

NATIONAL SCIENTIFIC MEDICAL MEETING 1995

Abstracts

ORAL PRESENTATIONS

IMMUNOLOGY

(O.1) CD8 $\alpha\alpha$ T LYMPHOCYTES IN HUMAN ADULT LIVER – EVIDENCE FOR EXTRATHYMIC T CELL DIFFERENTIATION

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Little is known about hepatic T lymphocyte subpopulations in the human liver. The aim of this study was to document the various subpopulations present in the liver and compare them to peripheral T lymphocytes in the same patients.

Normal hepatic tissue was obtained at time of transplant from five patients, and a single cell suspension of lymphocytes were prepared by standard methods. Cells were stained with monoclonal antibodies specific for CD8 α and CD8 β chains, CD4, CD8, CD3, $\alpha\beta$ TCR, and $\gamma\delta$ TCR, and analyzed by two and three colour flow cytometry.

Of the hepatic CD3+ cells, 71% were CD8+ and 25% were CD4+, with a CD4/CD8 ratio of 1:3 in contrast to the peripheral CD4/CD8 ratio of 2:1. 18% of the hepatic CD3+ cells expressed $\gamma\delta$ TCR. Significantly, CD8 $\alpha\alpha$ accounted for 27% [mean] of the total hepatic CD8+ population.

Conclusion: There is now evidence that the adult human gut can support extrathymic T cell differentiation. A significant population of hepatic CD8 $\alpha\alpha$ cells would suggest that the liver is also a site of extrathymic differentiation, which may have important implications for the understanding of autoimmunity and graft tolerance.

(O.2) LOCALISED INCREASE IN INTESTINAL $\gamma\delta$ TCR+ AND CD8+ LYMPHOCYTE POPULATIONS AND ENHANCED CLASS II ANTIGEN EXPRESSION: INDEPENDENT FEATURES OF COELIAC DISEASE

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Activated T lymphocytes may play a significant role in the pathogenesis of coeliac disease. Identification and quantification of T cell populations in subcompartments of the small intestine is now possible using flow cytometry.

The aim of this study was to examine phenotype and class II expression of CD3+ lymphocytes from the lamina propria and intraepithelial sub-compartments in patients with active coeliac disease.

Small intestinal biopsies were taken from 30 patients, 11 active coeliacs and 19 controls. A single cell suspension was obtained from the epithelial layer (EL), using chelating and reducing agents; the lamina propria (LP) was digested using collagenase. Cells were stained with antibodies specific for CD3, CD4, CD8, $\gamma\delta$ TCR and HLA-DR molecules and analyzed using flow cytometry.

Class II antigen expression was detected on a significant percentage of lymphocytes from normal small intestinal EL

(mean 34.87%; range 3.80-50.09) and LP (mean 20.60%, range 11.76-26.26). A significant increase was seen (mean 52.41%; range 22.78-86.34) in EL lymphocytes from active coeliacs when compared with controls. Class II antigen expression was similarly increased on lamina propria lymphocytes (mean 38.45%; range 14.39-68.76) when compared with controls.

T cell phenotypic studies showed an increase (mean 26.29%; range 14.58-51.80) in the CD3+ $\gamma\delta$ TCR+ population in the EL when compared with control patients (mean 9.57%; range 0-25.70). The $\gamma\delta$ infiltrate into the LP of coeliac patients was much less marked (mean 3.43%; range 0-6.92; controls: mean 0.79%; range 0-2.40). The significant change in the CD4:CD8 ratio seen in the coeliac epithelium (ratio 1:22; control epithelium, ratio 1:8) was not mirrored in the LP (1.3:1 in coeliac preparations and 1.4:1 in controls).

High class II antigen expression by coeliac intestinal T cells was common to both LP and EL. The increase in the $\gamma\delta$ TCR+ and CD8+ populations, however, was significantly more marked in the EL than in the LP suggesting that these features may be independent.

GASTROENTEROLOGY

(O.3) LABORATORY PARAMETERS IN THE ASSESSMENT OF CROHN'S DISEASE ACTIVITY

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One of the main problems encountered in the management of Crohn's disease is the accurate assessment of disease activity.

The present study set out to 1) determine the relationship between clinical assessment of activity by the two clinicians with the following laboratory parameters Hb., HCT, WCC, Platelets, ESR, Albumin, Alpha 1 Acid glycoprotein (AGP) and C-reactive protein (CRP). 2) correlate each laboratory parameter with four numerical indices of activity, the Crohn's disease activity index (CDAI), the Van Hee's disease activity index (AI), the simple index of Harvey and Bradshaw (SI) and the Fielding index and 3) correlate all eight laboratory parameters with each other.

194 assessments were performed on 56 patients, 184 obtained complete results. Following history and examination, two clinicians independently graded disease activity. After each, blood was taken for measurement of stated laboratory parameters and indices were calculated.

Four laboratory parameters; AGP, albumin, ESR and platelets, showed a highly significant correlation ($p < 0.01$) with all four numerical indices. AGP, ESR, platelets were the three parameters which correlated highly significantly ($p < 0.01$) with the seven remaining laboratory parameters.

Conclusion: AGP, ESR, platelets correlated highly significantly with numerical indices of activity and other laboratory parameters.

DERMATOLOGY

(O.5) RECALCITRANT PSORIASIS: WHEN IS TONSILLECTOMY INDICATED?

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Tonsillitis due to beta haemolytic streptococci is a well recognised triggering factor for both guttate and palmoplantar psoriasis. Between 25 and 50 percent of patients with psoriasis experience worsening of their skin condition after an attack of tonsillitis. We reviewed 13 patients with recalcitrant psoriasis exacerbated by recurrent tonsillitis who underwent tonsillectomy over four years. There were 12 females and one male with a mean age of 17 years, 6-28. Six patients had guttate psoriasis and seven patients plaque psoriasis. Patients were followed by chart review and postal questionnaire. Full follow up was available on all patients. Psoriasis cleared completely after tonsillectomy in 7 patients, improved in 3 patients and was unchanged in 3 patients. The guttate group did better than the plaque psoriasis group. We discuss the rational and indications for tonsillectomy in the psoriatic patient.

NUTRITION

(O.6) ASSESSMENT OF DIETARY FOLATE AND FOLATE STATUS IN A GROUP OF NON-PREGNANT FEMALES

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A specific role for folate in the prevention of both recurrence and first occurrence of neural tube defects has been established⁽¹⁾. All women planning a pregnancy are advised to increase their folic acid intake by 400µg/day over and above their current intake by increasing consumption of folate rich foods, by increasing consumption of folate fortified foods or by taking a folic acid supplement. Eighty non-pregnant females were assessed for dietary folate intake using the diet history method. Red cell folate was analysed to measure folate stores. The mean total dietary folate intake was 229 (79) µg/day. The mean red cell folate was 373 (133) µg/l.

Analysis of the dietary folate intakes divided into quintiles shows increasing folate stores from the lowest quintile of dietary folate with a mean of 143µg/d (95% CI, red cell folate 225µg/l to 319µg/l) to the highest quintile of dietary folate with a mean of 345µg/d (95% CI, red cell folate 387µg/l to 506µg/l).

These findings are of relevance given the recommendations for periconceptual folic acid intake. In agreement with Czeizel et al.⁽²⁾, we conclude that based on present dietary patterns, it is unlikely that females can achieve an extra 400µg/day of folic acid from food folates alone.

References

1. MRC Vitamin Study Group. Prevention of neural tube defects: results of the MRC Vitamin Study. *Lancet*. 1991; 338: 132-137.
2. Czeizel et al. Prevention of congenital abnormalities by periconceptual multivitamin supplementation. *BMJ*. 1993; 306: 1645-1648.

PLENARY SESSION

CARDIOVASCULAR

(O.8) THE IMPACT OF RECENT ANTIHYPERTENSIVE STRATEGIES ON HIGH BLOOD PRESSURE CONTROL: 1980-85 vs 1990-95

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Before 1985 drug management of hypertension comprised the "stepped care" approach, i.e. start with a diuretic (D), add a beta blocker (B), then a vasodilator (V) and/or neuronal blocker depending on the BP response. Of late ACE inhibitors (ACEI) and calcium blockers (CB) are among the most prescribed BP lowering drugs. This study compares the management of unselected patients in a hypertension clinic between 1980 and 1985 (209 patients) and 1990 to 1995 (180 patients). Other than age (51 vs 56 yrs, P<0.001) both groups had similar sex distribution, duration of follow-up (16 vs 16 months). B-Baseline. F-Follow-up. Cholesterol and potassium-mmol/l. Creatinine-µmol/l. *P <0.01, **P<0.001.

	Wt. (Kg)		Chol.		Creat.		Pl.K+		Mean BP			
	B	F	B	F	B	F	B	F	B	F		
80-85:	76	75	6.2	6.1	98	103	3.9	3.9	126	108**		
90-95:	77	75	5.8	5.8	108	114	4.1	4.0	122	109**		
% Use of drugs:	D		BB		VD		ACEI		CB		Cost/mth.	
80-85:	65		52		8		10		11		4	\$14.89
90-95:	53*		29*		2		7		62**		28**	\$31.54**

Drug management of hypertension has not improved in the past 10 years despite an inflation adjusted cost increase of more than two fold.

(O.9) UROKINASE TYPE PLASMINOGEN ACTIVATOR (u-PA) IS INDEPENDENTLY RELATED TO OUTCOME IN COLORECTAL CANCER

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Unrestrained growth of malignant cells must be accompanied by invasion for cancer to progress. Urokinase-type plasminogen activator (u-PA) is a serine protease capable of hydrolysing extracellular matrix and basement membranes, and has been implicated in tumour invasion and metastasis. Using immunohistochemical methods we have previously demonstrated that u-PA antigen level is of prognostic importance in Duke's B colorectal cancer (CRC)¹.

The aim was to determine the relationship between u-PA level, clinical features, tumour stage, tumour grade and patient survival following CRC resection. 105 CRC cases (63 males, 52 females; mean age 68 years, range 36-83) admitted to a single hospital.

Tissue level of u-PA antigen was measured on detergent extracts of CRCs and corresponding colorectal mucosa remote from the cancer using an ELISA assay (American Diagnostica). Results are expressed as a ratio of tumour u-PA to normal mucosal u-PA (ng/mg protein).

No significant relationship was seen between u-PA level and age (p=0.6), gender (p=0.23), tumour site (p=0.77), tumour size (p=0.75) or tumour stage (p=0.16). u-PA cancer/normal ratios were greater in poorly differentiated tumours (p=0.03). Patients with a high cancer/normal u-PA ratio had a significantly worse outcome than those with lower ratios (logrank test p=0.009). Cox regression analysis identified tumour stage (relative risk [RR] 2.6, p<0.0001) and cancer/normal u-PA ratio (RR 2.3, p=0.05)

as the only two independent prognostic features studied.

Conclusion: uPA antigen measurement may be a useful marker of colorectal cancer aggressiveness, and is capable of predicting prognosis independent of other clinical and pathological features.

Reference

1. Mulcahy et al. *Lancet* 1994, 3, ii, 583-4.

INFECTIOUS DISEASES/GU MEDICINE

(O.10) Fc γ RECEPTOR EXPRESSION AS AN EARLY INDICATOR OF BACTERIAL INFECTION

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Despite appropriate antimicrobial chemotherapy, the mortality rates associated with severe bacterial infections remain high. To improve prognosis, prompt diagnosis and treatment are essential. Thus, the development of early detection methods would be advantageous. Since IgG antibody binding receptors (Fc γ RI Fc γ RII and Fc γ RIII) are important mediators of phagocytosis, measurement of these receptors could be useful in the early detection of infection⁽¹⁾. In this study Fc γ R expression was measured on the neutrophils and monocytes of 38 patients suspected of systemic infection and compared to Fc γ R expression in 30 healthy blood donors. Of the 38 patients tested, 17 were blood culture positive, 7 were blood culture negative but had severe bacterial infection at localised sites and the remaining 14 had no cultural evidence of infection. Fc γ R expression was measured using flow cytometry. There was no significant difference in the expression of Fc γ RI on neutrophils or monocytes in patients with systemic Vs localised infection, (p=0.27, p=0.25) respectively. Fc γ RI expression was, however, significantly increased in both these infected groups, compared to patients without evidence of infection for neutrophils (p=0.0007, p=0.0001) and monocytes (p=0.03, p=0.02) and compared to controls, p<0.0001, in all cases. The expression of Fc γ RII did not differ significantly between the patient groups, although patients with systemic or localised infection were significantly different to controls for both neutrophils (p=0.003, p=0.01) and monocytes (p=0.004, p=0.0004). Measurement of Fc γ RIII was not useful in distinguishing the different patient groups from controls. This data suggests that increased Fc γ RI expression on neutrophils or monocytes may be a useful rapid indicator of bacterial infection.

Reference

1. Van de Winkel, J. G. J., Capel, P. J. A. Human IgG Fc receptor heterogeneity: molecular aspects and clinical implications. *Immunol. Today* 1993; 14: 215-21.

PUBLIC HEALTH

(O.12) NEONATAL BCG - IMPACT ON CHILDHOOD TB & TUBERCULIN SENSITIVITY IN TB CONTACT TRACING

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The efficacy and scheduling of BCG and its potential to interfere with the interpretation of the tuberculin test as a screening tool are debated. Counties without neonatal BCG have been shown to be associated with a higher rate of TB hospitalisation in the 0-14 year age group (relative risk 3.8, CI

1.7-8.9, p<0.001)¹. This study examines the impact of neonatal BCG on the tuberculin sensitivity in TB contacts.

Tuberculin (PPD RT 23) sensitivity using the Mantoux test (5 TU) was studied in relationship to BCG status in TB contacts attending a TB clinic in Dublin. A BCG scar was used as the indicator of vaccination.

Data on 1032 contacts of 96 cases of TB were examined. The mean age of the contacts was 32 years. 784 (76%) contacts had BCG scars from neonatal vaccination. 50%, 30% and 20% of the contacts had Mantoux results of 0-4 (negative), 5-14 (positive), 15+ mm (strongly positive) induration respectively. Tuberculin sensitivity increased sharply between 20-40 years of age, declining after 60 years. Contacts of sputum positive cases had larger tuberculin reactions. The presence of a BCG scar was not found to significantly influence the degree of tuberculin sensitivity (p<0.231) in any age group. Studies have shown that BCG given at older ages is associated with larger tuberculin reactions².

These data suggest that the optimum age for BCG may be at birth as it significantly reduces the incidence of childhood TB without interfering with tuberculin sensitivity in the contact tracing process using the Mantoux test.

References

1. Johnson, H. Neonatal BCG & childhood TB in the Republic of Ireland. *CDR* 1993; 3: R132.
2. Menzies, R, Vissandjee, B. Effect of BCG vaccination on tuberculin reactivity. *Am. Rev. Respir. Dis.* 1992; 145: 621-34.

RHEUMATOLOGY AND REHABILITATION

(O.13) ARTICULAR DAMAGE IN RHEUMATOID ARTHRITIS IS RELATED TO SYNOVIAL TISSUE MACROPHAGE POPULATIONS

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The contribution of individual synovial cell populations to articular destruction in rheumatoid arthritis (RA) is controversial. 28 patients with RA were studied prospectively by measuring disease activity and radiological articular destruction at entry and at review 6 (mean) (range 4-8) years later. In addition, synovial cell populations were quantified in detail at review. Correlations were sought between synovial cell populations and radiological course.

Mean radiological score deteriorated from 35 at entry to 90 at review (p=0.0001) despite improvement in all measures of disease activity. Significant correlations were identified between both lining layer (LL) depth (r=0.63) and sublining layer (SLL) macrophage count (r=0.59) and the extent of radiological destruction at review and also with radiological progression during the study (r=0.54 and r=0.68 respectively). In contrast, no lymphocyte subpopulation correlated with radiological course. Detailed analysis of 11 patients demonstrated reduced CD 14 expression compared to CD68 expression in the LL (p=0.003), unlike in the SLL, where expression of CD14 and CD68 were equivalent.

Since LL depth reflects LL macrophage accumulation, this study clearly demonstrated that macrophages throughout the synovium correlated with progressive articular destruction in RA. In addition, LL macrophages differ in their phenotype from those in the SLL, and may represent a distinct macrophage subpopulation which plays an important role in progressive articular destruction. These findings have important implications for the development of new therapies for patients with RA.

POSTER PRESENTATIONS

ENDOCRINOLOGY/METABOLISM/LIPIDS

(P.1) THYROTROPHIN RECEPTOR ANTIBODIES IN HYPEREMESIS GRAVIDARUM

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Hyperemesis Gravidarum (HEG) has frequently been associated with thyroid hyperfunction. In the present study the prevalence of Thyrotrophin Receptor Antibodies (TRAb) in whole serum and IgG concentrates prepared in serum from patients with HEG was compared with those obtained from "well" patients studied during the first trimester of pregnancy (T1) and in non-pregnant controls. TRAb was measured using a radioreceptor assay. Sera and IgG concentrates which produced inhibition of ^{125}I TSH binding to thyroid membranes $>15.0\%$ were termed positive. TRAb were positive in 7/56 (12.5%) of patients requiring hospitalisation for HEG. Of 19 "well" T1 pregnancy patients, one (5.2%) was TRAb positive. Similarly only 1/22 (4.5%) of non-pregnant female controls was TRAb positive. When IgG concentrates were prepared from sera by PEG (50%) precipitation, positivity increased to 10/11 (91.0%) in HEG and a 16/19 (84.2%) in "well" T1 pregnancy. In order to investigate a possible role for hCG in influencing TRAb positivity in pregnancy, known concentrations of hCG (62.5 - 500x10³ IU/L) were added to an incubation mixture containing TRAb negative serum. Inhibition of ^{125}I TSH binding increased from 6.4%-22.3% with increasing hCG. The results suggest the presence of a non-hCG TSH binding inhibitor in sera from patients with HEG. They also emphasise the need to exert caution in interpreting results of TRAb investigations, particularly in IgG concentrates prepared from pregnancy sera.

(P.2) NEONATAL THYROTOXICOSIS - A CASE REPORT

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We present a most unusual case of neonatal thyrotoxicosis in premature twins. The mother of the twins has Graves disease, was thyrotoxic for two years, becoming hypothyroid one and a half years prior to delivery during which time she was maintained on L-Thyroxine. During pregnancy she developed rising levels of thyrotrophin receptor antibodies (TRAb) which had been absent in early pregnancy rising to 70% inhibition of ^{125}I labelled TSH binding at 26 weeks gestation. Twin boys were delivered vaginally at 30 weeks + 6 days gestation. Both boys were significantly hyperactive. Twin 1 developed intermittent tachycardia which resolved spontaneously, he displayed no inability, persistently fed well and had good weight gain. Peak TRAb on Day 2 was 61.4%. Twin 2 developed tachycardia from day 8 which became increasingly severe necessitating treatment with propranolol. Weight gain was also poor despite adequate intake. The twins, now nine months of age remain under follow-up. At review both twins are thriving and propranolol treatment has been discontinued for twin two. These findings demonstrate the importance of thyrotrophin receptor antibodies (TRAb) in monitoring neonatal thyrotoxicosis. The report outlines the course of neonatal thyrotoxicosis and demonstrates the need for careful evaluation of offspring born to mothers with thyroid disease.

(P.3) SECONDARY HYPERPARATHYROIDISM IN ELDERLY SUBJECTS WITH HYPOVITAMINOSIS D: PREVALENCE AND CORRECTION

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Bone disease is a serious and common problem in the elderly causing hip, vertebral and other bone fractures. Hypovitaminosis D predisposes to the development of bone disease. An intermediate and reversible stage is hypovitaminosis D osteopathy and associated secondary hyperparathyroidism (SHPT) with accelerated bone loss.

A large number of publications have reported a high prevalence of hypovitaminosis D in elderly subjects. Secondary hyperparathyroidism in association with hypovitaminosis D is now being diagnosed with increasing frequency probably due to the advent of more sensitive assays for intact parathyroid hormone. The effect of high dose Vitamin D supplementation in correcting SHPT in a patient with stress fractures is presented; serum PTH decreasing from 6.9 - 2.2 pmol/L as serum 25(OH)D increased from 14-128 nmol/L. The concentration of serum 25(OH)D necessary for restoration of serum PTH to the adult reference range may be as high as 70 nmol/L in patients who have developed SHPT.

(P.4) - See p. 53

(P.6) NEUROPATHIC DIABETIC ULCER: A CASE-CONTROL STUDY

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We carried out a case-control study of diabetic neuropathic ulcers (DNU) drawn from all patients attending the diabetes service in our hospital between 1990-93 and found 31 patients with DNU. These were age, gender, duration and DM-type matched with diabetic controls who did not have DNU. A range of clinical and psycho-social variables were compared. All subjects underwent a standardised clinical and bedside neurophysiological examination and Beck Inventory for depression. Neuropathy was documented by: a clinical scoring system (modified from Lehtinen 1989) and biosthesiometry vibratory perception threshold (VPT) with abnormal results age adjusted. The group median age was 65 years, 66% male, DM median duration 14 years. DNU patients (v/s controls) had a high prevalence of overt nephropathy 68% v/s 26% ($p = 0.003$), proliferative retinopathy/maculopathy 71% v/s 39%, ($p = 0.003$), peripheral vascular disease 48% v/s 16%, ($p = 0.008$), higher neuropathy examination score ($p < 0.01$) and abnormal VPT 82% v/s 48%, ($p = 0.01$). The groups did not differ in prevailing HbA1c, present or past alcohol intake, education, or Beck Inventory score. We conclude that DNU occurs in patients with more severe neuropathy and is linked to microvascular and peripheral vascular disease.

(P.7) SCREENING FOR DYSLIPIDAEMIA IN NIDDM-RELATIONSHIP TO MACROVASCULAR DISEASE AND OTHER RISK FACTORS

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Macrovascular complications are the leading cause of morbidity and mortality in NIDDM. Insulin resistance,

hyperinsulinaemia and dyslipidaemia may be contributory factors. We looked at the lipid profiles, risk factors and incidence of macrovascular disease in 160 non-insulin-dependent diabetics attending a diabetic outpatient clinic. 44 patients (28%), 31 male and 13 female were active smokers. 59 patients (37%) had hypertension. 27% of all patients had elevated cholesterol levels (>6.1 mmol/l), 33% had elevated non-fasting triglyceride levels (>3.0 mmol/l) and 44% had low HDL-cholesterol levels (<1.0 mmol/l). Approximately 25% of patients had evidence of macrovascular disease with more than two thirds of these having coronary heart disease. These patients were more likely to be male, to have hypertension and to have a family history of hypertension or ischaemic heart disease. This group also had a statistically higher mean cholesterol and LDL-cholesterol than the group as a whole. Only one patient was on lipid-lowering therapy in this group. In view of current opinion advocating treatment of significant dyslipidaemia in high risk subjects or those with coronary heart disease, a number of these patients may require more active intervention.

(P.8) LIPOPROTEIN Lp(a) IN ELDERLY AND VERY ELDERLY SUBJECTS

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Lipoprotein Lp(a) is a variant of low-density lipoprotein and subjects with values >30 mg/dl have greatly increased risk of coronary heart disease. Lp(a) levels are strongly influenced by genetic factors. It was of interest to measure Lp(a) levels in very elderly subjects, who as survivors of their peer group, might be expected to show a predominance of lower values of Lp(a) consistent with a reduced risk profile for atherosclerosis. In this preliminary study, 129 elderly subjects, who were apparently well and living in the community, were enlisted - 60 subjects > 90 years of age, 35 subjects > 80 years of age and 32 subjects 65-80 years of age. Lp(a) was measured by standard immunoassay methods (Immunozytm).

Lp(a) levels were asymmetrically distributed with Median values in >90, >80 and 65-80 year age groups of 11.5, 8.0, 10.6 mg/dl respectively. There were 30% of subjects in the >90 year old group who had values of Lp(a) >30mg/dl with 19.4% in the >80 year old group and 20.6% for the 60-80 year old group compared with 25% within the entire group. Lp(a) values, in the 'at risk' range for atherosclerosis, are present in a higher percentage of well nonagenarian subjects, than are present in 'younger' old groups. This finding is surprising in view of the expectation that risk factors for coronary heart-disease might be reduced in nonagenarian subjects who by virtue of their age have survived premature heart disease.

GASTROENTEROLOGY

(P.9) ACUTE FOOD BOLUS IMPACTION: AETIOLOGY AND MANAGEMENT

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Various oesophageal disorders have been implicated as causative factors in acute food bolus obstruction. The purpose of this paper was to investigate patients presenting with acute food bolus impaction and identify any underlying pathology.

In this prospective study over a two year period, 17 patients presenting with acute food bolus impaction were investigated. All patients, where possible, had full oesophageal investigation including Barium swallow, 24 hour ambulatory pH monitoring and oesophageal motility studies. Of these patients 8% demonstrated oesophageal pathology. Over 60% showed evidence of gastroesophageal reflux, while almost half had abnormal oesophageal motility patterns. 59% had previous food bolus impaction but only two of these had any definitive treatment in the past.

The results of this study suggest that underlying oesophageal pathology as a cause of acute food bolus impaction is evident in the vast majority of patients. It appears that such disorders have been underdiagnosed in the past due to inadequate investigation. We recommend that all patients presenting with acute food bolus impaction should be thoroughly investigated so that appropriate definitive treatment can be advocated and recurrences prevented.

(P.10) IS THE GENETIC DIVERSITY OF *HELICOBACTER PYLORI* IMPORTANT FOR THE CLINICAL OUTCOME OF GASTRODUODENAL DISEASES?

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Helicobacter pylori is associated with a wide range of gastroduodenal pathology from asymptomatic carriage through gastritis and/or peptic ulcer disease to gastric cancer. The aim of this study was to assess whether *H. pylori*-related diseases are associated with specific strains using randomly amplified polymorphic DNA (RAPD) fingerprinting technique. *H. pylori* stain was isolated from each of 40 individuals including 35 patients with duodenal ulcer, gastric ulcer, non-ulcer dyspepsia and five asymptomatic volunteers. The organisms were subcultured on chocolate agar for 3-5 days and the cells of each strain were harvested. *H. pylori* DNA was extracted by the phenol/chloroform method and amplified using the polymerase chain reaction-based RAPD with a combination of two 10-nt primers. Electrophoresis of RAPD products on 2% agarose gel yielded DNA profiles (fingerprints) of DNA of each strain. The fingerprints of strains were compared with their corresponding clinical gastroduodenal disease status. RAPD fingerprinting with a combination of the two primers yielded 10-20 main bands on the agarose gels. The profiles of the PCR products of DNA from all the 40 strains were different from each other. There were no specific bands that associated with the clinical outcome of gastroduodenal pathology. In conclusion, the strains of *H. pylori* may not be disease specific and the host response to the infection may determine the clinical outcome.

(P.11) OMEPRAZOLE PLUS ONE OR TWO ANTIBIOTICS TO ERADICATE *H. PYLORI*

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Eradication of *H. pylori* heals gastric and duodenal ulcers and dramatically reduces ulcer relapse rates. The combination of omeprazole (Om.) with amoxicillin (Am.) results in variable eradication rates. Preliminary studies suggest that omeprazole plus two antibiotics achieves higher eradication rates.

The aim of this study was to compare the efficacy of omeprazole in combination with one and two antibiotics.

Subjects with *H. pylori* gastritis \pm D.U., who had not received previous eradication therapy were enrolled. *H. pylori* status was assessed by histology, culture and a rapid urease test. Subjects were allocated to one of the following regimes;

Group 1: Om. 20mgs daily + Am 500mgs t.i.d. for 2/52

Group 2: Om. 20 mgs b.i.d. + Am. 1gm b.i.d. for 2/52

Group 3: Om. 20 mg daily + clarithromycin 250mg b.i.d. + metronidazole 400mgs b.i.d. for 1/52.

100 subjects were recruited (mean age, 44.6 years, range 17-82 year, 58 male).

Eradication rates were as follows: Group 1; 11/22 (50%), Group 2; 20/28 (71.5%), and Group 3 46/50 (92%). In Group 3, all 4 patients who failed to eradicate had primary metronidazole resistance and 1 had primary clarithromycin resistance.

Triple therapy with omeprazole is efficacious (92% eradication) and superior to dual therapy.

(P.12) DISTAL OESOPHAGEAL REFLUXATE AND MOTILITY IN PROXIMAL GASTRO-OESOPHAGEAL REFLUX

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Reflux into the proximal oesophagus may be associated with extra-oesophageal manifestations of gastro-oesophageal reflux disease. This study examined the correlation between distal oesophageal acid exposure refluxate pH, clearance of refluxate, oesophageal motility and proximal oesophageal reflux. Oesophageal manometry and 24 hour dual channel pH monitoring were performed in 105 patients; group 1 (n=42) normal controls; group 2 (n=33) distal GORD; group 3 (n=30) distal and proximal GORD.

Results	Group 1	Group 2	Group 3
Proximal oesophagus % time pH <40.4 (0.1)	0.2(0.1)	3(0.4)*	
Distal oesophagus % time pH <4	2(0.2)	18(4)	18(3)
Reflux episodes > 5 min (no.)	1(0.2)	8 (2)	6 (1)
Mean Refluxate pH	3.7(0.2)	2.3(0.4)	2.6(0.6)
Mean wave amplitude	36(3)	28(3)	44(5)*
Upper sphincter pressure	53(5)	54(4)	53(4)
Lower sphincter pressure	10(1)	7(1)**	10(1)
Mann-Whitney U test	values: mean (sem)		

*p<0.01 group 3 v group 1 & 2; **p<0.01 group 2 v group 1 & 3

Proximal refluxers had greater oesophageal wave amplitude and lower sphincter pressures. Characteristics of distal reflux did not predict proximal oesophageal acid exposure. The pathophysiology of proximal reflux remains unclear.

(P.13) UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA) ANTIGEN CORRELATES WITH NEOPLASTIC STAGE OF COLORECTAL MUCOSA

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Urokinase-type plasminogen activator (u-PA) is a serine

protease which promotes degradation of extracellular matrix. The aim was to quantitate u-PA antigen in normal and malignant large bowel tissue, and to study the relationship between neoplastic progression and changes in u-PA profiles. 236 fresh-frozen tissue specimens from 113 patients, adenocarcinomas (n=105), adenomatous polyps (n=13), and normal colorectal mucosa remote from the tumour site (n=108). Levels of the u-PA antigen were measured on detergent extracted tissue using a sandwich ELISA assay (American Diagnostica). Results are expressed as mean values (ng/mg protein) with 95% confidence intervals (C.I.).

Mean u-PA expression was unaffected by gender (p=0.44), or age (p=0.27). u-PA expression was greater in colonic than rectal mucosa (p=0.01). There was a 4 fold increase in u-PA antigen level between control and malignant tissue. Polyps had intermediate u-PA levels. Tumours of patients with distant metastatic disease demonstrated the highest levels of u-PA.

Tissue	n	u-PA \pm 95 % C.I. (ng/mg protein)
Normal	(n=108)	0.15 \pm 0.02
Adenomas	(n=13)	0.42 \pm 0.13
Adenocarcinomas		
Locoregional	(n=90)	0.56 \pm 0.1
Distant metastatic	(n=15)	0.71 \pm 0.29.

Conclusion: u-PA antigen level appears to reflect the neoplastic potential of large bowel mucosa. High levels within adenomatous polyps support the concept that these are pre-malignant lesions.

(P.15) CENTRAL PONTINE MYELINOLYSIS POST LIVER TRANSPLANT NO ASSOCIATION WITH SERUM SODIUM FLUCTUATIONS

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The aim of this study was to delineate the association between serum sodium [sNa] and the development of central pontine myelinolysis [CPM] post orthotopic liver transplantation [OLT]. 38 patients underwent 43 OLT between January 1993 - January 1995. Serum Na concentrations were measured serially throughout the hospital course and plotted for the perioperative period. Metabolic parameters including glucose and pH values were also plotted.

Of 38 patients who underwent OLT, 3 developed CPM days 5-7 post surgery heralded by the onset of coma in 2 patients with subsequent seizures and spastic quadraparesis; the third patient experienced the 'locked-in' syndrome, with apraxia, hypertonicity and extensor planter responses. Two female patients underwent elective surgery for PBC [age 58 and 64 yrs] and one male for AIH [age 50 yrs]. All patients experienced slurred speech, ataxic gait, and shorterm memory loss. CT brain scan was normal in all patients, but MRI confirmed changes in the pons consistent with demyelination. The sNa concentration did not exceed 17mEq/L in any patient during the peri- and 48 hr postoperative period, and metabolic parameters were within normal limits prior to the development of neurological signs.

Conclusion: CPM occurred in 7.9% of patients transplanted and had no demonstrable relationship to sNa flux.

(P.16) WHO BEST ASSESSES CROHN'S DISEASE?

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Knowledge of the presence and degree of inflammation in Crohn's disease would be useful in multicentre therapeutic trials.

The purpose of the present study was two fold: a) to determine the relationship between clinical assessment of activity by two clinicians with four previously published indices, the Crohn's disease activity index (CDAI), the Van Hees activity index (AI), the simple index of Harvey and Bradshaw (SI), and the Fielding index, and b) for the first time, to study the internal correlation between these four indices.

A hundred and ninety four assessments were performed on 56 patients with Crohn's disease. Following each clinical assessment, the indices were calculated.

A good relationship was observed between the median indicial values and clinical gradings for all four indices. The best relationship was demonstrated with the AI with no overlap in 50% values with increasing grades of disease activity. All four indices demonstrated a good correlation with each other ($p < 0.01$). The best correlation was observed between more objective indices the AI and the Fielding index ($r = 0.79$) for first assessments only.

Conclusion: The Van Hee's AI is a reliable measure of inflammatory activity in Crohn's disease and would be useful in multicentre therapeutic trials.

**(P.17) THE MOLECULAR GENETICS OF A
HEREDITARY FORM OF COLORECTAL CANCER**

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We have been studying the molecular genetics of a family with an inherited autosomal dominant predisposition to colorectal cancer.

This family has a phenotype atypical of familial adenomatous polyposis (FAP), with an average age of diagnosis at 68 years, (later than classical FAP) but it falls within the range of hereditary non-polyposis colorectal carcinoma (HNPCC). However, some family members contain up to 25 colonic polyps, more than the usual number for HNPCC. There is a possibility that an attenuated form of FAP - attenuated adenomatous polyposis coli (AAPC) - is involved. This phenotype, represented by a later age of onset and fewer polyps than classical FAP, is due to less deleterious germline mutations in the APC gene. Attempting to elucidate the nature of this kindred's form of colorectal cancer, we have proceeded with genetic analysis. The results indicate that previously identified conserved and non-conserved single base-pair changes have been shown not to be responsible by single strand conformational polymorphism and heteroduplex analysis. Thus, we have undertaken linkage analysis of the APC gene on chromosome 5 (the disease locus for FAP), using 5 highly informative polymorphic markers flanking the APC gene to determine if alterations in this gene are responsible for the condition.

DERMATOLOGY

**(P.18) PORPHYRIN METABOLISM IN HEPATITIS C
INFECTION SECONDARY TO ANTI-D
IMMUNOGLOBULIN AND INTRAVENOUS DRUG
ABUSE**

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Hepatitis C virus (HCV) has been implicated as a possible triggering factor for porphyria cutanea tarda (PCT) with antibody prevalence ranging from 10% in Ireland to 76% in France. We therefore compared porphyrin metabolism in 2 groups of patients with HCV infection.

Group 1 comprised 34 Rhesus negative women immunised with anti-D immunoglobulin (age range 30-56, mean 44 yrs). Group 2, all HIV negative intravenous drug abusers (IVDA), included 14 male, 11 female (age range 16-43, mean 28 yrs) HCV positive patients (Elisa and RIBA 3). Haemoglobin, serum ferritin, liver function tests, Hepatitis A and B status, plasma and urinary porphyrins were measured. One patient in Group 1 was on oestrogen therapy. Three in Group 2 abused alcohol.

Porphyrin excretion was normal apart from 3 (12%) in Group 2 with elevated free erythrocyte protoporphyrin, ranging from 756-969 ng/L (normal < 590). Liver function tests were abnormal in 27 (76.4%) in Group 1 and 19 (76%) in Group 2. Ferritin levels were elevated in 2 (5.9%) at 267ng/mL and 671ng/mL (normal: 8-110) in Group 1 alone.

HIV and HCV infection are associated with significantly abnormal porphyrin metabolism. Four of 59 patients with HCV infection alone, had mildly abnormal porphyrin profiles. Other factors, including, progressive liver disease, genetic predisposition, older age, ethanol, iron overload and oestrogen therapy may be necessary to precipitate overt PCT.

**(P.19) MALIGNANT MELANOMA - THE CASE FOR
EARLY DIAGNOSIS**

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Melanoma is the most lethal of cutaneous malignancies accounting for 85% of skin cancer related deaths. The aim of this study was to assess survival and identify prognostic indicators in all melanoma patients treated at a single institution over a 9 year period. 232 patients (167 females, 65 males) mean age 50 years (range 5-92 years) were treated. All had stage 1 disease at presentation, lower limb (41%) was the most frequently affected site in females and trunk (38%) in males. 64% of the melanomas were invasive, 50% nodular and 46% superficial spreading. Survival curves were calculated using the Kaplan Meier methodology and the overall 5 year survival was found to be 81%, with the majority of deaths occurring within 2 years of diagnosis. Multivariate analysis using a logistic regression model identified Breslow thickness as being the only independent statistically significant determinant of prognosis, emphasising the importance of early diagnosis and prompt referral in this disease.

(P.20) BULLOUS ERYTHEMA AB IGNE

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The clinical manifestations of erythema AB IGNE are well described and consist of a rectangular red or brown macular dermatosis occurring most commonly on the lower limbs and backs of women. It occurs most commonly after prolonged exposure to infra red radiation at a level lower than that which produces an acute thermal burn. Reports of bullae formation in erythema AB IGNE are very rare. We report three cases of bullous erythema AB IGNE that presented to our clinics over a two year period. Histologically the split occurred at the level of the dermo-epidermal junction similar to that seen in second-degree thermal burns. Direct immunofluorescence of perilesional skin was normal in two patients. We have found only two previous cases of erythema AB IGNE associated with bullae formation in the literature^{1,2}. In one of these cases the histology suggested a coexistent lichen planus. In our three cases, there was no evidence of lichen planus. We propose that thermal injury in erythema AB IGNE may result in bullae formation, and that erythema AB IGNE is more frequently associated with sub-epidermal bullae than is hitherto reported.

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(P.22) CLINICAL SIGNIFICANCE OF IgA ASSOCIATED VASCULITIS

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Vasculitis may have many causes. Immunoglobulin deposition may be a non specific finding but IgA deposition is thought to be mainly associated with Henoch Schonlein Purpura (HSP) and may convey a greater risk of renal disease. We studied all patients diagnosed over the past seven years with vasculitis characterised by IgA deposits in the blood vessel walls. Patients were identified retrospectively from laboratory records and clinical details obtained from hospital notes. Twenty-seven patients (age range 17-70 years) with IgA vasculitis were identified, 14 females and 13 males. The diagnosis and associated findings are summarized in the table.

Diagnosis	No. of patients	Associated conditions
HSP	10	Renal disease 3
SLE	2	Renal disease 1
Bullous disorders	2	-
Hepatitis	1	Multi-organ failure
Leg ulcers	1	-
Drug rash	1	-
Eczema	10	-

Three of ten patients with Henoch Schonlein Purpura and one of two patients with SLE had renal disease. Therefore as with other forms of vasculitis underlying renal disease should be excluded, but IgA deposition in cutaneous lesions does not necessarily indicate underlying renal disease.

(P.21) AUTOSOMAL DOMINANT PSEUDOXANTHOMA ELASTICUM. IDENTIFICATION OF THE ASYMPTOMATIC OR CARRIER STATE BY ELECTRON MICROSCOPY

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PXE is a rare, hereditary clinically heterogenous disease of connective tissue. It may be inherited in an autosomal recessive or dominant (AD) manner. The incidence of AD inheritance is controversial. We report an Irish family in which 5 of 6 members showed evidence of PXE on electron microscopy (EM) examination of the skin.

The index case initially presented with visual loss and angoid streaks were detected on funduscopy. Skin examination was normal on initial presentation. Biopsies of flexural skin revealed elastic fibre abnormalities on EM confirming a diagnosis of PXE. His asymptomatic parents and siblings (N=3) were similarly assessed. Cutaneous examination was normal in all cases. One sibling demonstrated swollen fragmented elastic fibres with elastic Van Gieson stain. EM examination showed evidence of the characteristic elastic fibre abnormality in these cases and also in their asymptomatic 70 year old mother. The pedigree pattern clearly supports an AD pattern of inheritance. We propose that EM examination of clinically normal flexural skin is a useful tool in the detection of PXE or of the asymptomatic carrier state.

(P.23) AN EPIDEMIOLOGICAL SURVEY OF PSORIASIS

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We present epidemiological data on 456 patients with psoriasis vulgaris (probands) attending a dermatology clinic, directly questioned about age of onset and family history of the disease. 191 (41.9%) were male, 265 (58.1%) female, mean age was 28.3 SD ± 18.4, mean age of onset 21.5 SD ± 16.2. 405 (25.2%) presented before 40, M:F 1:1.4, 115 (25.2%) before 10, M:F ratio 1:17. Age of onset declined steadily for men after 40, in women a greater number still developed the disease. 198 (43%) of probands had an affected 1° relative, 24 (5.3%) a 2° relative. Probands with earlier age of onset had a higher % of affected relatives, 58.3% between 0-9, 7.1% between 40-49, suggesting stronger genetic influence with earlier onset. 333 (72.6%) of probands had neither parent affected, 121 (26.3%) had 1 parent and 4 (0.9%) both parents. 68 (20.5%) probands with neither parent involved, had another sibling affected. These results do not favour simple autosomal dominant or x-linked recessive or dominant inheritance. An autosomal recessive pattern with a lower than expected frequency due to delayed age of onset could account for our figure of 20.5%.

Reference

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**(P.24) DERMATOPHYTE ONYCHOMYCOSIS IN
PREADOLESCENT CHILDREN**

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Dermatophyte nail infection is regarded as rare in children with a reported prevalence of 0.2%, as compared to between 2-5% in adults, rising with the age of population studied. We document its occurrence in the paediatric age group with 3 case reports of tinea unguium occurring in healthy children, ages ranging from 7 to 14 years from different families, presenting over a 6 month period. All were asymptomatic but presented because of the distressing and dystrophic appearance of their nails. All cultured trichophyton rubrum species and only one had an associated tinea pedis. We show carriage of asymptomatic T.Rubrum on clinically normal toe-nails of other family members in 2 of the 4 cases, which may act as a reservoir for transmission of infection. We suggest that the prevalence of onychomycosis in children may be increasing and that certain subpopulations of young children are more at risk. We speculate as regards the lower prevalence in children, compared to adults but stress the importance of correct diagnosis at presentation by appropriate mycological assessment.

Reference

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**(P.25) ROLE OF APOPTOSIS IN SUBTYPES OF
MALIGNANT MELANOMA**

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Mutant p53 & bcl-2 inhibit apoptosis and allow tumour proliferation. In malignant melanoma bcl-2 expression is most prominent in the radial growth phase. In this study we compared bcl-2 expression in 13 nodular and 13 acral lentiginous malignant melanomas and looked at Ki-67 expression, a known proliferative marker and determined any relationship with prognostic variables. Mean bcl-2 staining score in the acral lentiginous group was 2.6 compared to a score of 1.7 in nodular variant ($P < 0.05$). Bcl-2 protein expression was not associated significantly with mitosis, Breslow thickness or survival. Percentage of positive Ki-67 cells varied considerably and did not correlate with mitotic index and survival. The novel observation of markedly increased bcl-2 expression in the acral-lentiginous group of melanoma suggests that this variant of malignant melanoma is biologically different from nodular malignant melanoma. We hypothesise that the acral lentiginous variant of malignant melanoma is protected intrinsically from stresses that induce cellular apoptosis, for example ionising radiation and chemotherapy.

(P.26) IMMUNOLOGY

OATS CEREAL IS NOT TOXIC IN COELIAC DISEASE

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The pathogenesis of coeliac disease appears to involve an immunological response to the ingestion of specific cereal proteins in wheat, barley and rye. The issue of oats toxicity is

controversial and was investigated in this study. 9 biopsy-proven coeliac patients in clinical and histological remission were challenged with 50g of oats daily for a 3 month period. Clinical, laboratory, histological and immunological markers of coeliac disease activation were evaluated. All patients remained asymptomatic throughout the challenge period and no laboratory evidence of malabsorption was found. There was no mucosal damage seen on routine histological examination of post challenge duodenal biopsies. Surface enterocyte height remained unchanged and intraepithelial lymphocyte counts were also unaltered following challenge. Furthermore, oats did not cause immunological activation since no rise in alpha gliadin or endomysial antibodies or in MHC class II staining of enterocytes was evident. This study demonstrates that oats is neither toxic nor immunogenic in coeliac disease and oats does not appear to contain the putative toxic peptide sequence found in the 3 other cereals.

**(P.27) MANIPULATION OF DONOR MARROW BY UV-B
LIGHT FACILITATES MISMATCHED BMT**

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A major complication of Bone Marrow Transplantation (BMT) is Graft versus Host Disease (GvHD) which is mediated by donor T cells. Abrogation of GvHD while preserving stem cell repopulating ability might allow an increase in the donor panel for BMT. *In vitro* evidence suggests that ultraviolet B light (UV-B) can inhibit T cell reactivity. A prospective study of time to engraftment, chimerism kinetics and long term repopulating ability (LTRA) of UV-B treated marrow precursors was performed in a murine BMT model. Irradiated animals were rescued with an inoculum of donor cells treated with varying doses of UV-B. Animals were sampled at weeks 1-4, 8, 12, 16, 20, 26 and assessed by PCR of Short Tandem Repeat Sequences. In semi allogeneic BMT, 20 animals were studied. At low UV-B doses ($< 1,000 \text{ J/m}^2$) donor engraftment was delayed, whereas doses of $2,000 \text{ J/m}^2$ or more never resulted in donor chimerism. There was no significant GvHD in control or UV-B treated animals. In the more immuno-aggressive allogeneic BMT 18 animals were studied. 5/6 control animals died of GvHD. At 1000 J/m^2 , there was no significant GvHD and 4/6 animals were long term donor chimeras. At $2,000 \text{ J/m}^2$ there was no evidence of GvHD but no animal became a donor chimera. These results indicate: 1. High doses of UV-B may affect stem cell function (semi-allogeneic studies). 2. There may be an optimal dose of UV-B that prevents development of GvHD while preserving LTRA of stem cells (allogeneic studies).

**(P.28) THE DIAGNOSIS OF COMPLEMENT DEFICIENCY:
STUDIES OF TWO IRISH FAMILIES WITH RECURRENT
MENINGOCOCCAL DISEASE**

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Complement deficiencies are best detected using haemolytic assays because these assays allow for screening for activity in

all components. Haemolytic assays have been developed that allow determination of both functional activity and identification of the missing component, when late acting complement component deficiencies (LCCD) exist. We have further developed this assay system to include activity of certain classical components such as C2, because C2 deficiency is the most common complement deficiency, but difficult to detect by antigenic assays. We applied these assays in studies in two Irish families. In one family a 14 year old girl from Co. Tipperary presented with a third episode of severe meningococcal septicaemia and meningitis. Testing revealed that she and a younger sibling have complete deficiency of the eighth complement component (C8D) whereas three other siblings, and the parents, have normal C8 activity. The other index case was a woman from Dublin with a history of recurrent meningococcal disease. She and two sisters were found to have complete C6 deficiency (C6Q0) (one sister was tested in the USA) and both these sisters have a history of meningococcal disease. Of three other siblings with no history of infection, one was tested and found to be complement sufficient, as were all the children of the index case and one affected sister. Several approaches to prophylaxis for these cases can be considered. They include counselling, the use of the quadrivalent meningococcal vaccine (which gives limited protection) and long term penicillin prophylaxis.

**(P.29) PASSIVE IMMUNISATION OF THE
GASTROINTESTINAL TRACT WITH HEN EGG
IMMUNOGLOBULIN**

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Gastrointestinal (GI) infection is a common cause of morbidity in young animals. Evidence is emerging that oral immunisation of the gastrointestinal tract with specific immunoglobulin (Ig) provides protection against intestinal pathogens. Hens immunised against such organisms lay eggs containing large amounts of specific Ig.

The aim of this study was to determine the usefulness of specific hen egg Ig against *Salmonella* in preventing infection, using the young calf as an animal model.

Twelve Isa Brown hens were immunised with *Salmonella*. Specific Ig levels reached a peak at 30 days post immunisation. These Ig laden eggs were collected, the yolks harvested and pooled.

An animal model of *Salmonella* induced gastroenteritis was developed using young calves. Forty five animals were divided into three groups. Two of these groups acted as controls, one receiving no egg yolk supplement, while the other received normal egg yolk from non-immunised hens as a supplement. The third group received a supplement of Ig rich egg yolk from immunised hens. All animals were orally challenged after five days with live *Salmonella*.

In the 2 groups of control animals, 14/16 animals given no egg supplement, and 9/13 animals fed normal egg, succumbed to infection within three days of challenge. However, in the group fed Ig rich eggs, only 4/13 animals succumbed to infection after challenge.

Therefore, specific hen egg Ig has a potential use in passive oral immunisation against GI infections.

**(P.30) INTERLEUKIN-10 ALTERS PHENOTYPE OF
PERIPHERAL BLOOD MONONUCLEAR CELLS**

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In asthma, dysregulation of bronchial T cell reactivity is associated with an imbalance within functionally distinct macrophage populations.

IL-10 inhibits cytokine production by activated macrophages and also reduces antigen-specific proliferation of human T cells. We investigated the effect of IL-10 on the phenotype of cultured peripheral blood mononuclear cells. Monocytes from six healthy volunteers were grown in culture for 7 days. IL-10 was added on day 5 to the differentiating macrophages; negative control and irrelevant cytokine (IL-12) control experiments were also performed. Double immunofluorescence studies were performed on macrophage cytopins using the monoclonal antibodies RFD1 and RFD7 to show the relative proportions of RFD1+ RFD7- antigen presenting cells, RFD1- RFD7+ mature phagocytes, and RFD1+ RFD7+ suppressive cells. The production of the inhibitory cytokine TGF β 1 in the culture supernatant was measured by lymphokine specific ELISA.

IL-10 reduced the relative proportion of antigen presenting cells (from 54% to 22% of total macrophages) ($p < 0.001$) and increased the proportion of mature macrophages (29% to 56%) ($p < 0.01$) and suppressive (17% to 22%) (p NS) macrophages. The concentration of TGF β 1 in the supernatant remained unchanged following the addition of IL-10.

In conclusion IL-10 may suppress antigen specific immunity and hence bronchial wall inflammation, therefore forming the cellular basis for new therapeutic approaches to asthma.

**(P.31) RAG1 AND RAG2 EXPRESSION IN HUMAN
LIVER: EVIDENCE OF T CELL DIFFERENTIATION**

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Success of engraftment in recipients of orthotopic liver transplantation has been reported to exceed that in recipients of other solid organ transplantation. These individuals seem to adopt a greater degree of tolerance to their hepatic graft, facilitating a reduction in immunosuppressive therapy. Such an observation suggests a possible functional role for the liver in the generation of graft tolerance.

It is our hypothesis that the liver is a site of extrathymic T cell differentiation and that tolerance to the hepatic graft arises when recipient stem cells mature and differentiate in the donor liver and emerge tolerant of donor antigen.

Expression of Recombination Activating Genes 1&2 (RAG 1&2) during T cell maturation is essential for rearrangement of gene segments that code for the T cell receptor (TCR). In this study RT-PCR was used to detect RAG specific mRNA from liver tissue. cDNA synthesis was carried out using random hexamers. Primers for first round and nested PCR of RAG1 and RAG2 were used. Bone marrow mRNA was used as a positive control for the reaction. RAG1 and RAG2 expression was not detected in peripheral blood. Using this approach RAG1

and RAG2 mRNA has been detected in extracts from four livers. Expression of these genes in liver provides strong evidence that T cells can differentiate within this compartment and supports the hypothesis that maturation of recipient T cells in the new graft may be a key feature of the tolerisation process.

**(P.32) A METHOD FOR THE DETECTION OF
ENDOMYSIAL ANTIBODIES IN COELIAC DISEASE
USING HUMAN UMBILICAL CORD TISSUE**

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Serum endomysial antibodies (EmA) have been used as an aid to the diagnosis of coeliac disease. This method involves the use of distal monkey oesophagus as substrate tissue. 100% specificity has been reported although sensitivity remains questionable. It has recently been suggested⁽¹⁾ that human umbilical cord might provide an alternative to monkey oesophagus. This study was carried out to compare the specificity and sensitivity of EmA estimation using human umbilical cord tissue (HUCT) and monkey oesophagus (MO) as target tissue.

HUCT was obtained after normal delivery and the cord vessels were dissected out, placed in OCT and snap frozen in liquid nitrogen. Sections were cut and stored at -70C. A modified immunofluorescence procedure was performed. A bright honeycomb fluorescence pattern indicated EmA positivity.

Sera from 53 adult patients being investigated for coeliac disease were studied. Histologically, 9 patients had active coeliac disease; of these 7 were EmA positive using HUCT and 6 using MO. Of 8 patients showing histological and clinical improvement on a gluten-free diet, 2 were EmA positive and 6 were EmA negative on both HUCT and MO. 30 patients had normal small intestinal histology; none of these had detectable EmA using either substrate tissue. 4 patients had other non-coeliac conditions and these patients were all EmA negative on both UCT and MO.

In summary, EmA estimation using HUCT is 100% specific and 78% sensitive and using MO is 100% specific and 67% sensitive. These results indicate the potential usefulness of HUCT as a screening test for coeliac disease.

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NEUROLOGY/NEUROSCIENCES

**(P.33) INVESTIGATION OF CHANGES IN NASAL
VISUAL FIELDS IN EARLY OPEN ANGLE GLAUCOMA
USING GOLDMANN PERIMETRY**

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Previous studies have demonstrated the changes seen in early open angle glaucoma using Goldmann perimetry to be general constriction of the visual field, arcuate scotoma in the visual field and the nasal step. Another study has shown that the nasal visual field can be enlarged by rotating the head by 30 degrees

in the direction opposite to that of the eye being tested in normal subjects with no ocular disease.

We examined the visual fields in two groups of subjects. The first group (the study group, n=20) consisted of patients attending ophthalmic clinics with a diagnosis of early open angle glaucoma who are on medical treatment with good control of intraocular pressure, evidence of optic disc cupping and no field loss on KOWA fields. The second group (the control group, n=20) consisted of age matched individuals with no evidence of optic nerve disease or any other ocular condition which could result in visual field changes.

After ocular examination, each subject had the visual field of each eye plotted with the head in two positions - namely straight ahead and rotated through 30 degrees in the direction opposite to that of the eye being tested. The two sets of fields in each subject were then compared for the presence (or otherwise) of nasal expansion and nasal scotoma.

Of the 38 eyes examined in the study group (2 eyes were unsuitable), 30 fields showed nasal expansion, 4 showed nasal reduction and 4 showed no change. The changes appeared thus:

Nasally expanded fields: Range = 1.6° - 13.3°, Mean = 4.9°,
Mode = 5.0°.

Nasally reduced fields: Range = 2.5° - 5.0°, Mean = 3.6°,
Mode = 2.5°

Of the 40 eyes examined in the control group, 37 visual fields showed nasal expansion, none were reduced and 3 showed no change. The changes appeared thus:

Nasally expanded fields: Range = 1.6° - 9.0°, Mean = 4.4°,
Mode = 3.3° & 5.5°

The presence of nasal reduction on rotation through 30 degrees is significant and could be used in the diagnosis and monitoring of open angle glaucoma.

**(P.34) TEMPORAL CONTRAST SENSITIVITY AS A
SCREENING PROCEDURE FOR EARLY OPEN ANGLE
GLAUCOMA**

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We investigated Temporal Contrast Sensitivity (TCS) in patients with early glaucoma, in order to ascertain the possible clinical value of this test in the early diagnosis of Chronic Open Angle Glaucoma (COAG), and as a margin screening procedure for COAG.

The study comprised of 108 patient eyes (Group 1) and 40 control; eyes (Group 2). Of group 1 almost half had a history of treatment for COAG, or were receiving treatment at the time of testing. The control subjects had Intra Ocular Pressure (IOP) <22mmHg, normal Snellen acuity and normal visual fields. The following tests were carried out on both groups: 1. Visual acuity - Snellen chart; 2. IOP - Goldmann applanation tonometer, 3. Assessment of vertical cup: disc ratio - direct ophthalmoscopy; 4. Visual fields - Hensen field analysis; 5. TCS: modulation transfer functions were obtained using a sinusoidal flickering stimulus viewed with central fixation and plotted at frequencies from 5 to 50 Hz.

The Modulation Threshold Transfer Function (MTTF) is a plot of log sensitivity versus log temporal frequency (Hz) for a given mean luminance and subject. The MTTF of group 1 confirms published findings¹, indicating that the sensitivity is

greatest within the frequency range 7-20Hz and falls off at higher and lower frequency. No statistical difference was found between the two groups which could be considered useful for diagnostic purposes. However, on average the control group did consistently score a higher sensitivity (approx. 50), than the glaucomatous group (approx. 30) in the temporal frequency range 10-20Hz.

Previous studies indicated that this test could be used to assess contrast sensitivity function in order to diagnose COAG. Our study to date has not correlated with this finding.

Reference

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(P.35) ANTIBODY CROSS-REACTIONS BETWEEN GANGLIOSIDES AND LIPOPOLYSACCHARIDES OF *CAMPYLOBACTER JEJUNI*

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Guillain-Barré syndrome (GBS), an inflammatory demyelinating autoimmune disease of the peripheral nervous system, is frequently associated with serum antibodies against gangliosides. GBS often develops after enteric infection with certain serotypes of *Campylobacter jejuni* (0:2, 0:4 and 0:19). Mimicry by ganglioside-like structures in lipopolysaccharides (LPS) of *C. jejuni* has been suggested to link infection, anti-ganglioside antibodies and development of GBS. The purpose of this study was to investigate the cross-reactions of antibodies with gangliosides and *C. jejuni* LPS. Binding studies were performed using thin-layer chromatography with chemical- and immuno-staining. Binding of anti-GM1 antibodies to 0:19 LPS, and of anti-asialoGM1 antibodies to 0:19 LPS, but predominantly to 0:2 LPS, was observed. Anti-*C. jejuni* 0:19 antiserum bound GM1 and asialoGM1, whereas 0:4 antiserum did not bind these gangliosides. Sera from two GBS patients who had *C. jejuni* infection contained antibodies predominantly of the IgA class against GM1, asialoGM1, and GD1b, as well as against 0:2, 0:4, and 0:19 LPS. Ganglioside-like epitopes in *C. jejuni* LPS, and the predominance of IgA in both patients, support the possibility that immune reactions against *C. jejuni* contribute to GBS.

(P.36) A STUDY TO EXAMINE THE PUPILLARY LIGHT REFLEX IN DIABETES MELLITUS USING AN INFRARED LIGHT REFLECTION METHOD

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It has been well documented that autonomic neuropathy frequently develops in diabetes mellitus. Anatomically the iris consists of two muscle groups which control pupil size. Innervation is exclusively by the sympathetic and parasympathetic parts of the autonomic nervous system. By measuring pupillary reflexes to a light stimulus quantification of the autonomic reflex is achieved in a simple non-invasive manner. Previous studies have indicated that the autonomic nervous system may be affected by diabetes before symptoms and signs of diabetic neuropathy become evident. This suggests

that altered pupillary reflexes portray early autonomic neuropathy.

The pupillary light reflexes were measured in three groups of patients; 6 age and sex matched control subjects (group A), 6 diabetic patients with no symptoms or signs of autonomic neuropathy (group B) and 6 diabetic patients with a diagnosis of autonomic neuropathy (group C). A dynamic binocular infrared light reflex pupillographic method called IRLS was used. This method is simple, fast and easy to operate in contrast to previous techniques, such as, Ohrt's cinematographic technique and Friedman et al's use of electronic infrared pupillography. IRIS also measures the consensual pupillary reaction and provides response measurements with larger amplitudes and time resolutions than previous methods. The basis of this study was to investigate the ability of the IRIS technique to detect changes in the autonomic reflexes associated with diabetes mellitus.

The mean values of the constriction latency (CL) were, in group A 67 ms, group B 75 ms and in group C 79.5 ms, while the mean peak constriction velocity latency (MPCVL) values were, in group A 114 ms, group B 117 ms and in group C 123 ms. These results suggest a prolonged latency of the constriction reaction in both diabetic groups, and portray increasing latency values correlating with the development of autonomic neuropathy.

References

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2. J. P. H. Reulen, J. T. Marcus, M. J. Van Gilst, D. Koops, J. E. Bos, G. Tiesinga, F. R. De Vries, K. Boshuizen. Stimulation and recording of dynamic pupillary reflex: the IRIS technique, part 2. *Med. Biol. Eng. Comput.* 1988; 26, 27-32.

(P.37) NEUROLOGICAL MANIFESTATIONS OF B12 DEFICIENCY

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The aim was to ascertain the prevalence of neurological symptoms and signs associated with B12 deficiency seen in St. James' Hospital between Jan. '91 and Dec. '94.

A retrospective study was performed reviewing the records of all patients with B12 levels <100ng/l. Those without full neurological assessment and with pre-existing neurological disease were excluded. 57 patients were studied.

54% (31) had no neurological symptoms or signs whereas 46% (26) were symptomatic. Of those with neurological manifestations peripheral neuropathy was the most common finding (24) 92%. 27% (7) presented with distal paraesthesia alone. Absent ankle jerks were noted in 54% (14) and absent knee jerks in 23% (6). Posterior columns were often affected with reduced vibration sense noted in 38% (10), position sense in 31% (8) and soft touch 19% (5). Ataxia secondary to posterior column disturbance was noted in 23% (6). Spinal cord changes were rare with only 12% (3) developing spastic paraparesis. One patient complained of increased irritability and emotional lability and one of worsening short term memory. No visual or spincter changes were noted.

In summary posterior column changes and absent reflexes were most commonly noted in cases of B12 deficiency. Spinal cord or central changes were rare. We could find no correlation between the degree of symptoms and the measured deficiency.

(P.38) AN UNUSUAL CASE OF DEMENTIA AND PSYCHOSIS IN A YOUNG WOMAN

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We present the case of N.H., a 21 year old University student with a three month history of frontotemporal seizures and cognitive deterioration.

N.H. experienced episodes of disorientation, paranoid psychosis, speech disturbance and marked deterioration in short and long term memory.

Over the course of three months, she exhibited fluctuating neuropsychiatric symptoms and required assistance in dressing and feeding.

Neuropsychological testing revealed an overall decline in cognitive ability with predominantly right hemispheric dysfunction.

Investigations included: serum vasculitis screen, CSF and serum virology including HIV, Porphyrin screen, Toxicology screen, Amino acid screen, repeated CSF analysis, EEG (interictal), MRI brain with gadolinium, Vascular screen.

These tests revealed persistently elevated CSF protein but no other abnormalities.

Following a further deterioration she had a repeat EEG showing diffuse slow-wave activity.

She underwent biopsy of non-dominant frontal lobe and meninges.

Histological findings were abnormal suggesting a diagnosis of subcortical gliosis. This diagnosis is uncommon in this age group and is often confused with schizophrenia or organic psychosis.

The clinical manifestations and the extensive differential diagnosis of progressive frontal dementia and seizures in a young adult will be discussed.

(P.39) HISTOLOGICAL EVIDENCE FOR NEUROTOXICITY OF β AMYLOID IN RAT HIPPOCAMPUS

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β /A4 amyloid is thought to be responsible for much of the pathology observed in Alzheimer's disease. We studied its ability to induce neurodegeneration following intrahippocampal injection in rats. Male Wistar rats received injections of: a) Soluble β /A4 (1-40, 7.5 μ g) and N-methyl D-aspartate (4.4 μ g), b) Aggregated β /A4 and NMDA, c) Aggregated β /A4, d) Vehicle (water), intrahippocampally (CA1-CA3) via an indwelling cannula over a 3 week period. The hippocampal lesion, cannula tract areas and numbers of cell bodies within the pyramidal cell layer were measured in 10 μ m sections (week 8). All injections produced localised tissue destruction, neuronal loss and reactive gliosis. The relative damage was expressed as the ratio of total damage versus cannula damage. We found that aggregated β /A4 appeared to be substantially more damaging than soluble amyloid, while the vehicle alone had little effect. NMDA appeared to potentiate the toxic effect of the aggregated β /A4. This suggests that β /A4 is indeed neurotoxic, especially when aggregated and with co activation of NMDA receptors.

(P.40) CARDIOVASCULAR EVIDENCE FOR AUTONOMIC DYSFUNCTION IN ALZHEIMER'S DISEASE

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Abnormalities of the autonomic nervous system in Alzheimer's disease have been suggested by previous studies of the cardiovascular response to standing. In this study, 12 outpatients having Dementia of the Alzheimer Type (Clinical Dementia Rating, Score \leq 1; mean age \pm SEM, 74 \pm 2 years) were continuously monitored using Finapres and their responses to the Valsalva manoeuvre and positional change were compared with 12 age matched (73 \pm 1 years) healthy elderly controls. Mean resting supine blood pressure and heart rate were not different between the two groups. Although both groups had the predicted tachycardia during the Valsalva manoeuvre, on opening the glottis only the controls showed the typical bradycardia (-10.2 \pm 2.6 versus +6.2 \pm 3.7 beats per minute, b.p.m., for the patients, $P < 0.01$). When the subjects stood, there was a similar increase in systolic blood pressure for both groups. In contrast, whereas controls had a robust tachycardia (+18.6 \pm b.p.m.) this was not the case for the Alzheimer's patients (+5.8 \pm 2.8 b.p.m., $P < 0.01$). This indicates diminished baroreceptor cardiac reflexes in mild Alzheimer's disease.

(P.41) PATIENT KNOWLEDGE OF ANTIEPILEPTIC MEDICATION

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Success with long term prophylactic therapy requires patient compliance and education. We reviewed case records and questioned 35 consecutive outpatients with grand mal epilepsy concerning their medication. Patients were receiving largely mono-therapy carbamazepine (15), phenytoin (10) and sodium valproate (5). The mean age was 42 years (range 14-81); 14 were female. Almost half (43%) were fit free during the previous year. Most knew the name and dose (71%), some (23%) name only and 6% knew neither. About half reported drowsiness and tiredness with their medication and 31% claimed it caused hair loss. Only 5 (14%) did not attribute any side effect to their medication. Patients, including 2 on warfarin, were unaware of potential drug interactions, and almost 30% were unaware of possible problems with driving, drinking, alcohol or pregnancy despite prescribers advising on these topics when initiating therapy. On the other hand almost all knew what to do if a dose was missed, attended for therapeutic drug monitoring, and requested more information about medication. Additional education including written information and reminders concerning therapy could be valuable and would be appreciated by patients with epilepsy.

NUTRITION

(P.43) DIETARY COMPLIANCE IN ADULTS WITH COELIAC DISEASE

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Coeliac disease results from permanent intolerance to dietary gluten, a condition which requires the dietary exclusion of gluten for life.

This study was carried out to assess patients' understanding of the prescribed diet and of the importance of adhering to it.

A questionnaire was posted to 107 patients with biopsy-proven coeliac disease who attended the Coeliac Clinic in St James's Hospital, Dublin. An 85% response rate was obtained and all questions were answered by all respondents.

The majority (65%) felt that the gluten-free diet should never be relaxed, although some felt that they could relax the diet during social occasions (16%), when away from home (10%) or when asymptomatic (10%). Nevertheless, many patients (42%) admitted deviating from their prescribed diet (10% "often included gluten"). The consequences of poor compliance were not always appreciated, most realising that diarrhoea could result (91%), fewer being aware of weight loss (86%), anaemia (69%), food malabsorption (60%) or metabolic bone disease (27%). Factors contributing to difficulty in adhering to the diet included cost (97%), problems during social occasions (91%) and difficulty obtaining gluten-free products (55%). Neither time since diagnosis nor socioeconomic group were significant factors in determining difficulty with dietary adherence.

Poor dietary compliance appeared to be a considerable problem in this population of adult coeliac patients. Contributing factors may have included insufficient patient education and infrequent dietetic follow-up as well as insufficient availability of gluten-free products, cost and inconvenience of the gluten-free diet.

(P.44) A SURVEY OF NUTRITION INTEREST AMONG GENERAL PRACTITIONERS

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Nutrition plays an essential role in health and in the practice of medicine. General practitioners (GPs) receive little nutrition training despite their potentially important role in promoting healthy eating and in using therapeutic nutrition strategies in patient management.

A postal survey of 100 GPs in the Eastern Health Board area, randomly selected from the Irish College of General Practitioners' register, was carried out. A good response rate was obtained to the questionnaire (56%) and most of the questions (28 of 33) were answered by all respondents. Awareness of nutrition-related societies ranged from 4% (European Society for Parenteral and Enteral Nutrition) to 19% (The Nutrition Society). Almost all (96%) felt that nutrition was important in preventative health care, 77% believing it to be important in general practice. This contrasted with infrequent assessment of patients diets (40% once weekly, 36% once monthly) where only 51% reported having access to dietetic services. Although 98% believed that doctors should know more about nutrition, 28% felt their knowledge of nutrition was

adequate (49% were unhappy with their nutrition knowledge and 23% were undecided). Further nutrition education was of interest to 85%, 75% stating their willingness to attend lectures and seminars. The topics of greatest appeal were obesity (83%), diabetes mellitus (74%), cardiovascular disease (74%), nutrition in the elderly (74%) and nutrition in infants (66%).

If the substantial interest in nutrition expressed by the respondent GPs is representative, efforts to promote awareness of nutritional issues and to improve the nutrition knowledge of GPs would be well received.

RHEUMATOLOGY/REHABILITATION

(P.45) IDENTIFYING IRON DEFICIENCY BY SIMPLE LABORATORY MEASURES IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Anaemia of chronic disease (ACD) is a common feature in rheumatoid arthritis (RA) but iron deficiency anaemia (IDA) also occurs and may be difficult to identify. A marrow sample demonstrating absent iron stores confirms IDA but is invasive, time-consuming and expensive. This aim of this study was to identify simple laboratory measure which either separately or in combination were reliably predictive of absent marrow iron stores, thereby avoiding the need for marrow sampling.

Forty seven anaemic RA patients (males with haemoglobin (Hgb) <11.0g/dl, females <10.5g/dl) who were not taking iron supplements underwent a bone marrow aspirate and/or biopsy in addition to a full blood count, serum ferritin (Ferr) and iron saturation measurements. Mean (range) age was 62 (20-80) yrs and disease duration 12 (1-40) yrs. An evaluable marrow sample was obtained in 34 patients: 19 had IDA (no marrow iron stores identified) and 15 had ACD (iron stores present). A diagnostic algorithm was developed using the results of the blood samples measured. Patients with serum Ferr <40µg/L were diagnosed IDA; of the remaining patients, those with a mean corpuscular volume (MCV) >85fL were diagnosed ACD; of those still remaining, patients with serum iron saturation <14% were diagnosed IDA, and those 14% as ACD. This algorithm had 95% sensitivity and 82% validity for the differentiation of IDA from ACD in patients with RA.

This study demonstrates that IDA can be reliably identified by measuring serum Ferr, MCV and iron saturation in many RA patients, thereby avoiding the expense and trauma of a bone marrow biopsy.

(P.46) ADHESION MOLECULE EXPRESSION IN SERUM, SYNOVIAL FLUID AND MEMBRANE IN INFLAMMATORY ARTHRITIS

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Studies have examined adhesion molecule (AM) expression in long-standing RA where the AM profile may have been

influenced by factors other than RA. In addition, the relationship of synovial membrane (SM) to serum (Srm) and synovial fluid (SF) AM levels has not been examined. SM, SF and Srm were obtained from 13 patients with untreated inflammatory arthritis: mean (range) age 49 (26-75) yrs, disease duration 27 (3-84) mths and Ritchie index (RI) 11 (0-22). SM AM expression was assessed by routine immunohistology. Paired Srm/SF soluble AM (sAM) levels were measured by ELISA.

Mean Srm and SF sICAM-1 correlated (Tau (T)=0.48). Lining layer (LL) ICAM-1 expression was greater in those with more sub-LL (SLL) ICAM-1 expression (p=0.01) and both LL and SLL ICAM-1 was greater in those with higher SF sICAM-1 levels (p<0.02). Srm sICAM-1 levels correlated with both ESR (T=0.45) and RI (T=0.47) and RI was higher in those with greatest SLL ICAM-1 expression (p=0.03). Mean Srm sE-selectin correlated with SF sE-selectin levels (T=0.52) and was higher in patients with disease duration 12 mths (p=0.04). Extent of SLL E-selectin expression correlated negatively with RI (T=-0.61). SLL VCAM-1 extent correlated negatively with LL thickness (T=-0.48). No other correlations were seen between SM, SF or Srm levels of either VCAM-1 or E-selectin.

This study found that Srm sICAM-1 levels reflect ICAM-1 expression in SM and SF and also disease activity. In contrast, this pattern was not seen with either E-selectin or VCAM-1. For these reasons, Srm sICAM-1 levels may represent a useful marker for the disease process in inflammatory arthritis.

(P.47) RELATIONSHIP OF ICAM-1 TO E-SELECTIN IN SERUM, SYNOVIAL FLUID AND MEMBRANE IN INFLAMMATORY ARTHRITIS

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The inter-relationship of synovial membrane (SM), fluid (SF) and serum (Srm) adhesion molecule (AM) levels in untreated inflammatory arthritis has not previously been systematically examined. Matched SM, SF and Srm samples were obtained from 13 patients (9 with RA) with inflammatory arthritis: disease duration 3-84 mths, no previous steroid or disease modifying therapy. SM ICAM-1 and E-selectin expression was assessed by routine immunohistology. Srm and SF soluble AM (sAM) levels were measured by ELISA.

A consistent inverse relationship was seen between E-selectin and ICAM-1 levels in SM, SF and Srm. The number of E-selectin positive vessels per mm² inversely correlated with the % ICAM-1 + lining layer cells (Tau (T)=-0.57) and was significantly lower in those with more intense sublining layer ICAM-1 staining (p=0.03). The % E-selectin positive vessels (as a % of all blood vessels) inversely correlated with serum sICAM-1 levels (T=-0.54). Serum sE-selectin inversely correlated with the extent of ICAM-1 expression in the sublining layer (T=-0.55). SF sICAM-1 levels tended to be lower in those with more intense expression E-selectin in the synovial membrane. Finally, synovial vascularity (von Willebrand factor expression) was significantly less in those with more intense sublining layer ICAM-1 staining (p=0.04).

These results indicate an unexpected but consistent inverse relationship between E-selectin and ICAM-1 levels in previously

untreated inflammatory arthritis. This suggests that the accumulation within the synovium of cells expressing ICAM-1 is accompanied by a down-regulation of E-selectin expression by endothelial cells.

(P.48) AN ANALYSIS OF THE DISCREPANCY BETWEEN THE CLINICAL AND RADIOLOGICAL COURSE IN RHEUMATOID ARTHRITIS

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Cohort studies in rheumatoid arthritis (RA) have noted progressive radiological deterioration despite improvement in clinical measures of disease activity. Clearly, many of these routine measures are not sensitive to radiological progression. We sought to identify those clinical measures which best correlated with radiological course.

Serial clinical and radiological data were recorded in 58 patients with active RA enrolled in a prospective study and reviewed a mean (range) 6.1 (4-8) yrs later. All clinical measures of disease activity improved, including morning stiffness (p = 0.0007), pain score (p = 0.004), grip strength, Ritchie articular index (RAI), ESR and hemoglobin (Hgb) (all p = 0.0001). Overall, 77% had improvement in 4 or more measures of disease activity and ESR improved in 93%. In contrast, mean Larsen score (LS) deteriorated significantly from 37 to 88 (p = 0.0001). Only 4 patients had little or no deterioration in LS. Radiological deterioration (actual change as percentage of possible change in LS) during the study correlated with RAI (r = 0.5, p = 0.005), Hgb (r = -0.55, p = 0.002) and ESR (r = 0.51, p = 0.004) at review. In addition, radiological outcome (review LS) also correlated with RAI (r = 0.43, p = 0.017), Hgb (r = -0.49, p = 0.007) and ESR (r = 0.41, p = 0.024) at review.

This study highlights RAI, Hgb and ESR as clinical measures of disease activity which best reflect radiological deterioration.

(P.49) SYNOVIAL FLUID CD8+ T-LYMPHOCYTE PREDOMINANCE IN PSORIATIC ARTHRITIS EFFUSIONS

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There are clinical, serological, and genetic differences between rheumatoid (RA) and psoriatic arthritis (PsA) including differences in the mononuclear cell (MNC) populations accumulating in synovial tissue. This study examined by flow cytometry, matched peripheral blood (PB) and synovial fluid (SF) MNCs from 11 PsA and 19 RA patients using the following monoclonal antibodies: CD4, CD8, CD3, HLADR and CD14. Mean (SEM) %+ MNC were:

	RA PB	RA SF	PsA PB	Ps ASF
CD4	49 (2.7)	38 (2.5)	40(3.0)	22(2.0)
CD8	22 (1.8)	41 (1.8)	32(2.0)	56 (3.0)
CD4 / CD8ratio	2.7(0.3)	1.0(0.1)	1.4(0.2)	0.4(0.1)
CD3	67(2.6)	79 (2.9)	72 (1.5)	77 (4.0)
CD3 HLA DR+	5.3(1.0)	57(3.9)	9(3.0)	49 (9.0)
CD14	6 (0.7)	6 (1.0)	6 (0.8)	6 (1.0)

CD8+ cells were significantly higher ($p < 0.04$) and CD4+ cells lower ($p < 0.02$) in PsA PB and SF compared to RA. The ratio of CD4 to CD8 cells seen in PsA PB was significantly less than in RA PB ($p = 0.005$). The ratio of CD4 to CD8 was also less in PsA SF, with CD8+ cells predominating, as compared to RA where the ratio was 1:1 ($p = 0.0004$). CD4 counts were significantly less, and CD8 counts greater, in SF compared to PB in both PsA ($p = 0.03$) and also in RA ($p = 0.0001$).

In view of the association of PsA with class I HLA antigens, the predominance of CD8+ cells in PsA SF provides further evidence for a different pathogenetic basis in PsA as compared to RA.

(P.50) CUTANEOUS LYMPHOCYTE ANTIGEN ON PERIPHERAL BLOOD AND SYNOVIAL FLUID LYMPHOCYTES IN PSORIASIS AND PSORIATIC ARTHRITIS

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Cutaneous lymphocyte antigen (CLA), expressed by ~80% cutaneous T-lymphocytes in psoriasis, may be involved in lymphocyte homing to skin. It has been proposed that CLA+ T-lymphocytes may also traffic to synovium in psoriatic arthritis (PsA) where they may play a pathogenetic role. CLA expression was measured in matched PsA peripheral blood (PB) and synovial fluid (SF) and also normal and disease controls.

Thirty subjects were studied: 6 active psoriasis, 7 PsA (5 paired PB/SF samples), 12 rheumatoid arthritis (RA) (6 paired) and 5 healthy controls. Fresh heparinised PB and SF were examined by dual fluorescence flow cytometry to measure T-lymphocytic CLA expression using HECA-452 (*gift from Dr. Louis Picker, Dallas*). In PsA, SF %CLA+ lymphocytes were higher than PB in four of five paired samples studied but the difference did not reach statistical significance (10.9% v 4.5%, $p = 0.08$). This pattern was not specific to PsA and in RA, SF %CLA+ lymphocytes were also higher than PB in all six paired samples (14.7% v 5.6, $p = 0.03$). There was no significant difference between mean %CLA+ SF lymphocytes in PsA compared to RA (10.9% v 14.7%, $p = 0.36$). Mean PB %CLA+ lymphocytes tended to be lower in psoriasis than in PsA (1.9 v 4.9, $p = 0.06$) but there was no significant difference between mean PB %CLA+ lymphocytes in PsA, RA and normal healthy controls (4.9%, 7.8% and 5.2% respectively).

These data do not support the hypothesis that CLA+ lymphocytes selectively traffic to PsA synovium since similar numbers are seen in RA SF. Increased numbers of CLA+ lymphocytes in SF in both RA and PsA may reflect non-specific accumulation of activated CLA+ T-lymphocytes at sites of inflammation.

(P.51) HML-1 EXPRESSION BY PERIPHERAL BLOOD AND SYNOVIAL FLUID LYMPHOCYTES IN RHEUMATOID AND PSORIATIC ARTHRITIS

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HML-1 antigen is an adhesion molecule member of the B7

integrin family expressed by over 90% intraepithelial and 40% lamina propria lymphocytes but rarely expressed outside these settings. It may be involved in lymphocyte homing to the gut. Since a gut-derived antigen may play an aetiological role in rheumatoid arthritis (RA), HML-1+ T-lymphocytes might be expected to traffic to and accumulate in RA synovium. In this study, HML-1 expression was measured in matched RA peripheral blood (PB) and synovial fluid (SF) samples and also in normal and disease controls.

Twenty four subjects were studied: 12 RA (6 paired PB/SF samples), 7 psoriatic arthritis (PsA) (5 paired) and 5 healthy controls. Fresh heparinised PB and SF were examined by dual fluorescence flow cytometry to measure T-lymphocytic HML-1 expression. In RA, SF %HML-1+ lymphocytes were higher than PB in all (SF > PB x2 in four of six) paired samples studied (7.2% v 1.2%, $p = 0.03$). This pattern was not specific to RA and in PsA, SF %HML-1+ lymphocytes were also higher than PB in four of five paired samples (7.0% v 1.4%, $p = 0.08$). There was no significant difference between mean %HML-1+ SF lymphocytes in RA compared to PsA (7.2% v 7.0%, $p = 0.93$). There was no significant difference between mean PB %HML-1+ lymphocytes in RA, PsA and normal healthy controls (1.1%, 1.1% and 1.7% respectively).

These data do not support the hypothesis that HML-1 + lymphocytes selectively traffic to RA synovium since similar numbers are seen in PsA SF. Increased numbers of HML-1+ lymphocytes in both RA and PsA SF may reflect non-specific accumulation of activated HML-1+ T-lymphocytes at sites of inflammation.

(P.52) A PROPOSAL TO USE A LASER IN REVISION HIP SURGERY

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Precise, powerful and sometimes subtle in their effects, lasers are increasingly important medical tools which have yet to find any major application in orthopaedic surgery. In one area, the increasing numbers of re-operations carried out on total hip replacement patients cause considerable difficulty for orthopaedic surgeons. One particular problem lies in the removal of the bone cement inserted during the primary operation, without causing damage to the bone. In order to develop a method for differentiating between polymethyl methacrylate bone cement and bone during laser ablation, the laser-induced fluorescence from bone cement has been studied and compared to that from the bone. An Oriel multispec spectrometer was used to analyse and record the radiation emitted in the range 340-840nm during 248nm excimer laser ablation. There was very high intensity fluorescence from bone relative to that from bone cement and several peaks occurred in the spectrum of bone which were absent from that of bone cement. Monitoring of this emission has enabled controlled laser ablation of bone cement in contact with bone to be achieved in vitro with no damage to the naked eye. This has shown the potential of controlling the power of laser surgery to solve the problem of cement removal.

(P.53) GENETICS OF TUMOUR NECROSIS FACTOR ALPHA IN RHEUMATOID ARTHRITIS

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The aetiology of rheumatoid arthritis (RA) is believed to involve both environmental and genetic factors. A large part of the inherited component is associated with a shared epitope (SE) found in several DRB alleles. Tumour necrosis factor alpha (TNF α) both because of its chromosomal localisation in the major histocompatibility complex and biological effects, is a candidate gene underlying the genetic association of the MHC with susceptibility to, or severity of, rheumatoid arthritis. We have recently described the first known polymorphism in the TNF α gene and shown that the rare allele (TNF2) lies on the extended haplotype A1-B8-DR3-DQ2. We have therefore examined the genetic contribution of this polymorphism in RA.

147 unrelated adult Caucasian patients and 135 healthy controls were studied.

	TNF2-	TNF2+	OR
Controls	90	45	
Patients	95	52	1.1(0.7-1.8)

Disease activity was assessed clinically and radiologically at presentation and at three years and no association there was no association with any measurement and TNF genotype.

Although there was no overall association of TNF2 with RA we are now studying a larger group to see if it contributes to RA independently of the SE.

GENERAL PRACTICE

(P.54) ESTIMATION OF THE IMPACT OF SMOKING ON PRESCRIBING COSTS IN SPECIFIC AGE GROUPS IN GENERAL PRACTICE

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The objective of this study was to quantify the effect of smoking on the cost of drugs prescribed in specific patient age groups under the General Medical Services (GMS) scheme.

Details of ingredient cost for one month for each pharmaceutical item dispensed by pharmacists under the GMS scheme with respect to patients attending one large inner city practice were linked to patients' age and to smoking status derived from practice records. Age specific costs in 10 year groups were calculated for current, ex- and non-smokers.

Smoking status was available on 88% of the 1,976 persons aged 15 and over. Of these 47.5% were smokers, 8% were ex-smokers and 44.5 were non-smokers. Average expenditure per patient for current smokers was £9.00 vs £19.30 for ex-smokers and £6.80 for non-smokers. These differences were significant when the effects of age and sex were taken into account ($p < 0.01$). Expenditure for smokers was higher than for ex- and non-smokers up to the 35-44 age group, but from 45-54 upwards expenditure was much greater for ex-smokers than for current and non-smokers.

The demonstration that ever smokers cost considerably more in terms of prescribing than non-smokers should provide a

double incentive for GPs to educate their patients with regard to smoking, and to assist smokers to stop before incurring permanent damage to their health.

(P.58) CAN LIFESTYLE STRATEGIES REPLACE THERAPY FOR HYPERTENSION?

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This study compared non-drug treatment to standard drug therapy for hypertensives in general practice. Patients ($n = 45$) with controlled hypertension for at least 6 months (a BP $< 160/95$ mmHg) were randomised to continued medication (C) ($n = 24$) or withdrawal (W) ($n = 21$). Drug therapy was recommended if BP exceeded 160/95 mmHg on any visit. Both groups were counselled regarding lifestyle by their GP and reviewed at least monthly for 9 months. Both groups were initially similar for BP, heart rate, age, duration of therapy, total cholesterol and body mass index. 3 subjects (1 from the W and 2 from the C group) did not complete monitoring. There were no cardiovascular events. 71% of W subjects remained off drug therapy at 9 months (15 of 21) with mean BP of 144/85 mmHg (W) and 139/86 mmHg (C). No significant differences were observed in mean systolic or diastolic BP, heart rate, or body mass index between the two groups after 9 months (MANOVA). The W group had a 6% reduction in body mass index after 9 months. Successful W group patients had lower baseline diastolic BP than unsuccessful subjects ($p < 0.05$). On multivariate analysis, physical activity level at 9 months was the best predictor of change in systolic ($r^2 = 0.20$) and diastolic BP ($r^2 = 0.12$) over the study. A proportion of motivated hypertensive patients can cease drug therapy and be adequately maintained by lifestyle advice from their GP for at least 9 months. Cessation of drug therapy may be an important motivating factor for lifestyle change.

GERONTOLOGY

(P.63) HOSPITAL-ACQUIRED DIARRHOEA - ARE THE ELDERLY MORE AT RISK?

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Diarrhoea is a significant cause of morbidity, particularly in the elderly. It may result in increased hospital stay, risk of malnutrition and dehydration and is associated with an increased susceptibility to other nosocomial infections.

We undertook a prospective study of patients admitted to a General Hospital in a 4 month period to determine the causes of hospital acquired diarrhoea and risk factors for acquisition. 50 cases out of 2600 admissions were identified, 41 of these were over the age of 65 years. 18 cases were secondary to Clostridium Difficile; 15 of these were over 65 years and the other 3 were young debilitated adults. All cases had Barthel Scores less than 10/20 and many shared the same commode or were nursed in the same ward. 20 cases were caused by medications - Laxatives accounting for 13 cases, the remainder caused by antibiotics, NSAIDs or other medications.

The overall incidence of hospital-acquired diarrhoea is 1.9

cases per 100 admissions. Most cases are iatrogenic or caused by *Clostridium Difficile*. Elderly debilitated patients are particularly susceptible. More careful attention to appropriate prescribing of laxatives in the elderly and rigorous attention to infection control policies by hospital personnel may prevent many cases.

(P.64) COGNITIVE FUNCTION IN OLDER DIABETIC OUT-PATIENTS

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Cognitive impairment and clinical dementia have been suggested as chronic complications of Diabetes Mellitus. However, the prevalence and type of cognitive impairment in older diabetics has not been quantified. In this study 41 diabetic out-patients aged from 60 to 89 years and 28 age-matched non-diabetic out-patients were screened for cognitive impairment using the Standardised Mini-Mental State Examination (SMMSE).

SMMSE scores suggested cognitive impairment in almost 1 in 5 diabetics. On statistical analysis however, no significant difference was found between the two patient groups in mean SMMSE scores or in the proportion with SMMSE scores of 23 or below. In the diabetic group lower SMMSE scores were related to patient age, school-leaving age, depressive mood and living alone. Cognitive performance was not related to Hb Alc₂ or frequency of blood or urine glucose monitoring by patients.

OBSTETRICS/GYNAECOLOGY

(P.68) ANAL SPHINCTER ENDOSONOGRAPHY USING A 120° SECTOR SCANNER

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Conventional methods of assessment of the anal sphincters primarily provide functional rather than anatomical information. Anal endosonography is the only modality providing direct visualisation of the sphincters. The aim of this study is to evaluate the use of the 120° sector scanner (more widely available than the 360° transducer previously described) in the identification of anal sphincter defects.

75 women were examined in the left lateral and prone positions by a Toshiba PVL 516s sector scanner. Neither the patients' symptoms nor the results of anal manometry and pudendal nerve terminal latencies were known to the ultrasound operator and the examinations were assessed by two independent observers.

79% (n=59) had abnormal transanal ultrasound. Of these 19% (n=11) had defects of the internal sphincter; 20% (n=12) had external sphincter defects; 36 (61%) had defects of both. All patients had abnormal manometry. We conclude that endosonography using a 120° sector scanner provides a reliable and well tolerated adjunct to conventional methods for assessing the anal sphincters.

(P.69) MATERNAL ACTIVE AND PASSIVE SMOKING IN PREGNANCY AT HOME AND IN THE WORKPLACE

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Effects of cigarette smoking in pregnancy are well known. Maternal exposure to other people's cigarette smoke i.e. maternal passive smoking has been less well-defined and the effects are more subtle. The objectives of this study were to document the incidence of maternal passive smoking as well as active smoking in a pregnant population attending a public clinic. This information was collected by self-administered questionnaire. A presenting sample was taken.

The total number of women studied was 113. The response rate was 100%. 42% smoked during pregnancy. 35% never smoked. 23% were ex-smokers, of whom 35% stopped just before or during the current pregnancy. The incidence of passive and active smoking was higher in unemployed women compared to employed and housewife groups. It was also higher in single compared to married women. Of those who worked, 66% were exposed to passive smoking in the workplace. 49% of smokers received advice about risks of smoking during their-current pregnancy.

Conclusions: Maternal passive smoking is very common in pregnancy. Its effects, which may be subtle, should be studied formally. Antenatal advice should refer to its potential hazards.

(P.70) MATERNAL PREFERENCE FOR MODE OF DELIVERY AND SATISFACTION WITH MANAGEMENT IN LABOUR – A SURVEY OF 520 IRISH WOMEN

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Data on maternal satisfaction with care in labour and maternal preference for mode of delivery were gathered by anonymous questionnaire, distributed on the day of postnatal discharge to all women delivered in a six week period during the months of February and March 1994. Women whose babies had a congenital malformation or perinatal death were excluded. 520 women completed the questionnaire (a 63% response rate). Parity, health plan status, antenatal class attendance, awareness of delivery types, analgesia and labour length were studied. Visual analogue scores (VAS) were recorded for satisfaction with pain relief during and after labour and for care during labour. The majority of women (65% VAS 7 or >) were satisfied with care in labour. Factors significantly associated with such satisfaction were good analgesia during labour (specifically epidural), vaginal delivery, adequate preparation for labour and if personal concerns were listened to by staff. 98.5% had hoped for a vaginal delivery (VD) and 1.5% for caesarean section (CS) - (actual rates - 81% VD, 10% CS, 9% operative VD). 81% felt they had been adequately listened to by staff. Such results may help influence and shape future care of women in labour.

(P.71) CONTRALATERAL OVULATION AS A FACTOR IN ECTOPIC PREGNANCY

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The purpose of this study was to determine the incidence of contralateral corpus luteum in ectopic pregnancy and its relationship to clinical presentation and known risk factors.

A prospective study of all ectopic pregnancies presenting to an urban maternity unit over a 12 month period. Clinical details were recorded. Laparotomy findings were noted: site and condition of ectopic pregnancy, side of corpus luteum, evidence of pelvic pathology. Statistical analysis of data was by chi-squared test and Fisher's exact test. $P < 0.05$ was considered significant.

There were 28 ectopic pregnancies: 1 ovarian, 27 tubal, of which 18 had ruptured. A corpus luteum was identified at laparotomy in 24. The site of ovulation relative to the tubal pregnancy was ipsilateral in 18 (75%), and contralateral in 6 (25%). The mean duration of amenorrhoea, the bleeding pattern at presentation, and the incidence of tubal rupture were no different when transmigration of the ovum had occurred. There was no association between the laterality of the corpus luteum and the presence of risk factors for ectopic pregnancy.

Conclusion: These data suggest that the contralateral corpus luteum is not an aetiological factor in ectopic pregnancy.

(P.72) GENITAL WARTS AND CERVICAL CYTOLOGY

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The aim of the study was to determine the incidence of cervical dysplasia in patients presenting with condylomata.

Setting: A sexually transmitted disease clinic.

A prospective observational study on all first attenders with condylomata accumulata. Patient details included risk factors for cervical dysplasia: age of first coitus, previous partners, contraceptive use, and cigarette smoking. All but 6 women had a cervical smear taken.

98 new patients with genital warts attended the clinic in 12 months. 66 (71.7%) had negative cervical smears. 26 (28.3%) patients had cervical dysplasia: Mild (20), Moderate (5), Severe (1). Results were analysed using chi-squared tests. Age of 1st coitus, previous sexual history, cigarette smoking, oral contraceptive use, and distribution of genital warts had no significant influence on the likelihood of cervical dysplasia in these patients ($p > 0.05$).

Conclusion: A significant number of patients presenting for the first time with genital warts have cervical dysplasia. Coital activity, cigarette smoking, and wart distribution appear to have little effect on the risk of abnormal cervical cytology in these patients.

(P.73) THE INCIDENCE OF LOWER GENITAL TRACT PATHOGENS WITH GENITAL WARTS

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The aim of the study was to detect vaginal and cervical pathogens among patients presenting with condylomata accumulata.

Setting: A sexually transmitted disease clinic.

A prospective observational study on female patients presenting with genital warts. Details were recorded of gynaecological symptoms, coital and contraceptive history, and partner's genito-urinary symptoms. A cervical smear and full pelvic inflammatory screen were performed. Specific swabs were cultured for candida, trichomonas, chlamydia, and gonococcus.

Of 98 new patients with genital warts, 92 were screened. 45 patients (48.9%) had negative pelvic inflammatory disease screens. Pathogens detected on swab culture were as follows: Candida 27, Gardnerella 9, Chlamydia 8, Bacteroides 3, Trichomonas 0, Gonococcus 0. Only 16 of the 47 patients (34%) with positive cultures reported vaginal discharge on questioning.

Conclusion: Over half of these patients presenting with genital warts had vaginal or cervical pathogens. Most were asymptomatic, and hence screening for genital infection is worth considering in all patients with genital warts. There was a notable absence of trichomonal and gonococcal infection.

(P.74) THE PIPELLE ENDOMETRIAL DEVICE: AN ALTERNATIVE TO DIAGNOSTIC CURETTAGE

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In recent years, a variety of endometrial sampling devices are reported as alternatives to diagnostic curettage (D&C), for obtaining tissue for morphological assessment. These devices do not require anaesthesia, can be used in an out-patient department and can be easily repeated.

In this study, 127 consecutive endometrial samples obtained by the pipelle device were assessed morphologically. (The method of sample collection is illustrated.)

21.2% of the samples yielded either very scanty material or showed fragments of shedding endometrium, and therefore were unsuited for full evaluation. 79.8% of samples showed small fragments of endometrial tissue from the functional layer, with well preserved architecture. Of these, 57% showed proliferative pattern, 31% secretory pattern, 2% interval phase, 7% atrophic pattern, one case (1%) each of adenocarcinoma, atypical hyperplasia, cystic glandular hyperplasia (simple hyperplasia) and a placental site nodule. We believe that the pipelle endometrial sampler is an effective alternative to D&C, and it yields adequate material for morphological assessment in most cases. Recent reports call for regular monitoring of breast cancer patients on Tamoxifen therapy for endometrial lesions. We think that the pipelle endometrial sampler in combination with transvaginal ultra sound or hysteroscopy would be very useful in this setting.

(P.75) IRISH TRAVELLING WOMEN: AN OBSTETRICAL AND PERINATAL REVIEW

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The purpose of study was to review the obstetrical and perinatal outcome of Irish travelling women by retrospective chart review of 98 consecutive women delivering in this unit between Jan. 1993 and August 1994. The mean age was 26 years (range: 16-43); 9 < 20 and 4 > 40 years. The mean parity was 5 (range: 0-13); 22 were nulliparae; 28 were > para 4. Thirty-four had a history of miscarriage and 5 of neonatal death. Forty-two had a family history of inherited disorder and 19 of diabetes mellitus. Fifty-seven consumed alcohol and 36 smoked during pregnancy. Sixty two booked at > 18 weeks. Seven had a booking Hb < 10g/dl. Labour was induced in 54; 17 had Caesarean sections. The mean birth weight was 3.8 Kg; 2 (twins) were < 2.5 Kg; 15 were > 4 Kg. There were no perinatal

deaths but 13 infants had serious problems. No mother breastfed. A health education programme is required to meet the special needs of this section of our community.

(P.77) THE EFFECT OF LOW-DOSE ASPIRIN ON PROSTAGLANDIN FORMATION IN PREGNANCY

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The risk of thrombosis is increased in pregnancy and thromboembolism is the commonest cause of maternal death. Thrombosis may also play a pathogenic role in preeclampsia, in which placental infarction and ischaemia impairs fetal growth. In this study, we examined for evidence of increased platelet activation in pregnant subjects by determining the *in vivo* formation of thromboxane (TX) A₂. TXA₂ is the major cyclooxygenase product in platelets and is generated in response to platelet activation. Moreover, TXA₂ itself is a potent platelet activator acting to amplify the original signal.

TXA₂ formation *in vivo* was determined non-invasively by measuring the urinary excretion of its major enzymatic metabolite, 11-dehydro-thromboxane B₂ (TX-M). Urinary TX-M was markedly elevated in pregnancy (2317±541, n=7; normal <350 pg/mg creatinine). To address if this was derived from platelets, aspirin was administered in low dose either as regular oral aspirin 75 mg/day (RA) or a controlled release preparation (CA) which has been shown to be highly selective for platelet cyclooxygenase. Both preparations significantly suppressed platelet cyclooxygenase, determined as serum thromboxane B₂ *ex vivo* (257±43 to 12.9±3.7 ng/ml, n=7 for CA; 217±28 to 2.7±0.6 ng/ml n=11 for RA). To determine whether this effect was selective for platelets, prostacyclin formation was measured as the urinary excretion of its metabolite, 2,3-dinor-6-keto-PGF_{1α}. In pregnant subjects, excretion of PGI-M was elevated (476±54, n=7; normal <220 pg/mg creatinine) when measured on two separate days. Neither aspirin preparation altered prostacyclin generation. In contrast, urinary TX-M decreased by more than 90% following 7 days of treatment with either preparation.

Conclusions: Thromboxane formation is increased in pregnancy and this derives largely from platelets. These data demonstrate in a non-invasive fashion that platelet activation is increased in pregnancy. This in turn may contribute to the risk of thrombosis.

(P.78) RELATIONSHIP OF VITAMIN E TO PROSTAGLANDINS E₂ AND F₂ α IN THE LUTEAL PHASE OF WOMEN WITH MINIMAL STAGE ENDOMETRIOSIS AND A NORMAL PELVIS

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Peritoneal fluid (PF) concentrations of vitamin E,

prostaglandin (PG) E₂ and PGF₂ α were measured during days 20 to 23 of the luteal phase in 36 women with minimal stage endometriosis (MSE) and 16 with a normal pelvis but unexplained infertility (NP). The phase of the menstrual cycle was confirmed histologically. The PF was collected from the Pouch of Douglas at laparoscopy and kept frozen until analysed. Vitamin E was estimated using HPLC methods and PGs were measured by the radioimmunoassay techniques. The values given are mg/L (mean ± SEM). Women with MSE had vitamin E levels of 3.67 ± 0.43 compared with values of 4.87 ± 0.88 in the normal group (p<0.05). Peritoneal fluid vitamin E showed a significant negative correlation with its PGF_{2α} content in women with a normal pelvis (r=0.69; p<0.01) but not in women with MSE (r=0.26; p>0.05). In contrast the levels of vitamin E in the PF of normal women showed a positive correlation with its PGE₂ content (r=0.62; p<0.02) but not in women with MSE (r=0.30; p>0.05). From these results it appears that vitamin E plays an essential role in the synthesis and/or metabolism of ovarian PGs in the luteal phase and this function is abnormal in women with MSE. Such a role for vitamin E in the luteal phase has been recently suggested from animal studies¹.

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OCCUPATIONAL MEDICINE

(P.79) NURSES' EXPRESSED COMFORT IN AIDS PATIENT CARE AND ITS CORRELATES

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Although negative attitudes toward Acquired Immune Deficiency Syndrome (AIDS) patients have been reported¹, the quality of care delivered has been inadequately addressed. Therefore, the aims were, to measure: 1). Nurses' expressed comfort with AIDS care, 2). Behavioural intention toward AIDS patients, 3). Knowledge of AIDS, and 4). Attitudes towards AIDS. A random sample of both psychiatric and general nurses were surveyed, using an 150-item questionnaire comprising a). demographic details. b). a 80-item Nursing Care Expressed Comfort Scale which included 4 behavioural sub-scales measuring: willingness, avoidance, refusal intention and caution, c). 19 attitude items measuring: stress, prejudice, and risk perception d). a 21-item knowledge scale. A response rate of 97% (N=155) was obtained. While 63% (98) were willing to nurse an HIV/AIDS patient, 51% (78) would be uncomfortable with being assigned to an AIDS ward and 12% uncomfortable with nursing an AIDS patient. All respondents expressed some level of avoidance with regard some aspects of AIDS care. Five percent (8) were tested for HIV after an occupational injury. In the case of those who would be uncomfortable, the findings imply that the care AIDS patients receive may be less than desirable. The question then, is if voluntary allocation to AIDS care may be of more benefit to all parties involved.

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(P.80) HEALTHCARE EMPLOYEE AWARENESS AND KNOWLEDGE OF OCCUPATIONAL HEALTH SERVICES

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The health service is one of the leading employers in Ireland and Great Britain. Its occupational health (OH) services vary enormously or are absent in health boards and voluntary hospitals in Ireland. Health service employees are exposed to numerous hazards - for example needlestick injuries - so adequate use of their OH department is important. This project investigated i) the knowledge and attitude of health care workers within the United Kingdom National Health Service (NHS) regarding their OH department, and ii) their awareness of policy for needlestick injuries. A questionnaire was sent to 300 NHS employees: the response rate following a second mailing was 51%.

The results highlight deficiencies in employees' knowledge of their OH department, its staffing and the facilities available: 14% did not know its location, 28% had never visited it and 84% did not know by whom it was staffed. Staff were reluctant to attend their OH department for anything other than pre-employment assessment and vaccination.

Although over 17% of staff had experienced a needlestick injury within the last 12 months, 23% of staff remain unvaccinated against hepatitis B. Nearly three-quarters of respondents felt that they had never had any training in the subject and over 27% of respondents are unaware of the procedure following needlestick injury. These findings have significance for the content and format of newly developing OH services in Irish hospitals.

PAEDIATRICS/PERINATOLOGY

(P.81) rhDNase USE IN PAEDIATRIC CYSTIC FIBROSIS PATIENTS

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Recombinant human DNase hydrolyses DNA, present in large quantities in infected CF sputum, so reducing the sputum viscosity. 12 paediatric patients (6 male, 6 female) aged 9-17 years were selected. Criteria for selection were age >5 years, a positive sweat test and FVC on spirometry between 40-70% of predicted. The study was an open trial with both clinician and patient aware of treatment.

All patients received a once daily aerosolised dose of 2.5 mgs rhDNase (Pulmozyme) for a period of 12 weeks. Baseline spirometry (FVC, FEV1) was performed on day 0, prior to starting therapy and repeated day 42 and day 84. Patients were asked to keep a daily diary of their respiratory symptoms, infections and their concomitant drug therapy during the study. Serial weights were recorded for each patient also. Spirometry: Average FVC for the group increased from 1.64L (SD 0.40L) 56.3% predicted (SD 9.57%) to 1.87L (SD 0.47L) 62.82% Predicted (SD 10.10%), $p=0.06$. Average FEV1 increased from 1.006 L (SD 0.27L) 39.9ZX predicted (SD 10.40%) to 1.196L (SD 0.34L) 48.25% predicted (SD 14.0%) $p<0.05$.

No serious adverse events were encountered among the patients studied and there was an average increase of 1.83

kilogrammes in weight with improved exercise tolerance observed. We conclude that rhDNase is well tolerated by Irish paediatric CF patients, with a statistically significant increase in FEV1, there was an increase also in FVC that failed to reach statistical significance. Further follow up studies are indicated to ascertain potential long term benefits of rhDNase therapy in this age group.

(P.82) HEAD GROWTH IN INFANTS WITH CONGENITAL PYLORIC STENOSIS

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Thirty seven out of a total of 44 infants with Congenital Pyloric Stenosis (PS) over the last 10 years had measurements of head circumference (HC) and weight at birth and diagnosis. Thirty one (89%) were male. A control group of 134 healthy infants was drawn from hospital and private clinics (50% male). A "Thriving Index" was derived for HC and weight:

$\frac{\text{Growth from birth (g or cm)} \times 100}{\text{birth weight (g) or birth head circumference (cm)}}$

divided by the age in weeks and expressed as % per week - head index (HI) and weight index (WI). Because these indices varied by age and sex, males only were compared at 3-4 weeks, 5-6 weeks, 7-8 weeks and 9-12 weeks. The pyloric male infants had a significantly lower HI at 3-4 weeks but more so from 7 weeks on: (median 1.06, range - 0.16 to 1.47; control: median 1.70, range 1.19 - 2.44). Regression analysis suggested this difference is related to the WI.

Early diagnosis is important to minimise the nutritional consequences of PS.

(P.83) DEMOGRAPHIC AND CLINICAL CHARACTERISTIC OF HIV INFECTED CHILDREN IN IRELAND

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This study presents the demographics and clinical manifestations of HIV infection in children in Ireland. It is a retrospective/prospective study. Children were identified at birth when maternal seropositivity was known (early), or if symptomatic (late) or at time of HIV diagnosis (dx) in a relative (late). All were monitored prospectively from dx, but for those identified late, data was also gathered from medical records prior to dx. Between '85 and '94, 30 infected children (20F, 10M) born to 27 mothers were identified. HIV was acquired vertically in 93%. Risk factors included maternal IVDU (44%), maternal partner HIV+ (41%), country of origin (11%) and unknown (4%). Clinical details are available on 28.11/28 (39%) were identified early and 17 (61%) late. 2/28 remain asymptomatic. 26 experienced symptoms of whom 14 developed AIDS at a median of 2.5yrs [range 0.2-6.6]. Symptoms include lymphadenopathy (23/28, 82%), organomegaly (82%), thrush (57%), FTT (36%), rec. bacterial infection (33%), opportunistic infections (21%), LIP (18%), dermatitis (14%) encephalopathy

(11%) and parotitis (10%). 23 children, median age 5.7yrs [range 0.8-9.8] survive of whom 9 have AIDS. The CD4 count in survivors ranges from 20-5630 cells/mm³. 12 receive antiretroviral therapy, 3 discontinued treatment, 1 refused and 7 have not reached criteria for therapy. 5 died [age 0.9 - 7.4yrs]. Causes of death included PCP (1), pneumonia (3), cardiopathy and pneumonia (1). Although 93% cases result from vertical transmission, only 39% are identified because of known maternal status in pregnancy. The predominantly late identification of cases prompts reassessment of current strategies of antenatal testing and mandates that clinicians be aware of symptoms that might suggest infection in a child.

(P.84) LIAISON CHILD PSYCHIATRY - A REVIEW OF SERVICE PROVISION

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Liaison child psychiatry involves a partnership between child psychiatry and paediatrics, to provide integrated medical and psychological care for children. A number of recent publications have described models of liaison child psychiatry service provision, but the actual work of such a service has not been described. The present study reviews the work of a liaison child psychiatry service in a 266-bedded paediatric hospital from January to December 1993. The service which was provided by three consultant child psychiatrists included two components, a) weekly psychosocial ward rounds with specialist paediatric teams, b) direct referrals from paediatrics to child psychiatry. Two hundred and thirty three young people were referred, representing 1.4% of all admissions during the same period. Reasons for referral included for clarification of the role of emotional factors in paediatric presentations in 104 cases (44%), and for assessment of deliberate self harm, anxiety or depression in 72 cases (30%). Rates of referral increased with age of the child, most being in the 11-15 year age range, with equal numbers of boys and girls being referred. Referral rates were much higher from paediatricians than from paediatric surgeons, although rates of emotional and behavioural disorder are equally common in children attending these services. Increasing awareness of the importance of psychological factors in the management of both acute and chronic paediatric disorders is focusing attention on the development and efficacy of liaison child psychiatry services.

(P.85) THE EFFECT OF A LACTASE ENZYME ON MILK OSMOLALITY

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Lactase enzyme reduces the lactose content of milks, and is available as "Lactaid" an "over the counter" preparation. We studied the rate of the reaction of Lactaid on milk lactose to determine if the recommended incubation time of 24 hours could be reduced to lessen the risk of infection.

Four different formulas were reconstituted according to the manufacturers' instructions. Osmolality was measured by the Fiske Os Osmometer over 24 hours without added enzyme, and with different concentrations of Lactaid.

The osmolalities of the same formula brand, reconstituted by

paediatric nurses, ranged from 320 to 382 mOsm/Kg and were higher than the manufacturer's quoted osmolality. There was a slight spontaneous change in milk osmolality over 24 hours. At 24 hours, osmolality ranged from 386 to 416 mOsm/Kg with one drop of added Lactaid; and from 474 to 591 mOsm/Kg with four drops. The rate of change of osmolality was maximum in the first four hours, and Lactaid exerted the majority of its effect within the first 12 hours.

Lactaid incubation time can be reduced to less than 12 hours. However the osmolalities achieved after incubation exceeded both the MRC1 and CONAPP2 guidelines for infant formulas. There is a wide variation in the osmolality of formulas reconstituted from powder.

References

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PSYCHIATRY

(P.89) POSTPARTUM DEPRESSION AND ELATION AMONG MOTHERS AND THEIR PARTNERS: PREVALENCE AND ASSOCIATED FACTORS

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Postpartum depression is well recognised. However, the occurrence of elation or hypomania in the postpartum period and the effect that childbirth has on partners is less understood. Over a six week period 385 mothers and their partners were asked to complete the Edinburgh Postnatal Depression Scale (EPDS) and the 'Highs' Scale and 82% (N=317) took part. At six weeks postpartum, 12% (N=29) of mothers scored 13 on the EPDS; higher scores were associated with bottle feeding (P=0.001), unemployment (P=0.003), failure to attend ante-natal care (P=0.02), babies that were difficult to manage (P<0.001), and maternal health problems (P<0.001). Only 1.2% (N=2) of partners scored 13 on the EPDS; higher scores were associated with fewer years in formal education (P=0.003) and unemployment (P=0.009). Using the cut-off of 8 on the Highs scale, at six weeks, 9.6% (N=23) of mothers and 13.3% (N=17) of partners were classified as 'cases'. Maternal 'highs' scores were associated with bottle feeding (P=0.03), fewer years in formal education (P=0.02), unemployment (P=0.02), and failure to attend for antenatal care (P=0.005). Partners' 'highs' scores related only to partner age (P=0.001). Depression and elation scores were strongly associated with one another in both the mother and partner groups (P=0.001). These findings suggest a complex and not mutually exclusive relationship between depression and elation in the postpartum period and identify possible predictors of mood disturbance in both mothers and their partners that may impact on treatment strategies.

(P.91) ANOREXIA NERVOSA COMPLICATING SYSTEMIC LUPUS ERYTHEMATOSUS; A CASE REPORT

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Systemic Lupus Erythematosus (SLE) has an incidence of 1/2000 and is an immunological disorder with a complex clinical

presentation and course. Anorexia nervosa (AN) is an illness of multifactorial origin and is estimated to occur in approximately 1% of 15-20 year old females. Both disorders are more prevalent among females. To date however there has only been one previous case report in the literature describing AN in a patient with SLE.

We describe the case of a 16 year old female who developed the classical features of DSM-III-R AN within a year of her developing and receiving treatment for SLE. Linking reasons for an association between these two disorders are discussed.

Conclusions: There was no evidence either clinically or using Magnetic Resonance Imaging to suggest that the emergence of an eating disorder in this patient was a manifestation of cerebral lupus.

(P.92) SUICIDAL IDEATION AND ACTS OF SELF-HARM AMONG WEST-DUBLIN SCHOOL CHILDREN

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This Study looks at rates of suicidal ideation and acts of self-harm among 13 and 14 year old School children in our catchment area of East Dublin.

4 Classes in 4 single sex Secondary Schools in East Dublin were chosen randomly, 2 male and 2 female. An initial agreement questionnaire was given following parental permission. All those with suicidal ideation at some time, and 20% of those with none were followed up with a detailed home interview.

87 children participated - 79.1% of total class population. Home interviews suggest 31.1% "Suicidal Ideation ever", 2.7% Self-harm rate - 4% of those interviewed felt suicide was a right under adverse circumstances. Only 35.1% would advise professional help to a friend with suicidal ideas.

Conclusion: This survey found lower levels of suicidal ideation than most North American studies. However, there is widespread acceptance of suicide as a desperate problem-solving exercise. Professional Services need a higher profile among this group.

(P.93) A 3 YEAR RETROSPECTIVE AUDIT OF ASSAULTS AGAINST PSYCHIATRISTS AND TRAINEES IN DUBLIN (1990-1993)

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A postal questionnaire was sent to 178 psychiatrists and trainees providing a service to the Eastern Health Board in the Dublin area. 147 replied (82.5% response rate).

57 had been assaulted (38.8%), 18 had been injured as a result (12.25%). The only distinguishing characteristic between those assaulted and those not, was that General Adult Psychiatrists were more likely ($P=0.01$) to be assaulted and Child Psychiatrists less so ($P=0.02$). Data were collected regarding 7% assaults. 63.2 assailants were male, 71% were known to the assaulted doctor, 43% were psychotic at the time of the assault and 25% were intoxicated. Weapons were used on 12 occasions - including 3 incidents with knives and one with an iron bar. Assailants were from 5 broad diagnostic groupings - personality disorder the most numerous group at 36.8%.

Conclusions: Assault rates approximate those of previous surveys in North America - 38.8%. Injury rates are lower

(12.25%). The low number of assaults in locked ward setting (30%) reflects the community orientation of the service.

(P.94) ATTITUDES TO PSYCHIATRY IN FINAL YEAR MEDICAL STUDENTS

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The attitude of medical students towards Psychiatry has relevance in the planning and structuring of medical curricula, and for patient management at the level of primary care. It is unclear from previous studies as to whether the clinical clerkship can influence the attitudes of medical students towards psychiatry.

Final year medical students attached to U.C.D. ($n=120$) were administered a series of three attitudinal questionnaires, before and after their eight week psychiatry clerkship. Anonymity was guaranteed. Data was coded and analysed using SPSS.

91% ($n=106$) of the class completed the questionnaires. There were 57 males and 49 females. The average age of the sample was 22 years sd (2.4). There was a significant increase in the mean score on the ATP (Attitude towards psychiatry questionnaire) post clerkship ($p=0.05$). Significantly more students expressed a wish to have a career in psychiatry post clerkship ($p=0.01$). Overall positive attitudes were expressed towards psychiatry, psychiatric treatment, and the need for psychiatric skills in general practice.

Conclusion: The eight week clinical clerkship in psychiatry would appear to have a positive effect upon the students' attitudes. It remains to be seen if this change will be transient or whether it will endure. We intend to follow this group prospectively and measure their attitudes towards psychiatry upon graduation and one year post-graduation.

(P.95) THYROID DISORDER IN A DOWN'S SYNDROME POPULATION

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As thyroid disease has been documented to be of a higher prevalence in individuals with Down's syndrome, an audit was set up to assess the thyroid status of 100 individuals with Down's Syndrome in the community and 36 individuals who were residentially based. In the residential sample, 25% ($n=9$) showed evidence of a thyroid disorder. 16.6% ($n=6$) had an established history of hypothyroidism and newly diagnosed cases accounted for 8.4% ($n=3$) of the sample. In the community based sample, 9% ($n=9$) showed evidence of a thyroid disease. There was one established case of hypothyroidism, and 8 new cases identified with evidence of a thyroid disorder.

The results from the audit emphasise the need to monitor the thyroid status in individuals with Down's syndrome. The average age in the residential sample was 28 years and in the community based sample, it was 32. This would indicate a youthful sample and as the incidence of thyroid disease has been found to increase over the age of 40 years, it again highlights the need for ongoing monitoring of thyroid status, regardless of age.

(P.96) THE EFFECTS OF GENDER AND HANDEDNESS ON THE NEUROPSYCHOLOGICAL PERFORMANCE OF PATIENTS WITH SCHIZOPHRENIA

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Many studies suggest that brain structure in patients with schizophrenia and that these patients also display a variety of cognitive deficits. This cognitive dysfunction may be influenced by factors such as gender or handedness.

27 patients with schizophrenia (DSM-III-R) were assessed on a complex neuropsychological battery devised to test a variety of functions. All tests were correlated with equivalent percentile norms to indicate the degree of impairment on each task. Patients were also administered a modified Annett handedness questionnaire and demographic information collected.

Cognitive performance of patients was impaired, when compared with equivalent percentile norms. Dysfunction of the frontotemporal region was evident, although impairment of the parietal lobe was equivocal. Further exploration of the data provided no evidence that this cognitive dysfunction may be influenced by gender. However, there is some evidence to suggest that the pattern of left- and right-handed individuals may differ.

This study was supported by the Health Research Board.

(P.98) REPEATED AMBULANCE CALLING IN OLD AGE —NUISANCE OR ILLNESS

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Previous studies of emergency ambulance calls suggest that up to 50% are inappropriate. However, there is no data in the literature concerning repeated or "nuisance" callers.

We describe three cases of repeated ambulance calling in elderly people in which the behaviour was directly related to an underlying psychiatric disorder, the effects of which were compounded by loneliness. Prior to psychiatric assessment these patients made up to 5 calls over a weekend. On each occasion the patients were transported to hospital, assessed and, in the absence of any physical findings, discharged home. This pattern persisted for several months in each case until they were referred for psychiatric assessment. The three patients, two women and one man, were diagnosed as having depression with mild dementia, Alzheimer's disease, and late onset schizophrenia with associated alcohol abuse respectively. Following appropriate intervention the calls stopped in two cases, and diminished significantly in the other.

The three case histories show that disturbed behaviour such as repeated ambulance calling in the elderly should raise the possibility of an underlying psychiatric disorder. Early identification and treatment can reduce patient distress and prevent the behaviour becoming habitual. The associated loneliness contributory to the behaviour can be tackled by maximising community support, and so more appropriate help-seeking behaviour can be introduced.

(P.97) QUALITY OF LIFE ASSESSMENT AMONGST SUBJECTS WITH SCHIZOPHRENIA ATTENDING A REHABILITATION CENTRE

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There is growing interest in assessing measures of deficit symptoms in studies of the course of schizophrenia. It is postulated that although overlapping, negative and deficit symptoms are not co-extensive. The Quality of Life Scale (QLS) is a 21 item scale, based on a semi-structured interview designed to assess deficit symptoms. Each item is scored on a 7 point scale providing 4 separate subscale scores and a total QLS score (maximum score is 126).

64 randomly selected patients with schizophrenia (DSM-III-R) who attended a rehabilitation centre were assessed using the QLS and the schedules for assessment of positive and negative symptoms of schizophrenia (SAPS and SANS). There were 31 males and 33 females with a mean age of 36.30 years (SD 12.13) and mean duration of illness of 10.55 years (SD 7.70). The mean QLS score was 51.70 (SD 21.50 and range 13 to 108) indicating moderate to severe impairment of functioning. Total SANS and all the individual SANS subscores were strongly negatively correlated with total QLS score ($p < 0.001$) as was duration of illness ($p < 0.001$). Educational attainment was associated with better quality of life. Age at diagnosis and gender were not correlated with QLS score. These findings suggest that premorbid functioning, duration of illness and negative symptoms adversely impact on the outcome of schizophrenia.

(P.99) POSTAL SELF EXPOSURE TREATMENT OF RECURRENT NIGHTMARES

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Recurrent nightmares occur in up to 5% of the population and are associated with insomnia, irritability, tiredness, anxiety and depression. Nightmares resemble phobias in that stereotyped cues trigger anxiety and result in avoidance behaviour. Several case reports and treatment trials support the value of behavioral treatment in recurrent nightmares. We have conducted a treatment trial to focus on the exposure method (also known as rehearsal relief). 171 suitable subjects were recruited following an advertisement in the media. They suffered weekly nightmares for at least a year and were randomised into one of three groups, exposure, relaxation or waiting list. The complete trial was administered by post including measures, diaries and treatments. Exposure treatment reduced the average frequency of nightmares by 50%; significantly better than relaxation treatment and waiting list control. Other measures including depression and anxiety diminished significantly in the exposure treatment group.

(P.100) SUICIDE IN PSYCHIATRIC INPATIENTS IN IRELAND

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An increase in suicide rates in psychiatric hospitals has been reported in Europe and U.S.A. in the past 25 years. It is important

to study hospital suicide rate in Ireland and factors associated with these deaths if risks are to be minimised.

Retrospective descriptive study of clinical, post mortem and inquest data reported to the Inspector of Mental Hospitals on all suicides in psychiatric hospitals or units in Irish Republic from 1982-1993. Rates of suicide calculated using 'person year method'.

There was an average 18 deaths per year in psychiatric inpatients accounting for 6% of all suicides per annum. The rate of suicide in short stay inpatients (stay less than one year) was 319/100,000. The rate for long stay (stay more than 1 year) 118 per 100,000. The suicide rate for all inpatients increased fourfold in a 100 years while the rate in the general population rose by a factor of eight. 35% of suicides were 25-34 years. 63 (47%) had depression and 52 (39%) schizophrenia. 46% made previous suicide attempt. The risk of suicide was higher the shorter the time interval after admission. 110 (74%) suicides in those registered as psychiatric inpatients occurred while patient was away from the hospital. 52 (35%) were absent without leave.

Conclusion: The high rate of suicide immediately after admission and the number who leave hospital emphasises the importance of careful management of patients at risk of suicide in a safe secure environment. The person year method is appropriate for monitoring changes in suicide rates.

PUBLIC HEALTH/EPIDEMIOLOGY

(P.101) HEALTH BEHAVIOUR OF PARENTS WITH YOUNG FAMILIES

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Lifestyle plays a key role in determining both the duration and quality of life. Personal advice from health professionals can exert a powerful influence on health behaviour of patients. We examined indicators of health behaviour in parents with young children in routine contact with the health service.

A cross-sectional study design was used. From Oct. '94 - Jan. '95, parents bringing their child for a routine developmental examination (at 9 mths approx., service uptake 80%) at Health Board clinics in a Dublin Community Care Area, including inner city and suburbia, were asked to respond to an area medical officer administered questionnaire.

Data on parents of 215 children are shown in the the Table below.

Mother not on folic acid supplements in early pregnancy	85%
Either parent currently smoking	47%*
Baby breast fed	39%*
No	61%
for up to 1 month	45%
For up to 3 months	25%*
No smoke alarm in the house	22%*
An open chip pan is used in the kitchen	7%
Baby sometimes put to sleep in the prone position	6%
Child not vaccinated against pertussis	

*Significantly associated with younger mothers and lower social class (X^2 , $P < 0.05$)

These data suggest that parents are responding to many health promotion initiatives. However, there remain opportunities at child screening clinics to further influence the health behaviour

of families with young children. The study suggests that a broad range of topics should be addressed, and prioritised in line with the targets of the National Health Strategy.

(P.102) SURVIVAL OF CHILDREN WITH DOWN SYNDROME IN THE EASTERN HEALTH BOARD FROM 1980-89

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The aim of this study was to document the survival of a cohort of children with Down Syndrome, identified from the Dublin European Register of Congenital Anomalies and Twins (EUROCAT), born in the Eastern Health Board area between 01/01/1980 and 31/12/1989 and to document factors influencing survival.

Information on survival was sought from multiple sources. Follow-up was attempted for each case until death or 1992 or until the date last known to be alive. Kaplan-Meier survival curves were calculated for the total cohort and for children born within the two time periods 1980-85 and 1986-89. Other prognostic factors studied included: maternal age, sex, mother's county of residence, season of birth and presence or absence of other congenital anomalies, specifically congenital heart disease (CHD) and gastro-intestinal anomalies. A multivariate analysis was carried out using Cox's proportional-hazards regression model.

The overall 10 year survival was 82% with no difference for the two time periods studied. Presence of CHD reduced 10 year survival to 73% ($p < 0.001$). This effect was largely due to the presence of atrio-ventricular canal defects. Other congenital anomalies and additional factors studied were not associated with decreased survival. These findings have relevance for service planning for children with Down syndrome. Long-term follow-up of children with congenital anomalies is clearly useful, however there is a need for simpler methods of establishing outcomes.

(P.103) A POPULATION-BASED STUDY OF THE EPIDEMIOLOGY OF DOWN SYNDROME OVER 10 YEARS IN DUBLIN, GALWAY, KILDARE AND WICKLOW

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We conducted a descriptive epidemiological study of Down syndrome (DS) in the 4 Irish counties covered by EUROCAT registries of congenital malformations for the years 1981-90 (Dublin, Kildare, Wicklow and Galway).

All DS cases born between 01/01/1981 and 31/12/1990 to mothers resident in the 4 counties were identified. Crude birth prevalence rates and maternal age-standardised rates (SPRs) were calculated for each county and for each year in the study period.

The crude birth prevalence for the 4 counties was 18.5/10,000. There was a fall in the total number of DS births over the decade, but less change in the crude birth prevalence due to

an increase in the proportion of mothers aged 35+. Galway had the highest crude birth prevalence of DS (23.5/10,000) but the SPR was within average for the 4 counties as a whole - 110.3, 95% confidence interval 86.7-139. The risk of having a DS child increased seventy fold from 1:1841 at age 15-19 to 1:26 at 45 years or older. Nearly half of all DS cases (47.4%) had at least one additional anomaly.

The parts of Ireland covered by EUROCAT have a high birth prevalence of DS births as compared with some other countries, but the maternal age-specific rates are not substantially different from those in large international studies.

(P.104) - See p. 53

(P.106) AN OUTBREAK OF "SLAPPED CHEEKS" SYNDROME (HUMAN PARVOVIRUS B19 INFECTION) IN A PRIMARY SCHOOL

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B19 causes erythema infantiosum (slapped cheeks syndrome). In childhood this is usually a mild self limiting infection. If contracted in pregnancy it may cause non-immune hydrops foetalis and foetal death in up to 10%. We describe the first outbreak of B19 infection in this country. In December, 1993, a cluster of 6 pupils with typical "slapped cheeks" rash occurred in a Dublin primary school and the diagnosis was laboratory confirmed using serology. Information leaflets on the infection were circulated to parents and management guidelines to physicians. In June, 1994, the parents of all pupils were asked whether their child had the suggested symptoms during the previous 6 months. 16% of pupils had such symptoms. Of these, 85% had slapped cheeks, 62% had rash elsewhere. The rash was evanescent (i.e. waxed and waned) in 72%. The mean duration of symptoms was 10 days. 57% reported spread to family members. 65% were aware of the illness which may have been due to the information campaign mounted at the time of the initial outbreak. 88% had not seen a similar rash before. None of the teachers had clinical symptoms. Six months after the initial outbreak, parvovirus IgG antibody was detected in salivary samples of 62% of the pupils, a level higher than that usually detected in the adult population. These data suggest that subclinical infection is common in primary school aged children.

(P.107) EPIDEMIOLOGY OF CONGENITAL ANOMALIES OF DIAPHRAGM (CAD) IN THE EASTERN HEALTH BOARD REGION FROM 1980-94

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This study was undertaken to describe the epidemiology of CAD in the Eastern Health Board region, using data from the Dublin registry of the EUROCAT database of congenital malformations. Congenital anomalies of diaphragm comprise mainly congenital diaphragmatic hernia and also include a small number of eventrations or absence of diaphragm. The SAS programme was used for statistical analysis. From 1980 to 1994, 116 cases of CAD were identified. The overall prevalence for 1980 to 1992 was 3.73/10,000 live and still births. The annual prevalence has, however, risen from 1.9/10,000 in 1980, to 4.5/

10,000 in 1985 to 5.2/10,000 in 1990. 87.9% (102) were livebirths and 12.1% (14) were stillbirths. 56% (65) were male and 43% (50) were female. There was one twin pregnancy and 115 singleton pregnancies. The mean birth weight was 2787.39 (sd 10259; range 560 to 49009). The mean length of gestation was 37.6 weeks. CAD was associated with other major congenital anomalies in 45.6%. The mean age of the mother at delivery was 29 years (sd 5.4 years; 16 to 43 years). It was the first pregnancy in 41.7% of mothers. 1.7% (2) had had a previous stillbirth. Using population based data that includes live and still births leads to more accurate description of the epidemiology of CAD.

(P.108) TUBERCULOSIS: A COMPARISON BETWEEN THE REPUBLIC OF IRELAND AND NORTHERN IRELAND

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We examined the incidence of TB in the Republic of Ireland and Northern Ireland in 1991. We showed that there is a significant difference between the incidences of TB with the Republic having relatively more cases.

Table 1: Incidence of TB per 100,000 population

Figure in parentheses = actual number of cases

	Republic of Ireland	Northern Ireland
Overall incidence	16.3 (582)	5.7 (90)
<15 yrs	5.8 (51)	2.3 (9)
15-34 yrs	9.7 (99)	1.8 (9)
35-54 yrs	15.5 (120)	5.2 (19)
>55 yrs	42.6	53
Proven (bacteriologically histologically)	7.8 (277)	3.5 (55)

Conclusion: There is a significant (real difference) between the incidence of TB in the Republic of Ireland and Northern Ireland. It is not explained by difference in counting or other extraneous factors.

(P.109) ASTHMA MORTALITY IN IRELAND AND THE UK 1980-1992

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Mortality from asthma in Ireland for the period 1980-1992 was examined using Vital Statistics Reports, and compared with similar data for the UK. Average age- (in 5-year intervals) and gender-specific rates were derived for three time periods (1980-84, 1985-89, 1990-92). For comparison between countries crude rates were adjusted to a European Standard Population by the direct standardisation method.

Age-specific mortality from asthma is <2/100,000 under 40 years. This was consistent over the 13 year period. There is some suggestion of decline in mortality in the 40-44 age group. The highest mortality occurs in elderly patients, with no

indication of a temporal trend. Age-standardised rates suggest that the overall mortality from asthma has not changed over the period covered by the study.

Comparing age-standardised rates between countries shows that for each time period asthma mortality is highest in Ireland, with Northern Ireland second, followed by England/Wales and Scotland. It also appears that the trend in asthma mortality in the UK is downward at present, whilst that in Ireland remains static. To what extent this is real, or related to inaccuracies in death certification in Ireland or in the other countries is impossible to say from this study.

(P.110) HIV REQUESTS IN A LARGE TEACHING HOSPITAL

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The aim of this study was to audit the HIV requests in a large teaching hospital. We analysed the number, source and risk category stated on the HIV request forms over the twelve month period, from 1 May 1993 through 30 April, 1994. All available information was entered onto an 'Epi-Info' database for subsequent analysis. We assessed age, sex, the actual source of requests, the rate of positivity by source, and the rates of positivity by age group.

In one year we performed 2,304 HIV tests, with 93 positives (4%). There was a slight male preponderance (56.8%), over female (43.2%). The bulk of requests came from the GUM clinic (62%), while 11% came from the fertility clinic, and 6% from the drug dependency unit. Most people were in the 20-40 age group. Of note was the lack of requests from the antenatal clinic and termination of pregnancy service. Positivity rates varied from 0.37% through 43%, depending upon the source of the specimen. The rate of positivity also varied by the risk category indicated, with the highest rate (33%) among IVDU's.

Based upon known seropositivity rates among certain populations (e.g. patients undergoing pregnancy termination), it appears that this teaching hospital may not be reaching certain risk groups.

(P.111) METHICILLIN RESISTANT STAPH. AUREUS

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Staphylococcus aureus is a common organism found on skin and in the anterior part of the nose in 30% of the population. It is usually susceptible to semi-synthetic penicillins such as methicillin or flucloxacillin. Methicillin is used in laboratory susceptibility tests and resistant staphylococci are referred to as Methicillin Resistant *Staphylococcus aureus* (MRSA). MRSA organisms were first isolated in the 1960s and numbers have increased dramatically since then. They are predominantly a hospital problem and can easily be spread from patient to patient and patient to staff members.

In 1993, INFOSCAN reviewed MRSA figures in the greater Munster area. Monthly figures from the various hospitals in the area were reviewed and the high risk areas were highlighted. Strict infection control measures were applied when an MRSA outbreak occurred in a unit i.e. appropriate isolation of affected

patients and reinforcement of good nursing standards. Since July 1993 an epidemic of MRSA has occurred in the INFOSCAN area. Monthly figures for MRSA have doubled since then, averaging 100 isolates a month.

The Department of Health has set up a working party to examine the problem. National Guidelines are due to be released in the immediate future in an attempt to contain this problem.

(P.112) HEPATITIS A IN MUNSTER

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Surveillance of infectious disease is an essential, integral component of Microbiology. INFOSCAN is an established communicable disease surveillance programme which monitored the recent epidemic of hepatitis A in the southern region of Ireland. Weekly notifications from all Microbiology Departments in Cork, Limerick, Tralee and Waterford were collated and analyzed to characterise this epidemic.

Diagnosis of hepatitis A illness in a centre is based on detection of IgM antibody to hepatitis A virus in serum. This presentation will display results of surveillance in the Southern Health Board area over a period of ten years, 1985-1994, and give detailed description of the most recent epidemic where over 500 cases were diagnosed. Monthly case notification varied from one to forty-nine cases over the years 1991-2. Age frequency and geographical distribution will be characterised.

From this data we can monitor the ongoing cyclical nature of hepatitis A illness and predict the next possible peak of the cycle. Preventative strategies will also be presented.

(P.113) PILOT STUDY TO INVESTIGATE THE INCIDENCE AND CAUSES OF CHILDHOOD ACCIDENTS OCCURRING IN PRIMARY SCHOOLS

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The NW section of N Cork CCA was chosen for this prospective observational study over the 93/94 school year. Data was collected by completion of questionnaire by the pupils' teacher following injury. The study involved 1137 pupils in 32 national schools. Response rate was 71.8%. A total of 17 accidents occurred resulting in 19 injuries, giving an accident-rate of 1.5 per hundred student-years; one accident per 66.6 pupils per year. Peak incidence was the 11-12 age group. Falls were the commonest cause of injury (64.7%). 1/3 of accidents occurred in the playground. 35.3% (6) of accidents resulted in fracture. Of 64.7% (11) of accidents which resulted in open wounds, gloves were used in one case when administering first-aid. 78.3% (18) of schools had an accident-recording policy. 17.4% (4) had a qualified first-aider on the premises and 52.2% (12) stocked disposable gloves. 87% (20) of schools had a safety statement and one school had legal proceedings pending following accident-occurrence. Mandatory reporting of school accidents is required. School Boards and Health Boards have a responsibility to understand the reasons for and nature of accidents in schools. However, the real issue is that of helping children to understand the nature of risk by exploring the safety of their own environment.

GENETICS

(P.114) A POPULATION-BASED COMPARISON OF THE EPIDEMIOLOGY OF BIRTH DEFECTS BETWEEN IRELAND AND LITHUANIA

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Ireland and Lithuania are small countries at the periphery of Europe with similar land area, population (3.5 million, 3.7 million) and number of births per year (50,000). The objective of this study is to compare the birth prevalence and mortality from major congenital anomalies between Ireland and Lithuania using the Dublin EUROCAT register and the Lithuanian national birth defect registry (LIRECA).

Both registries are population based and use multiple sources for case ascertainment. The Dublin register covers approx. 20,000 births per year and because it contains 15 years of data it can provide trend analyses. LIRECA is larger and covers the whole of Lithuania (approx. 50,000 births per year) but it only began in 1992.

Dublin EUROCAT had a high birth prevalence of neural tube defects in 1980 (47/10,000 births), but by the 1990s this had fallen to a level similar to that found in LIRECA (14.5/10,000 births). Dublin EUROCAT had a higher birth prevalence of chromosomal anomalies 21.7/10,000 births compared to: LIRECA (11.9/10,000 births). LIRECA had a higher birth prevalence of cleft lip and/or palate (11.2/10,000) vs. 8.7 for Dublin. Congenital anomalies caused 32% of infant deaths in Lithuania vs. 20% in Ireland in 1993.

This collaboration will allow both registries to learn from each other with regard to case ascertainment methods, and where important differences in birth defect prevalence are discovered in depth analysis will be done to try to identify aetiological factors.

(P.115) THE DUBLIN EUROCAT REGISTRY - A POPULATION-BASED REGISTER OF BIRTH DEFECTS COVERING 3 COUNTIES

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EUROCAT consists of a network of 30 population-based regional birth defect registries throughout Europe, the objective of which is the epidemiological surveillance of congenital anomalies in Europe.

The Dublin Registry which is the third largest in Europe, began in 1979 and covers all births in Dublin, Wicklow and Kildare using multiple sources of ascertainment for birth defects. These include birth notification forms, death certificates, HIPE and karyotyping records.

From 1980-1990 245,172 births were surveyed, including 1,922 stillbirths and 7,032 babies/fetuses with congenital anomalies were registered giving a prevalence rate of 28.7 per 1,000 births. Of all the EUROCAT registries, Dublin had the highest birth prevalence of neural tube defects for the period 1980-1990 (28.9/10,000), but this fell from almost 50/10,000 to 15/10,000 over the 11 year period. Of all the EUROCAT

registries, Dublin had the third highest prevalences of Down syndrome among live births (16.6/10,000), and the second highest number of liveborn Down children (405). Registry data has been used for a number of specific research projects, including a study of survival of liveborn Down children.

The Dublin EUROCAT register provides valuable baseline and trend data on the birth prevalence of all major congenital anomalies. It is also a potentially valuable resource for further aetiological and clinical research.

(P.117) AN ASSOCIATION STUDY OF NEUROTROPHIN 3 GENE POLYMORPHISM IN RELATION TO SCHIZOPHRENIA

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Epidemiological and Neuropathological studies suggest that abnormalities of brain development play a role in the aetiology of schizophrenia. It follows that trophic factors, such as neurotrophin 3 (NT-3), known to have a role in brain development are candidate genes for this disorder. A recent Japanese study presented evidence of an allelic association between a dinucleotide repeat polymorphism in the promoter region of the NT3 gene and schizophrenia in a population of 70 schizophrenics compared with 70 controlled. We have examined the frequency of the alleles at this polymorphism in 175 caucasian schizophrenic patients and 147 control subjects. In a test of all alleles together the patients and controls did not differ significantly in allele frequencies. However the male schizophrenics were more likely to have the allele previously found to be associated.

HAEMATOLOGY

(P.119) MOLECULAR PREDICTION OF RELAPSE AFTER MATCHED UNRELATED DONOR (MUD) MARROW TRANSPLANTATION

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Although the majority of children with acute lymphoblastic leukaemia (ALL) are cured following chemotherapy, the prognosis for patients in 2nd or subsequent clinical remissions (CR) remains poor. Allogeneic BMT is associated with a 40% disease free survival but is often limited due to lack of a HLA identical sibling donor. This study was undertaken to investigate hemopoietic chimerism following MUD BMT for ALL in 2nd or subsequent CR. Clinical outcome was unknown at time of study. Chimerism post BMT was assessed by amplification of polymorphic short tandem repeats using PCR. 17 patients have been evaluated from 1-18 months post BMT. 5 patients exhibited donor chimerism (DC); in 2 of these patients, DC persisted at all times post BMT and these patients remained in CR. In 3 patients DC evolved to mixed chimerism (MC) and was predictive of subsequent relapse. 5 patients exhibited stable low level MC (level of recipient cells <1%) and all remain in CR. 7 patients showed initially high or progressive MC post BMT.

4/7 relapsed in the first 6 months post BMT while 2 patients rejected their grafts with high levels of recipient cells. One patient showed increasing MC with subsequent emergence of a new non leukemic clone and clearly merits close monitoring. In summary a high incidence of MC was seen in this patient cohort. High levels of recipient cells or a switch from DC to MC between 16 months post BMT were predictive of subsequent leukemic relapse. Patients with DC or low level stable MC were long term survivors. Thus chimerism results were highly predictive of outcome in this patient group.

(P.120) EVALUATION OF IN VITRO CULTURE SYSTEMS FOR GROWTH OF PRECURSOR ACUTE LYMPHOBLASTIC LEUKEMIA CELLS

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Although ALL can be treated with chemotherapy/BMT, this may only result in reduction of disease burden without eradication of the leukemic clone. Persistence of low numbers of leukemia cells in patients in "apparent" clinical remission is termed Minimal Residual Disease (MRD) and may allow relapse prediction. Culture based studies were used to detect leukemic precursors in ALL patients. Initial studies focussed on two semi solid assays. Cells from 36 patients with B precursor ALL at diagnosis were grown using either assay system but leukemic blast cell colonies were only detected for 50% of diagnostic samples. This prompted a change to a system with allogeneic stroma as a feeder layer to prevent apoptotic death of ALL precursors. Stromal layers were grown from normal donor marrow in 25cm cell culture flasks. Intrinsic stromal hemopoiesis was abrogated by removing all non-adherent cells after 24 hours. When a confluent layer was obtained (4-6 weeks), it was detached and replated into wells of a 24-well culture dish. Bone marrow cells from patients with ALL (diagnosis/remission) were cultured on stroma for 7 days. Contents of the wells were removed and stained with an anti-CD19 antibody. Subsequent analysis on a FACScan (Becton Dickinson) allowed percentage recovery of B cells from the system to be calculated. 7 samples have been cultured in this system and % CD19+ cell recovery evaluated. Culture of further samples is required to test efficacy in the growth of ALL cells, particularly from remission samples.

(P.121) EFFECTS OF PYRIDOXAL-5'-PHOSPHATE ON ADP - AND THROMBIN-INDUCED AGGREGATION OF BLOOD PLATELETS

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To elucidate the mechanism of inhibition of platelet aggregation by pyridoxal-5'-phosphate (PLP). Platelet aggregation was determined using the Chronolog 430 aggregometer. Phospholipids were extracted by the method of Bligh & Dyer⁽¹⁾, separated by t.l.c., located by iodine vapour and extracted and analysed for phosphate (Bartlett⁽²⁾), PLP (10mM) was shown to inhibit aggregation of platelet rich plasma and of platelets resuspended in Tyrode solution. Analysis of

the phospholipid fractions showed that aggregation caused a decrease in phosphatidyl choline, phosphatidyl ethanolamine and phosphatidic acid with concomitant increase in the lysophosphatidyl choline and lysophosphatidyl ethanolamine and in the combined phosphoinositide/phosphatidylserine fraction. Inhibition of the aggregation by PLP was associated with inhibition of these changes in phospholipid components. These results point to the direct effect of PLP on phospholipase A2; an effect on phospholipase C is less clear and requires further study.

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(P.122) EFFECT OF PYRIDOXAL-5'-PHOSPHATE ON CALCIUM MOBILISATION IN BLOOD PLATELETS

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Ionised calcium plays a key role in platelet function⁽¹⁾. Pyridoxal-5'-phosphate (PLP) inhibits platelet aggregation⁽²⁾. This study was carried out to detect an effect of PLP on Ca²⁺ mobilisation in human platelets. Aggregation was determined on the Chronolog 430 aggregometer. Ca²⁺ was determined using fluo-3 indicator.

PLP(10mM) inhibited both platelet aggregation and Ca²⁺ mobilisation induced by RDP or thrombin, pointing to a direct effect of PLP on a receptor-mediated pathway for intracellular Ca²⁺ mobilisation associated with platelet aggregation.

PLP(10mM) potentiated both platelet aggregation and Ca²⁺ mobilisation induced by the Ca²⁺-ionophore, bromo-R23187. This potentiation was not observed in the absence of extracellular Ca²⁺. Here PLP may exert its effect through direct or indirect inhibition of Na⁺/H⁺ exchange, leading to cytosolic acidification, which in the presence of extracellular Ca²⁺ would facilitate exchange of H⁺ for Ca²⁺ mediated by the ionophore.

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(P.123) VOLUNTEER UNRELATED BONE MARROW DONORS FOR BONE MARROW TRANSPLANTATION

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Bone marrow transplantation is a curative therapy for a range of haematological disorders. The ideal donor is a HLA matched sibling but worldwide only about one third of patients eligible for transplant have such donors. The establishment of large international registries of HLA typed volunteer donors has allowed the increasing use of Matched Unrelated Transplants (MUD).

Since the establishment of the Irish Unrelated Bone Marrow Registry, 11 donors have donated, 1 in 1992, 1 in 1993 and 9 in 1994 for patients in Ireland (3), Europe (4) and U.S. (4). Ten have donated bone marrow and 2 donated peripheral blood stem cells (PBSC). The volume of marrow harvested under G.A. varied from 595 mls - 1,200 mls (mean 897 mls/depending on

patient weight). Engraftment occurred in 8/10 marrow harvests and in the PBSC harvest. One patient who failed to engraft subsequently engrafted with PBSC from the same donor. Six of the eleven patients are alive and well 4-15 months after transplantation. The most common complication suffered by donors was prolonged discomfort delaying return to work (3 female). One of the two donors who donated PBSC following GCSF developed moderate thrombocytopenia which resolved spontaneously. All but one of the marrow donors indicated their willingness to donate again if requested, but the complications of this procedure suggest that PBSC collection with GCSF may be a more acceptable method of harvest for donors. However, the effects of GCSF need to be carefully monitored as experience in normal donors is limited.

**(P.124) LYMPHOCYTE HOMING RECEPTOR (CD44)
AND PROGNOSIS IN PRIMARY GASTROINTESTINAL
LYMPHOMA**

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The lymphocyte homing receptor (CD44) is involved in lymphocyte adhesion to endothelial cells of high endothelial venules and lymphocyte exit from the blood. There is considerable evidence that it may be involved in haematogenous dissemination of malignant lymphoma. CD44 expression was determined in a series of 36 consecutive patients with primary gastro-intestinal non Hodgkins lymphoma who have been followed up for a period of up to ten years. The value of CD44 expression as a prognostic monitor was assessed and compared to staging, histology and other indices of prognosis.

58% of this series were CD44 positive. There was a significantly higher expression of CD44 (75%) among small bowel cases, compared with gastric lymphoma patients (44%). When 1 and 2 year survival rates for CD44 positive and CD44 negative patients were compared, expression of the CD44 molecule appeared to indicate a poorer prognosis over both time periods.

INFECTIOUS DISEASES/GU MEDICINE

**(P.125) RESPIRATORY PATHOGEN SUSCEPTIBILITY
ANALYSIS**

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INFOSCAN Editorial Board.

Current surveillance of pathogens causing infectious disease is vital to successful, efficacious therapy in patient care. INFOSCAN is an established communicable disease surveillance programme which monitors the susceptibility patterns of respiratory pathogens in the southern region of Ireland. Over a specified period, hospitals in Cork, Limerick, Tralee and Waterford collected data on susceptibility of respiratory pathogens, *Haemophilus influenzae*, *Streptococcus pneumoniae* and *Moraxella catarrhalis*. Centres in Cork, Tralee and Waterford utilise the Stokes Comparative method to determine susceptibility of pathogens. These data were collated by INFOSCAN. This presentation will show data assimilated over four consecutive years and highlight trends in resistance in *H. influenzae* and *S. pneumoniae*. Trends which show cause for concern with an increase in the penicillin resistant

S. pneumoniae to 20% in 1994. Sample size varied from 164 to 262 over the four years.

Continued surveillance of resistance rates for antibiotics used against respiratory pathogens is essential to determine probable efficacy for general practitioners and hospital clinicians. These data are provided annually by INFOSCAN in its quarterly bulletin.

**(P.126) EXPERIENCE WITH DAY-CASE INSERTION OF
LONG-TERM IN-DWELLING RIGHT ATRIAL
CATHETERS IN PATIENTS WITH AIDS**

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The need for longterm in-dwelling right atrial catheters (RAC) in the management of patients with HIV infection is common. Previously the insertion of RAC's required admission to hospital with the procedure taking place in theatre. More recently the insertion of these lines in radiology units in both HIV+ and patients has been reported. We review our experience of RAC insertion in AIDS patients on an outpatient basis in our radiology unit.

All patients requiring RAC's between Jan. '94 and June '94 were referred. Patients' age, risk group, sex, CDC staging, CD4 count, indication for insertion and past medical history were recorded. Patients were followed up for immediate and delayed complication rates, disease progression, presence of neutropenia and duration of line insertion. Patient tolerability was assessed informally by simple questionnaire.

All nine catheters were inserted successfully in right atrium within 24hrs of request. There were no malpositions as can occur with blind insertion in theatre. All patients were outpatients and were discharged on the same day as the procedure was performed. There were no immediate complications in this series and infection rates were comparable with previous surgical series. There is reduced risk exposure to anaesthetic and surgical staff as previously, line insertion required blind direct cut down (venotomy). This initial review supports the advent of this day case intervention service for immunocompromised patients.

MICROBIOLOGY

**(P.127) MYCOBACTERIUM MALMOENSE SPECIFIC
DNA PROBE FROM THE 16S/23S rRNA SPACER**

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Mycobacterium malmoense was first described in 1977. It is now recognised as an opportunistic human pathogen which can be difficult to identify using standard methods. In this study the nucleotide sequence of the 16S/23S ribosomal intergenic spacer region from five clinical isolates of *M. malmoense* has been determined, in order to develop a PCR based DNA probe assay to facilitate the early identification of this organism. The DNA sequence generated was compared with the intergenic spacer sequences of related organisms and a high degree of sequence homology was observed with *Mycobacterium avium*.

An oligonucleotide probe that specifically detects *M. malmoeense* was designed and the ability of the DNA probe to detect geographically distinct *M. malmoeense* isolates was investigated.

(P.128) ANTIBIOTIC AUDIT IN AN ACUTE GENERAL HOSPITAL

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Antibiotic audit of in-patients in the MMH is undertaken to evaluate both existing practices and the trends in treatment of infection. Information on the influence of microbiology reports on choice of therapy is also recorded. The audit is undertaken by examining patient's records on the wards, and consulting relevant nursing personnel and medical staff. Three hundred and forty four and three hundred and eight five patients were audited in 1993 and 1994 respectively. 60% received antibiotics in 1993 compared to 50% in 1991. 48% of surgical patients received antibiotics for prophylaxis in 1993 and this rose to 78% in 1994. The commonest infections treated were respiratory and urinary. Duration of therapy for urinary infections fell from eight to five days and for respiratory infections an increase from six to eight days was noted. There was a 15% increase in switch from IV to oral antibiotics over the period. Choice of antimicrobial agent was seen to be appropriate in the majority of cases.

(P.129) EPIDEMIOLOGICAL MARKERS IN STUDIES OF MENINGOCOCCAL ISOLATES FROM NORMAL AND COMPLEMENT DEFICIENT SUBJECTS

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Neisseria meningitidis isolates can be characterized by the use of epidemiological tools such as polysaccharide capsule serogrouping, class 1 and 2 outer-membrane protein sero-subtyping, and multi-locus enzyme electrophoresis. We used these assays to study case isolates from individuals with deficiency of the late acting complement components (LCCD). These individuals have increased susceptibility to recurrent meningococcal disease, but some disease manifestations may be less severe in the absence of complement activity. Alternatively deficient subjects may become infected with less virulent organisms. Sixteen *N. meningitidis* strains were recovered from cases with known LCCD (all C6 deficiency) and were compared with 122 routine case isolates (obtained from the same area, during the same time period). Common serogroups, particularly B, predominated in both patient groups. However, rare serogroups were significantly more prevalent in deficient patients. Sero-subtyping showed no significant differences. Multilocus enzyme electrophoresis revealed the same genetic diversity in isolates from both groups. However, the ET-5 complex (which is associated with epidemic disease) was found in 18% of the routine clinical isolates but in none from the LCCD subjects. Moreover, a highly significant finding

was that 8 of 16 isolates from LCCD subjects were in one ET cluster, F, totalling only 20 isolates. These results show a difference in the clonal composition of strains infecting LCCD subjects. A number of LCCD patients with meningococcal disease have now been identified in Ireland, and strain epidemiological studies need to be done.

(P.130) HEPATITIS E IN IRELAND

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Hepatitis E virus (HEV) causes an enteric non-A, non-B hepatitis (NANB). The main route of transmission is faecal-oral. Epidemics of this enterically transmitted NANB hepatitis have been reported in tropical countries with a high case-fatality rate among pregnant women.

Recently evidence is accumulating, indicating that HEV might be prevalent in Europe. To date, only one study on HEV prevalence in Ireland has been described. In this study there was no evidence of hepatitis E infection in 45 haemodialysis patients.

We investigated antibodies to HEV in sera from 500 antenatal patients and 100 consecutive samples sent to our laboratory for serological diagnosis of viral hepatitis. Antenatal samples are readily available, and represent the seroprevalence of HEV in the general population in Ireland. The viral hepatitis screens were negative for hepatitis A and B. Antibodies to hepatitis C were detected in 3 of the 100 samples.

Two (0.4%) of the 500 antenatal patients were IgG anti-HEV positive. Four (4%) of the samples sent for viral hepatitis screens had antibodies to hepatitis E.

Our results indicate a low prevalence of Hepatitis E in Ireland with figures similar to those in other European Countries.

(P.131) PULSED-FIELD GEL ELECTROPHORESIS CONFIRMS THE DISCRIMINATORY VALUE OF RAPD FINGERPRINTING OF ENTEROBACTER CLOACAE

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A study was undertaken to confirm the reliability of Random amplification of polymorphic DNA (RAPD) as a fingerprinting method for the gram negative organism, *Enterobacter cloacae*. Previously, a group of seven *E. cloacae* isolates, collected from an Intensive Care outbreak of infection with this organism, and two control strains, had been investigated with RAPD. The PCR-based fingerprinting method was readily applied to this organism providing sufficient discrimination to permit differentiation between strains with identical biochemical profiles and antibiograms. Subsequently these isolates have been further characterised by a second well established genotypic fingerprinting method - pulsed-field gel electrophoresis (PFGE). The bacterial strain to strain differentiation established by RAPD analysis was independently confirmed using PFGE, thus establishing the reliability of RAPD as a fingerprinting method for *E. cloacae*.

(P.132) TOTAL ANTIBODY AND IgM RESPONSES IN BOVINE HERPES MAMMILLITIS

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Bovine herpes mammillitis (BHM) is an ulcerative disease of the teats and udder which usually occurs in recently calved heifers and cows. It is caused by bovine herpesvirus 2 which is more closely related to human herpes simplex virus than to any bovid herpesvirus. To assess the usefulness of serology as a diagnostic/confirmatory method, 2,000 sera from unaffected cattle and 212 samples from 19 outbreaks of BHM were examined for antibodies using a serum neutralisation test incubated at 32°C. The presence of specific IgM in paired samples was detected by titre elevation in the presence of complement. Low titred antibody (GMT 8) was detected in 7% of the national herd. By contrast, in investigating the 19 outbreaks, high titred antibody (GMT 21) was detected in 89/114 single samples and in all herds examined. Much higher antibody titres (GMT 37) were present in cattle with BHM compared to their unaffected herd-mates (GMT 12). High IgM and total antibody titres were detected in the first of paired samples (GMT 42), demonstrating that antibody concentrations had peaked early and had begun to decline quickly (GMT 7 in second samples). The results demonstrate that a clinical diagnosis of BHM can be corroborated by the detection of high titred total antibody or IgM, often in the earliest samples collected.

(P.133) SPIKED SPECIMENS FOR EVALUATION OF MICROTITRE CULTURES IN THE ISOLATION OF CLASSICAL SWINE FEVER VIRUS

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Classical swine fever (CSF) is a peracute to chronic disease of domestic pigs and wild boar which continues to occur in extensive outbreaks in the EU. Ireland is at risk of importation of CSF virus (CSFV) via live pigs or meat products. Isolation of CSFV is currently performed in cell cultures grown on flying coverslips, followed by virus detection using fluorescent antibody staining. However, this method is unsuitable for examining large numbers of samples at multiple dilutions, as is required when investigating a suspected outbreak of a notifiable disease. A method using microtitre cell cultures and immunoperoxidase staining was developed. This was evaluated by spiking normal porcine organ homogenates and serum with CSFV and measuring virus recovery. Virus was detected 24 hours after cell culture inoculation, with peak titres being reached in 48 hours. Virus concentrations recovered from spiked serum were almost as high as from control samples, but a hundred-fold ($2 \log_{10}$) loss of virus activity occurred in the spiked organ samples. The presence of intracellular lipid or lipoprotein inhibitors of measles, dengue, herpes simplex and rabies virus has been reported previously. It is possible that these substances are widespread in nature and adversely affect attempts at virus isolation.

(P.134) CANDIDIASIS IN CRITICALLY ILL SURGICAL PATIENTS

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Fungal infections are a major cause of morbidity in critically ill surgical patients.¹ We assessed the incidence of candidiasis in a general surgical ITU, the characteristics common to patients with postoperative candidiasis and the efficacy of regular surveillance cultures in providing early detection. All surgical patients who remained in ITU for more than 24 hours were included in the study. The presence of established risk factors for the development of candidiasis was noted.² Twice weekly urinary surveillance cultures were taken. Blood cultures were performed where clinically indicated 50 patients were studied. 9 patients developed urinary candidiasis (18%), 2 of these developed a candida septicaemia. Distinguishing candidiasis patients from those with bacterial sepsis is a difficult clinical problem. Long hospitalisation and parenteral nutrition, multiple operations and antibiotics are well known predisposing factors to candidiasis. Similar predisposing factors were found to be significant in the present study also. Regular urinary surveillance cultures may be useful in the early detection and management of these patients.

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ONCOLOGY

(P.135) FAILURE TO METABOLISE SUPEROXIDE/RADICALS IN THYROID CANCER

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Cytochemical measurement of Glucose-6-Phosphate Dehydrogenase (G6PD) activity is routinely performed under an atmosphere of N_2 to prevent H^+ reacting preferentially with O_2 and thus being unavailable to reduce a neotetrazolium (NT) H^+ acceptor. G6PD activity was minimal when benign tissues were reacted under an atmosphere of O_2 . An unexplained finding was that in many malignant tissues a significant amount of G6PD activity is retained under O_2 . In this study G6PD measured in frozen sections from benign thyroid tissues (N=14) gave a mean of $33.4 \pm 0.7U$ under O_2 . In contrast, malignant thyroid tissues (N=6) demonstrated O_2 insensitivity in that significant G6PD activity was retained under O_2 (N_2 $39.2 \pm 1.0U$; O_2 $37.4 \pm 1.0U$; 95% G6PD activity retained). O_2 insensitivity in malignant tissues has been attributed to the inability of such tissue to remove superoxide radicals. Frozen sections of thyroid tissue were incubated with the enzyme superoxide dismutase (SOD; 42-4201U/ml) prior to G6PD measurement. Addition of SOD abolished the O_2 insensitivity of G6PD in the malignant thyroid rendering its behaviour similar to benign tissues which were themselves unaffected by exogenous SOD. The findings provide

a theoretical basis for the O₂ insensitivity phenomenon based on failure of malignant to metabolise O₂ radicals and demonstrate that this investigation is a true metabolic index differentiating between benign and malignant thyroid tissues.

**(P.136) OESTROGEN AND PROGESTERONE
RECEPTORS IN TAMOXIFEN ASSOCIATED
ENDOMETRIAL LESIONS**

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Breast carcinoma is a leading cause of death in women. Endometrial cancer is the commonest genital tract cancer with a lower mortality especially because it can be diagnosed at an earlier stage. Tamoxifen, a synthetic non-steroidal, anti oestrogenic drug is widely used as adjuvant therapy for breast cancer in post menopausal women with positive oestrogen receptors. Current trials are exploring the use of Tamoxifen as a prophylactic agent in women at high risk of developing breast cancer.

Lately there has been an accumulation of reports suggesting a possible association between Tamoxifen treatment and induction of endometrial pathologies such as endometrial hyperplasia, polyps and carcinoma.

This presentation is part of our study, aiming to evaluate the oestrogen and progesterone receptor status by using microwave antigen retrieval technique and subsequent avidin - biotin peroxidase complex method in these endometrial lesions, and the possibility, if any, of predicting which of the Tamoxifen treated patients will develop such an endometrial pathology. We carried out the receptor assay in 6 cases, 3 of which had a history of Tamoxifen therapy. In our short study, the receptor status in the endometrial lesions does not show any relationship with the history of Tamoxifen therapy, but status was related to grade of tumour in all cases.

**(P.138) LONG TERM RESULTS OF RADIOTHERAPY TO
THE LOWER LEG**

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All patients receiving radiotherapy for lower leg lesions between 1988 and 1992 in Exeter following recalibration of radioactive sources, were studied for a period of 2-6 years to

assess: the incidence of radionecrosis, natural history of the process of radionecrosis and results of surgical intervention by various reconstructive techniques.

A total of 25 patients were studied and the natural history of the process of radionecrosis showed two clinical patterns; immediate (primary) radionecrosis and late (secondary) radionecrosis. The incidence of primary radionecrosis corresponded well to reported levels of approximately 15%. The incidence of secondary (late) radionecrosis however showed an incidence approaching 30%.

Reconstruction with split skin grafts were universally unsuccessful and our experience showed the effectiveness of fasciocutaneous flaps in the surgical management of this difficult condition.

An early combined audit between our departments has stopped the practice of radiotherapy to the lower leg for common skin malignancies.

**(P.139) BILATERAL FREE TRANSVERSE RECTUS
ABDOMINUS MYOCUTANEOS (TRAM) FLAP FOR
BREAST AND CHEST WALL RECONSTRUCTION
(Case Report)**

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Breast cancer is the most common malignancy in women, affecting one out of every nine women some time in their lifetime. The most effective treatment for breast cancer today is surgery, either alone or in combination with chemotherapy, radiotherapy or both. Restoring a natural appearing breast with few scars and minimal secondary deformity of the donor site is a challenge. TRAM flap is popular today because it adds bulk to the chest wall and is autologous. Reconstruction with free TRAM flap compared with the pedicle conventional TRAM flap is more reliable.

A 58 year old women who had had bilateral mastectomies in the past, and was on the waiting list for breast reconstruction, on arrival was found to have bilateral local recurrences. She underwent wide excision of both mastectomy scars, followed by bilateral free TRAM flap operation for chest wall reconstruction .

The case and the result will be discussed.

PATHOLOGY/CYTOLOGY

(P.140) MERKEL-CELL CARCINOMA OF THE SKIN

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Merkel-Cell Carcinoma (or Neuroendocrine Carcinoma) is a rare skin tumor with variable clinical features that can easily

be confused with basalioma, spinocellular epithelioma, and malignant melanoma. A histologic diagnosis also may prove difficult because of a similarity to certain forms of malignant lymphoma, metastatic pulmonary small cell carcinoma, malignant melanoma and primary extraskeletal Ewing's sarcoma of the dermis.

This report reviewed three clinical cases treated in this department, with a view towards obtaining early diagnosis and better prognosis.

(P.141) CAUSES AND OUTCOME OF ACUTE ABDOMINAL EMERGENCY SURGERY IN SIERRA LEONE

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The aim of this retrospective study is to review causes and outcome of acute abdomens in a rural hospital in Sierra Leone where facilities were limited. The surgical service was provided by western trained physicians without postgraduate surgical training and by experienced theatre nurse aids with little formal training.

All cases of acute abdomen hospitalised from Oct '92 until Oct '94 who required surgery were identified by review of theatre books, ward records and patients notes. EPI-INFO was used as a database and for statistical analysis.

173 cases, 53% male, 4% < 14 yrs, were identified. Operative diagnoses included; ectopic pregnancy (N 43), strangulated hernia (N 34) of whom 15 required bowel resection, incarcerated hernia (N 9) appendicitis (N 15), normal appendix (N 5), uterine rupture (N 9), perforated ulcer (N 8), pelvic or tubal abscess (N 7), volvulus (N 6), primary bacterial peritonitis (N 5), obstruction due to adhesions (N 5), traumatic bowel injury (N 4), intussusception (N 3), and other miscellaneous. 90% survived to discharge after a median post operative stay of 8.5 days (range 7-127). Of 18 deaths 83% occurred in the first 3 days. Predictors of poor outcome included ileal perforation, usually due to typhoid, and resection of bowel in strangulated hernia.

These results show that acute abdominal surgery can be done at district level in poor countries using limited facilities even by staff without extensive surgical training. The range and nature of pathology differ from Western series in the high incidence of ectopic pregnancies and strangulated hernia

(P.142) GLUTATHIONE S-TRANSFERASE ISOENZYMES AS INDICATORS OF LIVER PATHOLOGY

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Measurements of serum enzyme patterns are important diagnostic indicators of liver damage: enzyme measurements

most commonly used in this way include alkaline phosphatase, alanine and aspartate aminotransferases and γ -glutamyl transpeptidase. It has been suggested that glutathione S-transferase (GST) may be a better diagnostic enzyme for liver damage in a variety of clinical conditions.⁽¹⁾ In this present study, we have studied the levels and isoenzyme patterns from groups of patients diagnosed as suffering from chronic active hepatitis (group 1, n=8), cholestasis (group 3, n=9) and cholestasis complicated by active cell damage (group 3, n=6). Although the standard liver test enzymes are elevated in the second group, GST activity is within the reference interval for this enzyme (0.35U/mg, n=100) while significantly elevated in the other groups. Hepkit™ ELISA assays indicate that Alpha class GSTs are the predominant isoenzymes in these samples. Mu class isoenzymes were detected using a qualitative Mukit™ ELISA assay in 57% group 1 and 25% group 3 samples while no group 2 samples gave positive results for these enzymes. Alpha class GSTs were expressed in 100% group 1, 40% group 2 and 100% group 3. These results probably reflect GST polymorphisms in the human population. Based on these measurements, we suggest that low levels of GST, accompanied by elevation in the standard liver test enzymes may help to distinguish cholestasis from cholestasis complicated by active cell damage.

Reference

1. Hayes, P. C. et al. Clin. Chim. Acta. 1990: 172, 211-216.

(P.143) MUSCLE BIOPSY FINDINGS IN PATIENTS INVESTIGATED FOR MALIGNANT HYPERPLASIA

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Malignant Hyperthermia (MH) is a serious disorder, dominantly inherited, which results in muscle contracture and hyperthermia, provoked by volatile agents and muscle relaxants commonly used in anaesthesia. There are few reports of muscle biopsy findings in patients undergoing investigation for MH. Whether a specific "MH myopathy" recognisable by histological criteria exists remains uncertain. We studied muscle biopsies from 111 patients undergoing investigation for possible MH for histological/histochemical abnormalities. Seventy eight biopsies were normal, 33 showed some myopathic features. When compared with results of muscle contracture tests using caffeine and halothane, there was no direct relationship between contracture test results and histological findings. However, a higher incidence of myopathic features was found in MH probands i.e those who had experienced a clinical episode of hyperpyrexia, probably reflecting prior muscle damage. A few biopsies showed other muscle pathology e.g. mitochondrial myopathy, Thomsen's disease. Eight large kindreds within the group were studied in detail. Specific histological features tended to be found within individual families e.g. mitochondrial excess, fibre type distribution patterns. The results suggest that there are no specific "Malignant Hyperthermia Myopathy" biopsy features, but that biopsy is often abnormal in probands and may be useful in indicating other muscle disease.

**(P.144) BILE DUCT EPITHELIAL CHANGE IN A
UNIQUE FEMALE COHORT OF TYPE 1b HEPATITIS C**

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Type 1b hepatitis C virus (HCV) is said to be associated with more severe progressive liver damage than infections with other types. We have studied bile duct epithelium in a cohort of 30 women with longstanding HCV infection.

Needle biopsy (Menghine) of the liver was performed under ultrasound control. Specimens were stained with Haematoxylin and Eosin, Haematoxylin and Van Gieson, Periodic Acid-Schiff and Perl's Prussian Blue stains. Histological features were assessed independently by two histopathologists (M.S., C.D.). Immunohistochemistry using AE1/AE3 anti cytokeratin monoclonal antibodies (ICN immunobiochemicals) by the Avidin/Biotin horse radish peroxidase method was carried out in 30 of the biopsies. 17 normal control liver biopsies were used.

Antimitochondrial antibodies were absent in all cases. The ratio of bile ducts to hepatic arteries were significantly higher (2.53 ± 1.33) in the HCV group compared to normal controls. Absolute bile duct epithelial cell proliferation was present involving single bile duct epithelial cells, cords of cells and formed bile ducts within portal tracts, along limiting plates and hepatic septa. Bile duct damage was not a consistent finding in the study.

Conclusions. This study shows conclusively that bile duct epithelial proliferation is a significant feature of type 1b HCV hepatitis. While bile duct damage is a feature of HCV infection a more significant finding in this study was bile duct epithelial proliferation.

PHARMACOLOGY/THERAPEUTICS

**(P.145) ANGIOTENSIN II: ADRENERGIC CONSTRICTOR
ACTION IN MAN**

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We have investigated the effect of local intra-arterial infusions of A II into the brachial artery of healthy volunteers during blockade of post-synaptic α receptors with phentolamine. The response was compared to that seen with A II infused during nitroprusside administration at a dose designed to give a similar dilator response to phentolamine.

A II (6.25, 25 & 100 pmol/min) was infused alone and then together with sodium nitroprusside (4 μ g/min) and phentolamine (40 μ g/min) in eight healthy volunteers. Forearm blood flow was measured by strain gauge plethysmography.

The percentage reduction in forearm blood flow produced by AII 100pmol/min in the phentolamine pre dilated vascular bed was significantly lower than that seen in the sodium nitroprusside pre dilated forearm bed (28.1 ± 2.9 v $52.9 \pm 4.2\%$; $p=0.006$). Comparison of the rate of change of blood flow in response to quadrupling doses of A II during blockade of α

receptors with phentolamine and during nitroprusside administration was calculated from the mean slope of the dose response curves. The mean slope during nitroprusside administration (-0.16 ± 0.025) was significantly greater than that during blockade with phentolamine (-0.098 — -0.020) ($p=0.046$).

Conclusions. We conclude that a significant part of the vasoconstrictive action of exogenous A II on forearm resistance vessels in man is sympathetically mediated.

**(P.146) CHANGING PROFILE OF DIURETIC
HYPOKALEMIA - A TEN YEAR STUDY OF THE
IMPACT OF FRUSEMIDE-AMILORIDE**

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A ten-year (1984-1993) prospective study of 16,605 admissions to an internal medicine unit identified 620 patients with hypokalemia ($K \leq 3.4$ mmol/l) at the time of admission. Initially, (1984/85), admission hypokalemia was associated with diuretic therapy (ratio, diuretic-associated to non-diuretic = 3.5:1) Admission with diuretic-associated hypokalemia (DAH) was caused or precipitated by hypokalemia (H) in 79%. A prescribers' education programme emphasising use of frusemide-amiloride reduced significantly H admissions within two years ($p < 0.0001$). This new situation indicates highly significant changes in DAH/non DAH admissions with H: most H admissions are not now related to diuretics; in DAH, frusemid-eamiloride admissions have higher K levels (3.2 vs 3.0mmol/l) and less morbidity from equal K levels; other drugs e.g. corticosteroids, bronchodilators are key precipitants in 62% of admissions with frusemide-amiloride DAH; admissions with frusemide-amiloride DAH are no longer caused by H alone. We conclude that frusemide-amiloride has led to beneficial changes in incidence and profile of DAH in hospital admissions.

**(P.149) ORAL OR INTRAVENOUS ANTIBIOTICS: THE
EFFECT OF INTERVENTION**

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We⁽¹⁾ have shown that oral antibiotic therapy has advantages over intravenous in terms of duration of hospital stay, ease of administration and cost in the treatment of mild to moderate community acquired lower respiratory tract infections (LRTI). However the vast majority of patients admitted to our hospital with this diagnosis receive intravenous antibiotics. We sent all doctors a copy of our previous report⁽¹⁾ with the recommendation that oral antibiotics be used for LRTI except in severely ill, immunocompromised or patients unable to

tolerate oral therapy. We compared the use of intravenous to oral antibiotics pre and post-distribution of the recommendations.

Results	No. of Patients	IV%	Oral%
1993 November (pre)	100	83%	17%
1994 January (post)	100	64%	36%
1994 March	100	72%	28%
1994 September	100	79%	21%

While initially our recommendations produced a significant ($p < 0.05$) increase in the use of oral antibiotics, over time, there was a drift back towards baseline levels. Additional methods of continuous intervention are required to achieve long term effects.

Reference

1. Chan, R. et al. *Ir. J. Med. Sci.* 1993; 162: 39.

We wish to acknowledge the contribution of the Pharmacy Department and support from the Health Research Board.

(P.150) LIMITED IMPACT OF RE-INSTATEMENT OF MEDICINES TO LIMITED LIST

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The General Medical Services (GMS) scheme provides medicines free of any charge to approximately 36% of our population. We looked at prescribing of ulcer-healing agents and analgesics between 1989 and 1993 to determine if the re-introduction in 1991 of alginates/antacids and certain analgesics had any impact on histamine H2 antagonist/omeprazole and non-steroidal anti-inflammatory (NSAID) prescribing respectively. Data was obtained from the GMS lists of top 100 drugs each year. Post re-instatement, alginates/antacids were used extensively - 48,000 of 459,000 (10%) ulcer-healing items in 1991; 196,000 of 655,000 (30%) by 1993 - but histamine H2 antagonist prescribing continued to rise, implying no substitution occurred, and fell only in 1993 when prescribing incentives were introduced. Omeprazole use rose from 5,000 items in 1990 to 62,000 in 1993, possibly indicating consultant/hospital influence⁽¹⁾. Prior to the re-introduction of paracetamol, its combinations and dextropropoxyphene in 1991, the alternative analgesics were NSAID's, dihydrocodeine or morphine. NSAID's comprised 1.25m (85%) of 1.46m analgesic items dispensed in 1991 and rose to 1.3m items in 1992, before falling to 1.17m in 1993 (71% of 1.7m items). The less expensive re-introduced agents accounted for the rise in total analgesic use. Prescribing changes were temporally more related to introduction of budgetary incentives than to the re-introduction of therapeutic alternatives and prescribers appear to use such items in addition to, not instead of more expensive options until there is good incentive to change.

Reference

1. McGettigan, P. et al. *Br. J. Clin. Pharm.* 1994: 37-512P.

Supported by the Health Research Board.

(P.151) AWARENESS OF THE CRITERIA FOR REPORTING ADVERSE DRUG REACTIONS AND RESPONSE TO INTERVENTIONS

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Spontaneous reporting of adverse drug reactions (ADR's) by yellow cards is the most widely used surveillance system for the safety of drugs in clinical practice, however, fewer than 10% of ADR's are reported. We surveyed 240 hospital doctors and of 118 respondents, over half (54%) had never reported and of reporters, 49% had just one ADR. Just 20% of respondents knew all the NDAB reporting criteria. Seriousness of the reaction was the most important reason for reporting while unavailability of yellow cards was considered the most important deterrent. Having previously identified unavailability of yellow cards as a constraint to reporting⁽¹⁾, we made yellow cards prominently available in wards and clinics and for three months inserted one upon admission into patients' charts. Prescribers were reminded regularly of their availability. During the three months of interventional activity, the NDAB received 29 ADR reports from this hospital compared with 12 in the preceding three months. Cessation of visual and verbal reminding was followed by a drop to 14 reports in the next five months despite continued availability of yellow cards.

Clinicians appreciate that ADR's should be reported but have poor knowledge of reporting criteria. They are responsive to intensive intervention but availability of yellow cards alone is insufficient to ensure reporting. The NDAB must enhance awareness of the need to report and educate doctors regarding reporting criteria while the profession must participate actively in ensuring the safety of medicines.

Reference

1. Feely J. et al. *BMJ* 1990; 300: 22-23.

Supported by the Health Research Board.

(P.152) OXIDATIVE STRESS IN HYPERTENSION AND INCREASED RESISTANCE TO LDL OXIDATION IN PATIENTS ON COMBINED THERAPY

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We⁽¹⁾ reported increased plasma lipid peroxidation, measured as malondialdehyde (MDA) in hypertensive patients. Our further

study now shows higher levels (1.23 ± 0.2 vs 1.05 ± 0.2 $\mu\text{mol/L}$, mean \pm SD, $p < 0.005$) in patients on single drug therapy ($n = 24$) as opposed to combined ($n = 27$). As several antihypertensive drugs had been shown to protect low-density lipoprotein (LDL) against oxidation promoted by copper ions *in vitro*, we investigated the relationship of antihypertensive drug therapy to copper-induced oxidation of LDL in patients with essential hypertension. We compared two groups ($n = 11$) of sex and age matched patients treated either by combined antihypertensive drugs or by a single antihypertensive drug. The major natural antioxidants such as plasma vitamin C and E, vitamin E in isolated LDL, erythrocyte vitamin E and erythrocyte glutathione were measured and there was no significant difference in respect of these factors between the two groups. The onset and progression of copper induced LDL oxidation was assessed by measuring the lag phase of production of conjugated dienes in an isolated LDL solution with continuous monitoring spectrophotometry at 234 nm through 4 hours. In patients on combined antihypertensive drug therapy, there was a significantly increased lag phase when compared with single antihypertensive drug treated patients (67.0 ± 32.6 vs 46.6 ± 9.9 minutes, mean \pm SD, $p < 0.05$) indicating the increased resistance of LDL to oxidation. Our data suggests that in hypertensive patients, there may be less oxidative damage and increased resistance to further damage in those on combined drug therapy.

Reference

1. Y. Wen et al. *Ir. J. Med. Sci.* 1994; 163 (suppl 13): 41.

Supported by the Irish Heart Foundation.

(P.153) ASSAY OF HUMAN ERYTHROCYTE SODIUM-DEPENDENT LITHIUM EFFLUX: THE IMPORTANCE OF TIMING OF BLOOD SAMPLING

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High activity of erythrocyte sodium-lithium countertransport (SLC) system is associated with essential hypertension. It is a genetically-determined trait and has been reported to be stable over prolonged periods in individuals. However, it is becoming increasingly evident that the transport system is susceptible to modulation, both acutely and chronically, by various factors. In this study, we observed temporal variations in SLC over a period of ten hours (08.00 - 18.00h) in healthy volunteers.

The activity of the transporter in 140mM sodium chloride at mid-day was 0.219 ± 0.032 mmol/l cell. h (mean \pm S.E.) and was higher than that in the morning (0.196 ± 0.029 ; $p < 0.01$). Kinetic characterisation of the transporter indicated that its affinity for external sodium, K_m , was unaltered during the experimental period. However V_{max} was maximum (0.354 ± 0.051 mmol/l cell h; $p < 0.010$). Its value in the evening (0.316 ± 0.042 mmol/l cell h) was lower than at mid-day ($p < 0.045$) but higher than in the morning ($p < 0.037$). Changes in SLC V_{max} correlated with neither the corresponding changes in plasma cortisol nor that in aldosterone. However, they correlated significantly with those in plasma renin activity ($p < 0.001$); although the regression analyses data indicate that changes in renin activity do not wholly account for the observed changes in the V_{max} of the transporter ($r^2 = 0.448$).

We conclude that changes in SLC activity occur during the day in healthy volunteers and is partly due to associated changes in plasma renin activity.

RESPIRATORY

(P.154) β_2 -INTEGRIN EXPRESSION ON CIRCULATING BLOOD NEUTROPHILS FROM PATIENTS WITH CYSTIC FIBROSIS

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Lung disease is the major cause of morbidity and mortality in cystic fibrosis (CF). Lung destruction results from chronic pulmonary inflammation, characterised by a massive influx of neutrophils from the bloodstream. Recently, hyper-expression of the β_2 -integrin (CD18) adhesion molecules on circulating neutrophils has been observed in patients with Adult Respiratory Distress Syndrome (ARDS). It is suggested that this may contribute to the excessive influx of neutrophils to the lung observed in ARDS. To assess whether similar mechanisms might be operating in CF, we compared surface expression of CD18 on circulating neutrophils from 10 CF patients and 10 control subjects of similar age and sex. Peripheral blood leukocytes were labelled with FITC-conjugated antibody to CD18 and analysed by flow cytometry. Results were calculated as the mean fluorescence intensity (MFI) of CD18-labelled neutrophils. No difference in surface β_2 -integrin expression on circulating neutrophils between CF patients (MFI = 54.6 ± 15.8) and control subjects (MFI = 57.2 ± 10.8) was observed. Only one CF patient displayed an MFI value above normal range (i.e. $>$ mean control value + 2SD). Thus, in CF, over-expression of β_2 -integrins on circulating neutrophils does not seem to contribute to the excessive accumulation of neutrophils in the lung.

This work was supported by the Cystic Fibrosis Association of Ireland.

(P.155) EFFECT OF NEBULISED RECOMINANT DNase ON MEDIATORS OF INFLAMMATION IN CYSTIC FIBROSIS

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In Cystic Fibrosis (CF), the connection between hyperviscous mucous, bacterial infection and inflammation suggests that the antimucolytic agent DNase, may, in addition to reducing airway obstruction, also attenuate the infection/inflammation cycle. The aim of this study was to examine the effect of DNase therapy on markers of neutrophil-dominated inflammation in CF. Blood and sputum samples were collected from fifteen stable CF patients prior to initiation of nebulised DNase therapy and at six and twelve-weeks thereafter. Plasma samples were analysed for interleukin-8 (IL-8), α_1 -protease inhibitor (α_1 PI) and neutrophil elastase in complex with α_1 PI (NE-PI). Sputum samples were assessed for IL-8, α_1 PI and levels of active neutrophil elastase (NE). Twelve weeks of DNase therapy failed to reduce plasma levels of either IL-8 or α_1 PI. A significant decrease in sputum levels of α_1 PI was observed over the twelve-

week treatment period (pre-treatment: 35.6±6.7 mg/ml; post-treatment: 8.75±3.0 mg/ml, p<0.002). This was not accompanied by a similar decrease in sputum levels of either IL-8 or NE activity, although a downward trend in NE activity was noted (pre-treatment: 946±123 μunits; post-treatment: 707±85.8 μunits, p=0.058). These results indicate that short-term treatment with nebulised DNase has little effect in attenuating underlying inflammation in CF.

This work was supported by the Cystic Fibrosis Association of Ireland.

(P.156) CD4+CD8+ T-CELLS IN GRANULOMATOUS LUNG DISEASE

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Extrinsic allergic alveolitis (EAA) and sarcoidosis are two granulomatous lung diseases characterised by an expansion of lung T-cells. In active sarcoidosis an increase in CD4 relative to CD8 T-cells is seen, resulting in a raised CD4/CD8 ratio. In EAA the increase in both CD4 and CD8 T-cells is similar. Recent studies indicate that interleukin-4 can induce the transformation of CD4 to CD8 T-cells via a CD4+CD8+ intermediate. By assessing BAL samples from EAA and sarcoidosis patients for the presence of CD4+CD8+ T-cells, this study set out to examine whether a difference in the level of CD4 to CD8 transformation might contribute to the different pattern of T-cell expansion observed in these two diseases. BAL cells recovered from EAA (n=6) and sarcoidosis (n=28) patients were double labelled with fluorescent anti-CD4 and anti-CD8 antibodies and analysed by flow cytometry. Paired samples were labelled with anti-CD3 (pan T-cell) antibody and the percentage of CD3+ cells that were CD4+, CD8+ and CD4+CD8+ calculated. The percentage of CD4+CD8+ cells was found to be significantly higher in the EAA group compared to the sarcoidosis group (EAA = 9.1±4.6, sarcoidosis = 2.0±0.42, p<0.005). These results suggest that differences in the level of transformation of CD4+ to CD8+ cells might indeed contribute to the differential T-cell expansion observed in EAA and sarcoidosis.

(P.157) DYSPHONIA AND INHALED STEROIDS: A PROSPECTIVE STUDY

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Although inhaled corticosteroid therapy is of undoubted benefit in the management of asthma, dysphonia is a recognised sequela. This study was designed to examine longitudinally the effect of inhaled steroids on the voice and vocal cords of newly diagnosed and previously untreated asthmatics.

Twelve subjects were recruited and underwent voice and vocal cord assessment prior to and 3 months after starting inhaled steroid treatment. Each patient acted as their own control. The assessment consisted of 1) rating dysphonia using a visual analogue scale, 2) acoustical analysis of the voice and 3) videostroboscopic examination of vocal cord activity.

Five subjects have been fully assessed. Before treatment 4 had normal voices and 1 was mildly hoarse. Vocal cord pathology was noted in 3 subjects. After 3 months of inhaled steroids

dysphonia was noted in 1 subject, no voice changes in 3 subjects and an improvement in the voice of the other subject were seen. Vocal cord bowing was found in 2 subjects, improvement of vocal cord pathology and no vocal cord changes were seen in 2 and 1 subjects respectively.

The significance of these findings and the results from 7 other subjects will be discussed.

(P.158) VIDEO-ASSISTED THORACIC SURGERY FOR SPONTANEOUS PNEUMOTHORAX

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Video-assisted thoracic surgery appears to be a viable alternative to conventional thoracotomy when surgical management of spontaneous pneumothorax is required. Apical pleurectomy and bullectomy can be performed with this approach thus sparing the patient the morbidity associated with formal thoracotomy. Using video-assisted techniques, we have performed 140 procedures on 130 patients, between January 1992 and January 1995, including 33 patients with spontaneous pneumothorax. The male : female ratio was 1.4:1. Age ranged from 17 to 84 (mean 38.7). The two main therapeutic strategies were apical pleurectomy in all patients (33) and blebectomy/bullectomy in 29 (88%). There was one hospital death (hospital mortality = 3%) in an elderly patient who developed multiorgan failure post bullectomy and persistent air leak. One patient (3%) required conversion to formal thoracotomy. Mean postoperative chest tube drainage was 3.1 days and mean postoperative hospital stay was 6.1 days. There has been no recurrence of pneumothorax in this series. Our evidence indicates an expanding role for video-assisted thoracic surgery which is now an option in the management of patients with spontaneous pneumothorax.

(P.162) RENAL FUNCTIONAL RESERVE IS ABSENT IN SEVERE COPD

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Renal functional reserve (RFR) is the normal increase in renal blood flow (RBF) in response to a protein load, which may be diminished in severe COPD. We investigated this using Duplex Ultrasonography in 17 stable hypoxaemic COPD pts. and 5 mild COPD controls. Mean (SD) PaO₂ was 8.2 (1.08), PaCO₂ 6.2 (0.71)kPa, FEV₁ 0.74 (0.27)l in the hypoxaemics, and PaO₂ 10.8 (0.66), PaCO₂ 5.2 (0.3) and FEV₁ 1.55 (0.43)l in controls. 10/17 pts. were hypercapnic. The pulsatility index (PI) (an index of RBF) was measured with an Acuson 128 scanner at baseline and 30, 75, 120 and 165 mins. after a 250g steak. The PI should decrease with increasing RBF.

Results: The PI fell normally in the controls, was unchanged in the normocapnic pts., and rose in hypercapnics.

PI	Fasting	75mins	PI Change	P value
Control pts.	1.06	0.93	-0.13	<0.005
Hypoxaemic + normocapnic	1.04	1.01	-0.03	ns
Hypoxaemic + hypercapnic	1.03	1.1	0.07	<0.05

We conclude that there is evidence of sub-clinical renal impairment in pts. with severe COPD, which is more marked in hypercapnics.

**(P.163) THE IMMUNOPATHOLOGY OF SUDDEN
ASTHMATIC DEATH**

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We investigated the immunopathological profile of the proximal airways in five patients (3 female, 2 male) who died from severe asthma. Blocks of tissue from the second generation right middle lobe bronchus were obtained within 24 hours of death and flash-frozen in liquid nitrogen. Double immunofluorescence and immunoperoxidase techniques were performed using monoclonal antibodies directed against CD4, CD8, CD68, RFD1, RFD7, EG1 and EG2 surface markers. Frozen biopsy sections of human palatine tonsil served as positive controls. Each section had a negative control (buffered saline) and an irrelevant control (monoclonal antibody to B cells). Airway inflammation was characterised by an epithelial mononuclear cell infiltrate on H&E staining.

There were significant increases in macrophages (predominantly of the RFD1+, RFD7- antigen presenting cell subset), T cells (the majority expressing CD8: suppressor/memory cells) and eosinophils with equal EG1 and EG2 expression.

We conclude that: fatal asthma is associated with increased numbers of suppressor/memory T-cells, antigen presenting macrophages and activated eosinophils present in the bronchial wall; fatal asthma results from uncontrolled peribronchial inflammation.

**(P.164) REGULAR BRONCHODILATORS ARE NOT
HARMFUL IN ASTHMA PATIENTS ON INHALED
STEROIDS**

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It has been suggested that regular inhaled beta agonists may be harmful in asthma. We studied 12 patients with asthma in a prospective, randomised single-blind, single-dummy, three-period crossover trial comparing placebo (2 puffs tds), salbutamol (200mcg tds) and oxitropium bromide (200mcg tds) for 28 days each. Computerised spirometry and bronchial reactivity to histamine were obtained on entry and after each treatment period. Symptom scores, use of rescue bronchodilator and peak expiratory flow rates were recorded daily.

There were no significant differences in bronchial hyperresponsiveness during salbutamol, oxitropium or placebo treatment periods. There were no significant differences in baseline FEV1, symptom scores or morning and evening PEFr between treatment groups. The use of rescue bronchodilator was significantly less in the salbutamol period compared to placebo.

In conclusion, regular treatment with inhaled salbutamol or oxitropium bromide is not associated with deterioration in asthma control in patients on concomitant inhaled

corticosteroid therapy. Our data suggest that although current concerns about inhaled beta agonists may be misplaced in these patients, regular bronchodilator use does not confer any advantage over intermittent therapy.

**(P.165) ASTHMA IN IRELAND: HOW WELL IT IS
MANAGED. A PRELIMINARY REPORT OF A
COMMUNITY SURVEY**

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Since the publication of international guidelines for asthma management there has been considerable interest in audit in asthma. To date there has been no community audit of asthma management in Ireland. The Asthma Society of Ireland therefore undertook a community based survey through Irish pharmacies over 7 days beginning 30th May 1994.

25 pharmacies were selected to represent the national demographic profile. All prescriptions for asthma medicines were eligible for inclusion. 23 questions were delivered by the pharmacist to define patient details and overall management of disease in the previous year. To assess their understanding of the different types of treatment, patients were asked to identify "reliever" or "preventer" from a series of photos.

Of 486 patients 285 had complete data. The high loss was due to a surprising 25% of prescriptions being collected on behalf of patients. 59% of patients held medical cards. 72% of patients were managed by their GP alone with 23% having combined GP/specialist care. 66% were taking preventative therapy. Whereas 48% of patients had taken inhaled steroids in the past year, an amazing 50% had at least one crash course or oral steroids over the same period and 15% were on regular oral steroids. 64% of patients had their peak flow measured at some time but had never had their inhaler technique assessed. 29 of those 189 on preventative therapy misidentified a reliever as a preventer. Of the 33 patients overusing beta-agonists, only 5 were not on regular preventative therapy. 16% were using a nebuliser regularly. 22% of all patients missed 2 weeks off work or school. 67% of patients were happy with their understanding of their illness.

In conclusion, patients were generally well informed but had fears about inhaled steroids. A high proportion of patients were taking oral steroids indicating sub optimal control. Beta-agonist overuse was relatively uncommon. It was disappointing that so few patients had their technique checked. Strategies to deal with these deficiencies will be discussed.

ANAESTHESIOLOGY

**(P.166) LATE PRE-EMPTIVE EFFECT OF HIGH DOSE
SYSTEMIC OPIATES**

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We investigated the pre-emptive effect of high dose systemic opiates over a 7 hour postoperative period. 38 ASA 1 patients undergoing abdominal hysterectomy, using standardised premed. and GA, were studied. A randomised double-blind design was employed - Group A received Alfentanil 70ug/kg over ten

minutes beginning 15 minutes before incision; Group B received Alfentanil 70ug/kg over 10 minutes beginning 15 minutes after incision. In recovery 2mg IV boluses of morphine were administered every 10 minutes until comfortable. PCA delivered IV morphine was used for postoperative analgesia. VAS pain rating at rest and on movement and morphine consumption were recorded at 6, 12, 24, 48 & 72 hours. VAS pain scores and PCA morphine consumption were analysed using 2-way ANOVA. Demographic data was similar in both groups. The VASR scores were similar throughout. The VAS_M scores were higher in Group A at 48 and 72 hours. The results demonstrate similar morphine consumption over the initial 24 hours. Group A demonstrate less morphine consumption between 24-48 hours than Group B - 20.1±3.2 vis 23.2±4.0 - and significantly less between 48-72 hours postoperatively - 3.3±1.5 vis 15.1±4.3 [p<0.02]. The morphine consumption results suggest a pre-emptive effect of high dose opioids which begins to emerge from 24 hours and is more marked at 48-72 hours. The VAS_M score results are difficult to interpret but possibly suggest the presence of an ongoing pre-emptive effect of PCA morphine use.

**(P.167) EUROPEAN NOSOCOMIAL INFECTION
SURVEY: ANALYSIS OF IRISH DATA**

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The incidence and mortality of Nosocomial Pneumonia in I.C.U. is ill defined. Diagnostic criteria were devised by EURONIS* Committee and applied prospectively throughout Europe. This paper analyses the Irish data.

9127 patients from 325 I.C.U.s in 14 European Centres were recruited. Ireland provided 205 patients from 10 I.C.U.s. Incidence of mechanical ventilation was 62.4% (Ire.) 58.6% (Eur.) APACHE II > 21, 9.7% (Ire.), 21% (Eur.), surgery before administration 63.7% (Ire.), 41.9% (Eur.), SDD 0% (Ire.), 6.6% (Eur.).

Results:	Ire. %	Eur. %
Incidence of Pneumonia	11.7	11.8
Mortality	14.15	14.3

Organisms (Irish Group)	
G. Positive	16.6%
G. Negative	38.8%
Fungus	2.7%
Polymicrobial	16.6%
Unidentified	25%

Conclusion: This survey provides authoritative figures on the incidence and mortality of nosocomial pneumonia in Irish I.C.U.s and these results concur closely with European data. Gram positive and polymicrobial infection may be commoner than traditionally believed. Despite the difference in utilization of SDD the incidence of pneumonia is the same.

* European Nosocomial Infection Survey.

**(P.168) DIFFERENTIAL NEUROLOGICAL RECOVERY
AFTER SPINAL ANAESTHESIA**

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There is growing acceptance of spinal anaesthesia for ambulatory surgery. Recently, ambulatory epidural analgesia was associated with significant proprioception impairment, even with normal motor power, possibly undermining safe

ambulation⁽¹⁾. Evaluation of detailed, clinical neurological recovery after spinal anaesthesia has not been reported.

We examined 15 men (mean age 72 years, range 59-87), undergoing transurethral resection of the prostate (TURP). Each patient had a full clinical neurological examination of the lower limbs pre-operatively, and at 30 minutes, 2, 3, 4, 5, 6 and 8 hours postoperatively, by the same observer. All patients received 3 mls plain bupivacaine (0.5%) via a 229 spinal needle at L2/3 or L3/4.

Median time (hours, interquartile range) to recovery of motor power sufficient for walking (6.0 (5.4-6.5)) was longer than for complete recovery of proprioception (5.6 (5.0-6.0), vibration sense (5.0 (4.3-5.6)) and spinothalamic sensory (5.6 (5.1-6.3)) modalities.

These results suggest that elderly males may safely be allowed to ambulate after spinal anaesthesia, when lower limb motor function has fully recovered. The contrasting outcome in epidural studies may be related to endocrine and age-related factors.

Reference

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**(P.169) ELECTROTRANSDERMAL DELIVERY OF
HYDROMORPHINE FOR POSTOPERATIVE ANALGESIA**

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A prototype electrotransdermal device was employed in a clinical setting, examining delivery of hydromorphone. Patients were women following surgery receiving analgesic medication by patient-controlled analgesia. A randomised double blind placebo controlled study examined the reduction in PCA morphine use by electrotransdermally administered hydromorphone. Hydromorphone was delivered from a circular gel of area 7cm², containing 32mg hydromorphone hydrochloride. The current was 0.12mA/cm² for 1 hour followed by 0.5A/cm² for 23 hours. The patch was removed and replaced by a fresh one at 12 hours.

Following a log of about six hours, hydromorphone administered by this method caused a significant reduction in morphine use. The mean total amount of morphine was reduced by 36% by the concomitant administration of hydromorphone. Tolerability was good. One patient in the active group had erythema under both the active and the passive gels at 36 hours.

The results support a clear morphine-sparing effect of concomitantly administered hydromorphone. The application of a small electric current can considerably enhance transdermal delivery of opioid analgesics: initially resulting in rapid delivery, thereafter providing sustained delivery until patch removal, whereupon there is a rapid cessation of delivery and a rapid fall in blood concentrations

**(P.170) CAUSAL FACTORS IN POST ANAESTHESIA
RESIDUAL PARALYSIS**

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Despite the use of intermediate acting neuromuscular blocking

(NMB) drugs and peripheral nerve stimulators (PNS), post anaesthesia residual paralysis remains a problem^{1,2} We studied the genesis of this problem.

Following Ethics Committee approval and informed consent, we studied 45 patients having general anaesthesia involving the NMB drug Atracurium. The Myograph 2000 was used and response to continuous train-of-four (TOF) stimulation at the ulnar nerve recorded. Residual paralysis at extubation, defined as TOF < 0.7, was determined. Also, interval from last Atracurium to reversal, duration of surgery and whether a PNS was used by the responsible anaesthetist. The responsible anaesthetist was blinded to the myograph recording and routine anaesthesia care was independent of the research. Mann-Whitney U test was used for statistical purposes.

Residual paralysis was found in 66% at extubation. Adequate reversal was significantly associated with a greater duration of surgery, a longer interval from last Atracurium to reversal and spontaneous recovery at the time of reversal. Use of a PNS was inversely associated with years of anaesthetic experience and had no effect on the incidence of residual paralysis.

The authors acknowledge support from the Health Research Board.

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(P.171) INDUCTION DOSE OF PROPOFOL: THE EFFECT OF ALCOHOL INTAKE

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Chronic alcohol intake may increase the induction dose of propofol⁽¹⁾. The clinical endpoints and electroencephalographic (EEG) changes during induction of anaesthesia are well known^(2,3). The aim of this study was to compare the induction dose of propofol between drinkers and non-drinkers using clinical and EEG endpoints of anaesthesia.

We studied 24 male patients before surgery. Patients were divided into drinkers (> 30 units alcohol/week,) and non-drinkers (0 units/week,). Anaesthesia was induced by propofol at a rate of 200 mls/hour. The dose requirements of propofol to achieve loss of verbal contact, loss of eyelash reflex, and loss of ability to hold a 20ml. syringe were noted. The EEG was monitored (Lifescan, Diatex, California), and the dose of propofol and blood propofol concentrations required to achieve burst suppression was recorded. Data were analysed by analysis of variance and Dunnetts test.

Propofol requirements (mg/kg) at endpoints: (*P<0.05)

	Drinkers (n=12)	Non Drinkers (n=12)
Loss of verbal contact	2.1 ± 0.7	1.5 ± 0.4*
Loss of eyelash reflex	2.5 ± 0.8	1.7 ± 0.3*
Drop syringe	2.8 ± 0.9	2.4 ± 0.8
Burst supp.	8.9 ± 2.5	6.8 ± 2.1 (P=0.07)
Bld. propofol conc. µg/ml.	8.6 ± 2.6	8.9 ± 3.2

Age and weight did not differ significantly between the two groups. Drinkers required more propofol for loss of both verbal contact and eyelash reflex. Dose requirements of propofol are increased in patients who drink more than 30 units of alcohol/week. The similar blood propofol levels at burst suppression suggest a pharmacokinetic contribution to this difference.

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(P.172) A NOVEL USE OF INTRATHECAL BACLOFEN BY CONTINUOUS INFUSION

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Baclofen is an effective antispasmodic agent, structurally similar to the inhibitory transmitter GABA. It functions by binding to GABA receptors in the spinal cord and thalamus, inhibiting mono and polysynaptic reflexes. This suppresses the abnormal response to muscle stretching or cutaneous stimulation that leads to spasticity. Intrathecal baclofen has been used for relief of spasticity associated with disseminated sclerosis and spinal injury.

A previously healthy 7 year old male sustained accidental hypoxic brain damage. He developed severe spasticity in all 4 limbs. Minimal stimulation caused paroxysmal increase in flexor tone, causing total body rigidity. In adolescence he developed marked kyphoscoliosis. The degree of spasticity precluded surgical correction due to the risk of rod extrusion. A trial of intrathecal baclofen reduced spasticity sufficiently to allow surgical intervention. Spinal fusion was performed from T1 to L4. Intra-operatively an intrathecal catheter was implanted, tunnelled and connected to a Medtronic implantable infusion pump. An intrathecal baclofen infusion was increased from an initial rate of 0.05 mg/24 hours to 0.8 mg/24 hrs. over a 5 day period. Spasticity and range of movement markedly improved, with total cessation of the intermittent paroxysmal body rigidity. Baclofen therapy will be continued indefinitely

Conclusion: Continuous baclofen infusion via an implantable pump is not only useful in treatment of intractable spasticity, but also permitted corrective orthopaedic surgery, thus halting progression of the skeletal deformity and preventing development of respiratory compromise.

Reference

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(P.173) QUANTITATIVE ASSESSMENT OF PATIENT PREFERENCE FOR ANAESTHESIA FACE MASK

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Pre-oxygenation prior to induction of anaesthesia, a time associated with stress⁽¹⁾, is becoming routine in many hospitals. It is no longer used solely prior to rapid sequence induction. Clear PVC anaesthesia masks, some scented, are available as an alternative to the traditional rubber mask. The aim of this study was to assess and quantify patient preference for the type of face mask used for preoxygenation.

In the induction room, prior to induction of anaesthesia after baseline monitoring and intravenous access had been established, 23 ASA class I-III patients aged 17-72 years were randomly allocated to preoxygenation using a Bains circuit with either a standard black rubber face mask or a King systems' "Fresh scent" clear PVC mask. After two minutes they were asked to assess the acceptability of the procedure using a 100 mm Visual Analogue scale (VAS). The process was then repeated using the second mask. Patients were then asked if they had a preference for the type of mask used.

18 patients preferred the "Fresh Scent" while 5 preferred the black rubber face mask. Overall from the VAS patients found

preoxygenation more acceptable with the "Fresh Scent" (7.4 mm ± 8.7) compared to the black rubber mask (23.1 mm ± 26.3).

Use of the clear mask may contribute to a more relaxed and compliant patient, better preoxygenation and a smoother induction.

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(P.174) CARDIAC SURGERY PATIENTS: A STUDY OF ANAESTHESIA FACE MASK PREFERENCE

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Patients undergoing cardiac surgery are often awake on arrival in the anaesthetic room. Prior to induction of anaesthesia they are pre-oxygenated. This is recognised as a time of increased stress. Stress should be avoided thus preventing increased myocardial work and oxygen demand with possible risk of ischaemia⁽¹⁾.

The aim of this study was to determine whether patients undergoing open cardiac surgery had a preference for the type of face mask to be used for pre-oxygenation and during induction of anaesthesia.

63 patients, ASA II-IV, aged 45-79 yrs scheduled for cardiac surgery were visited pre operatively. The practice in the anaesthetic room was explained and that we were studying face mask preference. The patients were presented with a black rubber mask, a Kings systems' clear PVC "Fresh Scent" (mint) and strawberry scented masks. A brief description of each mask was given in random order. Patients were asked to breathe through the masks and express any preference. Results were analysed using X² test.

Pt preference	Fresh scent	Strawberry	Black	No pref.	Totals
Male	23	18	1	1	43
Female	13	7	0	0	20
Totals	36	25	1	1	63

95% patients preferred the PVC masks (p<0.001), but with no significant difference between the scents.

Use of the PVC masks, which patients preferred, may reduce stress and help prevent the risk of cardiac ischaemia.

Reference

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(P.175) SUXAMETHONIUM IN CHILDREN: A COMPARATIVE STUDY OF MYALGIA AND INTUBATING CONDITIONS

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The incidence of suxamethonium myalgia in children is reported to be low⁽¹⁾, but has not been previously assessed in a randomised fashion. 70 children undergoing adenotonsillectomy were randomised to receive either deep inhalational anaesthesia with halothane (n=33), or suxamethonium 1mg.kg-1 (n=37) for intubation following induction with thiopentone 6mg.kg-1. Variables recorded included intubating conditions, respiratory

complications, fasciculation score and the incidence of post operative myalgia (POM). Intubating conditions were significantly better (p<0.01) and anaesthetic time reduced (p<0.001) in the group who received suxamethonium. The incidence of myalgia was low in both groups (one patient in each group). This study shows that when suxamethonium is administered as part of a standard anaesthetic regimen, it does not appear to increase the frequency of POM in children. The use of suxamethonium optimises intubating conditions while reducing anaesthetic time.

Reference

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(P.176) A COMPARISON BETWEEN 2 TECHNIQUES FOR MEASURING CARDIAC OUTPUT - OESOPHAGEAL DOPPLER (OD) VERSUS PULMONARY ARTERY CATHETER (PAC) THERMODILUTION

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Measurements of cardiac output were done simultaneously using 2 different methods in 18 patients undergoing liver transplantation - OD versus PAC thermodilution. Measurements were recorded during Phase I, II, III of the transplantation - each phase giving rise to very varied haemodynamic situations (Bland + Altman Analysis).

Results

	r correl	r2 mean diff in 2 techs	(d) L/min	2SD L/min ±	Mean CO L/min	% 2SD is of mean CO
Phase I	0.8	0.65	-2.8	2.4	7.75	30%
Phase II	0.57	0.334	0.19	3.6	6.2	58%
Phase III	0.62	0.39	0.04	5.2	9.2	56%

Conclusion: In this study there was not close agreement between the two methods - particularly at higher cardiac output values. Even though the PAC thermodilution is the accepted technique, it is not inherently accurate thus the lack of close agreement between the 2 methods does not indicate which is the more accurate measurement technique. However, the agreement is sufficient to enable us to use either method for trend monitoring. Advantages of doppler are low cost, safety, simplicity, continuous beat by beat monitoring of blood flow.

(P.177) A REVIEW OF THE UTILISATION AND DEMANDS ON A NEWLY OPENED INTERMEDIATE CARE FACILITY

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A High Dependency Unit (HDU) is defined as an area for patients that require more intensive observation, treatment and nursing care than can be provided on a general ward. The economics, the improved nurse/patient ratio and the rationalisation of intensive care utilisation justify the need for such a facility⁽¹⁾. In a 491 bedded hospital with a complement of 18 intensive care beds, we present a 4 month audit of a newly opened 8 bed HDU. We review the demands of the various specialities in terms of utilisation and percentage occupancy.

	% Utilisation	% Bed Day Usage
Vascular Surgery	8.4	14.1
General Surgery	21.1	23.5
Cardiothoracic	44.1	40.2
ENT Surgery	4.5	3.0
Orthopaedics	2.8	4.2
Medicine	17.4	13.9
Urology	1.7	1.1

The existence of intermediate care facilities has been endorsed by several workers and its favourable effect on patient care demonstrated^{1,2}. This review demonstrates the demand on the facility by the different disciplines and highlights the need for HDU availability.

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CARDIOVASCULAR

(P.178) A MODEL FOR CALCULATING THE COSTS OF LONG TERM DRUG THERAPY FOR LOWERING SERUM CHOLESTEROL

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The cost of long term drug therapy for treatment of elevated cholesterol is unknown. By combining data from the Mater Hospital Cholesterol Screening Study (normal volunteers, average cholesterol by age, 25-64 (N=954) with population data (National Census 1991) the absolute numbers of individuals with cholesterol values greater than 5,6,7 and 8mmol/L were determined. Using anticipated life expectancy by age (Irish Life Actuarial) a model for calculating lifetime costs of drug therapy was generated (Table below).

Age (yrs)	Total No. ¹	Cholesterol mmol/l				Life expectancy (yrs) ²	Total nos. people Chol .7+2 risk factors ³
		% of population	.5	.6	.7		
25-34	495.391	20	24	2.3	0.5	16.2	-35
35-44	463.5-3	42	15	4	1	36.6	3129
45-54	344.566	42	23	5	2	27.3	800-
55-64	277.115	31	39	9	1.5	19	13040

-1. National Census data 1991

-2. Irish Life Actuarial Data

-3. Risk Factors (smoking, hypertension, previous CHD, family history of premature CHD)

Based on the above data

Simvastatin 20mg daily, long term treatment

Total No. People × life expectancy × annual cost (£671)

	Total cost IRE
All chol .7	£1447 Million
All chol .7 - 2 risk factors	£380 Million

Conclusion: Long term drug therapy for lowering serum cholesterol is expensive. The cost of coronary events averted is considerably less. Ways of targeting lipid lowering therapy are needed.

(P.179) AUDIT OF THROMBOLYTIC THERAPY BY A PREDICTIVE INSTRUMENT FOR MYOCARDIAL INFARCTION MORTALITY

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The outcome of 85 consecutive patients (mean age 65.9±11.7 years) with confirmed myocardial infarction was audited using a predictive instrument for mortality⁽¹⁾

Seventeen patients (20%) died within 6 weeks of admission: the predictive instrument predicted an overall mortality of 27.0±23.5%. None of the 30 patients (35%) predicted to have a mortality below 12% died. Those who died did not present later than survivors (6.4±5.9 vs. 6.1±8.6 hours), but were older (75.4±8.7 vs 63.5±11.1 years, p <0 .001), Forty six patients (54.1%) were given thrombolytic therapy. These patients presented earlier (4.1 +/-3.6 vs. 8.5 +/-10.8 hours, p<0.02) and were younger (63.5±10.7 vs. 68.6±12.2 years, p<0.05) than the 39 patients not given thrombolytics. There was a mean delay of 83±51 minutes between admission and thrombolytic administration. Only 3 of the 17 who died received thrombolytics. The actual mortality rate of those not given thrombolysis was 36% compared with a predicted rate of 33.9±28.1%: both higher than th predicted (21.1±16.5%, p<0.02) and actual (6.5%) mortality rate of those given thrombolytics. There may be a bias against giving thrombolytics to severely ill patients, since all 6 patients with shock were not treated. Of the rest not treated only 2 had an absolute contraindication; other reasons were: non-diagnostic ECG changes (12 patients), late presentation (3 patients), bleeding risk (5 patients), age (2 patients), hypertension (2 patients), no reason (7 patients). Conclusion: the predictive instrument identified those most likely to die from acute infarction and, hence, those most likely to benefit from thrombolysis.

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(P.180) HAEMORRHAGIC RISKS OF LONGTERM ORAL ANTICOAGULATION IN A NON-TRIAL MEDICAL ENVIRONMENT

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Four hundred and ten consecutive patients attending a special anticoagulation clinic over a one year period were asked to complete a questionnaire concerning their warfarin treatment.

The total number of patient years on warfarin was 2870. Of the 410 patients, 59 (14%) admitted to 88 bleeding episodes, of which 36/88 (41%) required admission to hospital or to casualty for treatment and 52/88 (59%) required only a lowering or temporary cessation of warfarin therapy. The annual rate of non-fatal bleeding requiring attendance at hospital for treatment was 1.3%. The annual total non-fatal bleeding rate was 3%.

Conclusion: The calculated annual non-fatal bleeding rate of 3% and the 1.3% annual rate of major bleeding requiring attendance at hospital are similar to those reported in randomised clinical trials of anticoagulation for stroke prevention in atrial fibrillation.

Thus, oral anticoagulation is as safe in an ordinary medical setting as in a closely supervised trial setting and more extensive

use of longterm oral anticoagulation for stroke prevention in atrial fibrillation should not lead to an unacceptably high rate of anticoagulant-related haemorrhage.

(P.181) INTERNATIONAL TRIALS AND NATIONAL PRACTICE: A QUESTIONNAIRE SURVEY ON THE TREATMENT OF ACUTE MYOCARDIAL INFARCTION

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To establish current clinical practice in the care of patients with acute myocardial (AMI), a questionnaire survey of 50 consultant physicians was performed. There were 42 (84%) responders.

All use aspirin in the acute setting. 38/42 (90%) give thrombolysis in CCU only; 4/42 give thrombolysis in casualty also. 36/42 (86%) use streptokinase only, regardless of patient age or site of AMI. 6/42 (14%) use TPA for anterior AMI in patients under 60. ACE inhibitors are given by 34/42 (81%) in patients with anterior AMI and evidence of LV dysfunction. ACE inhibitors are neither given routinely nor given before day 3 by any physician surveyed. Magnesium is checked routinely by 8/42 (19%) and given routinely by none. The percentage of AMTs considered for angiography in the individual physician's units varied from 10-50%.

Conclusion: Despite the recent depth of literature supporting the use of TPA, early ACE inhibition and magnesium in the treatment of AMI, current practice predominantly is streptokinase, selective late ACE inhibition and no magnesium. The reasons for the dichotomy between the favourable results of randomised trials of therapy in AMI and clinical practice are unknown.

(P.182) DIABETES, RETINOPATHY AND THROMBOLYSIS

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Usage of thrombolysis in Myocardial Infarction (MI) is the major recent development in cardiology. Patients with Diabetes Mellitus (DM) and MI have a poorer prognosis and need thrombolytic therapy. Recent trials of thrombolysis demonstrated a greater benefit in diabetic patients compared to controls, and a similar complication rate. Additionally, in a group of 148 diabetic patients receiving thrombolysis, 7% of whom had documented retinopathy, no retinal haemorrhage occurred. Indeed, there is only one recorded case of retinal haemorrhage after thrombolysis. However, the British National Formulary states that diabetic retinopathy is a contraindication to thrombolysis.

The aim was to assess the influence of retinopathy on the administration of thrombolysis to diabetic patients with MI.

An audit using a retrospective chart review was carried out on all 1994 casualty admissions with DM and MI. Data collected included; demographic details, symptom duration, if fundoscopy was performed, mydriatic usage, thrombolysis and contraindications, if not given.

12 patients were admitted with DM and MI (12M, 4F). The mean age was 63.3 years (range 54-74). The mean symptom

duration before admission was 6.3 hours (range 0.5-24). 33.3% (4/12) received thrombolytics. 83.3% (10/12) had fundoscopy documented, mydriatic usage was not recorded in any chart. 33.3% (4/12) had documented retinopathy and all four did not receive thrombolysis. Four further cases did not receive thrombolysis; one had CPR, two had delayed diagnoses and one had no reason recorded. Conclusion: All diabetic patients with MI were considered for thrombolysis. 83% of diabetics had fundoscopy to exclude retinopathy. Diabetic retinopathy is a practised contraindication to thrombolysis in this hospital.

(P.184) PHARMACOLOGY OF A NOVEL GPIIb/IIIa ANTAGONIST WITH ANTIPLATELET ACTIVITY SUPERIOR TO CONVENTIONAL THERAPY

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Platelet aggregation and adhesion is mediated through glycoprotein (Gp)IIb/IIIa: an adhesion receptor The primary ligand is fibrinogen which binds via the sequence Arg-Gly-Asp(RGD). Hence RGD-containing peptides are antagonists at the receptor. However peptide antagonists induce an active conformation of the receptor and the appearance of novel epitopes: ligand induced binding sites(LIBS). The function of LIBS is unclear but they may be involved in cell activation and thus indicate partial agonist activity. We examined a novel non-peptide GpIIb/IIIa antagonist (NPA), which binds to the RGD recognition site, in 9 patients with stable angina. Platelet aggregation was assessed in response to thrombin related agonist peptide(TRAP) alone and in combination with collagen (agonist pathways unaffected by aspirin). LIBS expression was measured by flow cytometric analysis.

The NPA dose dependently suppressed platelet aggregation to TRAP (86.5±4.9%, mean±SEM) and TRAP/Collagen (86.8±3.7%) and prolonged bleeding time in all patients (>30 mins in 8/9 cases). In contrast to previously described peptide antagonists, LIBS expression was not induced.

Aspirin is a weak inhibitor of platelet aggregation and adhesion. In contrast this NPA shows marked antiplatelet activity. This class of drug offers a novel and alternative approach to antithrombic therapy which is more potent than aspirin.

(P.185) CYCLOOXYGENASE INHIBITION DOES NOT ALTER FOREARM VASCULAR RESPONSES TO SEROTONIN IN HEALTHY VOLUNTEERS

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Serotonin has been reported to stimulate prostacyclin release⁽¹⁾. In 1988, Blaise et al reported that inhibitors of cyclooxygenase augment serotonergic responsiveness in canine coronary arteries⁽²⁾. Serotonin produces a biphasic response on the forearm resistance vessels of healthy volunteers, At low dose vasodilatation occurs and at high dose there is a constrictor response. We have investigated the role of cyclooxygenase in the forearm vascular responses to serotonin in healthy

volunteers. Ten healthy volunteers aged 25-36 years were studied. Serotonin was infused into the brachial artery in 5 incremental doses 0.003-30 ug/min for 2 minutes each. Forearm blood flow was measured at baseline and following each dose using venous occlusion plethysmography. Indomethacin (100 mg) was then administered orally and after 90 minutes the serotonin infusions were repeated. Results were analysed using paired t-tests and Dunnett's test of multiple comparisons. Vasodilatation occurred at doses 0.003 to 3 ug/min and vasoconstriction at the highest dose (30 ug/min). There were no significant differences in the vascular responses to serotonin following indomethacin, indicating that products of cyclooxygenase are not involved.

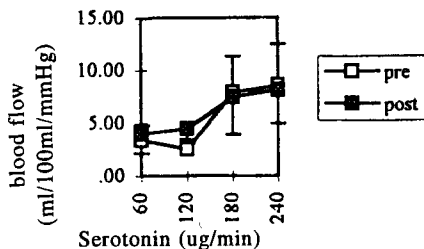


Fig. 1. Arteriolar responses to serotonin pre and post indomethacin.

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(P.186) THE HAWKSLEY RANDOM-ZERO SPHYGMOMANOMETER (RZO); EFFECT OF TWO METHODS OF PRESSURE RELEASE ON THE ACCURACY OF THE RZO

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The RZO sphygmomanometer, a widely used modified mercury device with a variable 'zero' correction, has been reported to be inaccurate.

Four recently serviced RZO machines were compared with a standard mercury device under static conditions.

A cuff connected to a standard and RZO machine, was placed around a glass jar. An unblinded controller set a random pressure on the standard whilst two independent blinded observers recorded the mercury level on the RZO. Residual pressure was then released through the hand valve and through a rapid release technique and the zero level on the RZO was noted. One hundred measurements using each method were made for each RZO.

A pressure decay curve was constructed using the hand valve. The RZO underestimated pressure compared with the standard sphygmomanometer using both methods. The modified technique consistently reduced the size of the error ($p < 0.005$) with a mean reduction from 1.64 to 0.79mmHg.

The pressure-time curves can be described by the biphasic log linear curve $Ae^{-at} + Be^{-bt}$.

In conclusion, overestimation of the zero in the RZO caused by a residual pressure tail in the system contributes to the machine's inaccuracy. Rapid pressure release improves this.

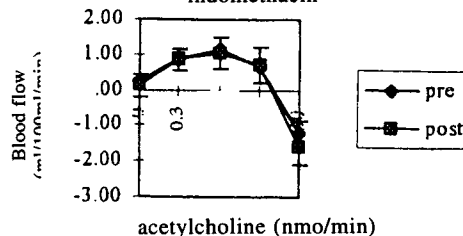
(P.187) CYCLOOXYGENASE INHIBITION DOES NOT MODIFY FOREARM VASODILATOR RESPONSE TO ACETYLCHOLINE IN HEALTHY VOLUNTEERS

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In 1988 Robert Furchgott discovered the obligatory role of the vascular endothelium in the vasodilatory response to acetylcholine⁽¹⁾. Acetylcholine is now known to stimulate muscarinic receptors on the endothelial cell surface, resulting in production of nitric oxide. Local infusion of acetylcholine and measurement of vascular response is now a widely used technique for assessing the function of the vascular endothelium in vivo. L-NMMA, a stereospecific inhibitor of nitric oxide, has been found to only partially inhibit vasodilation to acetylcholine⁽²⁾. This suggests that another vasodilator substance such as a cyclooxygenase product may be involved. Ten healthy volunteers (age 49-57 years) underwent brachial artery cannulation. Forearm blood flow was measured at baseline and following local drug infusions using venous occlusion plethysmography. Acetylcholine was infused at 60, 120, 180 and 240 nmo/min for 2 minutes each. Indomethacin (100 mg) was then administered orally and after a period of 90 minutes the infusions were repeated. Results were analysed using paired t-tests and Dunnett's test of multiple comparisons. Acetylcholine caused a dose-dependent increase in blood flow. There was no significant change in basal or stimulated flow following indomethacin. In conclusion, cyclooxygenase products do not influence forearm vascular responses to acetylcholine in healthy volunteers.

Fig. 1. Arteriolar responses to acetylcholine pre and post indomethacin



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(P.188) PARTIAL AGONIST ACTIVITY OF PLATELET GLYCOPROTEIN IIb/IIIa ANTAGONISTS DETECTED AS AN INCREASE IN TXA₂ FORMATION *IN VIVO*

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RGD-containing peptides and other antagonists of the platelet glycoprotein (GP) IIb/IIIa may induce a high affinity binding site for fibrinogen and the expression of cryptic sites, termed ligand-induced binding sites (LIBS). Such changes may represent partial agonist activity. The functional relevance of LIBS was examined in a canine model of coronary thrombolysis induced by t-PA. The GP IIb/IIIa antagonists, RO43-5054 (n=11) and RO44-9883 (n=12), were infused at increasing doses

of 2-10ug/kg/min, 30 min prior to t-PA. RO43-5054 induced LIBS expression, as measured by binding of monoclonal antibody D3 to platelets, by flow cytometry, whereas RO44 had no effect. Both drugs abolished platelet aggregation *ex vivo* and inhibited coronary reocclusion, which is platelet dependent. Neither RO43-5054 nor RO44-9883 altered plasma t-PA levels. Both drugs increased the rate of bleeding compared with t-PA alone, but there were no differences between the two drugs. Urinary 2,3-dinor-TXB2 (TXM), an index of platelet activation *in vivo*, was measured using gas chromatography, mass spectrometry. Following reperfusion, urinary TXM increased in the RO43-5054 group to 31+9ng/ml (n=4), similar to controls. This increase was blunted in the RO44-9883 treated group (9+2.5ng/ml, n=4). Hence, GPIIb/IIIa antagonists that do not induce LIBS result in greater suppression of platelet activation *in vivo*, although without any discernable functional benefit in this model. The persistent generation of TXA2 with LIBS-expressing antagonists, suggests that such antagonists have partial agonist activity.

(P.189) THE LEARNING CURVE FOR NEW CORONARY DEVICES

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Since 1990, percutaneous coronary angioplasty (PTCA) procedures have been performed in 82 patients using new coronary devices (stents = 70, atherectomy = 12). We compared the major complication rate of patients undergoing new device intervention with patients undergoing conventional PTCA during this time. All stented patients were aggressively anticoagulated (Aspirin, intravenous heparin until INR > 3, Warfarin for 1-3 months). Results are tabulated below.

	Total PTCA experience	New Device PTCA
Patient No.	1249	82
Mortality (in hospital)	1%	1.2%
Acute occlusion	9%	9.7%
Q wave MI	5.6%	6.1%
Emergency CABG	1.3%	3.7%
Vascular repair	—	2.4%

No patient required blood transfusion or dropped haemoglobin > 2g/dl.

Conclusion: the requirement for emergency CABG was greater in the "new device group". Otherwise new device PTCA at our institution had a low major complication rate. In particular the the of vascular repair (2.4%) and absence of significant haemorrhage is encouraging.

(P.190) LONG TERM OUTCOME FOLLOWING CORONARY ARTERY BYPASS GRAFTING FOR ISOLATED LAD STENOSIS

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Disease involvement of the left anterior descending coronary artery [LAD] is associated with an adverse outcome. The purpose of this study was to detail the clinical profile of patients who

had coronary artery bypass grafting [CABG] for isolated disease of the LAD, and to assess their 4-10 year clinical outcome. Patients were identified from the operative records of all hospitals performing cardiac surgery in Ireland from 1984-1990. Cine coronary arteriograms and clinical case notes from the time of operation were reviewed. Follow up on 283 patients was by postal questionnaire or telephone interview and was complete in 100%.

The left internal mammary artery was used as a conduit in 246 patients [87%]. Median duration of follow up was 6.6 years. Survival was excellent, being 97% at 5 years and 86% at 10 years. At time of follow up, 263 [93%] of patients were alive, 195 [69%] were free of angina, 17 [6%] had a myocardial infarction and 32 [11%] had cardiac failure. Repeat cardiac surgery was required in 15 patients [5%], with 1 having cardiac transplantation.

Conclusion. Patients undergoing CABG for isolated LAD disease have an excellent prognosis. Where possible internal mammary artery grafts were used.

(P.191) IMPACT OF CIGARETTE SMOKING ON OUTCOME POST BYPASS SURGERY FOR ISOLATED LAD STENOSIS

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Cigarette smoking predicts an adverse outcome following coronary artery bypass grafting [CABG]. The purpose of this study was to detail the effect of smoking on a highly select group of patients who had CABG for single vessel left anterior descending [LAD] coronary artery disease. Patients were identified from the operative records of all hospitals performing cardiac surgery in Ireland from 1984-1990. Follow up on 283 patients was by postal questionnaire or telephone interview and was complete in 100%

The vital status and clinical events for all patients relating to their smoking history are tabulated below

	Continuers	Quitters	Never	Starters
Pt. No.	36	164	81	2
Alive	33 (92%)	155 (95%)	73 (90%)	2 (100%)
Angina	8 (22%)	57 (35%)	22 (27%)	1 (50%)
MI	3 (8%)	9 (5%)	5 (6%)	0 (0%)
CCF	5 (14%)	20 (12%)	7 (9%)	0 (0%)
ReDo	4 (11%)	8 (5%)	3 (4%)	0 (0%)

Conclusion: Of patients with single vessel LAD disease having CABG, 12.7% continued to smoke. While continuers were less likely to suffer from angina to quitters, they were more likely to die, have a myocardial infarction [MI], suffer from cardiac failure [CCF], or require redo CABG.

(P.192) SERIAL CHANGES IN CARDIAC OUTPUT DURING NORMAL PREGNANCY; A DOPPLER ULTRASOUND STUDY

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The direction and magnitude of change in cardiac output (CO) during the third trimester remains controversial. This

controversy is founded in part on the small numbers studied and the methodological difficulties in obtaining reproducible measurements of CO non-invasively. Doppler flow velocity profiles and aortic root cross sectional area measurements using transthoracic ultrasound are an accurate and reproducible method for non-invasive measurement of CO. We performed serial measurements of CO on 5 occasions from 24 weeks gestation to term and once during the puerperium in 26 normal pregnancies (156 measurements in total).

Results: Absolute values & % change from baseline.

Gestation /wks	Heart Rate /bpm	Stroke Volume/mls	CO / l/m
24	82.8 (19.5%)	60.2 (-11.1%)	5.6 (7.7%)
28	89.9 (29.0%)	66.4 (-1.9%)	5.92 (26.5%)
32	91.4 (32.8%)	76.7(13.3%)	6.96 (48.7%)
36	84.9(22.5%)	77.9(15.1%)	6.45(37.8%)
38/40	81.5 (18.0%)	71.4 (5.4%)	5.66 (20.9%)
4 wks postpart	69.3 (0.0%)	67.7 (0.0%)	4.68 (0.0%)

Conclusions: In this study, CO increased in a linear fashion until the end of pregnancy. Thereafter, it reached a plateau and ultimately declined before term, though not to baseline. These observations have management implications for patients with serious heart disease complicating pregnancy.

(P.193) VALUE AND LIMITATIONS OF DOBUTAMINE STRESS ECHOCARDIOGRAPHY IN THE DETECTION OF CORONARY ARTERY DISEASE

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The purpose of this study was to determine the value of Dobutamine stress echocardiography (DSE) in the detection of angiographically significant coronary disease (> 70% reduction in coronary luminal diameter). DSE and angiographic studies were performed in 78 patients of whom 59 (77%) had significant ischaemic heart disease (IHD). The overall sensitivity and specificity of DSE for IHD was 90% and 68% respectively. The sensitivity was 100% (14 of 14) for multivessel disease. Sensitivity for detection of those with double vessel disease was 91% (11 of 12) while for single vessel disease it was 88% (29 of 33). No patient had a symptomatic arrhythmia or complications from induced ischaemia.

Conclusion: DSE is a safe technique. It predicts the presence of significant IHD. The value of DSE in detecting angiographically significant IHD in a low risk population remains to be determined.

(P.194) PRELIMINARY EXPERIENCE WITH PERCUTANEOUS BALLOON MITRAL COMMISSUROTOMY USING THE INOUE TECHNIQUE

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The role of percutaneous transvenous mitral commissurotomy (PTMC) in treating patients with mitral stenosis remains to be clarified. We report our initial experience with the transeptal flow directed Inoue PTMC technique in 11 patients. The mean age was 55 ± 13 years. Pre-procedure assessment included transoesophageal echocardiography with detailed anatomic and

functional analysis of mitral valve pathophysiology. All patients were New York Heart Association (NYHA) functional class III or IV. The procedure was successful (mitral valve area > 1.5 cm², improvement in functional class and no complications) in 10 patients, ie a 91% procedural success rate. Mitral valve area increased from 0.95 ± 0.2 to 2.18 ± 0.8 cm² (mean \pm SD). Transmitral pressure gradient fell from 12 ± 8 to 4 ± 5 mmHg (mean \pm SD) while NYEHA functional class improved by >1 grade in all patients, falling from 3.5 ± 0.5 pre to 1.4 ± 0.5 post procedure. There were no major complications. In 3 patients mitral regurgitation increased by a single angiographic grade.

Conclusion: In this initial experience, PTMC was a safe and effective alternative to surgical mitral valvotomy in selected cases.

(P.195) MATERNAL HEART DISEASE COMPLICATING PREGNANCY AT THE NATIONAL MATERNITY HOSPITAL, DUBLIN 1968-1988

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During the years 1969-1988, 669 pregnancies (486 patients) complicated by maternal heart disease were managed at the National Maternity Hospital. Medical and obstetrical management was conservative. Aetiology of heart disease and outcome of pregnancy are tabulated below.

	1969-78	1979-88
Total pregnancies	77,841	86,414
Pregnancies with MHD*	5/1000	3/1000
Aetiology of MHD	N (%)	N (%)
-rheumatic	323 (84%)	194 (69%)
-congenital	52 (13%)	67 (24%)
-miscellaneous	12 (3%)	21 (7%)
Mortality in MHD		
-maternal	2 (0.5%)	1 (0.35%)
-foetal	20 (5.2%)	19 (6.7%)

*MHD = maternal heart disease.

Conclusions: (1) Most maternal heart disease has a benign outcome and can be managed conservatively. (2) The prevalence of maternal heart disease complicating pregnancy has declined. (3) There has been a decline in the prevalence of rheumatic heart disease complicating pregnancy with a relative increase in congenital and miscellaneous conditions.

(P.196) A BODY SURFACE MAPPING ALGORITHM FOR THE AUTOMATED DETECTION OF ACUTE MYOCARDIAL INFARCTION

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The purpose of this study was to evaluate an algorithm for the detection of acute myocardial infarction, based on body surface mapping. A portable mapping system incorporating a self adhesive 64 electrode harness which can be applied rapidly to the chest was used to map healthy control subjects and patients with acute MI. At each of the 64 electrode sites QRS and ST-T iso-integrals, and 11 other features of the QRST segment are measured. In addition new variables are derived which describe the 3-dimensional geometric surface of the map. Using a training

set of maps recorded on 80 controls and 69 patients with MI, 14 variables were identified which correctly classified 79/80 of the controls (specificity = 98.8%) and 65/69 of the MIs (sensitivity = 94.2%). The algorithm based on these 14 variables was applied prospectively to a further 48 control subjects and 59 patients with MI (10 anterior, 31 inferior, 13 inferoposterior, 2 posterior, 1 lateral, 1 inferior with right bundle branch block and 1 anterior non-Q wave MI). All 48 control subjects (specificity = 100%) and 57/59 of the MIs (sensitivity = 96.6%) were correctly classified. This algorithm demonstrates a high level of sensitivity and specificity for the early detection of MI. It will be applied to patients with atypical ECG changes such as ST segment depression only and it is hoped that it will improve detection of MI in such patients thus enabling the appropriate administration of thrombolysis.

(P.197) AUDIT OF A HOSPITAL ANTICOAGULANT CLINIC

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154 consecutive patients completed a questionnaire stating why and for how long they expected to take warfarin and if they were aware of certain problems with long term anticoagulation. The clinic doctor then correlated this with the information on each patient's anticoagulant card, which should include indication for anticoagulation, target International Normalised Ratio (INR) and expected duration of treatment. The indication for anticoagulation was stated on the card in 84% of cases, known by 68% of patients and unknown in 5%. These indications included valvular heart disease and atrial fibrillation (70%) and complications of ischaemic heart disease (15%). The expected duration of treatment was given on the card in 44% and known by the patient in 59%. It was assumed to be lifelong in a further 15% as the indication in these cases was valve replacement. The INR target range was stated in only 17% of cases. Patients indicated that they were aware of the potential for drug interactions and the possibility of bleeding after surgery or dental work in 48%, 40% and 49% of cases respectively. This audit reveals shortcomings in the completion of anticoagulant cards with basic details such as duration and target anticoagulation range often omitted. The study also revealed that continuing patient education is needed as knowledge of long term risks of anticoagulation was poor.

(P.198) A COMPARISON OF DIGITAL SUBTRACTION ANGIOGRAPHY WITH DUPLEX SCANNING AND COLOUR FLOW MAPPING IN THE ASSESSMENT OF CAROTID ARTERIES

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The aim of this study was to compare the use of digital subtraction angiography with duplex scanning and colour flow mapping in symptomatic patients with suspected extracranial

carotid artery disease. 103 patients underwent both selective carotid arteriography and duplex scanning with colour flow mapping. The two examinations were performed within a few days of each other in all cases. Angiographic stenosis measurements were recorded in each patient using a digital subtraction technique and dedicated equipment. Measurements were similarly obtained using duplex ultrasound scanning and colour flow mapping. Measurements obtained from the 103 patients were placed in recognised groups of severity. In 93% of cases arteries demonstrated to be sonographically normal were confirmed normal on angiography. However, in patients with higher grade stenoses (greater than 70%) agreement was rather less at 79%. Overall agreement between the two modalities occurred in 71% of cases. Conclusion: We have demonstrated that duplex sonography can reliably identify normal and minimally diseased vessels. However, in higher grade stenoses we would recommend the greater sensitivity of angiography as a standard part of the imaging protocol.

CRITICAL CARE MEDICINE

(P.199) ASPECTS OF NOVEL INSTRUMENTATION FOR REAL-TIME MONITORING OF LACTATE AND GLUCOSE USING MINIATURIZED FLOW SYSTEMS WITH INTEGRATED BIOSENSORS

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C. Urban, I. Moser, G. Jobst, Technical University, Vienna.

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F. Dempsey, D. Diamond, M. Smyth, Dublin City University.

*Project Co-ordinator

The concept of Total Chemical Analysis System (TAS) which encompasses automatic sampling, sample transport, preparation and detection and which transforms chemical information into electronic information was first proposed by Manz.⁽¹⁾ The ultimate objective of this project is to produce a functional model of a miniaturized Total Chemical Analysis System (μ TAS) suitable for application in real-time monitoring of clinically important analytes particularly lactate and glucose. Equipment miniaturization would increase speed of analysis and reduce consumption of reagents which may be expensive and harmful to the environment. Details on two aspects of the project will be presented - 1) the improved performance obtained with amperometric enzyme membrane electrodes using Lactate Oxidase/Glucose Oxidase Sandwich membranes in combination with flow injection analysis (FIA). The linear lactate concentration increased from 1.5mM to 20mM by combination with EA using a volume injection of 25. μ l. 2) the fabrication and performance parameters of integrated thin film lactate and glucose sensors. The relative effects of potential interferents in clinical application were studied and show that ascorbic acid and uric acid interference is negligible. Paracetamol at a concentration 10 times the therapeutic concentration causes a reading error less than 0.5mM/L for glucose.

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(P.200) MICRODIALYSIS AS A SAMPLING SYSTEM FOR CONTINUOUS MONITORING OF BIOCHEMICAL ANALYTES

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Probes for continuous monitoring of blood pressure, temperature and oxygen status of blood in the critical care of patients have been developed. The application on a total chemical analysis system for continuous monitoring of analytes is under development. The sample for analysis could be withdrawn through a microdialysis probe inserted subcutaneously or directly in blood. Microdialysis is a diffusion based method by which small molecules can be removed from living tissue for analysis. The sample obtained is free from macromolecules (mainly proteins) and may be introduced directly into microanalytical systems without further purification. The aims of this presentation are to report the effects of perfusion flow rate, temperature and dialysis membrane size on microdialysis efficiency as judged by relative recovery of lactate and glucose in in-vitro studies. Relative recovery of lactate and glucose decreased from 93% to 10% as perfusion flow rate increased from 1.5 to 20 μ l/min. Dialysis efficiency was not significantly altered by temperature change within the physiological range - efficiency altered by 0.33% and 0.54% per degree Celsius for lactate and glucose respectively in in-vitro experiments. The relative recovery of lactate increased from 10% to 100% as microdialysis membrane surface area increased from 10mm² to 80mm².

(P.201) GLUTATHIONE-S-TRANSFERASE AS A MARKER OF LIVER INJURY IN CRITICALLY ILL PATIENTS

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We measured the incidence of subclinical liver damage in intensive care (ICU) patients by measuring serum levels of α glutathione S-transferase (GST), a marker of acute liver damage¹.

37 patients had serial GST levels measured (on admission to ICU, +8hrs, +16hrs, +24hrs, and once daily thereafter) by radioimmunoassay. Routine physiological parameters were noted.

54% of patients had abnormal GST - 78% of this group had increases in AST or ALT subsequently. Patients with increased GST had a higher APACHE II (illness severity) score on admission ($p < 0.05$, unpaired t-test). No physiological variables predicted increases in GST. Use of inotropes was associated with increased GST. 6 of the 17 patients with no increase in GST had elevated AST or ALT on admission to ICU; in these AST and ALT decreased after admission. No patients developed liver failure.

We conclude that GST has a place in the detection of acute liver damage in critically ill patients. It could allow more sensitive monitoring of ongoing liver damage, earlier clinical intervention, and earlier detection of recovery.

Reference

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(P.202) CLOSED TRACHEAL SUCTION DOES NOT REDUCE BACTERIAL CONTAMINATION OF HANDS AND AIR

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Hypothesis: that "closed" suction of the trachea (where the suction catheter is within a plastic sheath) contaminates the hands of carers and the air less than "open" method (where the carer holds the catheter through a sterile glove).

50 studies were performed on 25 patients with tracheal tubes or tracheostomies. Each study involved performing "open" and "closed" suction once, separated by two hours. The hands of carers were imprinted on culture plates before and after each treatment; two plates assessed airborne contamination.

	Colony	Count (Mean, S.D.)	
	Hands pre	Hands post	Airborne
Open	140 (166)	251 (208)*	18.5 (10)
Closed	151 (180)	198 (176)*	15.0 (9)

*= $P < 0.01$ compared to before, ANOVA.

Conclusions: "Open" and "closed" tracheal suction are associated with similar degrees of bacterial contamination.

(P.203) LOW PERI-OPERATIVE DO₂ IN CARDIAC SURGERY - EFFECT OF DOPEXAMINE

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Inadequate tissue perfusion occurs during routine cardiac surgery. Shibutani has suggested that the critical level of oxygen delivery (Crit DO₂) in cardiac surgery is 300-00 ml/min/m². Dopexamine improves oxygen delivery. This study prospectively analysed the effect of prophylactic dopexamine on oxygen delivery in low risk patients undergoing elective coronary artery bypass graft (CABG) surgery.

23 consenting elective patients without ventricular dysfunction were enrolled in a double blind, placebo-controlled study. They received either a prophylactic infusion of dopexamine at 2 μ g/kg/min (N=12) or saline (N=11). Serial oxygen delivery (DO₂) and oxygen consumption (VO₂) were measured at 12 pre-determined intervals. Crit DO₂ was calculated using split linear regression analysis from grouped measurements in early (0-5 hr) post operative and late (6-24 hr) post-operative periods. The number of DO₂s in each group falling below the Crit DO₂ were compared.

The Crit DO₂ for the early period was 356 ml/min/m² and 342 ml/min/m² for the late period. 57.5% of all DO₂ measurements fell below the Crit DO₂ in the early post-operative period compared to 33.9% in the late period. Analysis of the mean DO₂ for each patient in each time period shows some evidence that dopexamine augments oxygen delivery in the early (0-5 hr) post operative period ($p = 0.057$).

The Crit DO₂ results correspond with those of Shibutani. 57.5% of measured DO₂s fell below the calculated Crit DO₂ in the early post CPB period. In this period a smaller proportion of the DO₂s (Dopexamine group) fell below the Crit DO₂ relative to controls. Despite absence of ventricular dysfunction failure to reach Crit DO₂ in the post-operative period was common.

(P.204) IS REPEAT EXPLORATIVE LAPAROTOMY OF VALUE IN PATIENTS WITH SEPSIS IN THE INTENSIVE CARE UNIT?

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The objective was to describe the incidence, pre-operative findings, post-operative findings, diagnostic methods and outcome of patients going from the ICU for a repeat laparotomy in search of abdominal sepsis.

Methods: Retrospective review of medical notes.

Fifteen patients age 19-82 years were included. Mortality was 60%. In 14 cases clinical examination was abnormal as was the relaparotomy. In one case clinical examination and ultrasound scan were negative but relaparotomy was still undertaken which also proved negative and the patient died. Radiology was employed in 7 cases and concurred with clinical examination.

Patient Type	No.	Abnormal Re-laparotomy	Age, Mean and SD	Average time to Re-laparotomy	Require MV/ CVVHD /Notropes	Radiology contributed to Re-laparotomy
Survivors	6	6	50.3/22	10	2	4
Non-Survivors	9	8	68/8.9	3.6	9	3

Conclusion: Relaparotomy which is abnormal had a 13% survival rate. Increasing age and multisystem organ failure were associated with an increase in mortality.

(P.205) DOWN'S SYNDROME INCREASES MORBIDITY AFTER CARDIAC SURGERY IN CHILDREN

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A previous study has indicated that Down's syndrome may adversely effect mortality rates after surgical correction of certain defects. The Paediatric Risk of Mortality (PRISM) score is a validated illness severity score used to predict patient outcome in a Paediatric Intensive Care Unit (PICU) setting. The aim of this study was to assess whether the presence of Down's syndrome contributed to morbidity and mortality in the PICU in children undergoing cardiac surgery, using the PRISM score as a guide to likely outcome.

The data from 521 consecutive patients entering the PICU following cardiac surgery was prospectively collected, and the PRISM score and predicted mortality rate calculated.

52 (10%) of the patients had Down's syndrome of whom 4 died. 49 of the remaining 469 patients also died. The mortality rates were correctly predicted for both groups by the PRISM score. Morbidity was higher in the Down's syndrome group with a significantly longer period of ventilation ($p=0.01$) and duration of stay in PICU ($p=0.05$). To assess whether this was related to a difference in procedures, or to Down's syndrome a homogenous group of patients undergoing Tetralogy of Fallot repair was assessed. The PRISM score again correctly predicted mortality rates, but patients with Down's syndrome had twice the duration of ventilation and PICU stay ($p=0.05$).

In conclusion Down's syndrome appears to influence morbidity but not mortality following, cardiac surgery.

(P.206) PULMONARY HAEMORRHAGE AND BAROTRUMA IN HOMOCYSTINURIA

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Homocystinuria is an autosomal recessive metabolic disorder, usually involving beta cystathionine synthase deficiency. Untreated patients develop a marfan-like syndrome and have a propensity to thromboembolic phenomena⁽¹⁾.

A 33 year old male with Homocystinuria and marfanoid features presented to A/E with a 3/52 history of malaise, cough, haemoptysis and petechial rash. He sustained a respiratory arrest and following resuscitation, developed a septic syndrome. Frank pulmonary haemorrhage was noted.

Differential diagnosis was of either meningococcal septicaemia or bronchopneumonia. The sepsis syndrome resolved over three days. No definite pathogen was identified. Apart from pulmonary failure, organ function remained normal. Appropriate nutritional support was maintained from the outset. Aspirin and dipyridamole therapy were continued as prophylaxis against thrombosis.

Pulmonary haemorrhage (>400ml/day) remained significant, requiring regular blood transfusions over a three week period. Systemic vasculitis were excluded. A pulmonary arteriogram failed to demonstrate either vessel occlusion or arteriogram malformation. An arch aortogram to demonstrate bronchial arterial supply was normal. Barotrauma with recurrent pneumothoraces and interstitial mediastinal emphysema occurred over his five week ventilatory period.

Life threatening pulmonary haemorrhage and recurrent pneumothoraces have not previously been reported in patients with homocystinuria.

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(P.207) TWO UNSUSPECTED CASES OF CARBON MONOXIDE POISONING AND THEIR OUTCOME FOLLOWING HYPERBARIC OXYGEN TREATMENT

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Nine and sixteen year old brothers presented to Casualty comatose. Both had been previously well and no history suggestive of substance ingestion or exposure was given. At presentation the brothers had Glasgow coma scales of 4 and 5 respectively. The younger brother showed seizure activity. Arterial blood gas estimation revealed metabolic acidosis. Toxicology screen was negative. Both patients were intubated, ventilation controlled and intensive care monitoring undertaken. Carboxyhaemoglobin analysis (requested empirically) revealed toxic levels of 31% in the 9 yr. old and 37% in the 16 yr. old. Both patients were managed with hyperbaric oxygen treatment at 3 atmospheres for 45 minutes on two occasions. Carboxyhaemoglobin levels reduced in the 9 yr. old from 31%—4%—3% post treatment and levels in the 16 yr. old reduced from 37%—4.5%—3.5% post treatment. Despite better clinical condition at presentation the 16yr. old had a more prolonged recovery.

These cases highlight:

- (1) The importance of suspecting a diagnosis of carbon monoxide poisoning in circumstances of coma of unknown origin.
- (2) Initial clinical status did not correlate with initial measured levels of carboxyhaemoglobin.
- (3) Despite evidence of severe poisoning at presentation longterm sequelae were minimal following prompt hyperbaric.

**(P.208) ROUTINE MANGANESE SUPPLEMENTATION
IS UNNECESSARY DURING SHORT TERM
PARENTERAL NUTRITION**

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Routine supplementation of trace elements is common in patients receiving total parenteral nutrition. This practice may be both unnecessary and unsafe. For many trace elements, only severe prolonged deficiency will lead to clinical symptoms¹. On the other hand, routine supplementation may give rise to toxic effects. The proprietary preparaffon Addamel® has been discontinued following reports of Manganese toxicity. As Manganese is excreted primarily in the bile, this is most likely to occur in patients with cholestasis². Monitoring of serum Manganese levels is an attractive option but may be impractical because of long delays in obtaining results. For these reasons, it has been our practice not to give Addamel® or Additrace® to patients receiving short term parenteral nutrition (less than 2 weeks). We do, however, give Zinc to all patients as Zinc deficiency is common in the critically ill³. We have reviewed the nutrition records of 227 patients. 38 patients (34%) received Addamel® and 78 patients (17%) received Additrace®, but only after 2 weeks of feeding. This was not associated with adverse effects. In contrast, 212 patients (93%) received Zinc (average 303 µmol daily). We conclude that routine Manganese supplementation is unnecessary during short term parenteral nutrition.

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REGISTRAR'S PRIZE

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OATS CEREAL IS NOT TOXIC IN COELIAC DISEASE
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The pathogenesis of coeliac disease appears to involve an immunological response to the ingestion of specific cereal proteins in wheat, barley and rye. The issue of oats toxicity is controversial and was investigated in this study. 9 biopsy-proven coeliac patients in clinical and histological remission were challenged with 50g of oats daily for a 3 month period. Clinical, laboratory, histological and immunological markers of coeliac disease activation were evaluated. All patients remained asymptomatic throughout the challenge period and no laboratory evidence of malabsorption was found. There was no mucosal damage seen on routine histological examination of post challenge duodenal biopsies. Surface enterocyte height remained unchanged and intraepithelial lymphocyte counts were also unaltered following challenge. Furthermore, oats did not cause immunological activation since no rise in alpha gliadin or endomysial antibodies or in MHC class II staining of enterocytes was evident. This study demonstrates that oats is neither toxic nor immunogenic in coeliac disease and oats does not appear to contain the putative toxic peptide sequence found in the 3 other cereals.

**WEIGHT LOSS IMPROVES POSTPRANDIAL
ABNORMALITIES CHOLESTEROL SYNTHESIS IN
OBESE INSULIN RESISTANT SUBJECTS**

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Abnormalities in postprandial cholesterol homeostasis have been recorded in the insulin resistant state. Obese insulin resistant subjects show an increase in endogenous cellular cholesterol synthesis postprandially while normal weight control subjects downregulate this synthetic pathway postprandially. We examined postprandial endogenous cellular cholesterol synthesis in obese subjects before and after enrolling in a weight reducing program. 9 obese insulin resistant subjects were studied for 7±2 months. Blood was drawn fasting, at 30 minutes and at 4 hours after consuming a carbohydrate rich meal. Lymphocytes were isolated and incubated with ¹⁴C acetate to measure de novo cholesterol synthesis. Insulin resistance was determined from the fasting insulin to glucose ratio while the ratio of the change in insulin from 0 to 30 minutes to the change in glucose over the same time yielded a index of insulin secretion. Weight and BMI fell from 101.6±9.6 to 92.7±8kg {p<0.001} and from 37.5±2.9 to 34.4±2.4kg/m² {p<0.001} respectively. Fasting lipids did not change. There was a decrease in insulin resistance from 3.04±1 to 2.0±0.6 (p=n/s) and in insulin secretion from 31.3±10.1 to 20.3±8 {p<0.05}. At baseline there was a rise in cholesterol synthesis postprandially from 362.1±73.2 to 502.6±124.4 pg/mg cell protein {p<0.05} but after weight loss

this postprandially increase was no longer seen - 334.4 ± 76.5 vs 298.2 ± 41.7 { $p=n/s$ }. Represented as % change from fasting value the initial $49.6 \pm 23.7\%$ rise postprandially fell post wt loss to $1.8 \pm 14.4\%$ { $p < 0.05$ }. Weight loss in our obese patients was accompanied by a reduction in the postprandial insulin surge and a decrease in postprandial cholesterol synthesis.

EFFECTS OF NITRIC OXIDE SYNTHASE INHIBITION IN HEALTHY PIGS AND IN AN IMPROVED PORCINE MODEL OF ENDOTOXIC SHOCK

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Vascular overproduction of the vasodilator nitric oxide (NO) causes pathological vasodilatation in endotoxic shock (ES). Thus NO synthase inhibitors including NG-nitro-L-arginine methyl ester (L-NAME) have been administered to endotoxaemic patients. This treatment restores blood pressure but reduces cardiac output (CO). In healthy pigs we have shown that CO is restored by the selective arterial vasodilator nicardipine indicating that reduced CO is due to increased afterload. To establish whether these findings could be applied to an appropriate pathological situation, we aimed to optimise an existing porcine model of ES and to assess the effects of L-NAME and of subsequent vasodilatation with nicardipine on CO in this model. In three groups of six pigs ES was induced by administration of *E. coli* lipopolysaccharide endotoxin (LPS, $160 \mu\text{g kg}^{-1}$ as a 30 minute infusion) with concomitantly inhaled NO to attenuate pulmonary vasoconstriction and intravenous fluids to maintain preload. Systemic and pulmonary vascular resistances (SVR, PVR) and CO (thermodilution) were measured at 30 minute intervals. This protocol produced an appropriate model of ES 60 minutes after the start of the LPS infusion (SVR 96 to $53 \text{ kPa l}^{-1} \text{ sec}$; PVR 14 to $15 \text{ kPa l}^{-1} \text{ sec}$; CO 6.5 to 8.51 min^{-1}). In two groups L-NAME (5 mg kg^{-1} between 75 and 85 minutes after the start of LPS infusion) increased SVR (to $111 \text{ kPa l}^{-1} \text{ sec}$) but increased PVR (to $32 \text{ kPa l}^{-1} \text{ sec}$) and reduced CO (to 6.21 min^{-1}). One of these groups subsequently received nicardipine ($50 \mu\text{g kg}^{-1}$ between 135 and 145 minutes) which reduced SVR (to $69 \text{ kPa l}^{-1} \text{ sec}$) and PVR (to $26 \text{ kPa l}^{-1} \text{ sec}$), temporarily restoring CO (to 6.61 min^{-1}). It may be possible to coadminister vasoconstrictors and vasodilators in ES in doses titrated to restore SVR without increasing PVR or reducing CO.

PORPHYRIA CUTANEA TARDA ASSOCIATED WITH HEPATITIS C AND HIV INFECTION

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Hepatitis C infection (HCV) has been suggested as a triggering factor for porphyria cutanea tarda (PCT). Patients with PCT have been found to have a hundred fold increase in

HCV antibody prevalence compared with blood donors, ranging from 10% of PCT patients in Ireland to 79% in Spain. There are at least four patients in Ireland who have been diagnosed with both HCV and PCT. In addition, HIV infection has also been associated with significantly abnormal porphyrin metabolism. However, the role of HCV infection alone in precipitating PCT is unclear. We therefore studied porphyrin metabolism in 2 groups of patients with HCV infection.

Group 1 comprised 34 Rhesus negative women immunised with anti-D immunoglobulin (mean age 44 yrs, range 30-56). Group 2, all HIV negative drug abusers (IVDA), included 25 HCV positive patients, 14 male, 11 female. The mean age was 28 yrs with an age range of 16-43 yrs. Haemoglobin, serum ferritin, liver function tests, Hepatitis A and B status were assessed. Plasma porphyrins, 24 urinary uroporphyrins, coproporphyrins, aminolevulinic acid and porphobilinogen were measured. A liver biopsy was performed on all patients in Group 1 and one in Group 2. One patient in Group 1 was on oestrogen therapy. Three patients in Group 2 abused alcohol.

Porphyrin excretion was normal in Group 1. In Group 2, however, 3 (12%) had elevated free erythrocyte protoporphyrin, ranging from 756 - 969 ng/ml (normal <590). Liver function tests were abnormal in 27 (76.4%) in Group 1 and 19 (76%) in Group 2. Ferritin levels were elevated in 2 (5.9%) at 267 ng/ml and 671 ng/ml (normal: 8 - 110) in Group 1 alone.

In our two separate population groups with HCV infection alone we found no evidence of PCT. However, 3 had evidence of porphyrin metabolic derangement. Hepatitis C infection alone is not sufficient to cause PCT. Additional co-factors such as genetic susceptibility, iron overload, alcohol abuse and oestrogen therapy appear necessary for induction of PCT, as all 4 patients with PCT had such additional risk factors.

MOBILISATION OF BLOOD PROGENITORS FROM PATIENTS WITH CHRONIC MYELOID LEUKAEMIA

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The natural history of chronic myeloid leukaemia (CML) is unaffected by standard chemotherapy. Treatment with interferon- α produces cytogenetic remission in only a few patients. Allogeneic bone marrow transplantation is curative, but only a small minority of patients are suitable because of age or lack of donors. For these reasons, attention has recently focussed on autologous transplantation. Although the bone marrow of patients with CML appears 100% Philadelphia chromosome (Ph⁺) positive, there is evidence that patients have some residual Ph⁻ negative progenitors. Carella and others have selectively harvested these cells after myelosuppressive chemotherapy. We have mobilised peripheral blood progenitor cells (PBPC) from 7 patients with CML in first chronic phase with idarubicin 8 mg/m^2 on days 1 and 2 and cytosine arabinoside 200 mg/m^2 bd on days 1-5 followed by G-CSF until the end of PBPC harvesting. Short term cultures indicated an adequate yield of PBPC in 517 patients. In 316 evaluable patients PBPC were predominantly Ph⁻ negative (5/90, 2/60, 2/90 metaphases Ph⁺ positive). One patient has been given high-dose chemotherapy and a PBPC infusion and has engrafted well with predominantly Ph⁻ negative haemopoiesis. We conclude that Ph⁻ negative PBSC can be mobilised from patients in first chronic phase CML.

AGE-RELATED IMPAIRMENT OF FOREARM VASODILATOR RESPONSES TO SEROTONIN

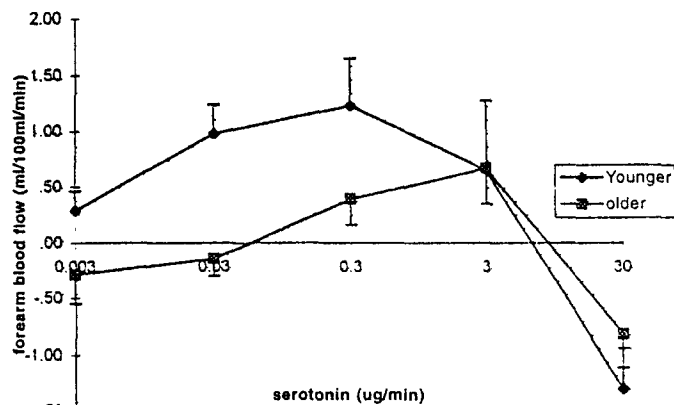
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Serotonin produces a biphasic response in the forearm vascular resistance bed of healthy volunteers, vasodilatation occurring at low dose and vasoconstriction at high dose. In vitro studies have shown that the vascular relation to serotonin is endothelium-dependent^[1]. Age-related impairment of flow mediated endothelium-dependent vasodilatation in the human forearm circulation has recently been reported^[2]. We have studied forearm arteriolar responses to serotonin in young and older non-smoking healthy volunteers. Nine young subjects (age range 25-32 years) and eight older subjects (age range 48-63 years) underwent cannulation of the brachial artery for the local infusion of drugs. Forearm blood flow was measured at baseline and following each drug infusion using venous occlusion plethysmography. Serotonin was infused in 5 incremental doses 0.003-30 µg/min for 2 minutes each. Results were expressed as change in forearm blood flow (ml/100ml/min) and analysed using multivariate analysis of variance and Dunnett's test of multiple comparisons. Serotonin produced a biphasic response in both groups with vasodilatation occurring at low doses and vasoconstriction at the highest dose (fig 1). In the older group however, vasodilatation was significantly impaired when compared with the younger group. There was no difference

between groups in the vasoconstrictor responses at the highest dose of serotonin. In conclusion, there is impaired vasodilatation to serotonin in older subjects. This may be due to age-related impairment of vascular endothelial function.

Fig 1. Arteriolar responses to serotonin in young and older subjects



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ENDOCRINOLOGY/METABOLISM/LIPIDS

(P.4) MACROVASCULAR DISEASE IN NON-INSULIN-DEPENDENT DIABETES MELLITUS (NIDDM): A PRELIMINARY REPORT FROM THE MATER HOSPITAL DIABETES DATABASE

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Macrovascular disease is the major cause of morbidity and mortality in NIDDM. Although its aetiology is multifactorial, it has been suggested that therapies used in the treatment of NIDDM may increase the risk of atherosclerosis in this patient population.

To evaluate the effects of diabetes treatment on the macrovascular complications, the prevalence of ischaemic heart disease (IHD), cerebrovascular disease (CVD), and peripheral vascular disease (PVD) was evaluated in 3 groups of NIDDM

patients treated with diet alone (group A, N = 644), oral hypoglycaemic agents (group B, N = 1124) and insulin (group C, N=339). The prevalence of angiopathies was as follows:

	PVD	IHD	CVD
GROUP A	7.9%	19.4%	3.2%
GROUP B	12.6%	21.8%	3.3%
GROUP C	16.0%	13.9%	3.5%

Hypertension, hypercholesterolaemia or smoking prevalence did not differ between groups. However, the prevalence of patients with proteinuria was significantly higher in group C (12.7%) in comparison with groups B (9.0%) and A (5.4%) respectively (p<0.05). Thus, insulin treated NIDDM patients have a reduced prevalence of IHD and have higher prevalence rates of PVD. The increased occurrence of the latter might partly be explained by the increased prevalence of proteinuria in this group.

PUBLIC HEALTH/EPIDEMIOLOGY

(P.104) STUDY OF SUICIDE VERDICTS IN THE DUBLIN CITY CORONER'S COURT 1989-1994

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This study was a retrospective review of the 1,336 inquests held in accordance with the Coroner's Act 1962 in the Dublin City Coroner's Court over the period 1989 to 1994 with particular reference to death by suicide. The study aimed to assess the correlation between the number of verdicts of suicide returned by the Coroner or jury and the number suggested by the clinical case records. Only in the final six months of the period studied was it permissible in law to return a verdict of

suicide following its decriminalisation in July 1993. The study also examined the age, sex, marital status and psychiatric history of the suicide victims and the methods employed. The results show a difference between the clinical number of suicides and suicide verdicts returned in accordance with the legal standard of proof. Suicide accounted for 288 deaths (22%). The male to female ratio was 7 : 3 and the incidence was highest in the 25-34 year age group. The majority were single. Almost 2/3 had a psychiatric history. The most common methods in males and females were hanging and drug overdose respectively. The study identified candidates most vulnerable to suicide where prevention may be possible. Amendment of the law to allow the Coroner return a clinical verdict for Central Statistics purposes should be considered.