SEVENTEENTH SIR PETER FREYER MEMORIAL LECTURE and SURGICAL SYMPOSIUM September 23rd & 24th, 1993

SESSION I

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COLORECTAL SURGERY - STOMA RELATED **MORBIDITY**

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The trend towards definitive one stage emergency large bowel surgery and the avoidance of a defunctioning stoma at anterior resection is partly driven by the perceived morbidity and low closure rate of temporary stomas. There is little recent data on stoma-associated morbidity. Hence the aim of the study was to examine stoma related complications and closure rates in patients undergoing large bowel surgery with a colostomy (AP resections excluded). Over a five year period 77 patients had colostomies (41 male, mean age 61.1 years). 45 patients had emergency surgery. Of the emergency operations 78% had end colostomies, the majority of which were Hartmann's. In the elective setting 69% of the patients had loop colostomies, the majority of which were performed in association with anterior resection. Underlying pathology was carcinoma 48%, diverticular disease 36%, inflammatory bowel disease 2.7% and miscellaneous 13.3%. Revision rates, complications (necrosis, stenosis, prolapse, hernia) closure rates and associated morbidity are shown in the table.

Revision Complications Closure Closure comp elective (n=32) 2 (6.2%) 3 (9.4%)21 (65.6%) 1 (4.7%) emergency (n=45) 2 (4.4%) 7 (15.5%) 28 (62.2%) 3 (10.7%)

Colostomy related complications were similar in those undergoing either emergency or elective surgery but closure rates were significantly lower in the emergency group especially in those who had a Hartmann's procedure for cancer (25%). Of the patients who did not have their colostomy reversed over half of these died within one year. Stoma closure morbidity was significant and one patient died undergoing reversal of Hartmann's. These data confirm the contention that both formation and closure of defunctioning colostomies are associated with significant complications, and one third of patients will not have their colostomies reversed.

MORPHOLOGY AND STAGING OF COLON CANCER DIAGNOSED ON BARIUM ENEMA

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The current availability of high quality double contrast barium enemas has had a significant impact on the accuracy of radiologic examination in the diagnosis of colon cancer. This study was performed to identify the specific radiologic signs which indicate accurately the stage of disease.

A list of all patients with colon cancer over a two year period to June 1991 at the Hospital of the University of Pennsylvania,

was made by computer search of pathology, radiology and medical case records. One hundred and fifty two patients were included. The morphology of the lesion as detected by barium enema was categorised as polyp less than 2 cm. diameter, polyp greater than 2 cm. diameter, plaque or ulcerated lesion, a carpet lesion and annular or semi-annular lesion. The pathologic report was used to assess the staging.

Overall tumor stage was higher in patients with annular or semi-annular tumours. Muscularis propria invasion was most marked in patients with annular lesions, but submucosal invasion was prominent in patients with polypoid masses greater than two centimetres. 44% of patients with annular lesions had lymph node metastases while 21% of those with large polyps had such tumour spread. Liver metastases were seen in none (0%) of the patients with lesions other than the two previously mentioned.

In conclusion, the findings of an annular tumour on barium enema is associated with a higher stage and more likelihood of metastatic spread than any other lesion.

GASTRIC ALKALINE SHIFT DOES NOT RELIABLY PREDICT OESOPHAGEAL BILE REFLUX

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Oesophageal bile reflux is difficult to measure requiring radioisotope imaging or unphysiological aspiration studies. Oesophageal alkaline shift is unreliable in detecting bile in the oesophagus. Supine gastric alkaline shift (GAS) (gastric pH>4 for > 10% time) may indicate duodenogastric reflux and has been used to predict oesophageal alkaline reflux.

A new probe which detects bilirubin in the oesophagus based on its spectrophotometric properties (Bilitec 2000, Synecic Medical) was used in this study to determine whether GAS and oesophageal pH>7.5 are reliable predictors of oesophageal bile reflux. Fourteen patients underwent simultaneous dual channel (gastric and oesophageal) pH and oesophageal bile monitoring. A positive bile study was taken as Bilitec reading (absorbance) >0.15 for more than 5% of the supine period.

Results

	Positive bile study (n=7)	Negative bile study (n=7)	p value*
Absorbance>0.15, supi	ne		
[mean % time (sem)]	29.5 (11.0)	1.0 (0.6)	p<0.001
GAS, supine			
[mean % time (sem)]	5.1 (2.7)	12.7 (4.9)	ns
Oes. pH>7.5, supine			
[mean % time (sem)]	0.4 (0.3)	6.5 (2.6)	p<0.05
DeMeester acid score	82.5 (27.7)	10.0 (4.0)	p<0.005

*Wilcoxon rank sum test

Five of the seven patients with a positive bile study had a normal gastric alkaline profile. Two patients with Barrett's oesophagus had oesophageal bile reflux in the presence of a normal acid score indicating that alkaline reflux may dilute the pH to give a "normal" acid profile.

These data suggest that neither gastric or oesophageal alkaline shift reliably predict gastrooesophageal bile reflux. Such reflux may occur in the presence of both normal and acidic oesophageal pH profiles.

4 GLOBUS PHARYNGEUS AND GASTRO-OESOPHAGEAL REFLUX

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Previous investigators in the past have demonstrated an association between globus pharyngeus and gastro-oesophageal reflux. With the advent of ambulatory 24 hr. pH monitoring, the strength of this association has been questioned.

Oesophageal manometry, prolonged ambulatory pH monitoring and endoscopy were performed prospectively in 21 patients with globus pharyngeus. 10 were male and 11 female with a mean age of 39 years. 8 patients (38%) had proven gastro-oesophageal reflux (all upright pattern). A further 4 (19%) patients had periods of reflux which correlated significantly with globus pharyngeus. Manometric study showed hypertonicity of the upper sphincter in only 1 patient. At follow-up, only 6 (29%) patients treated with a H2 antagonist reported improvement in symptoms.

Although an association exists between globus pharyngeus and reflux oesophagitis the poor response to treatment suggests that other factors must be invovled.

EPICARDIL STIMULATION PRODUCES A FALL IN LOWER OESOPHAGEAL SPHINCTER TONE

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Many patients with treated ischaemic heart disease (IHD) have persistent chest pain and on investigation up to 50% of these are found to have gastro-oesophageal reflux disease (GERD). The link between these two pathological entities remains unclear.

The effect of epicardial stimulation on lower oesophageal sphincter (LOS) tone was studied in 7 adult mongrel dogs, acting as their own controls. Epicardial stimulation was produced by friction and a pressurised water jet on the left ventricle. LOS tone was continuously monitored using a sphinctometer (Gaeltec Ltd., Isle of Skye, UK) and blood pressure monitored via an intra-arterial catheter.

Results [mean (sem)]

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	Control 1	Epicardial	Control 2 Friction	Water Jet
LOS tone (sphinctometer)	13.0 (2.2)	6.2 (1.7)*	13.6 (2.4)	5.0 (1.2)*
Mean blood pressu (mmHg)	92 (8)	72 (7)*	90 (8)	70 (5)*

^{*} p<0.03 vs control Wilcoxon signed rank test

LOS tone was reduced in five of the seven animals in response to both friction and the pressurised water jet. This occured in association with a significant fall in the mean blood pressure.

These data demonstrate that LOS tone may be reduced by epicardial stimulation. This change may be due to activation of receptors in the myocardium of the left ventricle. This may explain the high incidence of GERD in patients with ischaemic heart disease.

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ROLE OF SURGERY IN PEPTIC ULCER DISEASE

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The role of surgery in peptic ulcer disease is controversial. Currently the majority of operations performed are for complications of gastroduodenal ulceration. A retrospective study of patients undergoing surgery in the last 18 months for peptic ulcer disease was conducted. Thirty seven patients underwent surgery.

Seven patients (19%) were operated on for bleeding gastric ulceration and seven patients (19%) for a bleeding duodenal ulcer. One patient was found to have a bleeding gastric ulcer along with a perforation. A further thirteen patients (35%) with perforated duodenal ulcers underwent emergency surgery. Ten patients (27%) were operated on electively. Five patients (13%) had vagotomy and pyloroplasty. Three (8%) had vagotomy and gastrojejunostomy and finally, two patients (5%) had Bilroth 1 gastrectomy. The mean age of patients undergoing emergency surgery for bleeding ulcers was 72.3 years. Male to female ratio was 1:1. In the bleeding group six patients (42%) were suffering from shock at the lime of presentation and out of these, four patients (28%) underwent emergency surgery within 24 hours. The exact bleeding point was endoscopically visualised preoperatively in eleven patients (78.5%). In all eleven patients (78%) had vagotomy, pyloroplasty and underrunning of the bleeding point and three patients (21%) had underrunning of the bleeding point and Losec infusion post-operatively. Early postoperative haemorrhage in two patients (15%) required Polya gastrectomy. The mortality rate in upper G.I. bleeders was 21% (3 patients) and was due to severe underlying medical problems.

We feel that surgery has a vital role in the treatment of complications of peptic ulcer disease. However, the place of elective surgery is rapidly diminishing.

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ERYTHROMYCIN ACCELERATES GASTRIC EMPTYING
FOLLOWING PANCREATICODUODENECTOMY: A
PROSPECTIVE, RANDOMIZED, PLACEBOCONTROLLED TRIAL

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Delayed gastric emptying (DGE) is a major cause of morbidity following pancreaticoduodenectomy, occurring in up to 40% of patients. The pathogenesis of DGE has been speculated to involve factors such as peritonitis from anastomotic leaks, ischemia to the antropyloric muscles, and gastric atony in response to either resection of the duodenal pacemaker or reduction in

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circulating motilin levels. This study tested the hypothesis that erythromycin, a motilin agonist, reduces the incidence of early DGE following pancreaticoduodenectomy.

Methods: Between November 1990 and January 1993, 115 patients undergoing pancreaticoduodenectomy were recruited into this prospective, randomized, placebo-controlled trial. The patients received either 200 mg of I.V. erythromycin lactobionate Q.I.D. (n=57), or an identical volume of 0.9% saline (n=58) from the third to the tenth postoperative days. On the tenth postoperative day, a dual isotope nuclear medicine gastric emptying scan was performed.

Results: The erythromycin and placebo groups were comparable with respect to multiple pre-, intra- and postoperative factors. The erythromycin group had a 38% reduction in the incidence of DGE (19% vs. 31%), and a significantly reduced (p<0.05) need to reinsert the NG tube for DGE (6 pts. vs. 15 pts.). Erythromycin significantly reduced (p<0.05) the percent retention of liquids at 30 min and solids at 30, 60, 90, and 120 min:

% Retention of Solids

Group	30 min	60 min	90 min	120 min	
Erythromycin Placebo	80±31 91±1 J}*	69±4 _{82±2} }**	63±4 _{78±2} }**	57±4 _{71±3} }**	
*p < 0.01, **p = 0.01 by Chi square.					

There were no major adverse reactions to erythromycin.

Conclusions: Erythromycin is a safe, inexpensive drug that significantly accelerates gastric emptying following pancreaticoduodenectomy and reduces the incidence of DGE by 38%. The use of erythromycin to decrease DGE after pancreaticoduodenectomy appears appropriate.

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RECOMBINANT ALPHA-I-ANTICHYMOTRYPSIN ATTENUATES PANCREATIC INDUCED LUNG INJURY.

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Alpha-l-anti-chymotrypsin (ACT) is an endogenous serine protease inhibitor which binds and neutralizes leucocyte proteases such as elastase and cathepsin G, inhibiting neutrophil chemotaxis and degranulation. Neutrophil infiltration is central to adult respiratory distress syndrome and may result in part from an imbalance between leucocyte proteases and endogenous protease inhibitors. The aim of this study was to evaluate the role of recombinant ACT (rACT) in ameliorating lung injury associated with pancreatitis. Sprague-Dawley rats (400 500grm) were randomized into controls (saline infusion) or pancreatitis groups, which were treated with saline or rACT (50mg/Kg). Myeloperoxidasc (MPO) was employed as a monitor neutrophil traffic in the lung, and wet: dry lung weights (WD) as a measure of pulmonary endothelial permeability. Lungs were also evaluated histologically.

	Control n=8	Pancreatitis n=9	rACT treated n=8
MPO (u/grm)	2.08±0.5	7.8±1.1	4.68±0.7*@
WD	3.2±0.1@	12.±3.3	4.2±0.5@

^{*=}p < 0.001 vs. control, @=p < 0.05 vs. pancreatitis (mean \pm SEM)

Caerulein (5mg/Kg/hr) induced pancreatis in all animals with an increase in serum amylase from 1851±208 (control) to 5198±924 (pancreatitis), p<0.05. Pancreatitis induced pulmonary neutrophil influx and produced significant pulmonary microvascular leak. Both neutrophil influx and pulmonary microvascular injury were attenuated by rACT. These data support the hypothesis that deficient endogenous protease inhibition may be responsible for the neutrophil mediated lung injury in pancreatitis, suggesting a therapeutic role for recombinant protease inhibitors such as alpha-l-antichymotrypsinogen.

10 GALLBLADDER MUCIN HYPERSECRETION AND CHOLESTEROL SUPERSATURATION: AN IMPORTANT INTERACTION IN CHOLELITHIASIS IN THE PRAIRIE DOG.

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University.

In the prairie dog model of cholelithiasis, hypersecretion of gallbladder mucin occurs prior to gallstone formation and neither the mechanism nor media Tors of mucin hypersecretion have been identified. The aims of this study were to examine the role of cholesterol and proslaglandins (PGE 2, PGF 2α) on mucin synthesis in an *in vivo* model.

Methods: 4 groups of adult female prairie dogs (N=26), maintained on cholesterol free chow were anesthesized with ketamine and the gallbladder (GB) exposed. Suture-ligation of the cystic duct with sparing of the neurovascular supply was performed to prevent entry of hepatic bile in the GB and bile removed using a catheter placed in the fundus. The GB was washed and the following solutions instilled: 1) model bile (MB, total lipid l0g/dL) CSI 0.6; 2) MB CSI 1.4; 3) vesicles with Ch: PL ratio 0.2:1; 4) vesicles with Ch: PL ratio 2:1. Mucin synthesis was measured by standard explant culture incorporation of 3H-glucosamine and is expressed as dpm/mg explant protein. PG assay was performed for strips of mucosa incubated for 30 min in Krebs buffer by RIA.

Results: There was no histological injury to the GB epithelium. Mucin synthesis and secretion was increased in animals given MB CSI 1.4 compared to those with unsaturated MB, CSI 0.6 (205, 435 + 13365 versus 127,655 + 9527 dpm/mg protein, p < 0.003) without any change in PG synthesis. A similar increase was seen in animals treated with cholesterol supersaturated vesicles (Ch: PL 0.2:1; 173,000 \pm 11,019 versus Ch: PL 2:1; 205,936 15,184, p < 0.01) again without change in PG synthesis. However, PGE 2 and PGF 2 α levels were higher in animals treated with MB of either CSI 0.6 or 1.4 compared to those receiving vesicles suspensions (p < 0.002).

Conclusion: Cholesterol supersaturated bile is a powerful stimulus for mucin synthesis and this effect is also seen with cholesterol supersaturated vesicles and appears independent of PG. We speculate that net cholesterol flux into the gallbladder mucosa is a stimulus for the early mucin hypersecretion seen in this model of cholesterol cholelithiasis.

PROGNOSTIC PARAMETERS IN RENAL CELL CARCINOMA A. I. Butt, M. H. Vazir, R. Sullivan, C. E. Connolly, H. C. Bredin.

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A retrospective analysis of fifty consecutive patients with

renal cell carcinoma was carried out. The tumours were classified in accordance with (1) Clinico-pathological stage, (2) nuclear grade, (3) cell type and architecture, (4) the presence and absence of intermediate sized filments cytokeratin and vimentin detected by monoclonal antibodies. Patient survival curves were constructed by the Kaplan-Meier method using the BMDP statistical package. Our findings demonstrated that increasing clinical stage and nuclear grade generally correlated with a decrease in patient survival. Patients with clear cell tumours survived better than those with granular (p = 0.0043) and mixed (p = 0.0022) tumours. There was no statistical difference in survival in patients whose tumours were vimentin positive versus vimentin negative. Very few tumours stained negative for cytokeratin and these latter patients had a favourable prognosis.

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THE IMPORTANCE OF THE INCIDENTALLY DETECTED RENAL CELL CARCINOMA

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Renal cell carcinoma (RCC) is a relatively uncommon tumour accounting for approximately 3% of adult malignancies. Despite advances in chemotherapy; radiotherapy, and immunotherapy the prognosis for RCC has remained largely unchanged. Recent years have seen an increase in the incidence of RCC detected incidentally, largely due to the greater availability and utilisation of diagnostic imaging modalities such as ultrasonography, and CT scanning. The relevance of these incidentally detected tumours has not been clearly defined. It is possible that earlier detection of these incidental tumours will result in a significant survival advantage. We review 187 cases with a clinical diagnosis of RCC over the 20 year period 1972-1992, with specific interest in the incidentally detected tumours, the presenting features and the change in diagnostic methods.

The male/female ratio was 2:1. While 54% of patients presented with frank haematuria, 43% with pain, and 35% with a palpable loin mass. Only 7% had the "classical triad" of pain, haematuria and mass. Of patients with a history of frank haematuria only 60% had red blood cells on urine microscopy at admission. 57% of ESRs were elevated and 14% of patients were hypertensive. Analysis of the pathological specimens identified lymph nodes in 50 or which 12 (24%) contained metastases. Distant metastases occurred in 14 (7%).

The definitive diagnostic investigation was ultrasound, (U/S) in 44%, intravenous urography (IVP) in 28%, angiography in 18%, and CT scanning in 8%. However, the changes in radiological technology over the last 20 years have been superimposed on these data with U/S and CT becoming available in the mid 70's and early 90's respectively.

Twenty four (13%), patients had "incidentally" detected tumours. These had been diagnosed by IVP in 11 (46%), U/S in 10 (42%), and CT scanning in 3 (12%). Nephrectomy was performed in 22 of these patients. Fifteen (63%) had Tl lesions, compared to 36% in the symptomatic group. No positive nodes were identified. Two patients had metastatic disease at presentation. This subgroup have presented with smaller tumours of a lower grade and stage, and may have a better outlook.

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ADJUVANT THERAPY IN STAGE I MALIGNANT MELANOMA: RESULTS OF A PROSPECTIVE RANDOMISED TRIAL

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We report the results of a prospective randomised trial of adjuvant therapy in high risk nonmetastatic malignant melanoma. Twenty six patients with stage 1 malignant melanoma of thickness greater than 1.5mm or Clarke's level 3 were randomised to receive either adjuvant treatment (DTIC and Interferon, n=14) or observation (n=12). Ethical approval was obtained. Mean age for males (n=8) was, 45 years and for females (n=18) was 48.3 years. Mean thickness in the treatment group was 2.9mm (range 0.8 - 7.0mm) compared to 2.6mm (0.76 - 5.0mm) in the observation group. Immunotherapy with DTIC and Interferon was given in cycles; all patients completed the treatment schedule. At five years 6 deaths had occurred in the treatment group and two deaths in the observation group (p < 0.5, confidence interval 0.6 - 10.4). Metastatic melanoma was confirmed in all eight patients. Mean thickness in the mortality group was 3.8mm. Statistical analysis identified the relative risk of mortality to be 2.6 times greater in the treatment group when compared to the observation group. In view of these results the randomisation was suspended.

Conclusion: Adjuvant treatment with DTIC and Interferon in high risk stage 1 malignant melanoma confers no benefit and is associated with an unacceptable mortality rate.

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RESIDENT PERITONEAL MACROPHAGE TUMOUR CYTOTOXICITY IS MEDIATED BY A SINGLE SIGNAL STIMULATORY PATHWAY

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The requirement of single signal vs dual signal stimulation for initiation of murine peritoneal macrophage (PMØ) cytotoxicity is assessed. Specifically the macrophage activating factors Lipopolysaccharide (LPS), Interferon- α (IFN- α) or their combination were used to induce the development of tumouricidal activity in murine PMØs. PMØs were harvested from female CD-I mice (6-8 weeks old) and were stimulated in-vitro for 24 hours with LPS (lmg/ml) and IFN-g (1000 units/ml) alone and in combination. The ability of the PMØs to kill WEHI 164 tumor cells was then assessed using the Cr⁵¹ release assay and generation of superoxide anion (O₂-) by reduction of Ferricytochrome C. Experiments were performed \pm anti-TNF monoclonal antibody \pm superoxide dismutase and \pm catalyse.

	WEHI 164 Cytotoxicity	O ₂ -
	% killing	nmols/mg protein
Control	26.5 ± 0.7	0.0187 ± 0.001
IFN-g	84.5 ± 9.75	0.0310 ± 0.003
LPS	60.5 ± 9.25	0.0340 ± 0.002
LPS ± IFN-g	71.1 ± 5.05	0.0280 ± 0.0011

Data = $mean \pm SD$

Initial results indicate that PMØs stimulated with LPS or IFN- α only have a higher cytotoxic ability against the WEHI 164 sub clone 13 cell line compared to a combination of these slimuli. This is also confirmed by the release of superoxide anion, a cytotoxic secretory product. These results imply that a single rather than a dual stimulatory signal is sufficient to increase tumouricidal activity in resident PMØs.

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A STUDY OF pS3 LOSS OF HETEROZYGOSITY AND RAS MUTATIONS IN BARRETT'S CANCERS

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Barrett's oesophagus is a pre-malignant condition with a 40-120 fold increased risk of developing adenocarcinoma within the columnar epithelium. The molecular genetic events involved in malignant transformation of this epithelium are unknown. We studied a total of 52 oesophageal cancer specimens for loss of heterozygosity of the tumour suppressor gene p53 on chromosome 17. Heterozygosity was determined on uninvolved resection margins. Loss of heterozygosity (LOH) was determined in tumour DNA samples following amplification by polymerase chain reaction of a polymorphic Msp I restriction site. There were 22 squamous cancers, 10 adenocarcinomas and 20 Barrett's cancers analysed. Of informative cases, LOH was documented in 5 of 12 tumours - 2 squamous, 2 Barrett's and 1 adenocarcinoma.

In addition 17 Barrett's cancers were studied for C-Ki-ras codon 12 mutation. All seventeen cancers were negative for ras mutations.

In conclusion although pS3 LOH in Barrett's cancers occurs with similar frequency to other oesophageal cancers neither ras mutations nor pS3 LOH appear to act as major determinants of malignant transformation, in oesophageal carcinoma.

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ALTERATION OF HOST ANTI-TUMOUR ACTIVITY FOLLOWING SPLENECTOMY

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Splenectomy is commonly undertaken in the treatment of upper gastrointestinal tumours such as gastric and pancreatic carcinomas. However, the effect of this procedure on subsequent host anti-tumour cytotoxicity is unclear. The aim of this study was to assess the effect of splenectomy on host macrophage (MØ) mediated anti-tumour cytotoxicity in the early post-operative period. 100 female CD-1 mice were randomised into one of three study groups; Control (C), Laparotomy and sham splenectomy (L) and Splenectomy (S). 24 hours post-operatively peritoneal cells were harvested by lavage and the macrophage subpopulation studied for the release of; Superoxide anion $(O_2$ -), a cytotoxic secretory product, Nitric Oxide (NO); a tumourostatic agent, Tumour Necrosis Factor (TNF), and for the ability of the cells to kill the Wehi 164 tumour cell line.

	O ₂ - nmol/90 mins	NO mmols/72 hrs	TNF pgms/105 MØ	Killing cpm/l05 M0
C	0.5±0. 1	55±5	0.64	78
L	17±0.2@	25±2 @	0.95 @	218 @
S	2.5±0.7*	9 <u>±</u> 4*	1.4 @	248@

Data = mean±sem *p<0.05 versus other groups. @p<0.05 vs controls

S was associated with increased release of the cytotoxic products superoxide anion and tumour necrosis factor by peritoneal macrophages. This correlated with a significantly higher killing of tumour cells in vitro by macrophages harvested from the splenectomy group 24 hours post operatively. The tumourostatic L-arginine matabolite nitric oxide was however significantly reduced indicating that killing of this tumour cell line appears to depend on TNF production and $\rm O_2$ - release rather than on L-arginine dependant mechanisms. In conclusion, splenectomy is not associated with a detrimental effect on macrophage mediated cytotoxic mechanisms within the peritoneal cavity in the early post operative period.

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INTERLEUKIN-2 mRNA TRANSCRIPTION AFTER THERMAL INJURY

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Serious traumatic and thermal injury have been shown to result in decreased secretion of interleukin-2 (IL-2) from activated T cells. The aim of this study was to determine whether defective IL-2 secretion after thermal injury is a result of preor post-transcriptional influences. Peripheral blood mononuclear cells (PBMC) from patients following thermal injury and normal controls were isolated and cultured in vitro in the presence or absence of Phytohaemagglutinin (PHA) stimulation. IL-2 production was determined using a bioassay. Total RNA was isolated and messenger RNA (mRNA) was analyzed by Northern blotting. IL-2 secretion and mRNA expression were both decreased in PBMCs from thermally injured patients. We therefore utilized a nurine model in order to determine if the decrease in mRNA for IL-2 was simply due to a change in the kinetics of expression after thermal injury or due to a decreased rate of nuclear transcription of IL-2. Twenty male A/J mice were divided into two groups. Half were thermally challenged (with institutional and national ethical approval) and half were sham controls. Splenocytes were harvested seven days later and stimulated for varying amounts of time with Concanavalin A before RNA isolation. In vitro stimulation of murine splenocytes revealed the kinetics of expression of mRNA to be similar in both sham and thermally challenged mice. Nuclear run-on analysis of murine splenocytes showed the transcription of IL-2 following thermal injury to be decreased compared to sham controls. We conclude that mRNA expression for IL-2 is decreased following thermal injury and propose that the defect is mediated at a pretranscriptional level.

TAUROLIDINE PERITONEAL LAVAGE AS A PROPHYLAXIS AGAINST POST-OPERATIVE INFECTION IN COLORECTAL SURGERY; A RANDOMISED DOUBLE-BLIND CONTROLLED TRIAL OF 300 PATIENTS

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Intra-operative peritoneal lavage (IOPL) using the antiseptic taurolidine reduces infective morbidity in established peritonitis. To determine the prophylactic effect of taurolidine IOPL, 300 patients were randomised to receive either taurolidine or saline IOPL at the completion of elective colorectal surgery, having previously received bowel preparation and prophylactic antibiotics. Bacterial culture swabs were taken from the region of surgery before and after IOPL. Post-operative infections were monitored.

The results of pre- and post- IOPL swab cultures were significantly different between treatment groups ($X^2 = 13.31$, p = 0.004). Of the 150 patients who received taurolidine, 28 (18.6%) had positive pre-IOPL swabs, compared to 35 of 150 (23.3%) in the saline treated group ($X^2 = 0.72$, p = 0.40). Of the 28 taurolidine treated patients with positive pre-IOPL swabs, 17 (60.7%) had negative post-IOPL swabs, representing reduced sepsis. In comparison, only 8 of 35 (22.8%) saline treated patients demonstrated a similar reduction ($X^2 = 7.8$, P = 0.005). The 33 post-operative infections were evenly distributed between treatment groups.

In conclusion, results of bacterial culture swabs suggest that taurolidine IOPL is significantly more effective in reducing bacterial numbers in the region of surgery than saline IOPL. However, this microbiological improvement does not reflect in reduced rates of post-operative infections.

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SURGERY FOR IDIOPATHIC THROMBOCYTOPENIA -CURRENT RESPONSE RATES AND FUTURE PROBLEMS

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Introduction. We reviewed the clinical and haematological success of splenectomy for Idiopathic Thrombocytopenic Purpura in our unit. Operation records, clinical indications, pre-operative treatment, post-operative course and follow up details were recorded.

Results. Fifty-five patients underwent splenectomy for ITP over a 10 year period. The diagnosis was simply idiopathic in 50 but in the past two years 5 patients have required splenectomy for ITP associated with HIV infection. Pre-operatively all patients had undergone a trial of steroid therapy and the indication for surgery was initial non-responders, relapse after successful immunosuppressive treatment or continual dependence on steroid medication. The lowest platelet counts pre-operatively ranged 2-63 x 103/ul with a mean of 17.9 x 103/ul. Operative treatment was by splenectomy through a mid-line laparotomy in 52 and by laparoscopy in three. There were no hospital mortalities or significant morbidity. Laparoscopic splenectomy was associ-

ated with a short hospital stay and rapid recovery and afforded protection to the surgeons and the theatre staff by reducing contact with the patients blood and thereby reducing the risk of HIV transmission. Follow up was achieved in 45 patients to date (mean 19 months, range 1-125) and showed a success rate of 41 (93%) when defined by the absence of symptoms and the documentation of platelet counts above 100 x 103/ul. Three patients (with platelet counts 8, 72 and 91) required further medical treatment. Two were given immunoglobulin after platelet antibodies were identified and one received steroids and azathioprine. There was a successful outcome in each. One patient with a postoperative platelet count of 90 x 10³/ul was clinically well and over her short follow up of 7 months has not been treated further. Only one patient has died since operation and this was a man 9 years post splenectomy and was from a myocardial infarction. The recent patients with HIV infection have all responded well and have normal platelet counts.

Conclusions. This study has shown a high success rate (93%) for splenectomy in ITP and that immunological techniques are available to rescue those who do not respond. The arrival of HIV associated ITP is a cause for concern and, in these, operative treatment may be safely carried out using laparoscopic techniques. In the latter the prognosis may be related more to the underlying HIV infection than ITP.

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ALTERNATIVE MANAGEMENT OF LOCALLY AGGRESSIVE BONE TUMOURS

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The aim of this study is to review treatment of locally aggressive bone tumours using cryosurgery rather than en bloc resection, with particular interest in functional outcome, complications and local recurrence.

Treatment of 17 patients between the age of 9 and 51 years is presented. The average length of follow up was 38 months. There were 13 lower limb, 1 upper limb and 3 pelvic lesions. Four tumour types were identified as being suitable for treatment by this method. These were: Giant Cell Tumour (7), Aneurysmal Bone Cyst (6), Chondromyxoidfibroma (3) and Low Grade Chondrosarcoma (1).

All patients were treated with mechanical curretage, cryotherapy and local application of phenol. The resulting bony defects were filled with autogenous bone graft in 6 patients, polymethylmethacrylate in 4 patients and a combination of bone graft and polymethylmethacrylate in 1 patient. The defect did not require reconstruction in 6 patients.

Functional evaluation was carried out using the system of the International Symposium on Limb Salvage (1989). On average 86% of premorbid function was restored at follow up. There were 2 superficial wound infections which resolved early in the post operative period with antibiotic treatment. One patient developed a deep infection which required curretage and soft tissue reconstruction and went on to sound bony and soft tissue healing. There was 1 pathological fracture and 1 patient has premature closure of the proximal tibial physis. 94% of the group are disease free at follow up as 1 patient developed local recurrence.

Our results compare favourably with en bloc resection and demonstrate the ability to gain adequate local control without recourse to more aggressive resection and more difficult and extensive reconstruction.

SESSION II

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ARGININE ENHANCES WOUND HEALING AND IMMUNE FUNCTION IN AN ELDERLY POPULATION

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The elderly account for an ever increasing proportion of the population. Wound healing and infectious problems account for the majority of morbidity and morality in the geriatric surgical population. In this study we sought, using a randomized double blind control trial, to determine whether oral supplementation with the immunomodulatory, semi-essential, amino acid arginine would enhance immune function and wound healing capacity. Forty five healthy volunteers, aged >65 were divided into two groups receiving either arginine asparate (n=30) (17g free arginine) or placebo (n=15). Dietary intake of food was not controlled. A polytetrafluroethylene (PTFE) implant was inserted subcutaneously into the right deltoid region and a 2 x 2 cm split thickness wound was created on the lateral aspect of the upper thigh and assessed daily until complete re-epithelialization was achieved. Mitogeneic response of peripheral blood lymphocytes to Concanvalin A, Phytohaemagglutinin, Pokeweed mitogen and allogeneic target cells were assayed at the beginning and end of supplementation. The hydroxproline content of the implants was determined as an index of reparative collagen synthesis. Nitrogen balance, blood chemistry and lipid profiles were compared before and after supplementation. Arginine supplementation significantly enhanced the hydroxproline content of the PTFE implants (26.49±2.39ug/cm) compared to controls (17.41±2.04ug/ cm), with an increase in total protein (43.47±3.85ug/cm) versus controls (21.95±2.5). There was no significant difference in the rate of epithelialization between the two groups. Response of peripheral blood lymphocytes to mitogenic and allogenic stimulation was significantly enhanced in the arginine supplemented group. Two weeks of arginine supplementation led to an improved and positive nitrogen balance (2.0±0.4gN) when compared to controls (0.11±0.47gN) p=0.01. No adverse effects were observed at this dosage of arginine.

The data suggest that enteral arginine supplementation may be of benefit to an elderly population in improving wound healing and immune responses and furthermore arginine is well tolerated in this age group with no untoward side effects being recorded.

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TOXIC SHOCK SYNDROME IN BURNS IN THE WEST OF IRELAND

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Toxic Shock Syndrome is a serious type of Staphylococcal Toxemia with a well defined set of clinical features. It has been reported in many clinical situations including Burns. It is associated with high mortality rate (average of about 11%).

A three year review of 71 burn cases at University College Hospital, Galway, revealed 8 cases of Toxic Shock Syndrome. 6 out of 8 cases occurred in young children. Majority of cases occurred in scalds. All cases grew Staph. Aureus on culture.

The diagnosis was made entirely on clinical grounds using the simplified criteria of Toffee and Williams (Fever, rash, hypotension, myalgia, vomiting and diarrhoea, mucosal erythema, and absence of other etiologies). Immediate treatment was started with i.v. antiobiotics on clinical suspicion. Fortunately no deaths occurred in this group due to this complication.

In this paper we discuss the etiology, diagnosis, treatment and prevention of Toxic Shock Syndrome in burns.

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INTRACELLULAR DYSFUNCTION FOLLOWING THERMAL INJURY - THE ROLE OF CYCLIC AMP

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Serious thermal injury is known to result in severe immunosuppression. This study was performed to investigate the role of Cyclic AMP (CAMP) in T cell dysfunction following thermal injury. Forty male AJ mice were randomised into two groups, half were subjected to a 20% scald burn and half were sham burned. Mice were sacrificed on days 4, 7, and 10 post burn. Their splenocytes were pooled and cultured in the presence or absence of prostaglandin E2 (PGE2). Intracellular CAMP levels were determined by radioimmunoassay. Splenocytes from normal mice were incubated with dibutyryl CAMP in order to determine the effect of elevated intracellular CAMP. Cells were analysed for proliferation (3 HT uptake), interleukin 2 production (CTLL bioassay), and IL 2 p55 receptor (IL 2R) expression (flow cytometry). All experiments were repeated with similar results. Levels of CAMP in splenocytes from burned animals were found to be significantly elevated on day 7 post burn compared with controls (p<0.05). This corresponds to the time period when we have previously shown IL-2 production to be maximally depressed following thermal injury. Incubation of splenocytes with PGE2 resulted in raised levels of CAMP in both burn and sham groups. However, the increase was significantly greater in splenocytes from the burn group compared with controls on days 4 and 10 (p<O.Ol). IL-2 production was significantly decreased by the addition of dbCAMP to splenocytes from normal mice stimulated with Con A (p<0.05). Significant IL-2 inhibition was not observed when dbCAMP was added to cells stimulated with a combination of phorbol ester and calcium ionophore, which bypasses all cell membrane events. IL 2R expression on splenocytes was unchanged by the addition of dbCAMP to the cultures. Cellular proliferation was significantly decreased by addition of dbCAMP to splenocytes stimulated with Con A. We conclude that intracellular CAMP levels are elevated following thermal injury in this model. Moreover, an increased sensitivity to PGE2 is found after burn injury. Incubation of splenocytes from normal mice with dbCAMP leads to immune dysfunction similar to that seen in burned mice. We propose that increased CAMP is an important mediator of T cell dysfunction following thermal injury.

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A ONE YEAR PROSPECTIVE STUDY OF PAEDIATRIC BURNS IN AN IRISH PAEDIATRIC BURNS UNIT

K. J. Cronin, P. Butler, M. McHugh, G. Edwards. Department of Plastic and Reconstructive Surgery, Our Lady's Hospital for Sick Children, Crumlin, Dublin 12. Burns are the fourth leading cause of injury death in children causing 1,500 deaths per annum in the USA. The majority of paediatric mortality and morbidity result from domestic accidents which are preventable. A prospective audit of paediatric burns from January to December 1992 was undertaken at our Burns Unit to outline the profile of the paediatric burns problem in Ireland. A total of 336 patients were referred (80% self referrals, 15% tertiary referrals, 5% GP referrals). 16% (57) of patients required admission and 84% (112) required prolonged dressings. Mortality was comparable to other centres at 1.8%. The patient profile was generally similar to that seen in other developed countries with some notable exceptions. Firstly, there was a high incidence of sunburn injuries requiring hospital treatment particularly among young infants. Secondly parental knowledge of first aid and safety precautions in the home were extremely poor. Also most parents did not know of the neoplastic risk associated with early childhood sunburn. However, the most striking feature was that 90% of incidents occurred at home and were entirely preventable. The authors suggest that a public health campaign on this subject would go a long way towards reducing paediatric burns mortality and morbidily in Ireland.

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DEMONSTRATION OF LONG TERM TRENDS IN MORBIDITY AND MORTALITY BY SURGICAL AUDIT

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Regular audit meetings are now regarded as being an essential activity for any surgical department. Analysis of audit data collected over a long time period should demonstrate trends in morbidity and mortality that may not be apparent when adverse events are only reviewed on a monthly basis. In this study, morbidity and mortality information accumulated over a 6 year period from a monthly audit meeting was reviewed.

From 1987 to 1992, 17,588 patients were admitted under three general surgeons. 13,505 (76.8%) underwent operative procedures of which 11,261 (83.4%) were elective and 2,244 (16.6%) were emergency procedures. 328 patients (1.9%) died during admission of which 196 occurred after operative intervention. Complications occurred in 588 patients (4.4%). Malignant disease accounted for 31% of all deaths. Mortality rate for emergency aortic aneurysm repair was 60% (compared to 5% for elective repair). The operative mortality rates for non-variceal upper gastrointestinal bleeding and for closure of perforated peptic ulcer were 28% and 8% respectively. As regards morbidity, particular attention was paid to the incidence of thromboembolism and wound sepsis. The incidence of thromboembolic complications halved over the period reviewed. Wound sepsis was most common after gastric resection (6.3%), followed by appendicectomy (4%) and colorectal operations

This study gives an overview of activity and morbidity and mortality patterns in this unit. Occasional summation of audit data in this fashion should be an integral part of surgical audit. Emergency operation for the complications of peptic ulcer disease is still associated with high mortality. Prophylaxis of thromboembolic disease would appear to be reducing the incidence of this problem.

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AUDIT OF SURGICAL PRACTICE - COMPARISON OF ON-LINE VERSUS RETROSPECTIVE DATA COLLECTION

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Introduction. The aim of surgical audit is to maintain standards and ensure delivery of surgical care. The audit must be continuous and include all patients passing through the firm. Many of the information collection systems that are used for audit add a great deal of extra work to the surgical firm and as a result are poorly used and the information collected may be unreliable.

Aim and Method. The aim of this study was to compare the accuracy and completeness of data collected by two audit data collection systems. An information collection system was introduced which was integrated into the normal daily activity of the firm. The method assisted the normal day's work by providing an on-line patient list, summaries for duty hand-over, surgical log books for trainees and data for the monthly surgical audit meeting. We compared the completeness of data in this system with that in a standard commercially available system which had been in place for the previous year and which required retrospective data collection from additional proformas or chart review after discharge. A prospective comparison was performed over a three month period during which data collection was maximised in the established system. The hospital PAS (Patient Administration System) registry was used as the gold standard for patient numbers.

Results. The annual rate of admission to the unit included 1,100 in-patients and 600 Day-Ward cases. The completeness of collected data was 93% for the on-line system and 60% for the retrospective system (p<0.001 Chi sq) when compared to the hospital PAS computer registry. The time required to maintain the on-line system was less than 25% of that for the established retrospective system.

Conclusion. Collection of data for surgical audit should use a system which is current (on-line) and integrated into the normal work of the surgical team in order to be accurate and complete. If inaccurate, especially incomplete, data is collected and used to support resource allocation surgical care will decrease in quantity and or quality. The way forward requires integration of the PAS with the on-line clinical record.

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AN AUDIT OF SPLENIC SURGERY IN A REGIONAL HOSPITAL

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The increased risk of sepsis in patients following splenectomy has been well documented. Fear of overwhelming post-splenectomy sepsis resulted in a generalised trend towards splenic salvage among surgeons. However, splenorrhaphy and attempts at splenic salvage may predispose to significant morbidity often more serious than the increased susceptibility to infection associated with splenectomy and subsequent asplenia.

We reviewed 246 patients who underwent splenectomy in this institution over a 15 year period. Indications for splenectomy were considered under the following headings; haematological (n=116), trauma (n=69), visceral carcinoma (n=35) and miscellaneous (n=26). There were 28 deaths in the series, primarily among the visceral carcinoma and multiple trauma groups. Two deaths were recorded among patients undergoing elective splenectomy for benign disease. Thrombo-embolic complications were recorded in nine patients; respiratory tract infection in 36 patients and intra-abdominal abscess in two patients. Post splenectomy septicaemia was documented in two patients, neither of which was fatal.

We conclude that elective splenectomy for benign disease is a safe procedure with a low incidence of post-operative complications. Similarly, emergency splenectomy performed on otherwise healthy patients is associated with a low incidence of complications. The risk of overwhelming post-splenectomy sepsis is minimal among otherwise fit patients undergoing splenectomy.

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IS LOCAL ANAESTHESIA APPROPRIATE FOR BREAST BIOPSIES?

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In our Breast Unit, it is our policy to offer patients for day case breast biopsy a choice of general (G.A.) or local anaesthesia (L.A.). The L.A. may be augmented by sedation if required. This study was aimed to see how well tolerated this procedure was, under the different forma of anaesthesia. Lumps felt to be malignant on clinical, cytological or radiological grounds are admitted via our main ward and excluded from this study.

All patients consented to the study and their anxiety level measured on a visual analogue scale. Analgesia (both in hospital and at home), complications and length of time in hospital and off work were recorded. Patient satisfaction was gauged by asking them if they would make the same choice again.

Seventy-eight female patients with a mean age of 34.6 years (range 15 - 58) have completed the study to date. Three proved to have malignant lumps and the rest were equally divided between fibroadenomas, fibrocystic disease and other benign conditions. Twenty-six chose G.A., 48 L.A. and 4 L.A. with sedation. There were no significant differences in terms of age or pre-operative anxiety. Lumps were most common in the upper outer quadants with no difference between the sides.

Less than half the patients required analgesia in hospital and they required a mean of five doses at home (usually of mefenamic acid). Patients receiving L.A. spent an hour and a half less time in hospital. More than a third of patients had not returned to work before the third post-operative day. The type of anaesthesia did not affect either analgesia or return to work. Thirteen patients had complications (6/48 L.A. vs 7/26 G.A.; n.s.). Seven of these were wound haematomas.

Fourteen of the 48 patients who had L.A. would not make the same choice again, in comparison to 2 of the 26 G.A. patients and 2 of the 4 who chose L.A. with sedation. This difference is highly significant. Those patients unhappy with their choice were significantly more anxious preoperatively (6.7 + 1.6 vs. 4.5 + 2.4; p < 0.001 - t test).

In conclusion, there are few significant objective differences whether G.A. or L.A. is used; but some patients, particularly the more anxious ones are less satisfied with L.A.

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pLiv1: AN OESTROGEN-REGULATED GENE ASSOCIATED WITH LYMPH NODE INVOLVEMENT IN BREAST CANCER

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Oestrogen receptor (ER) status is an established prognostic marker in breast cancer. However, not all ER+ tumours respond to endocrine therapy and this may be due to a non-functional receptor in some cancers. Several oestrogen-regulated genes have been cloned and investigated as better markers of a functional ER. The expression of 2 such genes, pLivl and pS2, has been examined here in 74 cases of primary breast cancer.

Our results show that pLivl and pS2 are expressed almost exclusively in ER+ tumours, although they are not invariably coexpressed. Taking all 74 cases, pLivl, but not pS2, expression correlated with lymph node disease involvement (p<0.01). In ER+ tumours alone, pLivl expression was even more strongly associated with nodal disease: 15/18 (83%) of ER+pLivl+tumours were node positive while 20/23 (87%) ER+pLivl-tumours were node negative (p<0.00l). This association was further strengthened analysing small ER+ tumours (<2cm) alone with 11/12 (92%) node positive tumours being pLivl+ and 17/22 (77%) node negative cases pLivl negative. pLivl expression did not correlate with tumour size or lymphovascular invasion.

In conclusion, pLivl is a candidate gene for metastatic spread in ER+ breast cancer.

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IS AN AGGREGATE SCORING SYSTEM FOR MAMMOGRAPHIC ABNORMALITIES APPROPRIATE?

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Stereotactic localization and fine needle aspiration cytology (FNAC) has a role in the management of non palpable breast abnormalities. As part of the ECCLES breast screening programme over 18,000 patients with no palpable breast lesions had their mammograms scored 1-5 by by two radiologists - 208 patients in the range of 3-5 had localization biopsies and had prior stereotactic cytology. The cytological smears were scored as grade (1) benign, (2) acellular, (3) atypical, (4) suspicious and (5) malignant by an independent cytologist. Aggregate score was thus generated as the sum of mammogram and cytology scores. This study evaluated its potential in the management of screen detected abnormalities. Of 96 malignant lesions 70 were correctly diagnosed by cytology. The sensitivity (85%), specificity (98%) and positive predictive value (99%) of grade 4 or 5 cytology compares favourably with other series. Significantly all 60 patients with combined mammographic and cytology scores of 4 or less had true benign disease following excision biopsy and all 40 patients with an aggregate score of 8 or greater had malignancy. We now recommend repeat mammography rather than excision biopsy in patients with aggregate score less than 4 and primary wide local excision with a score of 8 or

FNAC: Fine needle aspiration cytology.

SAFE CRITERIA FOR SELECTION OF PATIENTS WITH PRIMARY OPERABLE BREAST CANCER FOR BREAST CONSERVATION WITHOUT RADICAL EXCISION

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A previous multivariate analysis of clinical and pathological features from this unit showed age, vascular invasion, tumour size, and nodal status to be predictive of breast cancer recurrence. New criteria for the selection of patients with primary operable breast cancer for breast conservation were decided upon. Breast conservation is now not advised in this unit if the tumour is >3 cms on clinical or radiological measurement or there is mammographic evidence of extensive or multifocal disease. In the presence of lymphovascular invasion, in or around the primary tumour, women aged over 50 years or women under 50 years of age with tumours measuring <1 cm are considered suitable to continue with this treatment. Re-excision is advised if the excision margin is <5 mm. All patients in this study received intact breast radiotherapy.

Between January 1988 and December 1992, 833 women aged 70 or less presented to this unit with operable (<5 cms) invasive cancers. Of these, 368 women were offered and chose breast conservation, and fulfilled the pathological criteria. 101 women had tumours <2 cm of special type and did not receive radiotherapy. These have been excluded from the study group. 267 women have proceeded to completion of treatment. At a median follow up of 24 months (range 3 - 57), 6 women (2.2%) have developed ipsilateral breast recurrence. In none, was this of the uncontrolled aggressive type.

Breast conservation without very wide excision is safe in women with tumours fulfilling the criteria described.

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TISSUE POLYPEPTIDE SPECIFIC ANTIGEN (TPS): A NEW SERUM MARKER OF PROLIFERATIVE ACTIVITY IN BREAST CANCER

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Serum tumour markers (TM) have been widely investigated in breast cancer. Current TM reflect tumour bulk and this unit has reported the use of some of these in managing metastatic disease. TPS is a novel serum marker in that it has been shown to reflect cell proliferative activity, rather than bulk, for a range of solid tumours (published data). Few studies have evaluated TPS as a marker in breast cancer.

We have assayed TPS in serum (U/L) from normal subjects (N=19), Stage I and II (N=19), Stage III (N=20) and Stage IV (N=20) breast cancer patients prior to any therapy. Mean serum TPS levels (with 95% confidence intervals) were: normals 76.69 (56 - 97), stage I/II 92.26 (61-122), stage III 217.58 (73 - 361) and stage IV 1183.75 (615 - 1752). Stage IV patients had a significantly higher mean level of TPS than Stages I - III with no overlap of confidence limits (ANOVA with range testing: p<0.001).

In Stage IV disease, serum TPS level showed no correlations with site of metastases, response to endocrine

therapy, duration of response nor survival from metastases.

Conclusion: Serum TPS assay is a useful indicator of metastatic spread in breast cancer.

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SCREEN DETECTED BREAST CANCERS CARRY A BETTER PROGNOSIS

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Breast screening aims to save years of life for women who would otherwise have died prematurely from breast cancer. In order to achieve this it needs to detect breast tumours that are of smaller size, better grade and type and earlier stage than those presenting symptomatically. The UK National Breast Screening Progamme offers mammographic screening to women aged 50-64 years. We have compared the tumours detected in the first 5 years of screening with those presenting symptomatically to our unit over the same time period.

S	Symptomatic	
Total cancers (50 - 70 yrs	450	267
Invasive	93%	76%
DCIS	7%	24%
Invasive Cancers		
< 2 cms	64%	89%
Grade I	19%	42%
Grade III	46%	16%
Lymph nodes involved	33%	16%

An estimate of the effect of these changes in tumour characteristics on prognosis can be obtained using the validated Nottingham Prognostic Index:-

•	Good	Moderate	Poor	
Screen detected	71% 34%	25% 52%		Chi-square
Symptomatic	34%	3270	14%	p<0.0001
Expected 15 year survival	80%		42%	13%

The results for the first five years of breast screening indicate that it has significantly increased the numbers of good prognosis cancers.

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CAN PRIMARY TUMOUR IMMUNOHISTOCHEMISTRY IDENTIFY NODE NEGATIVE PATIENTS AT RISK OF EARLY DISEASE RELAPSE?

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Early disease relapse in patients with early (i.e. node negative) breast carcinoma remains an unpredictable problem. To date, there have been few prognostic indicators as to which patients with stage 1 (node negative) disease might benefit from adjuvant therapy.

This study attempts to evaluate whether primary breast tu-

mour immunohislochemistry has a role to play in predicting tumour recurrence in the first five years, following presentation, with reference to the MCA, CA15-3, EGFr and cerbB2 antigens. These were compared to traditional markers such as ER values and a known histopathological grading system.

Sixty-six patients were included in this study (mean age 48.5, range 35-86) 44 were stage 1 (node negative) and 22 stage 2 (node positive). The mean follow up period was 72 months (range 9-92). Of the node negative group, 45% developed tumour recurrence within the follow up period versus 59% of the node positive group. In those node negative patients that had recurrence 55% expressed a low tumour immunoreactivity (<30% of cells) to MCA, and CA153 and a high pathological grading score (>6). These were significant (p<0.05) indicators of early relapse. In node positive disease primary expression of EGFr was a significant indicator of early relapse. Expression of cerbB2 proved to be disappointing in both groups.

MCA, CA15-3 primary tumour expression and a high pathological grading score may have role in selecting a subgroup of node negative patients at risk of early disease relapse.

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IS AXILLARY DISSECTION NECESSARY IN SCREEN DETECTED BREAST CANCER?

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The results of the first round prevalence screening in a mammography screening program were assessed. The aim of this study was to analyse histological factors in patients found to be node positive or negative, to determine whether axillary dissection is necessary in all cases. Eighty four cancers were detected. On level 2 axillary clearance, 21 were node positive and 63 had no nodal involvement. The nodal blocks deemed negative on initial H+E staining were stained with monoclonal antibody to epidermal membrane antigen to detect micrometastases. 8% of node negative patients were found to have micrometastatic disease. Tumour size, grade and type were assessed to determine, if any difference existed between the node negative and node positive groups.

Tumour Grade	Node Pos	Node Neg	Tumour Size	Node Neg	Node Pos
1	5%	3.2%	<lem< td=""><td>15.8%</td><td>5%</td></lem<>	15.8%	5%
2	20%	54%	1-2cm	42.8%	25%
3	75%	42.8%	2-3cm	35%	35%
			3-4cm	3.2%	10%
			>4cm	3.2%	25%

The presence of nodal metastases or micrometastases could not be accurately predicted by any characteristics of the primary tumous taken either separately or in combination. We therefore, recommend that for all prevalent cancers detected by mammographic screening, axillary clearance is necessary.

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A TEN YEAR REVIEW OF BREAST CARCINOMA IN A DISTRICT GENERAL HOSPITAL

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A retrospective review was performed, over a ten year period,

extending from 1979 to 1988, of all patients presenting to this unit with primary breast carcinoma. An analysis of stage at presentation, operative treatment, histology and survival was performed.

A total of 202 patients were included in this study. The mean age of patients at presentation was 56.6 (0.9) years (mean (SEM)), with a range of 24 to 84 years. One male patient presented during the study period. 33.7% were premenopausal and 66.3% of patients were postmenopausal. 55% of tumours presented on the left side. The majority of tumours presented in the upper outer quadrant (56%).

Stage of disease at presentation was as follows; Carcinomain-situ 6%; Stage 1, 14%; Stage 2, 25.4%; Stage 3, 14% and Stage 4, 12%. 15% of patients had segmentectomy and the remainder had simple mastectomy with axillary clearance. Histopathological analysis revealed; 6% carcinoma in situ; 75% infiltraling ductal; 16% lobular and 3% other. 25.5% of tumours were ER negative and 74.5% of tumours were ER positive. 90% of patients received adjunctive therapy. This included radiotherapy in 50%, chemotherapy in 29% and tamoxifen in 63%

Complete follow-up was available in 98% of patients. The median follow-up was 48 months with a range of 4 to 132 months. 32% experienced disease recurrence and 26% of patients died from their disease.

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500 BREAST CANCER PATIENTS WITH FOLLOW-UP

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This is a review of 500 female breast cancer patients, who have been treated and followed-up through our Breast Clinic. Data has been collected prospectively and entered into a computer database. The follow-up ranges from 3 months to 22 years.

The mean age at presentation was 55.8 years (range 25 - 90). Five patients had bilateral cancers and 21 have subsequently developed a contralateral tumour. One hundred and thirty-one patients were pre-menopausal. 78 peri-menopausal and 291 post-menopausal. Oestrogen receptor status was positive (>200 fmol/g wet weight) in 64% (207 of 325 cases), and 43% (94 of 220 eases) were progesterone receptor positive (>200 fmol/g wet weight).

The histology of the tumour was infiltrating ductal carcinoma or infiltrating carcinoma (NOS) in 402 (80%), infiltrating lobular carcinoma in 72 (14%), and other histology in 26 (5%). Carcinoma-in-situ was seen in addition to the tumour in 230 (46%). Complete clinical \pm histological staging in 443 eases was as follows: Stage 1 (n=84). 2A (162), 2B (126), 3A (26), 3B (29) and 4 (16).

Initial surgery of the breast was mastectomy in 318 cases, quadantectomy / wide local excision in 147 cases, biopsy only in 13 cases, local excision in 9 cases and no surgery in 13 cases. Axillary node clearance was performed in 415 cases, nodes were sampled in 35 cases and not operated on in 60. Eighty patients (16%) had chemotherapy, 132 (26%) radiotherapy and 264 (53%) had tamoxifen.

The ten year disease free survival was 39% (including local recurrence) and the overall ten year survival was 63%.

C-MYC OVER EXPRESSION AS MARKER FOR PATIENTS AT RISK OF DEVELOPING BREAST CARCINOMA

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Activated cellular oncogenes may have a role in the pathogenesis of human malignancy. One such oncogene, c-myc, has been implicated in the control of cell division and differentiation of normal and malignant breast tissue. In a previous study we have demonstrated a similar incidence of c-myc over expression in patients with ductal carcinoma in situ and invasive ductal cancer when compared with normal breast tissue, thus suggesting that c-myc over expression may be an indicator of cell proliferation.

The aim of this study was to evaluate c-myc products in benign breast tissue of patients who subsequently developed breast carcinoma.

Materials and Methods. Group 1: Histological specimens of benign breast disorders; no subsequent breast cancer with mean follow up of 18 years (n=23).

Group 2: Histological specimens of benign breast disorders in patients who developed breast carcinoma 1 to 8 years later (n=21).

Group 3: Histological specimens of the breast carcinomas which subsequently developed in group 2 (n=20).

Specimens were stained using the indirect immunoperoxidase method with 9E10 monolconal antibody. Positive results were awarded for strong nuclear staining.

Results

Group	1	2	3
Number (%) of			
positives	3(13%)	13(62%)	12(60%)
-	p<0.0001	1 vs 2, & vs 3	

Conclusion: The study demonstrates a clear association between c-myc over expression and subsequent breast carcinoma. This over expression is not found in benign breast disorders of patients who do not develop subsequent breast carcinoma.

SESSION III

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INTRA-ABDOMINAL RECOMBINANT TISSUE PLASMINOGEN ACTIVATOR REDUCES POSTOPERATIVE ADHESIONS

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Postoperative adhesions have been attributed to reduced peritoneal plasminogen activator activity. This study evaluated high and low dose intraperitoneal (IP) recombinant tissue plasminogen activator (rt-PA) on adhesion formation and on anastomotic healing. Ninety male Sprague-Dawley rats were divided into 6 groups. Adhesions were induced in groups 1-4 using two established models. In groups 1 and 2, a 2 mm gallstone was placed in the upper abdomen along with 2 ml sterile bile. Group 2 animals received IP rt-PA (2.5 mg/kg). In groups 3 and 4, a one cm² flap of peritoneum was excised from the left lateral sidewall. Group 4 animals received IP n-PA (1.0mg/kg). In groups 5 and 6, the colon was divided 3 cm distal to the caecum and reanastomosed with 3/0 Polydioxanone suture. Group 6 animals recived IP rt-PA (2.5 mg/kg). Laparotomy was performed one month later and the incidence, site and grade of adhesions recorded. In groups 5 and 6, the anastomotic segments of colon were removed with a 2 cm cuff at each end, and tensiometry studies performed using a JJ Tensile Testing Machine.

Group	1	2	3	4
	Control	rt-PA	Control	rt-PA
Adhesion	12 (80%)	1 (7%)	9 (60%)	5 (33%)
X2 analysi	s p <	< 0.001	n	.s.

Tensile strength (mean \pm SD) in group 5 animals was 2.53 \pm 0.52 Newtons (N) and 2.98 \pm 0.8 N in group 6 (n.s.). The results of this study suggest that high dose IP rt-PA may reduce the incidence of adhesion formation without inhibiting anastomotic healing.

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MANAGEMENT OF HEPATIC SECONDARIES FROM COLORECTAL CANCER (CRC). ARE WE DOING ENOUGH?

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Of the 1669 new cases of colorectal cancer diagnosed each year in the Republic of Ireland, approximately 300 (15-25%) will have liver secondaries at the time of initial presentation. Of these an estimated 27% are amenable to surgical resection and there is sufficient evidence (Adson et al) to show that a significant number of such patients will benefit from liver resection with improved survival rates of 25%. Without surgery survival is on an average 8 months. Heald et al. have shown that the current surgical practices among consultants treating such patients is varied in the United Kingdom. In an effort to determine if a consensus exists between consultant surgeons in the Republic regarding methods of screening, diagnosis, treatment and follow up, an anonymous postal survey of current surgical practice was undertaken. Questionnaires were sent to 76 General

and Hepato-biliary surgeons, resulting in a 79% response rate. All surgeons currently treat patients with CRC, seeing a mean of 25 patients annually, of which approximately 20% present with liver secondaries at initial presentation. Pre-operative screening is undertaken by 92%, employing LFT's (39%), ultrasound (59%), CT scanning (24%) and tumour markers (31%). Intraoperative screening is employed by 96% of the surgeons. 31% of the consultants perform liver resections personally while 10% refer these patients to tertiary centres. Chemotherapy as a method of treatment is employed by 76% of surgeons. Postoperative screening is employed by 95% using LFT's (56%), ultrasound (77%), tumour markers (35%) and CT scanning (16%) of cases.

Conclusion: In view of this survey we conclude that despite available evidence in favour of surgical treatment in patients with liver secondaries from colorectal cancer this option is not being as widely employed, in the Republic of Ireland, as perhaps it should be!

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LAPAROSCOPIC NISSEN FUNDOPLICATION

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The Nissen Fundoplication (NFP) is well established as a surgical treatment for refractory gastro-oesophageal reflux disease (GORD). Recent advances in laparoscopic technique permit extensive dissection and suturing with minimal surgical invasiveness. To demonstrate the suitability of a laparoscopic approach to NFP, we report our experience with 8 patients who underwent the procedure. Six patients were male and 2 female. Mean age was 44 (±12) years. Mean duration of symptoms was 2.5 (±1.3) years. Surgical indications included benign peptic stricture (n=2), regurgitation (n=3) and severe reflux symptoms refractory to Omeprazole (n=3). Pre-operative assessment included endoscopy and biopsy, 24 hour PH monitoring, oesophageal motility studies and barium swallow. Seven of the 8 procedures were successfully completed laparoscopically. One patient was converted to open operation following initial laparoscopic dissection. The mean anaesthesia time was 220 (±40) minutes. The mean post-operative stay was 3.4 (±0.8) days. All 8 patients experienced symptomatic improvement at 6 month follow up. Four patients who underwent post-operative PH and motility studies confirmed normal PH profile and lower oesophageal sphincter tone.

We conclude that laparoscopic Nissen Fundoplication is a technically feasible, safe and effective anti-reflux operation.

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LAPAROSCOPICALLY ASSISTED COLONIC RESECTION

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Laparoscopic colectomy has been shown to be technically possible though time consuming and expensive. This unit has had extensive experience in the laparoscopic management of a variety of intra-peritoneal pathologies. This study investigates a realistic role for laparoscopic techniques in colon resections.

Over an 18 month period, eight patients were scheduled for

laparoscopically assisted colonic resection comprising: right hemicolectomy (3); left hemicolectomy (2); anterior resection (2); and abdomino perineal resection (1). Following establishment of a pneumoperitoneum an umbilical port was placed for visual examination of the peritoneal cavity. Four quadrant ports were then placed sequentially. Full mobilisation of the colon onto its mesentery was then accomplished including mobilisation of the hepatic and splenic flexures as appropriate. A short transverse incision was then placed to allow delivery of the mobilised tumour and colon. This enabled resection and anastomosis to be performed with ease whether hand sewn or stapled (anterior resection). One patient was found to have a frozen pelvis and loop colostomy was performed. In one obese patient for left hemicolectomy the anatomy could not be clearly identified and the abdomen was formally opened. One patient with myaesthenia gravis had a right hemicolectomy with endotracheal intubation or formal muscle relaxation.

We emphasise a number of points: (i) the operating time is doubled when compared with standard open surgery, (ii) early gut recovery and patient mobilisation is universal though not necessarily associated with earlier patient discharge, (iii) accurate tumour localisation and screening for synchronous lesions by pre-operative contrast studies is essential when employing this technique.

This early experience encourages us to continue to explore the techniques of laparoscopically assisted colonic resection.

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LAPAROSCOPIC-ASSISTED COLECTOMY: IS IT A FEASIBLE ALTERNATIVE?

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Laparoscopic-assisted colectomy is the most recent addition to the large number of accepted laparoscopic procedures which are now in widespread practice. In this study we report on 12 cases of laparoscopic-assisted colectomy carried out since the introduction of this technique in our hospital in January 1993. Twelve patients (7 men, 5 women, age range 33 - 73 years) who required elective colorectal excision were admitted to hospital for this procedure. Five patients had surgery for inflammatory bowel disease (proctocolectomy and ileostomy n=4; sigmoid colectomy n=1), five patients had anterior resection for rectal carcinoma and two patients had anterior resection for rectal prolapse. In all cases the principles of "open" colorectal surgery were adhered to with special reference to inferior mesenteric artery ligation and identification of the ureters. Two-handed laparoscopic techniques were ulilised using 12mm disposable trocars (ENDO-PORT, Autosuture) through which a variety of dissecting and grasping instruments were introduced. The ENDO-GIA 30 stapling device was used in all cases to divide the bowel as well as ligating major blood vessels. The mean operating time was 222 minutes with a range of 165-300 minutes representing our learning curve. There was no mortality, and morbidity included one wound infection, one chest infection and in one case the late (14 days) development of a colo-vaginal fistula. Two patients had to be converted to open operation, one due to unclear anatomy and a second because of the presence of undetected liver metastases. Per-operative blood transfusion was a mean of 3 units (range 0-13). Two of the 12 patients were ventilated for 24 hours post operatively. In the cases of rectal carcinoma pathological assessment of resected tumour showed a satisfactory clearance. In all patients in which an anastomosis was performed (cross-stapling technique) a gastrograffin enema was found to be normal at 7 days. Mean hospital stay was 18.3 days (range 7-33 days) with the cases of inflammatory bowel disease being responsible for lengthy stays. We conclude that laparoscopic-assisted colectomy can be peformed safely with a substantial patient benefit which increases with the number of cases performed. In relation to oncological acceptability in the patients with carcinoma, larger numbers and a longer follow-up will be necessary belore making a decision on widespread acceptance of this procedure.

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AUDIT OF ONE YEAR'S CHOLECYSTECTOMY PRACTICE AT MAYO GENERAL HOSPITAL

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One hundred and thirty two patients had cholecystectomies performed over a one-year period at Mayo General Hospital. Eighty five (64%) had a laparoscopic procedure attempted while forty seven (35%) had open cholecystectomy. Eight (9%) of eighty five who had laparoscopic cholecystectomies attempted were converted to an open procedure. The morbidity following both procedures is documented in Table I.

Table I

Laparoscopic Cholecystectomy Open Cholecystectomy

(1)	N=85)	(N=47)
Mortality	_	_
Conversion	8	_
Respiratory Dysfunction	7	3
Bile Leak	1	-
Haematoma	2	_
Mean Hospital Stay (Days)	3	7

Morbidity is higher following laparoscopic cholecystectomy relative to open procedures Audit has demonstrated that the majority of the morbidity is related to dissection at the livergallbladder interface. Accuring from this audit we have developed a multifunction instrument to offset this morbidity.

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THE SAFETY AND ACCURACY OF INTRAVENOUS CHOLANGIOGRAPHY IN A DISTRICT GENERAL HOSPITAL – A RETROSPECTIVE STUDY

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Intravenous Cholangiography (I.V.C.) has been advocated pre-operatively, particularly since the introduction of laparascopic cholecystectomy. It has not gained favour in some centres owing to poor image quality and a fear of contrast reaction.

Of the 109 I.V.C.'s performed in our hospital from January 1989 to April 1993, 106 case notes were studied, only one I.V.C. was unsuccessful in a cirrhotic patient. Patients ages range from 20 to 82 with a mean age of 60; 76 patients were female. Meglumine Iotroxate (BiliscopinShering) contrast was used in

all patients. Only two patients (1.8%) had minor reactions of periorbital oedema and thrombophlebitis.

Indications for I.V.C. included recent acute cholecystitis, a hisory of jaundice, a history of pancreatitis and post cholecystectomy pain.

Of the 105 successful I.V.C.'s, 64 proceeded to cholecystectomy (24 laparoscopic and 40 open). The remaining 41 did not have surgery owing to medical unfitness, normal investigations, postoperative investigations and various other reasons.

Sixty-three of the 64 who had surgery were found to have stones in the gallbladder (there was one case of cholesterosis). I.V.C. suggested 42/64 (65.5%) cases had stones in the gallbladder and of 44 Ultrasound scans (U.S.) performed 38 (86%) suggested likewise.

Of the 64 operative cases 11 had exploration of the ducts following I.V.C. and Per-operative Cholangiogram (P.O.C.). Of the 11 ducts explored 8 were found to have stones. I.V.C. suggested a total of 12 to have duct stones and 5 of these were verified by exploration. Of 21 P.O.C. 7 suggested duct stones and all of these were verified by exploration. Of the 64 operative cases there were 3 false negative I.V.C.'s (4.5%) and 4 false positive (6%).

Conclusion: We conclude in our small series that I.V.C. is safe from contrast reactions and accurately diagnosed common bile duct stones in 62.5% of cases.

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INVESTIGATION AND MANAGEMENT OF BENIGN BILIARY STRICTURES AND FISTULAE

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The management of benign biliary strictures and fistulae continues to represent a difficult problem. This study presents the experience of one referral hospital which investigated 15 such cases.

There were 11 female and 4 male patients (age range 22-76 years). The usual clinical presentations included right upper quadrant pain, jaundice, fever and chills.

Stricture or fistula aetiology was iatrogenic in 13 cases, pancreatic in 1 case, and due to sclerosing cholangitis in 1 case. Among the iatrogenic group, 6 patients had attempted repair of the stricture/fistula prior to referral to this unit. The previous unsuccessful repairs included Roux-en-Y Hepaticojejunostomy (4), Roux-en-Y Choledochojejunostomy (2), Hepaticoduodenostomy (1) and Longmire procedure (1). Two patients had more than one previous repair.

The diagnostic imaging studies performed in the pre-operative assessment included Percutaneous Transhepatic Cholangiography (10), E.R.C.P. (7), and H.I.D.A. scans (5).

One patient was treated by percutaneous transhepatic balloon dilation. The remaining 14 patients had surgical correction of the stricture or fistula. Twelve patients had a Roux-en-Y hepaticojejunostomy performed, one each a Choledochoduodenostomy and a Choledochocholedochostomy. There were no operative deaths. Post-operative complications included wound infection, septicaemia and one biliary leak. The range of followup has been 1 month to 4 years. Treatment is successful where the patient is asyptomatic and has normal L.F.T.'s or improved from pre-operative levels.

The patient who underwent percutaneous transhepatic balloon dilation has had a good result with short follow-up. Of those

treated surgically, one patient had recurrent episodes of cholangitis and developed secondary biliary cirrhosis.

Benign biliary strictures and fistulae are iatrogenic in most cases. Therapeutic approaches include non-operative procedures. The risk of recurrence requires that longterm follow-up is essential.

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EARLY EXPERIENCE WITH THE ANGIOSCOPE

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The use of intraluminal endoscopy or angioscopy is increasingly becoming a recognised tool in the field of vascular surgery.

Since the introduction of the video assisted angioscope to our unit in February 1993, we have performed 10 infra-inguinal vascular procedures in 10 patients using this technique: There were four above knee femoral-popliteal in situ vein bypasses, one below knee femoral-popliteal in situ vein bypasses, one below knee femoral-popliteal in situ vein bypasses. The indications for use of the angioscope in these cases was assessment of the patency of the vein graft, direct vision valvotomy and accurate identification of venous tributaries. In one case, angioscopic assessment of the vein graft showed the calibre of the vein to be unsuitable, despite preoperative Duplex scanning which suggested the vein was of adequate size. In a further three cases, the angioscope was used to assess the distal vessels following femoral artery thrombectomy (n=2) and to assess the distal anastomosis following a PTFE femoral-popliteal bypass.

There were no post operative complications directly attributable to the use of the angioscope in our experience. The obvious advantages of this technique include the accurate assessment of the calibre of a potential vein graft, the facility of direct vision valvotomy and the avoidance of an extensive thigh wound to isolate venous tributaries. Post operative Duplex scanning showed no evidence of AV fistulae in any case.

We conclude that the use of the angioscope provides an accurate adjunct to open vascular cases while providing all the advantages of minimally invasive endoscopic surgery.

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NEW TRENDS IN THE EVALUATION AND TREATMENT OF CAROTID ARTERIAL DISEASE

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Indications for carotid endarterectomy have become more clearly defined as a result of prospective studies confirming its benefits in patients with high grade symptomatic carotid stenosis. Similarly, duplex scanning is now being used more frequently in the investigation of carotid stenosis.

In order to determine whether these developments have led to a change in the investigation and management of carotid disease, we have evaluated referral patterns, investigative techniques and surgical indications in the last 100 carotid endarterectomies performed over a 4 year period.

Between 1989 and 1993, 93 patients (62 Male 31 Female; Mean Age = 65 years; Range 48-88 years) underwent 100 consecutive carotid endarterectomy operations.

No. of Operations	1989- 1991 48	1992- 1993 52
Indication for Surgery		
Symptomatic:		
<50% stenosis (Duplex)	3	0*
50-79%	12	13
80-99%	29	32
Asymptomatic/Contralateral Symptom	atic	
Disease		
<50%	0	0
50-79%	0	0
80-9 <u>9%</u>	2	1
"True" Asymptomatic		
<50%,.	0	0
50-79%	0	0
80-99%	3	4
Pre-op Angiography	40 (83%)	23(44%)**
Referral: Vascular Surgeon	31(64%)	16(31%)+
Physician	9(19%)	7(13%)
Outcome		
Transient Neurological Deficit	2	2
Permanent Neurological Deficit	3	1
Mortality	1	0

^{*} p<0.05 **p<0.05 +p<0.05 Chi-square test.

One patient developed a transient neurological deficit during carotid arteriography which resolved without sequelae.

These results indicate that the number of carotid endarterectomy operations being performed has increased. They also show that the number of angiograms performed prior to surgery has significantly decreased. The indications for surgery have also changed with significantly fewer operations being performed for less severe symptomatic stenoses. The trend towards the more selective use of pre-operative angiography appears to have been adopted to an equal extent by both referring physicians and operating surgeons. This approach towards less invasive investigative procedures and more specific surgical indications would not appear to have a deleterious effect on outcome.

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FIFTEEN YEAR AUDIT OF CAROTID ENDARTERECTOMY

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Both the North American and European carotid studies have found that surgery is the treatment of choice in symptomatic patients with high grade internal carotid artery (ICA) stenosis when surgical mortality and morbidity is less than 5%. For this reason surgical audit of carotid endarterectomy is essential.

409 CEA's were performed on 382 patients over a period of 15 years extending from 1978-1993. There were 262 males (64.8%) and 120 females (35.2%) with a mean age of 64 years (45-88). Atherosclerotic risk factors included increased blood pressure in 170 pts (41.6%), tobacco use in 339 pts (82.9%) while 23 (5.6%) were diabetics. 96 pts (23.5%) had a background of IHD.

Indication for operative intervention were stroke in 22.7%, TIA's in 58.4%, amaurosis fugax 6.6% while 4.6% had symptoms of vertebrobasilar insufficiency. The remaining 6.8% were asymptomatic with high grade stenosis of the ICA. 235 proce-

dures were performed under general anaesthesia, the rest under local.

Intraluminal shunts were employed in 174 cases (42.5%) while 28 arteriolomies were patched. Perioperative stroke occurred in 4 pts (1%) and 30 day mortality was 1.2%, all of which were cardiac related. Other post-op complications included TIA's (2.7%), 77% of which were ipsilerateral, transient cranial nerve palsies in 2.2% and wound haematoma in 1.7%. Postoperatively patients were reviewed at 1, 3, 6 and 12 months and annually thereafter. Mean follow up was 38.3 months. Late stroke occurred in 18 patients (4.47%) of which 14 (78%) were ipsilateral.

Duplex ultrasound scanning was performed on follow-up and this reveals restenosis in 65 patients (15.8%), 57 (87.7%) of which were asymptomatic.

CEA is a safe procedure when performed for symptomatic carotid artery stenosis with acceptable mortality and morbidity rates. Careful auditing of operative outcome and longterm follow-up is essential in order to establish a wider role of CEA in carotid artery disease.

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NEURO-VASCULAR FUNCTION IN PATIENTS WITH HAND-ARM VIBRATION SYNDROME AFTER CESSATION OF VIBRATION EXPOSURE - A PROSPECTIVE ASSESSMENT

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Hand-arm Vibration Syndrome (HAVS) is an occupational disease characterised by neurovascular dysfunction of the hands, resulting from repeated exposure to vibration over a prolonged period. The aim of this study was to prospectively assess the neuro-vascular status of patients who ceased working as a result of HAVS. Ten patients, were assessed prospectively to determine the extent of change in the initial neuro-vascular deficit. The interval between initial and subsequent testing was 10 months in all cases. The severity of the disease was staged according to the Stockholm workshop scale (S.W.S.) (vascular and neurological). Neurovascular status was assessed by vibrometry, aesthesiometry (depth and two point discrimination), dynamometry (grip strength) and digital rewarming after cold provocation.

	Initial ⁄Iedian	(Range)	ubsequent Median	(Range)
S.W.S. (Vascular)	1.5	(0-3)	2	(1-3)*
S.W.S. (Neurological)	1	(0-2)	1	(0-2)
Vibration threshold (mm)	1.06	(0.27-5.47)	0.85	(0.15-5)***
Depth perception (mm)	0.44	(0.18-0.8)	0.65	(0.18-0.8)***
2-pt discrimination (mm)	2.68	(0.58-5.38)	2.38	(0.35-4.79)**
Grip strength (L) (kg)	45	(28-50)	47.5	(36.5-66.5)**
Grip strength (R) (kg)	46	(29.5-63)	52.7	(42.5-61)
Rewarming time (L) (min	1.5	(1-15)	3.5	(1-14)***
Rewarming time (R) (min	1.5	(1-15)	4.5	(1-16)***

(Significance levels *p>0.05, **p>0.01, ***p>0.005, Wilcoxon)

The neurological deficit associated with HAVS may regress after cessation of vibration exposure, while the vascular deficit may progress.

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MEDIASTINOSCOPY: ITS ROLE IN SUPERIOR VENA CAVAL SYNDROME

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Mediastinoscopy is mainly used to assess the operability of carcinoma lung. Its role in the diagnostic work-up of Superior Vena Caval (SVC) Syndrome has been controversial, due to the fear of life-threatening haemorrhage and the delay caused in initiating prompt therapy.

A retrospective study of patients admitted with SVC syndrome was carried out. Thirteen patients of SVC syndrome underwent mediastinoscopy. Allhough other non-invasive investigations had revealed the site of SVC obstruction, mediastinoscopy was performed to obtain histological diagnosis. The mean age of the patients was 53.8 years. Male to female ratio was 10:3. Mediastinoscopy revealed malignancy in nine patients (69%). Three patients (23%) of small (oat) cell carcinoma, two patients (15%) of undifferentiated carcinoma, one patient (7%) of nonHodgkins lymphoma, one patient (7%) of squamous cell carcinoma, one patient (7%) of thymoma and one patient (7%) of germ cell tumor. Benign mediastinal fibrosis was diagnosed in three patients (23%). C.T. scans were performed on all patients. Superior venacavogram was performed only in the three patients (23%) of benign mediastinal fibrosis.

In all, mediastinoscopy provided accurate histological diagnosis in 12 patients (92%). One patient (7%) of idiopathic SVC thrombosis was diagnosed as thoracotomy. Rapid biopsy results enabled us to institute appropriate therapy early. Apart from a small wound haematoma, no other complication was encountered.

Thus, mediastinoscopy is not contraindicated in SVC obstruction. It is a quick and accurate investigation with a high diagnostic yield in experienced hands. In view of its low morbidity it should be carried out in the work-up of SVC syndrome if other lesser procedures failed to identify the lesion before blindly presuming a malignant cause and treating it.

SESSION IV

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NITRIC OXIDE ATTENUATES ISCHAEMIA-REPERFUSION INDUCED LUNG INJURY

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Limb revascularisation following aortic occlusion leads to lung injury dependant on activated neutrophil adherence. Nitric oxide inhibits neutrophil aggregation and adherence to endothelial cells. To determine in-vivo whether nitric oxide has a role in attenuating ischaemia-reperfusion induced lung injury, the effect of increasing or decreasing nitric oxide levels with L-NAME or SNP respectively, were evaluated in an aortic occlusion/lung injury model of 30 minutes ischaemia and 2 hours reperfusion (I:R). Sprague-Dawley rats (10/group) were randomized to controls; I-R; I-R treated with L-NAME (IOmg/kg); and I-R treated with SNP (0.4mg/kg) during reperfusion. Myeloperoxidase activity (MPO) measured pulmonary neutrophil influx. Pulmo-

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nary endothelial permeability was measured by wet:dry weight and bronchoalveolar lavage protein (BAL prot) and neutrophil counts (BAL PMN).

	Control	I-R	L-NAME	SNP
Wet:Dry Wt.	3.15±0.05	4.08±0.9*	5.±0.4@	2.8±0.2@@
MPO (u/g)	3.05±0.4	6.1±0.1**	8.9±0.7@	3.5±0.4@
BAL Prot (mg)	347±32	454±16*	581±40@@	330±61
BAL PMN	0.7±0.05	1.8±0.07**	2.7±0.16@	0.9±0.1@@

*p<0.05, **p<0.001 vs control; @p<0.05, @ @p<0.00I vs I:R. (Statistics by the unpaired Students t-test, values as Mean+SEM)

A significant increase in MPO activity and microvascular leakage was produced by I-R which was exacerbated further by administration of L-NAME. SNP therapy attenuated the I-R induced lung injury. These data suggest that nitric oxide in-vivo inhibits ischaemia-reperfusion induced lung injury, perhaps by inhibiting pulmonary neutrophil influx.

N-nitro-l-arginine methyl ester (L-NAME), sodium nitroprusside (SNP) ischaemia-reperfusion (I-R), myeloperoxidase (MPO), bronchoalveolar lavage protein and neutrophils (BAL Prot, BAL PMN).

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LUMINAL ADRENERGIC AGONISTS ACT VIA A LOCAL MECHANISM TO INFLUENCE ILEAL TRANSPORT

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Intestinal transport is controlled by neural pathways, hormones and luminal agents. Luminal adrenergic agents influence water and ion transport in the jejunum. This study tested two hypotheses: 1) luminal adrenergic agents influence ileal water, ion and glucose transport, and 2) these agents exert their effects locally and selectively.

Methods. Absorption studies (n=44) were performed on dogs with adjacent 25 cm ileal Thiry-Vella fislulas (TVF). Perfusion with 14C polyethylene glycol was used to calculate absorption of H_2O , ions, and glucose from the distal TVF. Experiments included three 1-hour periods: basal, luminal agonist infusion, and recovery. In group 1, agonists were administered to the distal TVF: norepinephrine (NE; α 1 > α 2 & B); phenylephrine (PHE: a1); clonidine (CLON; α 2); isoproterenol (ISOP; B). In group 2 the agonists were administered to the proximal TVF.

Results. Expressed as the change in absorption (ΔA) between the basal and infusion hrs in group 1: *p<0.05 by ANOVA.

Infusion	(n)	Dose	$\Delta A H_2O (ml)$	ΔA Glucose (mg)
NE	(n=8)	10 μg/min	+7.0±2.2*	+2±2
PHE	(n=8)	7.6 µg/min	+5.8±2.4*	+3±4
CLON	(n=8)	10 μg/min	-7.6±2.1*	-48±8*
ISOP	(n=8)	10 ug/min	-6.+3.3	-4+6

+ indicates increased absorption, - decreased absorption.

There were no changes in absorption in group 2, and no changes in heart rate in either group. Ion absorption paralleled H_20 absorption.

Conclusions. Luminal adrenergic agonists modulate ileal transport via a local mechanism. Inhibition of glucose absorption is selectively mediated via the α_2 receptor. Luminal proabsorptive α_1 agents may prove useful in pathologic secre-

tory such as intestinal transplants, diabetic diarrhoea or diarrhoea-associaled endocrinopathies.

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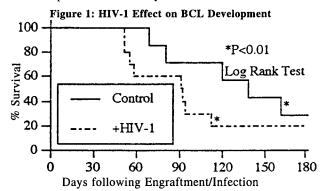
HIV-1 ENHANCES THE DEVELOPMENT OF EBV-INDUCED B-CELL LYMPHOMA IN VIVO.

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Individuals infected with Human Immunodeficiency Virus Type 1 (HIV-1), the causative agent in the Acquired Immune Deficiency Syndrome (AIDS) are at increased risk of developing aggressive lymphoproliferative disease (LPD) including highgrade B-cell lymphoma (BCL). Epstein-Barr virus (EBV) is implicated in the pathogenesis, following immunosuppression by HIV-1. Recent evidence, however, suggests a direct role of HIV-linB-cell transformation. Severe Combined Immunodeficient (SCID) mice develop human BCL following engraftment with human peripheral blood leukocytes (PBL) and infection with EBV. The ability of HIV-1 to enhance the development of EBV-induced BCL in this model was studied.

SCID mice were engrafted by intraperitoneal inoculation of $50x10^6$ PBL from 3 EBVseropositive donors (latent EBV infection; 10 mice per donor). Five mice in each group were infected with HIV-1 by pre-incubation of PBL with HIV-1IIIg (T-cell tropic virus; 10^6 infectious units/1 ml) for 2 hours prior to engraftment. Mice were monitored daily and killed when weight loss of $\geq 40\%$ occurred in combination with palpable abdominal tumours, or after 180 days (D). The day of sacrifice was taken as the end-point for each assay.



71.5% of mice (15 mice; 3 donors) engrafted with PBL containing EBV-latently infected B-cells (Fig. 1: Control) developed human BCL al a median of 119D following engraftment (range: 68-161D). 80% of HIV-1 infected mice (15 mice; 3 donors; Fig. 1: +HIV-1) developed BCL, at a median of 73.5D (range: 50-112D).

Mortality data within and between categories were compared for statistical significance using the Log Rank Test. There were no significant differences between donors in either category. Data from all mice in each category were used to construct mortality curves. Statistical significance is shown.

The SCID mouse provides an *in vivo* model of BCL associated with immunosuppression. In this model, HIV-1 infection led to statistically significant enhancement of BCL development. Possible mechanisms include the effects of cytokines or extracellular HIV-1 gene products elaborated by infected T-cells of cytokines or extracellular HIV-1 in the transformation of B-cells. Further elucidation of the mechanisms underlying the pathogenesis of B-cell lymphoma associated with immunosuppression may lead to the development of strategies

for the prophylaxis and treatment of this often fatal condition in the expanding population of patients with AIDS.

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RECOMBINANT ALPHA-1 ANTI-CHYMOTRIPSIN ATTENUATES THE LUNG INJURY ASSOCIATED WITH LIMB ISCHAEMIA-REPERFUSION

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Limb revascularisation following aortic occlusion may lead to a lung injury similar to the adult respiratory distress syndrome (ARDS). Activated neutrophils may play a central role in the pathogenesis of this lung, with neutrophil infiltration and associated tissue injury evident on histology. This neutrophilmediated tissue injury may result in part from an imbalance between leucocyte proteases such as elastase and cathespin-G. and endogenous proteases inhibitors.

Alpha-1 antichymotrypsin (ACT) is an endogenous serine protease inhibitor which neutralises leucocyte proteases and inhibits neutrophil degrangulation and chemotaxis. The aim of this study was to evaluate the role of recombinant ACT (rACT) in reducing the lung injury associated with limb ischaemiareperfusion, in a model of aortic occlusion (30 min) followed by reperfusion (120 min). Aortic occlusion was confirmed by Dopoler flow studies. Male Sprague-Dawley rats were randomised into three groups; control (n=9) treated with saline; ischaemiareperfusion (I/R) treated with saline (n=9); and ischaemiareperfusion treated with rACT (I/R+rACT) (n=8). Myeloperoxidase (MPO) activity, a haem containing enzyme specific neutrophils, was measured in pulmonary homogenates and used as a measure of neutrophil influx into pulmonary tissue. Lung parenchymal injury was assessed by light and electron microscopy (EM) studies. Pulmonary microvasacular leakage was evaluated by measurement of bronchoalveolar lavage protein (BAL). (Table, Mean ± SD)

	Control	I/R	I/R + rACT
	(n=9)	(n=9)	(n=8)
MPO (u/g)	3.05±0.4	6.1±0.1*	4.21±0.6†§
BAL (mg/ml)	347±32	454±16*	303±42†§
*=p<0.05 vs co	ntrol; †=0.05	vs control; §=1	<0.05 vs I/R

*=p<0.05 vs control; †=0.05 vs control; §=p<0.05 vs I/R Unpaired Students t-test

A significant increase in MPO activity was produced by I-R which was attenuated by rACT therapy. Recombinant alpha-1-anti-chymotrypsin therapy also significantly diminished the increase in pulmonary microvascular leakage seen after aortic occlusion and reperfusion. In addition, histological examination demonstrated that rACT therapy markedly reduced pulmonary tissue damage seen after I-R. These data suggest that the lung injury associated with ischaemia/reperfusion is neutrophil mediated and indicate a therapeutic role for recombinant protease inhibitors, such as alpha-1-antichymotrypsin.

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MYCOBACTERIUM PHLEI RESTORES IMMUNOCOMPETENCE TO IMMUNOSUPPRESSED BREAST CANCER PATIENTS

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Breast cancer is a disease that exhibits a wide range of

biological aggressiveness. Some present with early disease only to succumb quickly while some with advanced disease may survive many years. The reasons for this anomaly are unclear but it may in parts be due to the immune status of the patient at presentation. The aim of this study was to determine the cell mediated immune function of a small population of breast cancer patients at presentation and to investigate the possibility of modulating their immune response with a novel immunostimulant. The immunostimulant is a purified cell wall extract of Mycobacterium phlei (MCWE). Lymphocyte blastogenesis in response to the mitogens Phytohaemagglutinin (PHA) and Concanavalin A (Con A) was measured in 29 primary breast cancer patients and 10 healthy controls. The lymphocytes were separated from peripheral blood over ficoll and blastogenesis was measured in a scintillation counter after pulsing the cells with tritiated thymidine. MCWE was added to the cells in a dose of 5µg/ml. Mean blastogenesis in the control population was 27, 675 ± 2551 counts per minute (CPM). Addition of MCWE increased the mean blastogenic response to $52,393 \pm 4678$. Seven of the 29 patients (25%) were significantly immunosuppressed when compared to the control population with a mean blastogenic count of 15,803 \pm 2784 CPM, p<0.001. Blastogenesis was increased in this subpopulation to 41,266 ± 3675 with the addition of MCWE. In conclusion there exists a subpopulation of patients with breast cancer who are immunosuppressed at presentation. It remains to be seen whether these patients will prove to have a poorer prognosis. MCWE would appear to immunomodulate these patients and may have a role as an immunotherapeutic adjuvant in some patients with breast cancer.

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MERALGIA PARESTHETICA FOLLOWING LAPAROSCOPIC HERNIORRHAPY: AN ANATOMICAL ANALYSIS

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Laparoscopic inguinal hernia repair offers the benefits of earlier mobilization and return to work.

The efficacy, morbidity and long term outcome are however unknown. Thirty laparoscopic herniorrhaphies were performed by covering the defect internally with a mesh patch secured with staples. Two cases of meralgia paraesthetica, entrapment of the lateral cutaneous nerve of the thigh (LCNT) were encountered. Both patients required removal of the lateral clips which led to complete resolution of symptoms. We subsequently carried out an anatomical study on 10 cadavers examining the relationship between the LCNT and the internal/laparoscopic landmarks.

	°PT-LCNT	IEV-LCNT	DR-LCNT
Males	11.06 cm	7.18 cm	6.31 cm
Females	10.2 cm	6.09 cm	5.06 cm

These results demonstrate that the inguinal canal is 5 cm in length and the LCNT lies approximately 5 cm lateral to the deep ring. We conclude that mesh lengths of 6-8 cm are adequate to cover the defect and avoid lateral placement and entrapment of the LCNT. We have had no further cases of meralgia paraesthetica since adopting this practice.

°IEV - Inferior epigastric vessels

PT- Pubic tubercle

DR - Deep ring

TWENTY FOUR HOUR AMBULATORY MANOMETRY WITH pH DETECTS A HIGH INCIDENCE OF OESOPHAGEAL ABNORMALITIES IN PATIENTS WITH TREATED CORONARY ARTERY DISEASE

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A recognised sequel of treated ischaemic heart disease is persistent chest pain despite normal cardiac investigations. There is an established association between coronary artery disease and oesophageal pathology. Investigation of such non cardiac chest pain has been unsatisfactory to date due to the low pick-up rate of stationary and short term ambulatory oesophageal manometry.

Eight patients with treated ischaemic heart disease underwent 24 hour ambulatory oesophageal manometry and pH plus ECG monitoring. Symptoms were correlated with the parameters measured.

Results. Six of the eight patients had pathological acid reflux with a mean DeMeester score of 50.4 (6.4), one had nutcracker oesophagus and one had a normal study. Seven of the eight patients reported a total of 63 pain events during the 24 hour study period:

Pain Events

No. of Events (n=63)
Reflux related 50 (79%)
Motility related 63 (100%)
Both reflux and motility related 50 (79%)

All seven patients that reported pain events during the study period had associated oesophageal abnormalities. The symptom index (% of events with an associated abnormality) was 100% in all these patients. One patient who had a normal study had 6 episodes of pain, all of which were associated with acid reflux events, even though his overall profile was within normal limits.

These data suggest that oesophageal reflux events or manometric abnormalities are a frequent cause of pain in patients with ischaemic heart disease. Even when the 24 hour profile is within normal limits brief periods of acid exposure may precipitate symptoms. Simultaneous twenty four ambulatory oesophageal manometry and pH produces a high diagnostic yield in patients with treated ischaemic heart disease and persistent chest pain.

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PANCREATITIS-INDUCED A.R.D.S. CAN BE AMELIORATED BY NITRIC OXIDE

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Nitric oxide (NO) is an endogenous vasodilator which also inhibits neutrophil activiation and adherence to endothelial cells. Inactivation of NO by superoxide anion released from activated neutrophils, inducing neutrophil-mediated microvascular injury, may be central to adult respiratory distress syndrome. We evaluated the effect of increasing NO, with sodium nitroprusside (SNP) and of decreasing NO levels with N-Nitric L-Argining Melhyl Ester (LNAME), on lung injury associated with pancreatitis (Panc.). Sprague-Dawley rats were randomised to controls (saline infusion) or caerulein-induced pancreatitis groups, which

were treated with saline, sodium nitroprusside (0.4mg/Kg) or L-NAME (10mg/Kg). Myeloperoxidase (MPO) was used to measure neutrophil infiltration in the lung. Wet:dry lung weights and broncholavage protein (BAL prot.) were used to measure pulmonary microvascular permeability. Caerulein (5mg/Kg/hr) induced pancreatitis in all animals with an increase in serum amylase from 1851±208 (control) to 4743.8±646 (pancreatitis), 5591±805 (L-NAME) and 4195±305.5 (SNP); p<0.005.

	Control	Control L-NAME	Panc	L-NAME	SNP
(Mean±SEM)	(n=10)	(n=5)	(n=10)	(n=10)	(n=10)
MPO (u/g)	2.08±0.5	3.01±0.5	6.79±0.5*	9.01±0.3°	2.54±0.4@
Wet:Dry Wt.	2.85±0.2	3.09±0.3	7.01±0.5*	11.96±0.6@	3.8±0.37@
BAL prot (mg)	347±32	352±29	2539±222*	3707±309§	1389±182§

* p<0.001 vs control, @ p<0.001, °p<0.005, § vs Pancreatitis (Students unpaired t-test)

These data show that pancreatitis induced significant pulmonary neutrophil influx and pulmonary microvascular leakage effects, which were attenuated by sodium nitroprusside and exacerbated by L-NAME. These data support the hypothesis that inactivation or endogenous NO may in part be responsible for the neutrophil mediated lung injury in pancreatitis and suggest a possible therapeutic role for nitric oxide.

N-Nitro-L-Arginine Methyl Ester (L-NAME), Sodium nitroprusside (SNP), Pancreatitis (Panc.), Myeloperoxidase (MPO), Bronchalveolar lavage prolein (BAL prot).

SESSION V

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HYPERPARATHYROIDISM IN MULTIPLE ENDOCRINE NEOPLASIA, TYPES I AND II

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Background. The surgical management of primary hyperparathyroidism (HPT) in Multiple Endocrine Neoplasia (MEN) syndromes remains controversial. This study attempts to define a therapeutic approach to MEN I and MEN IIa related HPT

Patients and Methods. Between 1970 and 1991, 124 patients had surgery for MEN related HPT. Primary cervical explorations were performed in 84 patients with MEN I and in 18 with MEN IIa. An additional 22 MEN I patients had reoperative surgery. All MEN IIa patients had concomitant thyroidectomy for medullary thyroid cancer.

Result. Compared to MEN I, MEN IIa patients had a lower serum Ca2+, and fewer symptoms and complications of hypercalcemia. Multiple gland disease was evident in 90% and 83%, respectively, of patients with MEN I and MEN IIa. Primary explorations in MEN I, resulted in surgical cure in 94%, persistent hypercalcemia occurring in 0% following subtotal resection compared to 17% following more conservative resections (p=0.005). Failure to identify all 4 glands at operation resulted in a 19% failure rate compared to 3% when all glands were seen (p<0.05). In MEN I, 10 year cumulative recurrence rates were 17% for subtotal resections and 14% for conservative resections. In contrast, all MEN IIa patients, whether treated by subtotal or

conservative resections were cured postoperatively and none recurred over a median follow-up of 5.8 years.

Conclusions. In MEN I the surgical principles should be (i) Identification of all 4 glands, (ii) Subtotal resection to ensure cure and to facilitate possible reoperation and (iii) Excision of supernumerary thymic glands. In MEN IIa we should identify and resect all enlarged glands for cure, but routine subtotal resection need not be performed as recurrence is rare.

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CHANGING TRENDS IN THE MANAGEMENT OF PHAEOCHROMOCYTOMA

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Phaeochromocytomas are rare tumours which continue to pose considerable diagnostic and therapeutic challenges. This study reviews the experience at this unit with the management of phaeochromocytoma. Over a 14 year period (June 1978 to June 1992), 43 patients (14 male, 29 female; mean age 42 years) were referred for treatment of phaeochromocytoma. Biochemical confirmation of the diagnosis was by measurement of 24 hour urinary vallinylmandelic acid in 90% of cases. The imaging techniques used varied over the period under review: from 1980 onwards, venous sampling was replaced by CT scanning as the primary localising procedure. MIBG scintigraphy was employed in all patients between 1984 and 1987, but only in selected patients since then. Changes also occurred in the operative approach employed. Between 1978 and 1983 a midline or a flank incision was used, and from 1984 to 1992 a subcostal or a posterior (12th rib) approach was favoured in most patients. Operative (30 day) mortality was limited to one case. One patient died 24 months after operation with recurrent malignant phaeochromocytoma, and three patients died during follow-up from unrelated causes. The remaining patients have no evidence of recurrent phaeochromocytoma with a mean follow-up of 30 months, although four (9%) remain on antihypertensive medication.

Surgical treatment of phaeochromocytoma is safe and effective. CT scanning has emerged as the favoured technique for localising phaeochromocytomas. Greater confidence in the accuracy of localisation procedures allowed selected phaeochromocytomas to be removed safely through a posterior approach.

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SURGERY FOR HYPERPARATHYROIDISM IN GALWAY: A 10 YEAR REVIEW FROM 1982 TO 1991

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An audit of all patients who had surgery for hyperparathyroidism, in this unit, over a ten year period from 1982 to 1991, was performed. The presenting complaints, indications for surgery, operative procedure and post operative progress were analysed.

Of the 40 cases identified, 30 were female and 10 male. The mean age was 55.2 (2.5) years (mean (SEM)) with a range of 23 to 77 years. The most common presenting symptoms related to the renal tract (17 patients) while 8 patients were asymptomatic. Twelve patients had positive clinical findings and 8 had positive radiological signs of hyperparathyroidism. The mean preoperative serum calcium was 2.83 mM/L (range 2.06-3.48).

Histologically 29 patients had adenomas, 10 had hyperplasia and 1 had a parathyroid carcinoma. Of those with adenomas 10 had cell types identified. These were; chief cell 3 patients; clear cell 2 patients; and mixed cell 5 patients. One patient had 2 adenomas removed at operation.

The number presenting with primary and tertiary HPT were 27 and 13 respectively. Of the 27 patients operated on for primary HPT a single adenoma was found in 23 patients. Hyperplasia was found in 2 patients and multiple adenomas in one patient and a carcinoma was found in a further patient. Of the 13 patients operated on for tertiary HPT 8 had hyperplasia and 5 had adenomas.

Post-operatively 9 patients with primary HPT developed temporary hypocalcaemia and 2 developed permanent hypocalcaemia. Of the patients with tertiary HPT one developed temporary and one developed permanent hypocalcaemia. Five patients with primary HPT required re-exploration for persistent hypercalcaemia. Two patients with tertiary HPT had persistent hypercalcaemia.

The mean hospital stay was 14 days.

In conclusion, the result of this study show that the outcome of surgery for HPT in this centre are satisfactory and compare favourably with studies from other centres.

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SUBSTANCE P AND THE URETER

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Substance P (SP) nerve endings have been identified in the ureter, but no definite role has been established.

Ten adult mongrel dogs (12-20kg) underwent general anaesthesia and insertion of an indwelling nephrostomy. Five animals subsequently had a contralateral nephrectomy performed (Group 2). 20 weeks later urinary samples were taken from the renal pelvis via the indwelling nephrostomy. Distal ureters were then ligated and urinary samples taken thirty minutes later (animal care and investigations under licence).

Urinary SP concentrations were measured by RIA. Group 1 demonstrated a baseline secretion of SP of 0.871 ± 0.085 per 0. lml (mean \pm SEM). Group 2 had a higher baseline SP secretion (1.32 \pm 0.209). Following ureteric obstruction there were significant elevations in SP production. Group 1: 1.578 \pm 0.151 (p=0.001); Group 2: 1.872 \pm 0.304 (p=0.04). Ten isolated canine ureters were subsequently suspended in a standard water bath. SP was added in doses of 10 ng/ml-10 ug/ml and increased ureteric peristalsis was confirmed.

These data demonstrate that SP is released in response to ureteric obstruction and is shown to increase ureteric peristalsis. Thus SP may well have a central role in mediation of ureteric colic.

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ENDOTOXIN REGULATES EARLY HOST RESPONSE TO SURGERY

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Wound peptides regulate peritoneal immune function following surgery. Endotoxin (LPS) either endogenously derived from the gut or exogenously derived through the wound may also be

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involved. We hypothesized that intraperitoneal endotoxin plays a major role in regulating peritoneal immune responses following surgery. To evaluate this hypothesis 180 female CD-I mice were randomized to the following groups: control, laparoscopy with CO₂ inflation (no wound, no LPS), laparoscopy with air inflation (no wound, LPS exposure) and laparotomy (wound and LPS exposure). After 24 hours peritoneal cells were harvested and assessed for peritoneal immune function including macrophage (MO) function [superoxide anion (O₂-)]

Tumor necrosis factor (TNF) and Phagocytosis (Phago) of opsonized FITC candida] and surface Mac 1 expression [Ln Mean Channel Flourescence (LMCF)]. Neutrophil influx (PMNI) was also assessed. LPS translocation was assessed by a gavage technique using FITC LPS.

	O ₂ -(nmol/mg protein)	Mac 1 (LMCF)	TNF (pg/mg protein)	PMNI	Phago (%)	Gavage (LMCF)
Control	0.4±0.1	171±49	30±1	2±2	43±6	0±0
Laparoscop	y 0.6±0.2	159±12	40±10	15±4	41±3	0±0
(CO ₂)	1 4±0 2*	7712*	150±10*	24±10*	2712*	120125*
Laparoscopy (Air)	y 1.4±0.3*	//±3**	130110	24±10*	2112	128±25*
Laparotomy	2.0±0.5*	77±13*	190±20*	37±7*	16±3*	145±29

Stats=ANOVA with significance set al P<0.05. *=P<0.05 vs control.

Air inflation and laparotomy groups, i.e. those exposed to either exogenous or endogenous endotoxin show a significant increase in the translocation of FITC LPS as compared to Control and CO₂ laparoscopy groups. This is correlated with a significant increase in the peritoneal inflammatory response above that of the control and CO₂ inflation groups. However, there was a reduction in Mac-1 and phagocytosis. The absence of significant differences between air inflation and laparotomy groups indicates that LPS rather than wound factors is the principle mediator. These findings suggest that endotoxin plays a significant role in regulating peritoneal inflammatory responses in the early post-operative period and indicates a potential source of therapeutic intervention in the injured host predisposed to sepsis.

67 INTERLEUKIN-2 RECEPTOR EXPRESSION FOLLOWING BURN INJURY

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Background. Depression of cellular immunity, including failure of T-cell proliferation occurs following serious traumatic or thermal injury. While decreased IL-2 production following injury is undisputed, the status of IL-2R expression and activity in this setting is controversial.

Methods. In an attempt to resolve this controversy, with local ethical approval, 220 male A/J mice (n=22 per group) were subjected to a 20% scald burn injury or sham burn, sacrificed at 4, 7, 10, 14 or 21 days following injury and splenocytes harvested for in vitro studies. Parameters of IL-2R expression and function were assessed.

Results. Lymphocyte proliferation and IL-2 production were both consistently suppressed following burn injury to a maximum of 50% (p=0.016, t-test) and 60.1% (p=0.018) of sham

burns respectively at day 7. Addition of IL-2 to cultures of burned mouse cells restored the proliferative response to that of the sham burns at each time point, indicating the presence of functional IL-2R on burned mouse cells. IL-2R p55 chain mRNA expression in response to mitogenic stimulation was measured by Northern blot analysis at days 7, 10 and 14 and was unchanged in thermally injured animals. Phenotypic IL-2R p55 chain expression in stimulated cells, as measured by flow cytometry, was not changed at any time after injury. IL-2R function, assessed by binding of fluorescein labelled IL-2 to cell membranes was unchanged in burned animals on days 4, 7 and 21 and was increased by 117% (p<0.001) and 22% on days 10 and 14, respectively.

Conclusions. Thermal injury does not result in either quantitative or functional suppression of IL-2R. Thus the observed suppression of T-cell proliferation, following thermal injury, appears primarily related to abnormal IL-2 production.

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A NEW ERA OF EPILEPSY SURGERY

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Modem epilepsy surgery is one hundred years old. On 25th May, 1886, Victor Horsley, resected a post traumatic scar from the motor cortex of a 22 year old male and cured him of intractable seizures occuring more than 100 times a week. Wilder Penfield, revolutionised surgical thinking in 1947 with the publication of his temporal lobe series confirming the role of the amygdala and hippocampus in the genesis and propagation of temporal lobe seizures.

The last 10 years has seen an explosion in the surgical treatment of epilepsy. An additional epilepsy surgeon begins practice every 90 days in North America. This is the result of several factors. We now have sophisticated computerised seizure detection and monitoring technology. The technical advances in microsurgery, developed in the 1970's plus the appearance of the CUSA or ultrasonic aspirator has made epilepsy surgery safe and even easy. High performance CT scanning and magnetic resonance imaging now reveal otherwise undetectable small epileptic lesions.

The results of this surgical treatment of epilepsy in patients in Ireland has attracted International attention. More than 100 patients have undergone temporal lobectomy. The removal of the temporal neocortex only in 50 patients has established a unique category of patients with unilaterally anterior placed spike and wave seizures largely cured by surgery (REF). Twenty consecutive patients have had corpus callosotomy or split brain procedures in Dublin. Two thirds of these patients have had their devastating drop attacks converted to partial seizures. A significant number have had an unexpected reduction in their tonic clonic seizures.

The precise number of patients requiring epilepsy surgery in Ireland is unknown. Comparison with other western societies suggests up to 2,000 people in this country with intractable seizures would have their lives and the lives of their families radically altered by surgical intervention.

Reference

Keogan Et al. Temporal Neocorticectomy in Management of Intractable Epilepsy: Longterm Outcome and Predictive Factors. Epilepsia, 33(5); 852-861, 1992.

TRANS-THORACIC SYMPATHECTOMY - AN IMPROVED TECHNIQUE

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In this paper we describe our results with a new technique of transthoracic sympathectomy (TTS), which has been modified from the previously described transthoracic electrocautery (TTEC), in the treatment of hyperhidrosis.

The technique is as follows: Under general anaesthesia and with a double lumen tube in situ, the anaesthetist collapses the lung on the side to be operated on.

A cut-down dissection is performed over the fifth intercostal space in the mid-axillary line and the pleural cavity entered by blunt dissection.

The trochar is introduced without risk of pneumothorax and the telescope inserted and advanced over the apex of the lung.

Using a 5mm port in the second intercostal space in the midclavicular line, a probe is introduced to identify the sympathetic chain as it runs over the neck of the second rib.

Instead of simply cauterising this, a diathermy-scissors is used to cut and burn the chain under direct vision.

The lung is then allowed to reflate, the trochars are removed and the wounds closed.

Over a two year period, we have now performed this procedure 28 times on 16 patients. There were 13 females and 3 males with an age range from 15 to 37 years. Follow-up has been for a mean of twelve months (range 2 - 26 months), with no post operative complications. Three patients had a small pneumothorax which did not require drainage. There were no recurrences. In conclusion, this modified technique of transthoracic sympathectomy for treating hyperhidrosis is safe and effective.

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ABSORBABLE SUTURES IN TENDON REPAIR

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Synthetic absorbable sutures with greatly extended degradation times have been available for a number of years and are used extensively. Surgeons have been reluctant to use these materials in tendon repairs fearing a significant loss of tensile strength during the early critical phase of tendon healing. Polydioxanone (PDS) is a synthetic absorbable suture with an absorption halflife of six weeks for 0:0 gauge. The aim of the study was to compare the strength of tendon repairs using PDS with the commonly used non-absorbable prolene. We performed repairs on transected flexor digitorum longus tendons from the left hind leg of 28 rabbits. Half the repairs were with PDS, the others with prolene using a modified Kessler stitch. 40 rabbit cadaver tendons were available for tensile strength testing, 10 of which were transected and repaired with PDS, 10 repaired with prolene and the others left intact. Tendons were harvested at 3 days, 2 weeks and 4 weeks post surgery and tensile strengths obtained.

Tensile Strength	Intact n=20	Fresh n=20	3 days n=4	2 weeks n=20	4 weeks n=4
PDS	185.75	22.15		40.72	104.1
Prolene		17.0	19.26	35.25	95.5

By 4 weeks the repair strengths had increased dramatically due to a strong fibrous bond of tendon healing. By four weeks the contribution of the suture to the repair strength was negligible and therefore the inherent strength of suture material is only important before this time.

These results show that PDS repairs are as strong as prolene during the critical first four weeks of tendon healing with the added advantage of complete absorption within 180 days.

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THE CLINICAL ASSESSMENT AFTER PRIMARY DIGITAL NERVE REPAIR

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We have carried out a retrospective study on 88 digital nerve injuries (84 patients) who presented to the Department of Plastic Surgery in University College Hospital, Galway, between September 1989 and September 1991.

Surgery was carried out on 94% of the patients within 24 hours of the injury, using magnified loupes (X4.5) as no microscope was available.

Follow-up was done on these patients with a range of 8 to 32 months.

After clinical assessment using two point discrimination test, light touch test (Highet's method), stereognosis test, and sweating test, we had excellent results in 17% of our patients, good results in 51.1%, fair results were seen in 22.8% with 9.1% achieving poor results.

A close correlation between age and recovery of sensation has been confirmed as with smoking and nerve recovery. Results were better on nerves cleanly cut than for crushed nerves.

Magnified loupes gives a satisfactory result in nerve repair, and this study compares well with reported series.

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A SEASON OF FOOTBALL INJURIES - RUGBY Vs. SOCCER

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Sports injuries affect fit, young people and account for a small but significant proportion of the workload which attends A&E departments. Most of these are football injuries - both rugby and soccer. Our hospital has a large number of rugby clubs and schools in its catchment area and we decided to review and compare all rugby and soccer injuries which occurred during the 1992-3 season.

During the season, 871 footballers, equally divided between rugby and soccer, presented to the A&E department. School players accounted for 45% of rugby and 15% of soccer injuries. In soccer the goalie was the most injured player, with wingers the least injured. In rugby, the flanker was the most injured player, but other forwards and in particular the No. 8 was less likely to be injured than the backs. The referee only accounted for one injury.

With new laws in rugby, it was interesting that only 16 players were injured in scrums, and 24 in lineouts; 75 injuries occurred in rucks and mauls, 56 in open play and 254 from tackles; 12 werce due to violence. In soccer, tackling accounted for 228 injuries, jumping for the ball 100, open play 100 and violence 9. Slightly more injuries occurred in the first half of matches, and in the first half of the season, but these difference were not significant.

Significantly more rugby players had head injuries than soccer players (60 vs. 28: p < 0.001; test). None of these required more than 24 hour observation. Rugby players sustained 79 fractures, usually the clavicle and nasal bones; soccer players had 76 fractures, with hand/wrist and ankle fractures predominating. Thirty-one rugby and 28 soccer players had lacerations. Most injuries were classified as soft-tissue injuries - 276 in rugby and 314 in soccer. X-rays were performed in A&E on 87% of patients, 27% were referred to specialist clinics and 5% were admitted, with no differences between the sports.

In conclusion, in our area there are no significant differences in the number and severity of rugby and soccer injuries. Certain types of injury are more common in one type of football, but it could not be said that one sport was more dangerous than another. Whereas law changes in rugby have made some areas of the game safer, rucks and mauls are still a cause for concern. In soccer, jumping for the ball and tackling remain significant problem areas. Sports administrators need to be aware of these findings.

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OBSERVER VARIATION IN THE RADIOGRAPHIC CLASSIFICATION OF FEMORAL NECK FRACTURE

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We recorded inter and intraobserver variation in the classification of subcapital fractures of the femur by the Garden and Pauwels systems. Plain radiography of sixty patients were classified independently by four observers The observer variation was calculated by Kappa statistics which corrects the obtained values for the agreement expected by chance Observer variation was also assessed in the Garden system when lateral as well as an anteroposterior radiograph was used

With the Garden system on the first reading of the sixty anteroposterior radiographs, there was complete agreement in only 10 (17%), three out of four agreed in 31 (52%) cases of agreement with high intraobserver variation. On the second reading, there was no increase in the level of agreement with a small intraobserver variation. When the radiographs were classified using both an anteroposterior and lateral view, there was no significant improvement in the level of agreement.

Of note is that in sixteen of the sixty cases on the first reading, the disagreement in classification was so great by one or more observers that surgical excision of the femoral head would have resulted as opposed to femoral head salvage. With the Pauwels system, on reading of the sixty radiographs, there was full agreement in only four cases (7%), three of four observers agreed in thirty (50%) and only two of four observers agreed in twenty-six (43%) cases reflecting a significantly low level of agreement

This study has demonstrated that the intraobserver variation for both the Garden and Pauwels classification systems is unacceptably high, even though the observers were aware that the results would be analysed. In conclusion, we suggest that this observer variation be clearly borne in mind in clinical decision-making and assessment of intracapsular hip fracture literature.

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CASELOAD OR WORKLOAD - AUDIT OF A YEAR'S OPERATIVE WORK IN A REGIONAL ORTHOPAEDIC UNIT

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To assess the meaningfulness of a year's worth of audit relating to all the patients who went to the operating theatre, simple counting of the number of cases is not enough. To translate the caseload which is the actual number of cases into workload which is the quantity of work represented by these operations, all the operative procedures were weighed for complexity according to the British United Provident Association "Schedule of Procedures". Accordingly they were divided into grades of complexities from minor to complex. Each grade has a corresponding "Intermediate Equivalent Value" (I.E.V.) which was given to each procedure and the score was added to calculate the workload.

This analysis of all the operative work was done for one year (1992) for the definitive assessment of the workload for the unit as a whole and of all the four teams involved.

Also noted was:

- The number of cases which were (a) emergencies (b) urgent (c) scheduled.
 - Number of procedures out of hours.
 - Grade of surgeon.

Results. The total operative caseload for the year 1992 was 3504 as compared to the workload of 3176.45.

As the caseload of one team differed from the other the operative workload as measured in "Intermediate Equivalent Values" provided an accurate reflection of each surgical team.

- 7.1% of operative cases were true emergencies, 55.6% urgent and 36.6% elective.
- The consultants are doing the maximum no. of cases, in our study the average was 58.77%, whereas this figure for S.H.O.'s was 1.52%, the Registrar's doing the rest.
 - 25% of cases were done out of hours.

Conclusions

- Use of I.E.V. gives a more accurate assessment of the amount of work being done in theatre than a simple counting of case numbers and is to be recommended.
- The availability of a 24 hour theatre facility for trauma cases would be very beneficial and cost effective: only 7.1% of cases were true emergencies but 25% of cases were done out of hours because of the lack of theatre space during regular hours.

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CAN VENOUS FUNCTION OR SWELLING BE IMPROVED AFTER ANKLE FRACTURES

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Ankle fractures are frequently associated with prolonged limb swelling. This may be related to calf venous pump dysfunction which also occurs. Earlier mobilisation of the internally fixated limb or the application of a graduated compression stocking to the injured limb if immobilised in plaster may help to minimise these complications.

Air plethysmography was used to measure parameters of venous function - ejection volume fraction (EVF) and residual venous fraction (RVF) - immediately after surgery (week 0), and at 6, 12, and 18 weeks. Limb circumference was also measured at 5 and 10 cms from the lateral malleolus. Patients were randomised to standard immobilisation in plaster for 6 weeks (Group 1, N=10), or plaster immobilisation along with the application of a compression stocking (18mm Hg at ankle, 8mm Hg below knee) for 6 weeks (Group II, N=10). A group without plaster undergoing immediate mobilisation (Group III, N=7) was also analysed. The differences (A) between each group's fractured and non fractured (control) limbs were calculated for each parameter and compared between the groups at each time point. Data are expressed as Mean ± standard deviation.

		WEEK		
	0	6	12	18
^EVF (Gl) %	41.7±22.X	39.0±23.7	19.9±23.2	4.7±6.3
^EVF (GII) %	53.7±20.3	38.2±20.1	22.3±7.5	16.8±16.4
^EVF (GIII)%	49.8±26.9	31.9±18.6	13.8±10.5	11.3±13.6
^RVF (GI) %	64.6±21.4	42.2±13.2	16.5±17.2	11.4±10.2
^RVF (GII) %	65.9±28.3	60.5±21.3	26.0±11.X	22.7±22.4
^RVF (GIII) %	44.0±21.5	39.5±29.7	16.1±12.7	3.5± 5.9

Early mobilisation (GIII) did not significantly improve calf venous function in comparison to plaster immobilisation alone (GI). The addition of a compression stocking (GII) also failed to improve EVF or RVF in comparison to immobilisation alone. In contrast, the difference in limb circumference (at least 10 cms) between fractured and control limb was significantly less in the stocking group than in those treated by immobilisation alone both at 12 weeks: 0.37 ± 0.46 cms vs 1.03 ± 0.72 cms (p < 0.04 student's t test) and at 18 weeks: 0.45 ± 0.30 cms v 1.15 ± 0.72 cms (p < 0.03). Earlier mobilisation did not reduce limb swelling.

We conclude that limb swelling may subside more rapidly in the immobilised fractured limb if a compression stocking is applied while the limb is in plaster. The observed reduction in limb swelling in the absence of a corresponding improvement in calf venous pump function suggests that factors other than venous dysfunction are contributing to limb swelling following ankle fractures.

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200 ACUTE HEAD INJURY ADMISSIONS TO A NATIONAL NEUROSURGICAL CENTRE: TYPES OF INJURY, MANAGEMENT AND OUTCOME

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Head injury is the leading cause of death and disability for persons under thirty-five years of age. We reviewed the last 200 patients admitted to our Neurosurgical Unit (NSU) in order lo assess the types of injury sustained, the treatment administered and the final outcome. There were 150 males and 50 females with an age range = 1-83 years (mean = 28.4; mcdian = 22.5) of whom 57% were under the age of 25 years. Road traffic accidents

(RTA) accounted for 47% of all injuries (vehicle = 19%; pedestrian = 17.5%; motorcycle = 6%; bicycle = 4.5%). Falls accounted for a further 35% and assault = 7.5%. There was a history of alcohol in 29.9% of adult cases (43/144). Patients were admitted directly to the NSU as well as being transferred from all parts of the country; distance travelled (km); range = 0-255; mean = 72; median = 32. Duration (hours) from time of injury to arrival at the NSU; range = 1-288; mean = 26; median = 18. Fifty-four percent of injuries occurred at weekend and Bank Holidays. Patients were categorised according to the Glasgow Coma Scale (GCS) into mild (GCS = 14-15; 27.5%), moderate (GCS = 9-13; 23.5%) and severe (GCS = 3-8; 49%) head injuries. Forty-six percent were transferred intubated. Skull fractures were present in 48% of cases and ahother 15% with depressed fractures. Extracranial fractures were present in 19.5% and 3% had pneumothoraces. Computerised Tomography (CT) revealed cerebral contusions, acute subdural haematomata, extradural haematomata and cerebral edema in 24%, 19.5%, 17% and 10.5% respectively. Eight percent of CTs were normal. Fifty percent of cases had required no neurosurgical intervention, 16% required a craniotomy and evacuation of a haematoma, 12.5% had intracranial pressure (ICP) monitors inserted and 12.5% had elevations of depressed skull fragments. Ventilation was required for 107 (53.5%) patients (duration (days) = 1-26; mean = 5.9; median = 5) and tracheotomy in 8.5%. Intensive Care Unit stay required for 116 (58%) patients (duration (days) = 1-33; mean = 6.6; median = 5) and total hospital stay (days) for all patients (n=200) = 1-168; mean = 15.5; median = 5. The Glasgow Outcome Score was 5 = Full Recovery = 55.5%; 4 = Disabled (independent) = 16.5%; 3 = Disabled (dependent) = 7.5%; 2 = Vegetative = 3.5%; 1 = Death = 17%. In conclusion, we confirm that head injuries are most commonly associated with young adult males and with RTAs. Approximately half of neurosurgical head trauma transfers are classified as "severe" and these have major rehabilitation, medical, social and fiscal implications.

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CHRONIC SUBDURAL HAEMATOMATA AND HEAD INJURY IN THE ELDERLY

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The treatment of Chronic Subdural Haematoma (CSDH) constitutes a significant proportion of the neurosurgical workload. CSDH are most commonly found in the elderly population following trivial head injury. We reviewed CSDH treated in our Unit with emphasis on age, mode of injury, treatment and outcome. We reviewed a 100 consecutive cases of CSDH over a 26 month period. There were 68 males and 32 females with an age range of 14-89 years (mean = 69 years; median = 72 years). Headaches, confusion, hemiparesis were the commonest presenting symptoms (49%, 43% and 37% respectively). The duration of symptoms (weeks) was; range = 1-10; mean = 1.9; median = 2. Ninety-five percent of patients had gradual onset of symptomatology. A definite history of trauma was recorded in 58% of cases; fall = 44%; RTA = 13%; struck by an object = 1%(duration since trauma (weeks): range 1-48; mean = 9; median = 3). Confusion and hemiparesis were the commonest clinical signs (38% and 34% respectively) although 29% of cases had a normal neurological examination. Computerised Tomography confirmed CSDH with 48% having left sided haematomata, 34%

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right sided and 18% bilateral. All patients were treated with Burr hole evacuations (13% under local anaesthegia), one patient required subsequent craniotomy. Eighty percent had clinical improvement post-op, 12% had no change, 3% had clinical deterioration and there were 5 deaths unrelated to the surgery. Morbidity (n = 6) included subdural empyema, cerebrovascular accident, seizure, respiratory tract infection, cardiac failure, deep venous thrombosis. Hospital stay (weeks); range = 1-104; mean = 13; median = 10.

In conclusion, we confirm that CSDH is a condition primarily of the elderly. Gradual onset of neurological symptoms in the elderly - with or without a definite history of trauma - should alert the clinician of the possibility of a CSDH. Burr hole evacuation is a safe and effective method of management.

SESSION VI

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CAUSES OF LONG TERM RENAL ALLOGRAFT FAILURE IN THE CYCLOSPORIN ERA

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Chronic rejection is the greatest cause of graft loss in Prednisolone and Azathioprine treated renal transplant patients (Foster et al 1989). Cyclosporine reduced the incidence of acute rejection and results in improved 1 year transplant survival. Comparison of the effects of different immunosuppressive regimens on the development of chronic rejection in a single centre has not previously been published.

Between Jan. 1980 and Dec. 1991, 435 renal transplants were performed with a mean follow up (to June 1993) of 5.6 years. 211 patients received Pred and Azathioprine and 224 Pred and Cyclosporin. Chronic rejection is defined as a slow progressive deterioration in graft function occurring after a minimum of 6 months function, with histological changes of arterial intimal proliferation (Alexis Carrel Conference on chronic rejection, Riksganson, 1992). 125 (28%) grafts failed in the first 6 months and were excluded from subsequent analysis, since by definition they could not have developed chronic rejection.

There were 310 patients remaining at risk. 136 received Azathioprine and 174 received Cyclosporin based treatments. Brief details of graft outcome are shown in the table below:

	Azathioprine	Cyclosporin
Total patients > 6/12	136	174
Graft still functioning	70 (52%)	141 (81%)
Chronic rejection	27 (20%)	12 (7%)
Acute rejection	5 (4%)	1 (0.5%)
Death with functioning graft	18 (13%)	12 (7%)
Other causes	16 (11%)	8 (4.5%)

Further detailed analysis and life survival data will be presented to show the changing pattern of long term outcome in the cyclosporin era.

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FREE FLAPS - THE LEARNING CURVEH. Rowley, M. J. Earley, T. P. O'Dwyer.Mater Misercordial Hospital, Dublin 7.

In March 1992 we began to use free flaps as reconstructive procedures following excision of floor of mouth and tongue tumours. The aim of our study was to examine the effect of the learning curve using this procedure in our unit. Fifteen patients underwent free flap reconstruction to repair defects following head and neck tumour surgery from the period of March 1992 until May 1993. The type of flap used was either free radial cutaneous or free radial osseocutaneous in fourteen of our patients. One patient had a free jejunal graft. We reviewed our cases and looked at factors including flap type, number of teams involved in surgery and operating time. Post operative factors examined included complications, length of time to commencement of feeding and length of time in hospital. There was a decrease in the complication rate, the length of operating time and the length of stay in hospital over the period studied. Reasons for these improvements are discussed and useful technical points which contributed to these improvements are described.

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PERCUTANEOUS NEEDLE CORE BIOPSY OF THE RENAL ALLOGRAFT: A COMPARISON OF THREE DIFFERENT METHODS

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Percutaneous needle biopsy remains the gold standard investigation for acute renal allograft dysfunction. We studied three different biopsy techniques to determine the safest and most reliable for obtaining adequate samples of renal cortex: (1) Blind vertical pass (BVP) with kidney palpation and biopsy with 18G trucut needle; (2) Ultrasound guided automated biopsy (USG) using 18G biopsy gun (Bard, Crawley); (3) Ultrasound guided automated biopsy with immediate examination (US+IE) of the specimen using a stereoscopic microscope.

440 biopsy cores were obtained from 280 consecutive separate biopsy procedures. There were no significant differences in complication rates between the three methods.

Method of biopsy	No. of biopsy procedures	No. of biopsy cores	Renal tissue present	Renal cortex present	No. glomeruli per core
BVP	69	96	80	63	5.9 ± 0.9
USG	144	262	245	218	11.7 ± 1.1
IIS ± IE	67	82	76	70	9.3 ± 1.1

BVP technique produced significantly less cores containing renal tissue (p < 0.01), fewer cores contained renal cortex (p < 0.01) and there were less glomeruli per core (p < 0.01) compared with both the ultrasound guided groups. There were no significant differences in the success rates of the USG and US+IE methods.

This study demonstrates that ultrasound guided methods are more successful than the blind pass technique. The added use of immediate examination using a stereoscopic microscope allows a 100% success rate in providing renal cortical tissue for diagnosis at a single biopsy procedure.

MANAGEMENT OF CALCULI IN LOWER ONE-THIRD URETER

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Objectives:

This is a retrospective analysis of 90 cases who presented in University College Hospital, Galway, from 1989 to 1992 with renal colic and subsequently diagnosed to have stones in the lower one-third of ureter. The objectives were:

- 1. comparison of the success rate of various modes of treatment.
 - 2. mean hospital stay.
- 3. evaluation of urine microscopy in diagnosis of ureteric colic.

Results:

В.

ICCSUI	113.			
A.	Dormia basket extraction	43.3% (39 cases)		
B.	Expectant treatment	35.5% (32 cases)		
C.	Ureteroscopy	10% (9 cases)		
D.	Meatotomy of ureteric orifice			
	and removal of stone from bladder	5.5% (5 cases)		
E.	Double J-stent and subsequent PCNL			
	or ESWI	4.4% (4 cases)		

Injury to ureter during Dormia basket extraction, complete ureteric obstruction and persistent pain were the indications for ureterolithotomy.

Mean hospital stay - 4.4 days.

Open ureterolithotomy

Urine Microscopy:

1. RBC in urine 71.2% (64 cascs)
2. No RBC in urine 20% (18 cases)
3. No record 8.8% (8 cases)

Serum calcium was within normal range in 89 patients. One patient had hypercalcaemia who subsequently was treated for parathyroid adenoma.

Conclusion:

Most of the lower ureteric calculi are successfully treated by Dormia basket extraction and conservative treatment is also successful in a high percentage of cases. Others can be managed by ureteroscopy or meatotomy. Only a few of them require open ureterolithotomy.

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LONG TERM FOLLOW UP OF SURGERY FOR STRESS INCONTINENCE

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Most reports on surgery for stress urinary incontinence are based on relatively short follow up. Short term success rates of up to 80% are commonly reported but we wished to determine the long term results of surgery.

The results of 150 patients undergoing surgery for stress urinary incontinence over a sixteen year period were reviewed and adequate follow up information was available in 118.

Mean age was 42 years (range 14-84 years) with a mean follow up of 28 months (range 2-154 months).

Procedure Marshall	No.	Dry at 6/52	Dry on Long Term Follow up
Marchetti	67	62	46
Stamey	26	22	13
Lapides	20	17	10
PV Sling	5	4	4
Total:	118	105 (89%)	73 (62%)

89% of patients were dry at six weeks following surgery. Seventeen patients underwent further surgery and 13 of these were dry on long term follow up giving an overall success rate of 73%. 44% of patients complained of urgency necessitating medical treatment.

Our early results compare favourably with other series but later follow up shows prolonged observation is required to fully assess the results of surgery.

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4.4% (4 cases)

MUCOSAL METABOLISM IN ILEAL CONDUIT AND ILEOCYSTOPLASTY

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Construction of an ileal conduit or ileocystoplasty exposes ileal mucosa to an altered luminal ecology which reduces luminal metabolic substrate availability. Glutamine is the preferenlial metabolic substrate of small bowel mucosa whereas butyrate is that of colonic mucosa. The aim of this study was to determine whether construction of an ileal conduit or ileocystoplasty changes metabolic substrate affinity in ileal mucosa.

Four endoscopic mucosal biopsies (4-15 mg wet weight) were obtained from healthy ileum at right hemicolectomy (n = 7), functioning ileostomy (n = 11), ileal conduit (n = 6) and ileocystoplasty at cystoscopy (n = 6). Each biopsy specimen was placed in tissue culture and assayed for metabolism of 14C radiolabelled glutamine or butyrate in a medium containing both substrates. Results were compared using Students t test.

	Glutamine (5mM)	Butyrate (10mM)
Ileum $(n = 7)$	0.74 ± 0.23	1.5 ± 0.4
Ileostomy $(n = 11)$	0.59 ± 0.12	1.8 ± 0.4
Ileal Conduit $(n = 6)$	0.49 ± 0.06	1.2 ± 0.4
Ileocystoplasty $(n = 6)$	$0.26 \pm 0.03*$	1.1 ± 0.2
umol/mg wet wt/h		mean ± SEM

^{*} p < 0.05 compared to ileal conduit and ileostomy.

We conclude that metabolic substrate affinity is reduced in ileal mucosa exposed to a urinary ecology and that these changes are most marked in ileocystoplasty.

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PROVISION OF BACKUP ARTERIOVENOUS FISTULAE IN PATIENTS ON CAPD

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Backup fistulae are provided for continuous ambulatory peritoneal dialysis (CAPD) patients on the rationale that many will require emergency haemodialysis during severe peritonitis episodes or CAPD failure from other causes.

Arteriovenous fistulae (AVF) form a large proportion of the routine surgical workload in dialysis units. Backup AVF accounted for more than 50% of the fistulae performed each year in Nottingham.

A preliminary survey confirmed that 42% of renal units in the UK currently have a policy for providing CAPD patients with backup arteriovenous fistulae.

We audited 176 patients who started CAPD between 1986-9 and have shown that over a median follow up period of 4 years the majority of patients (73%) do not require haemodialysis.

Of the 153 backup fistulae formed in 114 patients only 10 were ever used for emergency haemodialysis. Twenty three other patients required emergency haemodialysis but when required their fistulae were no longer functioning. The mean fistula patency times for this study compare very favourably with other published series, with 1 and 3 year patency rates of 73% and 60% respectively.

Backup fistulae are still provided as a routine procedure in many units throughout the Britain. This study has shown that most fistulae are not available for emergency haemodialysis when required. 94% of fistulae were never used for haemodialysis. We consider that it is no longer justifiable to perform backup fistulae in CAPD patients.

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LAPAROSCOPIC APPENDICECTOMY - ONGOING PROSPECTIVE AUDIT OF 100 PATIENTS

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Introduction. A recent randomised trial has shown a significant advantage in terms of patient recovery after laparoscopic appendicectomy when compared with the open approach. Following this we adopted a policy of laparoscopic approach in all patients with an indication for appendicectomy. In order to assess ongoing safety and efficacy we reviewed all patients who have presented to our unit with suspected acute appendicitis since we commenced laparoscopic surgery. Data was collected prospectively and the indication, diagnosis, problems encountered, post operative recovery and follow up details were recorded.

Results. One hundred patients have now undergone laparoscopy for a pre-operative diagnosis of appendicitis. The final diagnosis was acute appendicitis in 81, Ovarian or tubal cysts in 9, pelvic inflammatory disease in 1, diverticular disease in 1, infarction of the omentum in 1, and nonspecific abdominal pain without objective pathology in 7. In 11 patients the appendix was left in situ and of the 89 resected 81 showed acute inflammation. The appendix was removed laparoscopically in 81 and 8 required conversion to an open approach. The reason for conversion was perforation with severe faecal soiling in 3, difficulty in mobilising the appendix in 4 and an altered diagnosis in one (cystic hygroma of the peritoneum). Patients requiring conversion to an open appendicectomy required a median of 7 days in hospital after operation compared to 3 days after successful laparoscopic surgery. Recovery rates after hospital discharge have been maintained with the median time to return to work at 9 days. Four patients have had significant complications. One developed aspiration pneumonia post operatively, 2 had prolonged pelvic peritonitis requiring extended hospital stay or re-admission, and one developed a recurrent appendicitis one year later. Two others required re-admission for abdominal pain that settled on conservative management and two had diarrhoea.

Conclusion. Laparoscopy for the operative assessment and treatment of acute appendicitis is applicable to all-comers provided that there is a low threshold for conversion to open surgery. Many problems encountered can be managed laparoscopically. The earlier discharge, and particularly the rapid return to normal activities shown in the randomised trial has been maintained.

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LAPAROSCOPIC OOPHORECTOMY: A METHOD OF ACHIEVING TOTAL OVARIAN ABLATION IN BREAST CARCINOMA

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Premenopausal patients with breast cancer benefit from ovarian ablation as adjunctive therapy. Over a one year period, since the introduction of this technique into this unit, nineteen patients have undergone laparoscopic oophorectomy, in order to achieve complete ovarian ablation. This procedure was performed in seventeen patients at the time of presentation with their primary tumour and in two patients following recurrence. The average age of patients was 41.5 ± 0.9 years (mean \pm SEM).

The procedure was performed using a standard laparoscope and camera, introduced via a subumbilical (lOmm) port following creation of a pneumoperitoneum. A 12mm operating port was placed in both the RIF and LIF. Oophorectomy/haemostasis was achieved using the Endo-GIA (USSCI) and diathermy haemostasis. The ovaries were delivered via the RIF and LIF ports.

Complications were minor. One patient, the first, required conversion to an open procedure. This patient also suffered from a minor wound infection. In addition a further patient had a bleed from a port site which required transfusion but not re-exploration. Follow up ranged from 2 to 14 months. Three patients experienced moderately severe menopausal symptoms, the remaining patients experienced minor symptoms. It is concluded that laparoscopic oophorectomy is a safe, minimally invasive and cost effective method of achieving total ovarian ablation.

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AQUA INJECTION ASSISTED DISSECTION (AQUAID) - A HELPFUL ADJUNCT AT LAPAROSCOPIC CHOLECYSTECTOMY.

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Fifty seven consecutive cholecystectomies were performed over a one year period, of which fifty five (96%) were completed laparoscopically. Eleven (19%) patients had acute cholecystitis. Nine (14%) had a mucocele. Seven (12%) had partially intrahepatic gallbladders. Morbidity was predominantly related to dissection at the liver-gallbladder interface, and included gall bladder perforation, bleeding from gallbladder fossa and biliary leakage. This resulted in conversion (n=2), Haematoma requiring drain-

age (n=2), Respiratory dysfunction (n=4), Bile leak (n=1) There was no mortality or bile duct injury.

We have analysed the value of aqua injection assisted dissection (AQUAID) at the livergallbladder interface. For thirty seven (68%) patients a bipolar electrocautery was used to dissect the gallbladder from its bed with related morbidity in 9 (16%) (Table I). A polyfunctional instrument (P.C.I. instrumente FRG) was designed in our unit and utilised for aqua injection assisted dissection at the liver-gallbladder interface at eighteen (32%) laparoscopic cholecystectomies, none of whom had any morbidity.

TABLE I

Morbidity	Electrocautery Assisted Dissection (N=37)	Aqua Injection Assisted Dissection (N=18)
CONVERSION	2	-
RESPIRATORY	?	
DYSFUNCTION	N 4	-
НАЕМАТОМА		
- Open drained	1	-
- Radiological drainage	1	-
Bile Leak	1	-

Aqua injection assisted dissection at laparoscopic cholecystectomy has significantly reduced gall bladder dissection related morbidity.

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MINIMALLY INVASIVE MANAGEMENT OF GALLSTONE PANCREATITIS

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Laparoscopic surgery has become the routine for elective cholecystectomy, but its place in the management of biliary pancreatitis has not been identified. We assessed the first 265 laparoscopic chlolecystectomies performed in our unit and identified 22 patients who presented primarily with pancreatitis, found subsequently to be gallstone related. The mean age of the pancreatitis group was 54 ± 17 years. All patients presented with abdominal pain. Five were jaundiced. Ranson score severity of pancreatitis averaged 1.8 (Range 1-6). Standard management was to perform Endoscopic Retrograde Cholangio-pancreatography (ERCP) when the clinical and biochemical markers had settled. The time interval between presentation, ERCP, surgery and discharge are shown (Table I).

TABLE I

	Presntation to ERCP	ERCP to Surgery	Surgery to Discharge	Total Stay
Median (Days)	8.9	4.5	4	16
Range	2-15	2-35	1-21	9-63

ERCP was readily available and did not delay surgery. It showed stones in the common bile duct in five patients. Spincterotomy was performed in six patients and all ducts were cleared with one exception with multiple common duct stones. With this exception all went on to laparoscopic cholecystectomy. One of these required conversion to laparotomy for cystic artery bleeding. There were no other complications. The majority of patients had multiple small stones remaining in their gallbladder and it was not possible to accurately predict the presence of common bile duct stones prior to ERCP. Mean post operative stay was short but longer than that for patients without pancreatitis (2 days). No patient developed post operative pancreatitis. This study shows that combined ERCP and laparoscopic cholecystectomy is an efficient, safe and effective minimally invasive mode of management for biliary pancreatitis.

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LAPAROSCOPIC CHOLEYSTECTOMY: NOT A BENIGN PROCEDURE

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Laparoscopy is a technique which has been in use since the early part of this century. Developments in optics and fibre-optic technology and the introduction of the micro-camera and videoscreen has further revolutionised this technique. It now enjoys widespread application in the field of general surgery and in particular for cholecystectomy.

A prospective study was initiated upon the introduction of laparoscopic equipment in 1990. One hundred and fifty patients were entered into the study. Re-usable equipment was employed (Storz). Prophylactic antibiotics and low dose heparin were routinely used. Two consultant surgeons performed the procedures. Each had completed a training course in Britain.

Complications occurred in 17.1% of patients and included the following: two deaths; one from a PE and the second due to CBD necrosis; one common bile duct injury; one urgent laparotomy for a cystic artery bleed after a clip slipped. 5.4% of patients required transfusion; 4.5% had acute retention or UTI's; 1.8% had atelectasis; 1.8% had large subdiaphramatic or suphepatic collections and 2.7% had subumbilieal wound infections; an overall conversion rate of 11% was recorded.

Problems from the instruments occurred in 3 cases; in two patients the grasper broke and in one patient the screw on the scissors came loose.

During follow up CBD stones were found in 1.8% of patients. In addition one patient presented 16 months post op with hepatic metastases.

In conclusion laparoseopic cholecystectomy is not without complications. Routine use of disposable instruments has shown to be unnecessary thereby reducing costs substantially. The technique was introduced without a randomised controlled clinical trial. It remains to be seen whether further complications such as late CBD stenosis will emerge with time.

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MINIMALLY INVASIVE THORACIC SURGERY

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Video Assisted Thoracic Surgery (VATS) spares the patient the morbidity associated with formal thoracotomy. It allows

excellent visualisation of the intra thoracic structures for both diagnostic and therapeutic procedures. With advances in technology and operator familiarity, the role of VATS has continued to expand.

Using Video thoracoscopic techniques in 52 patients, we have been able to perform 56 procedures. We have found the applications of this procedure to be diverse, being both diagnostic (27) and therapeutic (29). The diagnostic procedures included lung biopsy (10), intrapulmonary masses (11), mediastinal mass (1), pleural effusions (4), pleural biopsy (1) and were associated with a high specificity and sensitivity. It allowed accurate preoperative staging of lung cancer, particularly helpful in assessment of resectability in N2 disease. It also allows assessment of the disease process in patients with malignant pleural effusion.

The therapeutic procedures included pleurectomy and blebectomy (8), excision of emphysematous bullae (2), trauma (3), lung resections (7), pericardial window (1), ligation of a patent ductus arteriosus (2), closure of broncho-pleural fistula (1), drainage of an empyaema space (2), oesophageal resection (1), para oesophageal hernia repair (1) and evacuation of haemothorax (1). These procedures were associated with minimal morbidity and short hospital stay. There were no intraoperative complications in either group and we did not have to revert to formal thoractomy in any case.

While we have reservations concerning the use of VATS for resection of malignant disease, our experience indicates an expanding role for Video Assisted Thoracic Surgery and we list as its chief advantages; reduced morbidity, and shorter hospital stay together with a high diagnostic facility and an expanding therapeutic role in both pulmonary and oesophageal surgery.

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LAPAROSCOPIC HERNIA REPAIR USING AN EXTERNAL NEEDLE

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Laparoscopic surgery has broadened the surgical therapeutic options for the patient presenting with an inguinal hernia. Over a 12 month period we performed 32 laparoscopic indirect inguinal hernia repairs in 30 patients. Criteria for selection were, patients less than 45 years of age without previous ipsilateral hernia repair. The repair involved formal laparoscopic suturing of the internal inguinal ring using a hollow external needle, introduced through the anterior abdominal wall. The suture material is passed through the needle and an external laparoscopic knot technique used. The mean follow up was 10.7 months (range 4-12 months). Anaesthetic time (AT) (mins), postoperative hospital stay (days), morbidity and recurrence were noted.

Results were:

N	AT (mins)	MORIBIDITY	STAY (days)	RECURRENCE
32	75	0	1.8	1

There was one recurrence. These results indicate that laparoscopic management of inguinal hernias using this technique is feasible. However, while these early results are encouraging, a stringent clinical trial and long term follow up will be necessary before the role of this new surgical procedure is validated.

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LAPAROSCOPIC SURGERY - IS IT COST EFFECTIVE?

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Use of laparoscopic techniques in surgery is now widespread, however the cost effectiveness of these procedures remains unclear.

Aim:

The aim of this study was to evaluate the cost effectiveness in adopting new laparoscopic procedures and to assess the value of maximal use of available laparoscopic equipment in reducing overall cost of these procedures.

Methods:

Study 1: Cost analysis of laparoscopic surgery was evaluated in 46 patients undergoing laparoscopic cholecystectomy (LC) compared with 22 patients who had the open procedure (OC).

Study 2: The cost effectiveness of maximal use of laparoscopic equipment was assessed in 18 patients who underwent a diagnostic Laparoscopy. End points assessed included operative cost, mean operative time and post-operative time according to the equation: Minimal Access Surgery (MAS) + exp. Hi-tech. equipment = less post-operative hospital stay + less ward staff requirement + less physiotherapy.

Results:

Study 1: Patients were age and sex matched in each group and mean operative time was identical (73 mins). LC was associated with reduced post-op. stay (3.7 days = LC vs 8 days = OC) and reduced overall cost (£1288 = LC vs 2138 = OC), indicating a mean saving of £910 for LC vs OC.

Study 2: Maximal use of laparoscopy avoided unnecessary appendicectomy in 11 cases (£1320 per case) and unnecessary laparotomy in 4 cases (£1320 per case). In the remaining 3 cases laparoscopy lead to subsequent definitive surgery.

We conclude that laparoscopic cholecystectomy is cost effective and that there is a reduction of the overall cost of laparoscopic operations when equipment is maximally used.