by heated blood (heated blood: median = 5.1, range: 1.0–5.8; $P < 0.01$ for heated blood vs blood, $P > 0.05$ for heated blood vs untreated control) but not by additional CsA (blood and CsA: median = 6.0, range: 5.6–6.0, $P < 0.05$ for blood and CsA vs untreated control). The induction of the allograft-prolonging effect of PBT may require a primarily vascularized allograft.

Studies on growth control of rat colonic mucosa

P. GREGORY, R. WHITEHEAD AND G. J. A. CLUNIE

Department of Surgery and Ludwig Institute for Cancer Research, Royal Melbourne Hospital, Parkville, Victoria

A rat model of colonic dysfunction-induced mucosal hypoplasia was used in order to elucidate factors involved in mucosal cell proliferation.

Wistar rats were given a Hartmann's procedure and the defunctioned mucosa allowed to become hypoplastic over the next 2 weeks. Attempts at reversing this hypoplasia using putative trophic compounds (via intraperitoneal infusion) and by the animals' own urine (by constructing a rectovesical fistula) were then performed. After 2 weeks of exposure, animals were killed and crypt cell production rates (CCPR) crypt length (CL), crypt surface area (CSA), and cellular morphology were assessed using computer graphic-assisted light microscopic analysis.

Bombesin, peptide YY, somatostatin, epidermal growth factor and 5-hydroxytryptane showed no effect on CCPR, CL, CSA or morphology. Pentagastrin (PG) and rat urine showed a marked response in reversing the hypoplastic mucosa CL and CSA. PG increased CCPR to normal, but urine showed no increase at 2 weeks. When urine was exposed immediately after defunction, mucosal hyperplasia occurred. PG and urine produced a change in the morphology of these crypts, producing a decrease in the goblet cell numbers as well.

It is concluded that urine and PG are able to expand certain cell compartments within the colonic crypts independent of mucosal workload and luminal nutrition. Further studies are underway to clarify the cell compartments expanded and the active components of urine.

Biochemical changes during and immediately following liver transplantation

R. BELL, G. KYD, K. WOODMAN AND A. G. R. SHEIL

University of Sydney, Department of Surgery, Sydney, New South Wales

A reliable indicator of liver graft viability and immediate function is yet to be determined. Standard liver function tests do not provide rapid allograft assessment. Readily obtainable indices such as changes in the recipient total body oxygen consumption and CO_2 production, and amino-acid clearance lack sensitivity and can only distinguish severe allograft dysfunction from normal function. A retrospective analysis of the biochemical parameters which occurred during 28 orthotopic liver transplantations at predetermined intra-operative and postoperative times were performed. Serum potassium fell uniformly, following revascularization as potassium was taken up by the viable hepatocytes. The serum levels of the hepatic transaminases, aspartate aminotransferase (AST) and alanine aminotransferase (ALT) rose immediately following revascularization of the graft, reaching a peak within hours and thereafter returning slowly to baseline values. While the rise in AST was more dramatic, the elevation in ALT was more prolonged as might be expected because of its longer half-life. Serum lactate rose steadily during both hepatectomy and the anhepatic period, but after revascularization the lactate level stabilized and then fell. Apart from one occasion when there was severe intra-operative shock, immediate liver graft function was moderately good, so that the significance or otherwise of the biochemical parameters as predictors of early graft function remains to be defined.

Lipid-A antibodies in donated blood

A. DILLEY, J. AKHTER AND D. R. HUNT

University Department of Surgery, St George Hospital, Kogarah, New South Wales

Lipid-A, the active fraction of endotoxin or lipopolysaccharide (LPS), is responsible for many of the systemic activities of LPS and appears to be structurally similar in many gram-negative organisms. Despite modern antibiotic therapy, gram-negative septicaemia is still associated with a high

morbidy and mortality. Hyperimmune serum with high levels of antibodies to lipid-A may have therapeutic potential in patients with septicaemia.

An enzyme-linked immunosorbent assay for antibodies to lipid-A using rabbit immune serum was developed and validated in order to detect antibodies in human serum.

Serum from 25 healthy blood donors was tested and, although 40% of undiluted samples gave extinction values above the background, when serum was tested at 1/100 dilution, only one of the 25 samples showed significant antibody levels.

It is concluded that healthy Australian blood donors are unlikely to be useful as a source for hyperimmune serum in the treatment of gram-negative septicaemia.