NATIONAL SCIENTIFIC MEDICAL MEETING
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Abstracts

PLENARY SESSION

ENDOCRINOLOGY

(O.1) GLUCOSE INTOLERANCE WITH GROWTH HORMONE REPLACEMENT

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The reported incidence of new cases of diabetes in adults receiving GH replacement therapy is very low. The risk of diabetes is increased, as insulin sensitivity is reduced in GH-deficient patients, and GH antagonizes the actions of insulin. This reduction is countered by an increase in insulin sensitivity by loss of central obesity and increased lean body mass in the treated state. We studied two groups of 20 patients of adult-acquired panhypopituitarism. One group (A) has taken GH continuously for over four years; group (B) entered a four month placebo-controlled cross-over trial. Results suggest a progressive statistically significant rise of glycosylated haemoglobin. Two patients, one from each group, developed frank diabetes and required oral hypoglycaemic agents.

| Glycosylated | Zero | 6 | 12 | 24 | 36 |
|--------------|------|---|----|----|----|
| Haemoglobin  | months | months | months | months | months |
| GROUP A      | 5.53 | 5.09* | 5.66** | 6.11** | 6.26** |
| GROUP B      | 6.06 | 6.4** | 5.66** | 5.96** | 6.26** |

Values are means; *p<0.05 and **p<0.01.

Most other studies show neutral effects on insulin sensitivity, with minimal incidence of glucose intolerance. This may be partly explained by the diversity of age, diagnosis (whether insufficiency or deficiency state), other pituitary deficiencies and replacement therapy, and possibly by dosage of GH utilised in these studies.

GASTROENTEROLOGY

(O.2) CLOSTRIDIUM DIFFICILE ASSOCIATED DISEASE - A HOSPITAL OR COMMUNITY PROBLEM?

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Clostridium difficile-associated disease (CDAD) is primarily a nosocomial condition. Community-acquired disease has been described but the incidence is low(1). During a recent outbreak, we prospectively reviewed all new cases of CDAD to determine what proportion of cytotoxin positive cases were community or hospital acquired. During a 4 month study period, 73 cases were identified. History of diarrhoeal episodes were recorded for each case. Selected isolates were typed using pyrolysis mass spectrometry (PMS). Community-acquired CDAD was defined as diarrhoea, on or within 72 hours of admission, in association with a positive stool cytotoxin test for C. difficile and in the absence of hospitalisation within 60 days. Sixty-five cases (89%) were hospital acquired. Fifteen patients (20.6%) had CDAD on admission; 8 (11%) were community acquired. 7 (9.6%) had been recently hospitalised (4 at St. James’s hospital, 3 at other hospitals). PMS typing of faecal isolates revealed that 2 predominant strains were responsible for the hospital outbreak; one of these strains was also isolated in community-acquired cases. This study suggests that the incidence of community-acquired CDAD may be higher than previously reported. We suggest that all newly admitted or transferred patients with diarrhoea should be screened for this organism.

Reference

1. Hirschhorn, L. R., Trnka, Y. et al. Epidemiology of community-acquired Clostridium difficile-associated diarrhoea. J. Infect. Dis. 1994; 169: 127-133.

GERONTOLOGY

(O.3) FREQUENCY OF ACTIVATED PROTEIN C RESISTANCE IN AN ASYMPTOMATIC NORTHERN IRELAND ELDERLY POPULATION

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Several studies have confirmed that activated protein C resistance (APC-R) occurs in 20-60% of thrombosis patients and is therefore more common than congenital deficiencies in the inhibitors of coagulation such as ATIII, Proteins C and S. Homozygosity for the Factor V (FV) gene mutation is associated with a 50-100 fold increased risk of venous thrombosis while heterozygosity is associated with a 5-10 fold increased risk. The mutation, however, is highly prevalent in the general population, a prevalence of 5% has been reported in several European countries. Its frequency in the population of Northern Ireland (NI) has not yet been reported. We screened a group of 72 generally healthy elderly individuals (av. age 81.3; range 76-97 years) on several occasions for APC-R using an assay based on the prolongation of activated partial thromboplastin time by the addition of APC. A mean ratio of 2.64 (range 1.72-3.46) was measured. Seven individuals (9.8%) had ratios <2.3 (av. 2.11; range 1.72-2.28). These subjects were then analysed for the FV mutation by PCR amplification and restriction analysis. The 4 individuals with the lowest ratios (av. 2.0; range 1.72-2.15) were found to be heterozygous for the mutation. None of these 4 individuals were deficient for Protein C, Protein S or ATIII. The frequency of APC-R (5.8%) within this NI elderly group is similar to that reported by others in the UK whose studies would have included a generally younger population. The successful ageing of these individuals perhaps underlines the low risk associated with heterozygosity. Alternatively a higher prevalence of the mutation may exist in the general population of NI, where the incidence of heart disease is one of the highest worldwide.
IMMUNOLOGY

(0.4) NEUTROPHIL HEAT SHOCK PROTEIN EXPRESSION CORRELATES WITH INCREASED APOPTOSIS FOLLOWING ENDOTHELIAL TRANSMIGRATION

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Neutrophils (PMN’s) undergo endothelial transmigration upon activation or in response to a chemoattractant. Such cells are stressed and have an increased capacity to incite tissue injury. Little is known about the effect of transmigration on PMN stress gene responses, PMN activation and ultimately apoptosis. The aim of this study was to evaluate the effect of PMN endothelial transmigration on stress gene responses and correlate this with activation state and apoptosis.

Human endothelial cells (ECU 304) were grown to confluence and PMN transendothelial migration was examined using costar transwells. Chemotaxis was induced by formyl-methionyl-leucyl-phenylalanine (fMLP). Flow cytometry was used to determine PMN receptor expression (CD 11b, CD 16, CD 18) apoptosis and phagocytosis. Heat shock protein (HSP) expression was evaluated by western immunoblotting.

fMLP-induced PMN transendothelial migration resulted in increased adhesion receptor expression (CD11b, CD18 p<0.05 v control) and phagocytosis (p<0.05 v control). Migrated PMN’s also had an increased rate of apoptosis (p<0.05 v control) as evaluated by propidium iodide uptake, histone release, and decreased FcγRIII (CD16 P<0.05 v control) expression. Furthermore increased PMN apoptosis correlated with induction of HSP 72 following transmigration.

Conclusions: Naive PMN’s that migrate through endothelium in response to a chemoattractant undergo activation. Such cells are subsequently programmed for induction of HSP 72 which may serve to preferentially induce PMN apoptosis rather than necrosis thus limiting tissue injury.

ONCOLOGY

(0.5) PROINFLAMMATORY CYTOKINE DETECTION IN PATIENTS WITH OESOPHAEGAL CARCINOMA

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The proinflammatory cytokines, TNFα, IL-8 and IL-6, may mediate host metabolic and immune responses to cancer possibly leading to paraneoplastic phenomena such as cachexia. The cellular origin of these cytokines in the cancer patient, in many cases, remains unknown. We examined proinflammatory cytokine levels intracellularly, using flow cytometry, in PBMCs from oesophageal cancer patients (n=14) and age and sex matched controls (n=10). TNFα and IL-6 levels were significantly increased (p<0.05) in PMA stimulated T cells and monocytes from the cancer patients when compared to the healthy controls. These results were confirmed using standard ELISA assays. Following collagenase digestion, increased levels of TNFα and IL-6 were detected in oesophageal tumour infiltrating T cells when compared to cells from normal mucosa. There was also increased production of TNFα and IL-6, but not IL-8, in malignant epithelial cells when compared to normal epithelium. These results show that both PBMC and tumour cell proinflammatory cytokine production are increased in patients with oesophageal carcinoma, indicating that a global dysregulation of proinflammatory cytokine production occurs.

PATHOLOGY/CYTOLOGY

(0.6) BIALLELIC EXPRESSION OF THE INSULIN-LIKE GROWTH FACTOR II GENE IN JUVENILE CANCERS

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The insulin-like growth factor II gene (IGF2) is imprinted. Thus, in contrast to most genes where both maternal and paternal copies (alleles) are transcribed into RNA and expressed, IGF2 is normally only expressed from the paternal copy (monoallelic expression). Alterations causing biallelic expression of IGF2 may lead to excess growth factor production, and thus, to tumourigenesis. This study evaluated IGF2 expression in a series of childhood cancers.

To date 41 tumours have been evaluated using PCR based methodology (26 Wilm’s tumours, 12 rhabdomyosarcomas, 3 miscellaneous). DNA was extracted and a polymorphic site Apal within the IGF2 gene was amplified and digested. This identified 10 samples as heterozygous for IGF2, meaning that separate maternal and paternal alleles were distinguishable. RNA from these informative samples was extracted. PCR amplified and restriction digested, to identify monoallelic versus biallelic profiles at the expression level. Samples with normal imprinting (monoallelic) displayed allele a (236bp) or allele b1/b2 (176/63 doublet). Biallelic samples displayed both alleles.

Using this approach 3/5 informative Wilm’s tumours and 2/4 rhabdomyosarcomas demonstrated biallelic expression.

In conclusion, biallelic expression of IGF2 was detected in a significant number of Wilm’s tumours and rhabdomyosarcomas, and should be considered, with other genetic alterations, as a candidate mechanism in tumourigenesis.

REGISTRARS' PRIZE

ANAESTHESIOLOGY

(0.7) THERMOREGULATION WITH THE SPACE BLANKET DURING PAEDIATRIC GENERAL ANAESTHESIA

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General anaesthesia impairs thermoregulation, with paediatric patients at higher risk of hypothermia than adults because of greater surface to volume ratio and higher metabolic rate. The space blanket reduces postanaesthetic shivering and increases skin temperature when used preemptively in adult patients(5). This study investigated its pre-emptive role in paediatric patients. 36 patients (age 1-11 years) undergoing general anaesthesia were randomised into two groups: Group 1 were wrapped in the space blanket prior to induction of anaesthesia; Group 2 received standard cotton covering only. Peripheral skin temperature (TP), from the dorsum of the hand and core temperature (TC), taken rectally, were recorded at 10 minute intervals. Anaesthesia was induced with 100% oxygen
and halothane and maintained by 50% nitrous oxide-oxygen, 0.75-1.5% halothane, with spontaneous ventilation. TC rose marginally in group 1 and fell in group 2 (not significant, NS). TP in groups 1 and 2 at induction and 20 and 30 minutes were, respectively, (mean ± SEM, Celsius) 31.4±0.33 vs 31.6±0.3, NS; 33.9±0.3 vs 33.4±0.3, NS and 34.5±0.4 vs 33.2±0.3, (p<0.05). Overall incidence of shivering was 14%, but not significantly different between the groups. The data suggests that preemptive application of the space blanket increases TP in paediatric patients during general anaesthesia and tends to conserve TC.

Reference
1. British Journal of Anaesthesia 1994; 72: 393-96.

DERMATOLOGY

(O.8) IS MONOCHROMATOR IRRADIATION TESTING USEFUL IN DIFFERENTIATING DRUG-INDUCED PHOTOSensitivity FROM CHRONIC ACTINIC DERMATITIS?

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Chronic actinic dermatitis (CAD) an uncommon, eczematous, photosensitive eruption is diagnosed on history, clinical examination, skin biopsy and abnormal light tests. Drug induced photosensitivity may look identical clinically, have a similar history and patients with CAD may be treated with potentially photosensitising drugs. We therefore reviewed all patients with CAD and compared their monochromator light tests with patients who had drug induced photosensitivity. Phototesting was performed on unaffected skin of the back with an irradiation monochromator; the minimal erythema dose (MED) determined for a series of wavelengths between 300 and 400 nm, in 14 patients with drug induced photosensitivity and 7 patients with CAD. Of ten females, four males with drug induced photosensitivity, age range 40-77 (mean 61 yrs), ten (71%), were photosensitive in the UVA range (320-370nm), the implicated drugs including, quinine, sparfloxacin, amiodarone, doxycycline, mefenamic acid, nalidixic acid, fenbrafen, diclofenac, enalpril and prochlorperazine maleate. Three patients with rosacea were photosensitive to doxycycline. The remainder (29%), were tested after discontinuation of the drug and their light tests were normal. In the CAD group, (four females and three males), age range 38-86 (mean 71.5 yrs), three patients (43%), were sensitive to UVA, UVB and visible light, four (57%) to UVA and UVB. In conclusion, UVA dissociated from UVB photosensitivity seems a relative but not absolute sign of drug induced photosensitivity. This pattern of light tests should prompt a detailed drug history to elucidate the causative agent. Phototesting should be performed while on the offending drug as testing days or weeks after discontinuation will give normal results.

GASTROENTEROLOGY

(O.9) ASSESSMENT OF FRACTURE RISK IN PATIENTS WITH CHRONIC LIVER DISEASE

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Metabolic bone disease occurs in up to 50% of patients with chronic liver disease (CLD). The aim of this study was to identify patients at risk of bone fractures by measuring bone mineral density (BMD) and markers of bone turnover and to assess the correlation of these with the severity of CLD. Twenty three patients with CLD had BMD measured by dual-energy X-ray absorptiometry scanning of hip and lumbar spine. Bone formation was assessed using serum levels of procollagen type 1 peptide, osteocalcin and bone alkaline phosphatase, and bone resorption was assessed using 2 hour urinary excretion of hydroxyproline, pyridinoline and deoxypyridinoline.

48% and 39% of patients had evidence of osteoporosis at the lumbar spine and femoral neck respectively. Biochemical results showed that 74% of patients had an increase in all 3 bone resorption markers and 42% had an increase in markers for bone formation. BMD at the lumbar spine was lower in patients with cholestatic liver disease compared to patients with other types of liver disease (p=0.004). No correlation was found between BMD and patient age, bilirubin, albumin, INR or duration of liver disease.

Conclusions: Osteopenia occurs in up to 62% of patients with CLD due to a high bone turnover state where bone resorption exceeds formation. Osteoporosis is most severe in those patients with cholestatics.

HAEMATOLOGY

(O.10) EPIDEMIOLOGY AND SURVIVAL RATES FOR ALL 632 LEUKAEMIA PATIENTS REGISTERED IN CORK AND KERRY OVER THE 8-YEAR PERIOD 1983/1990

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A detailed profile is presented of all 632 leukaemia and multiple myeloma (ICD-O code 169) patients registered by the Southern Tumour Registry during the 8-year period 1983/1990. Annual age-adjusted rates of 13.9 and 8.7 per 100,000 were seen for males and females respectively. These levels indicate a lifetime (up to 75 yr) risk of 1 in 68 for males and 1 in 116 for females. The main morphological sub-types registered were multiple myeloma (31%), CLL (25%), AML (18%) CML (9%) and ALL (8%). One, two and five-year survival rates were examined; age at diagnosis and lesion type were extremely significant factors in relation to patient outcome. The overall incidence levels indicate that Irish rates were relatively high by international standards.

References
1. Cancer, The Irish Experience. M J. Crowley
2. Muir, C., Warehouse, J., Mack, T., Powell, J., Whelan, S. Cancer incidence in Five Continents volume V.IARC Scientific Publications No.88. Lyon: International Agency for Research on Cancer, 1987.

PSYCHIATRY

(O.12) LOWER FREQUENCY OF APOE E ALLELE IN AN OLDER DOWN’S POPULATION

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Several studies have reported an association of the Apolipoprotein E allele e4 with Alzheimer’s disease. Individuals with Down’s syndrome (DS) are known to have an increased

5
risk of Alzheimer's disease. We are engaged in a prospective study on the effect of APOE genotype on the development and progression of dementia in Down's syndrome. We determined the APOE genotype of 77 DS individuals whose average age was 48. 12 of these individuals were demented using DSMIIIR criteria. APOE genotype was determined as described by Crook(C). The table summarises our results for this group and compares the allele frequencies with the frequencies in a sample of 182 population controls. The frequency of the E4 allele in the DS individuals (0.084) was less than half that in the controls (0.192) (Chi square 9.36, 1df, p=0.0022). We found no E4 homozygotes in the DS group whereas we would have expected between two and three. Schacter et al(D) have found a lower frequency of the APOE e4 allele in a study in French centenarians, which they attributed to its role as a risk factor in heart disease and Alzheimer's disease. We propose that the decreased frequency of ApoE e4 allele in DS may be due to the premature death of those DS individuals with this allele from either heart disease or dementia. This effect may be seen much earlier in DS perhaps due to the overexpression of the APP gene on Chromosome 21.

Allele number and Frequency E2 E3 E4
DS n=77 12 (7.8) 129 (83.8) 13 (8.4))
Controls n=182 20 (5.5) 274 (75.3) 70 (19.2)

References
1. Crook, R., Hardy, J., Duff, K. J. Neuroscience methods 1994; 53: 125-127.
2. Schacter, F., Delanef-Faire, L., Guenot, F. et al. Nature Genetics 1994; 6: 29-32.

POSTER PRESENTATIONS
ANAESTHESIOLOGY
(P.1) SPINAL ANAESTHESIA WITH COMBINED HYPERBARIC AND ISOBARIC BUPIVACAINE
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We assessed effects of reducing the volume of hyperbaric bupivacaine by giving half the volume as isobaric bupivacaine. When using 0.5% hyperbaric bupivacaine for spinal blockade, the segmental spread and cardiovascular effects of the block have been shown to be dependent on the volume of local anaesthetic injected.

40 patients undergoing elective surgery were studied in a prospective, randomised, double-blind trial: Group 1 (20 patients) received their local anaesthetic as two equal aliquots of 0.5% hyperbaric bupivacaine and 0.5% isobaric bupivacaine respectively; Group 2 (20 patients) received their local anaesthetic as two equal aliquots of 0.5% hyperbaric bupivacaine.

There was no significant difference found between the two groups with regard to maximal height of block (group 1, mean [range], T7 (T4-T11); group 2, T8 (T5-T11)), rate of onset of blockade, or time to maximal blockade (group 1, mean (SEM), 23.55 (2.41) min; group 2: 20.89 (2.95) min). There was no difference found between each group in either cardiovascular stability or vasopressor usage. The administration of a mixture of 0.5% isobaric bupivacaine and 0.5% hyperbaric bupivacaine confers no advantages over administration of the same volume of 0.5% hyperbaric bupivacaine alone.
0.001). There was no relationship between pain scores for throat pain or otalgia and the development of negative middle ear pressure. 8 patients recorded higher pain scores for throat pain at day 7 then day 1, only 3 of this group had negative middle ear pressure. Middle ear pressure reverted to normal at day 7 in 15/18 patients and in the remaining 3/18 it was normal at day 14. This study demonstrates the development of transient negative middle ear pressure following tonsillectomy in 69% of patients. This change is unrelated to the degree of postoperative pain nor is it associated with otalgia.

(P.4) PAIN IN THE POSTOPERATIVE RECOVERY ROOM
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Postoperative ward analgesia remains suboptimal. This may be partially related to inadequate early use of opioids to attain minimum effective analgesic concentration (MEAC). We examined the incidence and predictors of severe postoperative pain on admission and discharge from our postoperative recovery room (RR). Verbal pain scores were obtained in a pilot study of 202 patients on RR admission and discharge. Procedures were classed as open cavitary, laparoscopic, orthopaedic, ENT or body surface surgery. Intraoperative use and dosage of narcotics and nonsteroidal (NSAID) analgesics, anaesthetists’ experience (pre-fellowship or post-fellowship NCHD, consultant) were noted, and RR opioid usage recorded. Pain scores and analgesic use were examined using Mann-Whitney, ~2 analysis and logistic regression.

Moderate or severe pain was experienced by 25% of patients on either arrival or discharge. Median intraoperative morphine dosage was 5 mg. Opioid use was slightly (median morphine dosage 8 mg, P < 0.05) higher in patients undergoing cavitary surgery; these patients had the highest pain scores on RR arrival and departure. 21 patients (10%) received > 10 mg morphine intraoperatively. Discharge scores of 6/10 or higher occurred in 24 patients (12%). Opioid usage and pain scores were unrelated to level of training. NSAID use/nonuse was unassociated with differences in opioid use or RR pain scores. No morbidity attributable to analgesic use (desaturation, slow respiratory rate) occurred.

Nonattainment of MEAC is frequent after open cavitary surgery. Conservative opioid dosages continue to be employed despite inadequate early postoperative pain relief; this does not change with increasing experience. Reporting such findings in departmental audit may help to alter perioperative management; such data may serve as a baseline for future interventional studies.

(P.5) EFFECT OF DICLOFENAC AND PETHIDINE VERSUS PETHIDINE ALONE ON POSTOPERATIVE PAIN AND BLEEDING AFTER TONSILLECTOMY IN CHILDREN
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Diclofenac is frequently used for analgesia after tonsillectomy. Recently concern has been expressed about the effect of diclofenac on prolonging bleeding time. One recent retrospective study found its use in tonsillectomy was associated with an increase in reactionary haemorrhage.

We designed a randomised controlled study to compare the effects of rectal diclofenac and IM pethidine given at induction with pethidine alone, in children undergoing tonsillectomy. Fifty nine patients were entered into the study. There were 26 males and 33 females, mean age 6 years, range (3-13). Patients were randomised according to chart number. Thirty five patients received rectal diclofenac after induction. Twenty four patients acted as controls.

There were no significant differences in operating time or operative blood loss between the two groups. In the recovery room the diclofenac group was significantly less restless than the control group (P < 0.05, Chi squared test), with less crying, movement and agitation. There was no difference in postoperative recovery and no primary or reactionary haemorrhage. One patient in the diclofenac group developed a secondary haemorrhage.

This study demonstrates a significant reduction in restlessness in the recovery room in children receiving rectal diclofenac. No increase in reactionary haemorrhage was demonstrated. Diclofenac remains a safe and effective analgesic agent in children undergoing tonsillectomy.

(P.6) REDUCED MORPHINE REQUIREMENTS VIA PCA IN THE ELDERLY
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Elderly patients have decreased dose requirements for many drugs compared to the young. Few studies have examined dose requirements of opioids in the elderly when administered via patient controlled analgesia (PCA)1. We compared the PCA morphine requirements between young and elderly patients.

Records were retrospectively analysed from 1,000 consecutive patients receiving PCA for post-operative pain. Inclusion criteria (i) age less than 10 years or greater than 60 years, (ii) upper abdominal surgery, and (iii) morphine PCA usage.

238 patients fulfilled the inclusion criteria. 89 patients were young and 149 were elderly. The mean age in the young was 29 years and in the elderly was 69 years. 51% were female in the younger group, 40% were female in the older group. Pain scores at rest and on movement were similar in both groups 3.8 and 6.7 respectively in the young, 3.2 and 6.2 in the elderly, (p > 0.05, Students t-test). Morphine usage over 48 hours was 58 ± 32.1 mg in the young, and 37 ± 20.3 in the elderly. (Mean ± S.D.) (p < 0.05, Students t-test).

Elderly patients required significantly less morphine via PCA to achieve the same pain scores as the young. These findings are consistent with studies showing decreased requirements of other drugs in elderly.

Reference
(1) Perry, Clin. J. Pain, 1994; 10:57-63.
CARDIOVASCULAR

(P.7) UTILITY OF SLC AS A MARKER FOR CARDIOVASCULAR DISEASES: A RESULT OF CORRECT CHOICE OF KINETIC PARAMETER

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The erythrocyte sodium-lithium countertransport (SLC) is abnormal in essential hypertension and some other forms of cardiovascular disease (CVD) but the considerable overlap in its activity in patients with these conditions and in normotensive healthy subjects remains a strong point against its possible utility as a marker for CVD. We sought to address this issue in greater detail.

Twenty-nine hypertensive patients (19 with family history of CVD) aged 56.4 ± 1.9 years (mean ± SE) and 32 normotensive subjects (12 with family history of CVD) aged 45.9 ± 1.9 years, participated after informed consent. SLC were determined in 35, 50, 70, 100 and 140 mM sodium chloride; and the Vmax and Km of the transporter determined. Hypertensive and normotensive individuals with family history of CVD (n = 31) had higher SLC activity (0.33 ± 0.011 vs 0.238 ± 0.011, p < 0.0005), greater Vmax (0.473 ± 0.019 vs 0.397 ± 0.018 mmol/L cell/h, p < 0.006) and lower Km 56.0 mM (median) vs 95.5 (p < 0.001) than hypertensive and normotensive subjects without such a history (n = 30). However, none of these parameters was sufficiently discriminatory as evidenced by the considerable overlap in the scattergrams for the two groups. On the other hand not only was the median quotient Vmax/Km significantly different 7.89 vs 4.20 (p < 0.001), but also the scattergram separated the two groups. This may reflect an effect of hereditary factors on the identified rate-limiting step in the transport system.

(P.8) MORPHOLOGICAL CHANGES IN RAT MITRAL VALVE ENDOTHELIUM FOLLOWING NEONATAL CAPSAICIN ADMINISTRATION

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Capsaicin administration results in depletion of Substance-P sensitive nerves. This study was carried out to observe the impact on the morphology of mitral valve endothelium.

The experimental group received capsaicin i.p. on day four of life; control animals received drug vehicle only. Animals were anaesthetised by chloral hydrate and hearts were removed following perfusion of 4% glutaraldehyde, and were routinely processed for Scanning Electron Microscopy.

Normal endothelial morphology showed an ordered and structured pattern, with large raised nuclei covered in discrete microappendages: no zoning was observed over the valve surface. Following capsaicin administration, valves were seen to be torn and possessed a denuded endothelium. Nuclear bulges changed in both apparent height and area, with the surface partially denuded of microappendages.

One month following systemic administration of capsaicin to neonatal rats, a serious alteration of mitral valve endothelium morphology and integrity had occurred. Depletion of Substance-P may have resulted in mechanical insufficiency of the mitral valve.

This study was funded by the Health Research Board.

(P.9) A COMPARISON OF THE COSTS OF PERCUTANEOUS TRANSCAVENOUS MITRAL COMMISSUROTOMY AND OPEN SURGICAL VALVOTOMY

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Since its inception in 1984, percutaneous transvenous mitral commissurotomy (PTMC) has developed as a safe and effective alternative to open surgical valvotomy (OSV) in suitably selected cases. This report compares the cost of PTMC using the Inoue balloon to OSV.

We performed a detailed cost analysis (consumables, paramedical and medical staff, bed days, intensive care, imaging) of all PTMCs (n = 19) and OSVs (n = 11) performed at our institution over a 30 month period (Jan. 92 - Jun. 95). Costs are tabulated below.

| Procedure                      | PTMC       | OSV       |
|--------------------------------|------------|-----------|
| HOSPITAL DAYS - WARD           | £900 (n=4) | £2450 (n=10) |
| ITU/CCU                        | 0          | 3000 (n=3)  |
| PROCEDURE-consumables          | £2006      | £4347     |
| - staff                        | £435       | £4347     |
| - anaesthesia                  | 0          |           |
| - general                      | £47        |           |
| GEN LAB + ECG                  | £21        | £106      |
| X-RAY                          | £12        | £19       |
| TOTAL COST                     | £3501      | £9922     |

PTMC and OSV patient clinical profiles were similar and all had pre-procedural assessment by cardiac catheterisation and echocardiography. Conclusion. Though consumable costs are high (Inoue balloon = £1440 + VAT @ 21%), PTMC is cheaper than OSV because of shorter hospital stay and no requirement for ICU care.

(P.10) COMPLICATIONS ASSOCIATED WITH DOBUTAMINE STRESS ECHOCARDIOGRAPHY: EXPERIENCE IN 309 PATIENTS

G. Kane, T. Hennessy, M. Codd, D. Sugrue, H. McCann.
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With expanding applications and increasingly aggressive stress protocols, concerns about the safety of Dobutamine Stress Echocardiography (DSE) have arisen. The purpose of this study was to analyse prospectively the safety, adverse event profile, and complication rate of DSE.

Prospective data was recorded in a consecutive series of 309 patients undergoing DSE for diagnostic evaluation of chest pain, for risk assessment following myocardial infarction or for detection of hibernating myocardium. The maximum dose of dobutamine used was 50 mcg/kg/min in 24.6% of patients and 40 mcg/kg/min in 73.1%. Atropine was used in 6.8%. No patient died, suffered a myocardial infarction or had sustained ventricular tachycardia. Angina pectoris occurred in 28.5% of patients; non-sustained ventricular tachycardia in 2.3%; supraventricular tachycardia in 2.9%. Profound bradycardia requiring test cessation occurred in 1 patient. Pulmonary oedema developed in 1 patient. A hypotensive response was seen in 1.3%. No patient complained of nausea, tremor or headache. 6 tests were incomplete because of an adverse reaction.

Conclusion. DSE is safe. Side effects are rare and when they
occur are usually minor. Ischaemic pain is effectively treated by test termination and sublingual nitrates. Whether DSE requires supervision by a medical doctor remains controversial.

(P.11) DETECTION OF ISCHAEMIA BY DOBUTAMINE STRESS ECHOCARDIOGRAPHY IS CRITICALLY DEPENDENT ON THE A PRIORI PROBABILITY OF DISEASE

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The accuracy of dobutamine stress echocardiography (DSE) in detecting angiographically significant coronary artery disease (CAD) (≥50% diameter stenosis) in a population with a high a priori probability of disease has been established. The value of DSE in routine clinical practice, in particular in unselected patients with a low pretest likelihood of disease has not been well defined.

From 10/94 to 8/95 a total of 245 DSEs have been performed at our institution. 98 of these patients had exercise stress electrocardiography (TMET). Results are tabulated below.

| Clinical prob. of CAD | DSE | TMET |
|-----------------------|-----|------|
| High ≥90%             | 125 | 46   |
| Med (11-89%)          | 104 | 45   |
| Low ≤10%             | 16  | 7    |
| Diseased arteries (n) | nDSE | nTMET |
| Single Vessel         | 60  | 22   |
| Double Vessel         | 65  | 22   |
| Triple Vessel         | 71  | 30   |

Conclusion. While DSE is closely correlated with advanced CAD, in milder disease it is less precise. DSE is, however, significantly more accurate than TMET, particularly in the medium probability group.

(P.12) BENEFIT AND COST OF HMG-CoA REDUCTASE INHIBITOR THERAPY DEPENDS ON AGE AND SEVERITY OF CORONARY ARTERY DISEASE

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The 4S and the West of Scotland Coronary Prevention Study reveal almost identical results, with an approximately 40 per cent reduction in coronary artery disease (CAD) mortality over 5 years from HMG-CoA reductase inhibitor therapy. Decision analysis shows that the benefit and cost of these lipid lowering agents depends on the age of the patient and the severity of CAD present. Control patients in the West of Scotland Study had an annual mortality from CAD of 0.5 per cent: decision analysis shows that life long HMG-CoA reductase inhibitor therapy will gain 1.3 quality adjusted life years (qalys) if started at age 50 at a total cost of IR£10,586 or IR£3634 per qaly gained; by 70 years of age 0.5 extra qalys are gained, costing IR£4539 or IR£9609 per qaly. Patient with three vessel disease and an annual CAD mortality rate of 7.0 per cent, will gain 6.23 qalys if treated from age 50, costing IR£7534 or IR£1209 per qaly gained: 1.33 extra qalys are gained at age 70, costing IR£3564 or IR£2678 per qaly. Who will decide if lifelong lipid lowering is worth it for each individual patient?

(P.13) CORONARY RISK FACTOR MANAGEMENT IN A POST CORONARY ARTERY BYPASS GROUP OF PATIENTS. A PRELIMINARY REPORT

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Long-term outcome following coronary artery bypass grafting may be related to the prevalence of major risk factors and their treatment following surgery.

We aimed to establish the prevalence and current management of coronary risk factors in a group of consecutive patients attending our hospital. This is a report of the first 100 patients. Data was collected by a structured patient interview, chart review, physical measurements and blood sampling.

There were 74 male and 26 female patients, average age 61.5 years. The mean length of time since surgery was 2.2 years. Thirty-nine patients had a recurrence of angina and this occurred on average 11 months after surgery. As regards risk factors, 22 were active smokers, 56 were ex-smokers and only 22 had never smoked. Two thirds of the patients were taking regular exercise; only 6 took no exercise at all. Seventy-two percent of patients had a cholesterol greater than 5.5mmol/l, yet only 10 of the patients were on lipid lowering drug therapy and a further 16 were on a lipid lowering diet. Twenty-nine patients had a systolic BP > 160 or a diastolic BP > 90 and 15 of these were on antihypertensive therapy. Seventy-seven patients were overweight but most of these had received specific advice regarding weight reduction in the preceding year.

Our results show a high prevalence of treatable risk factors in this high-risk group with inadequate treatment in many cases. New combined primary and hospital care strategies for cardiac rehabilitation and long-term secondary prevention of coronary heart disease are required.

(P.14) FREQUENCY OF LEFT VENTRICULAR FAILURE FOLLOWING ACUTE MYOCARDIAL INFARCTION IN THE THROMBOLYTIC ERA

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If the goal of modern therapy of acute myocardial infarction (AMI) is preservation of myocardium, the occurrence of cardiac failure could be regarded as a treatment failure. In recent studies of IV thrombolysis and primary PTCA the frequency of left ventricular failure (LVF) following AMI has been as low as 3.5%. This very low rate might be explained by selection bias in patients recruited to randomized trials. The purpose of this study was to examine the frequency of LVF in a consecutive
series of unselected patients admitted with AMI to one centre during the period Jan. 1992 to Dec. 1994. During the study period a total of 850 patients were admitted with AMI. The frequency of LVF (bibal rales/S3) was 34% (n=289). An additional 7.5% (n=64) suffered cardiogenic shock (Killip IV). In univariate analysis, factors significantly related to the occurrence of LVF included advancing age (p<0.01) and failure to administer thrombolysis (p<0.05). Among factors not associated with LVF were female gender, smoking history and previous infarction. The hospital mortality for this population was 15%. In multivariate analysis LVF was a powerful independent predictor of mortality. In conclusion, unselected consecutive patients the frequency of LVF complicating AMI remains high and is a major determinant of mortality following AMI.

(P.15) NITRIC OXIDE SYNTHESIS INHIBITION AND VENTRICULAR FIBRILLATION

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Alterations in nitric oxide (NO) synthesis have been implicated in cardiomyopathy, ischaemic heart disease and septic shock. Recent work has suggested a possible role for nitric oxide in cardiac arrhythmogenesis. The effects of inhibiting NO synthesis with L-NAME (10 mg/kg) on cardiac electrophysiology have not been fully determined.

The dominant frequency of electrically induced ventricular fibrillation was determined in 10 anaesthetised pigs (30-42 kg) using a Fourier transform. The dominant frequency (7.8 ± 0.5 Hz in Lead II) was not altered by treatment (8.5 ± 0.5 Hz) with L-NAME.

In a group of 16 pigs (45-58 kg) the effect of L-NAME (10 mg/kg) was assessed in relation to energy required to defibrillate. There was no significant difference in the energies required to achieve successful defibrillation on 80% of attempts between the L-NAME group (104.9 ± 8.0 J) and the control group (111.1 ± 11.9 J), and on 100% of occasions, L-NAME (122.5 ± 11.5 J) and control (137.5 ± 13.1 J).

The results show that inhibition of NO synthesis has no significant effect on the dominant frequency of ventricular fibrillation or on the efficacy of defibrillation in the pig heart.

(P.16) USE OF ORAL FLECAINIDE IN CARdioversion FROM ATRIAL FIBRILLATION TO SINUS RHYTHM

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Standard treatment of acute lone A Fib includes admission to hospital and cardioversion with either intravenous drugs therapy or electrical DC cardioversion. Intravenous flecainide has previously been reported as successfully cardioverting A fib and oral flecainide has the potential of pharmacological conversion of A Fib to sinus rhythm, possibly avoiding hospitalization.

We have assessed the ability of oral flecainide to convert acute onset A.Fib. 26pts (21 male & 5 female) aged 23 - 83 yrs received either 100mg (7pts) or 200mg (19 pts) oral flecainide followed by a maintenance dose of 100mg bd. All pts were euthyroid. None had significant hypertensive, valvular or ischaemic heart disease. 23 pts had normal echocardiograms, 3 had mildly dilated atria.

Of the 26 pts 17 (65%) converted to sinus rhythm, 15 within 72 hrs and 2 at 12 and 21 days respectively. 2 of the 17 pts had mild left atrial enlargement. Of those who cardioverted 16 received 200mg and 3 100mg. These results indicate that oral flecainide has the potential for cardioversion of acute lone A fib to sinus rhythm. The results indicate that it is as effective as reported IV therapy for cardioversion and avoids the need for hospitalization.

CRITICAL CARE MEDICINE

(P.17) BRACHIAL PLEXUS INJURY – A COMPLICATION OF CENTRAL VENOUS LINE INSERTION

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A 26 year old self employed mechanic was admitted to the Burns Unit having sustained 40% full thickness burns. His hospitalisation was complicated by MRSA septicaemia, ARDS and early multi system organ failure. A central venous line was inserted into his right subclavian vein for IPN. 2 days later he complained of pain and was unable to move his right arm. Subsequently, he was found to have paralysis of all the muscle groups of his right upper limb apart from some flexor movements in his fingers with areflexia and sensory loss over the C5/C6 dermatomes. The findings were thought to be in keeping with a brachial plexus lesion. An MRI scan showed a “haematoma” or “fibrosis” around the brachial plexus. EMG studies revealed a complete lesion from C5/C7 with evidence of partial function at C8 and a good function at C4. Despite physiotherapy, at follow up 2 months later there was no improvement in the EMG findings. Though brachial plexus injury has always been considered a complication of central venous line insertion(1), there have been no cases described, in the literature in the last 10 years. Central lines are mandatory in major surgical cases but one must always be aware of the possible complications caused by them.

Reference
1. Kaye, C. G., Smith, D. R. Complications of central venous cannulation. BMJ 1988; 297: 572-3.

(P.18) CHANGES IN BODY MASS DURING ICU TREATMENT

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Body weight (BW) in ICU patients fluctuates due to alterations in body mass(4) and water(5) and is usually estimated rather than measured. We hypothesised that (i) estimated weights are inaccurate and (ii) changes in true body mass (TBM) are masked by changes in water content.

On admission, ICU patients whose expected length of stay (LOS) was > 5 days were placed on a bed incorporating 4 load cells (accuracy of ± 0.1 kg). BW was estimated by ICU staff.
MBW was then recorded 12 hourly under standard conditions. Changes in MBW due to pack insertion/dressing changes were excluded. We calculated TBM as MBW minus cumulative fluid excess, corrected for insensible losses.

Patients received standardized nutritional support from day 3 and urinary nitrogen on day 6 was calculated. We studied 20 patients whose mean (SD) age, MBW, LOS and APACHE II score were 44.3 yr (18.54), 70.5 kg (14.39), 10.0 days (6.78) and 18 (3.8) respectively. Mean error in estimated weight on admission was 10.3% (nurses) and 12.2% (doctors). Mean protein and calorie intake was 64 g and 1670 kJ/dl/day. Mean decrease in MBW during ICU stay was 0.22 kg/day (range 0.21 kg (gain) to 0.49 kg). Mean reduction in TBM was 0.56 kg/day (range 0.28-0.86 kg/day) and this correlated with urinary nitrogen loss (r=0.7). In ICU, (i) estimated weight is significantly inaccurate and should not be used in physiological calculations and (ii) rapid and significant decreases in body mass occur which may be underestimated due to fluid accumulation.

References
1. Cerra, F. B. Hypermetabolism, organ failure and metabolic support. Annals of Surgery 1987; 192: 570-580.
2. Roos, A. N., Westendorp, R. G. J., Frohlich, M., Meinders, A. E. Weight changes in critically-ill patients evaluated by fluid balances and impedance measurements. Critical Care Medicine 1993: 21: 871-7.

(P.19) LOSS OF BODY MASS IN ICU PATIENTS RECEIVING DOPAMINE

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Dopamine appears to influence pituitary function and is associated with decreased circulating human growth hormone and insulin-like growth factor (1) which could exacerbate catabolism, and therefore wasting, during critical illness.

At 12 hourly intervals from admission, patients whose expected length of stay exceeded 5 days, were weighed (measured body weight, MBW) under standardized conditions, using a bed incorporating 4 electronic load cells (accuracy ± 0.1 kg). Standard demographics, APACHE II score and use of dopamine by infusion was recorded. Changes in weight due to removal/insertion of prostheses, packs/dressings were excluded MBW was converted to true body mass (TBM) using measurements of cumulative fluid balance (1000 ml = 1 kg) and insensible loss. Patients received nutritional support, starting on day 3, based on their admission MBW. There were no significant differences in mean age, weight, length of ICU stay, admission APACHE II scores and mean daily protein/calorie intake between 14 patients who had received dopamine by infusion (group D) and 18 who had not (group ND). Mean (SD) decreases in MBW during ICU stay were 0.42 (0.08) kg/day (group D) and 0.20 (0.05) kg/day (group ND) (p<0.01). Mean decrease in TBM was 0.55 (0.10) kg/day and 0.35 (0.07) kg/day respectively (p<0.05). Thus group D were losing an additional 1.4 kg body mass per week relative to group ND.

The use of dopamine by infusion is associated with an accelerated loss of lean body mass during critical illness.

References
1. Van den Berghe, G. et al. Critical Care Medicine. 1994: 22: 1747-753.
2. Roos, A. N. et al. Critical Care Medicine. 1993; 21: 871

(P.20) SHORT TERM MORTALITY RATE FOR PATIENTS OVER 80 YEARS ADMITTED TO THE INTENSIVE CARE UNIT

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Age has been proposed as a criterion for health care rationing. The purpose of this study is to examine the in-hospital mortality for elderly patients admitted to our Intensive Care Unit. Patients, 80 years or older, admitted to the Intensive Care Unit (ITU) between 1/Jan/94 and the 1/Dec/95 were included. Data recorded included the patients age, sex, source of admission, specialty, APACHE II score, and length of stay. Mortality rates in ITU and after discharge to the wards were examined.

2336 patients were admitted to the unit. 66 (2.8%) patients were 80 years or older. 38 patients were male. Mean age at admission was 83 years. Mean APACHE II score was 18. The mean length of stay was 4.3 days. 15 (22%) patients died in ITU. A further 16 died on the ward. 46% of patients had an in-hospital mortality.

Conclusions: Although the short term mortality rate for this group of patients seems high, the rate is comparable to other studies. Age is not a sufficient factor in deciding upon admission restrictions.

Reference
1. Callahan, D. Old age and new policy. JAMA 1989; 261: 905-906.

(P.21) LIPOPOLYSACCHARIDE DOES NOT INDUCE NEUTROPHIL ADHESION TO HUMAN PULMONARY ENDOTHELIAL CELLS

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Adhesion of polymorphonuclear leucocytes (PMNs) to pulmonary endothelial cells is an initial step in the inflammatory process characterising the adult respiratory distress syndrome. Previous studies using human umbilical vein endothelial cells (HUVECs) have suggested that lipopolysaccharide (LPS) is a potent stimulus for PMN adhesion to endothelial cells. The aim of this study was to investigate the effect of LPS on PMN adhesion to human pulmonary artery endothelial cells (HPAECs). Human PMNs were coincubated with HPAECs with LPS (0.001-10 mg/ml) with 2% serum for 1 hour. The effect of phorbol myristate acetate (PMA) (125 ng/ml) was also examined. Percentage adhesion stimulated by PMA was 66±10SD. LPS did not significantly increase adhesion at any of the concentrations used. To confirm the activity of LPS PMNs were incubated at 37°C with 0.01-100 mg/ml LPS + 2% serum for 1 hour and labelled with fluorescent antibodies to the MAC1 adhesion molecule complex (CD11a/CD11b). FACS analysis indicated upregulation of both CD18 and CD11b. Thus in the system used, LPS did stimulate PMN adhesion molecule expression, indicating that the lack of adhesion reflects a difference in HPAEC response to LPS compared to that reported for HUVECs. This work was supported by The Health Research Board Ireland.
(P.22) 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.

Twenty subjects were recruited and underwent voice and vocal cord assessment prior to and 3 months after starting inhaled steroid treatment. 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.

Prior to commencing inhaled steroid therapy for their asthma 14 subjects had normal voices, 5 subjects were mildly hoarse and one was moderately hoarse. Vocal cord pathology was noted in 12 subjects, 2 patients had vocal cord nodules and the remainder were noted to have mildly oedematous cords together with a glottic chink. At 3 months follow up, improvement in voice was noted in 2 subjects, one patient felt more dysphonic but there was no change in vocal cord appearance. One subject was noted to have developed a mid glottic chink with no associated change in voice. One subject had clearing of mild vocal cord oedema and improvement in voice.

This study demonstrates that 60% of subjects commencing inhaled steroid therapy for asthma have mild vocal cord pathology. Voice is more likely to be improved following use of inhaled steroids for 3 months then made worse.

(P.23) COLLAGEN AND ELASTIN REMODELLING IN EMPHYSEMA - A HUMAN - ANIMAL COMPARISON

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Although the relationship between elastin degradation and emphysema is well known, recent evidence suggests that a more complex process of pulmonary remodelling occurs within the emphysematous lung. The aim of this study was to assess the extent of extracellular matrix remodelling by ultrastructural examination of its two major components, elastin and collagen. Emphysema was induced in rats by the intratracheal administration of porcine pancreatic elastase (1.2U/g body weight) and human lungs were obtained at surgical resection for lung carcinoma. Emphysema was confirmed histologically in both animal and human samples by measurement of the mean linear intercept. Matching sections were immersed in 2.5M NaOH and 88% formic acid to digest elastin and collagen respectively. Scanning electron microscopy with stereo-pair imaging allowed 3-D visualisation of elastin and collagen frameworks. The distribution of emphysema was primarily panacinar in rat lungs and centriacinar in human lungs. As expected in both types of emphysema, elastic lamellae were disrupted and perforated with multiple fenestrations. Accompanying this disintegration was a marked increase in thickness of collagen fibrils which in some cases coalesced imparting a sheet-like appearance to the airspace walls. Unique to human centriacinar emphysema, collagen formed helices which spiralled around alveolar septae to form bulky walls between adjacent airspaces. In conclusion, these findings lend support to the novel concept of aberrant collagen remodelling in the pathogenesis of emphysema.

(P.24) TREATMENT OF SMALL CELL LUNG CANCER IN A SMALL REGIONAL CENTRE

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Small cell lung carcinoma (SCLC) is the most aggressive of the four common cell types of lung carcinoma. Less than 10% of patients with SCLC are alive two years after diagnosis.

Staging procedures, treatment regimens and survival results were reviewed in a small regional centre to make a comparison with larger treatment centres.

Thirty-one cases of SCLC seen by one physician from 1985 to 1993 were reviewed. Staging was clinical. Treatment was undertaken in conjunction with the local Oncology and Radiotherapy services. 42% of patients had limited disease where as 58% had extensive disease at diagnosis. In patients with limited disease, 20% were alive at 18 months and there was a 10% long term survival rate i.e. greater than three years. Average length of survival in limited disease was 456 days. Survival results were comparable with those treated with chemotherapy alone and combination chemotherapy and radiotherapy. In patients with extensive disease the best results were from those treated with a combination of chemotherapy and radiotherapy with an average survival of 353 days. These figures compare favourably with those from larger multidisciplinary centres. The factors contributing to our relative success may relate to continuity of care achieved in a smaller centre.

(P.25) RESPONSE OF PATIENTS AND BED-PARTNERS TO NASAL CONTINUOUS POSITIVE AIRWAY PRESSURE (nCPAP) FOR OBSTRUCTIVE SLEEP APNOEA (OSA)

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Nasal CPAP is a very effective therapy for OSA, but is cumbersome, and compliance varies. We prospectively evaluated 91 consecutive OSA patients treated with nCPAP, who were asked to complete questionnaires before, and 2 to 12 months after starting therapy. This study intended to examine both the patient’s subjective response to nCPAP and their bed-partner’s impressions also. Replies were received in 84 (92%) patients. Patients were divided into 4 groups depending on whether they had a bed-partner, and according to their response to an initial question assessing overall improvement in sleep quality and daytime alertness with nCPAP, ranging from 0 (minimal/none) to +4 (excellent). Patients were called responders if they scored > 2. Group A (45 pts, 54%) were responders with bed-partners; Group B (10 pts, 12%) non-responders with bed-partners; Group C (15 pts, 18%), were responders (12 pts, 14%) and non-responders (3 pts, 4%) without bed-partners; and Group D (14 pts, 17%) had stopped nCPAP. Nine questions were directed at...
the bed-partner, and assessed their perception of changes in both the patient's and their own sleep quality, daytime alertness, mood and quality of life, and also to changes in the relationship between patient and bed-partner following institution of nCPAP. These questions scored from -1 (worse) to +3 (marked improvement). Significant improvement in all parameters for the patient (mean ± SD = 2.4 ± 0.7) were noted in group A. In addition, Group A bed-partners reported subjective improvement in the same parameters (1.7 ± 1.1). Group B improvements were less, (1.8 ± 1.0 in patients, and 0.6 ± 1.1 in partners). Overall, the data indicate a subjective success of therapy in 68% of patients, but the bed-partner's replies indicate this figure underestimates the true response rate. Furthermore, the results show significant improvements in the bed-partner's sleep quality, daytime alertness, mood and quality of life, indicating that successful treatment of OSA patients with nCPAP also gives significant benefits to their bed-partners.

(P.26) PURIFICATION OF NEUTROPHIL COLLAGENASE FROM PURULENT SPUTUM

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Neutrophil collagenase (MMP 8) is a member of the matrix metalloproteinases (MMPs), a family of highly homologous zinc endopeptidases which play a crucial role in many physiological processes. The aim of this project was to develop a purification system for MMP 8 from purulent sputum and raise polyclonal antibodies.

After initial extraction, contaminating proteins were removed with a zinc chelate affinity column. MMP 8 was then separated, from another closely related MMP, gelatinase b, on a Q Sepharose ion exchange column using a NaCl gradient. The final purification step was carried out with an orange sepharose affinity column.

SDS-PAGE analysis indicated the presence of purified protein with bands corresponding to latent neutrophil collagenase (85kD) and products of collagenase auto-degradation at lower molecular weights (55kD & 57kD). A 10-fold increase in specific activity was observed, with a 20% final yield, which provided mg quantities of pure enzyme.

This work is funded by Forbairt and The Irish American Partnership.

(P.27) CD30 EXPRESSION ON T LYMPHOCYTES DEFINES IMPORTANT DIFFERENCES IN THE IMMUNE RESPONSE IN INFLAMMATORY DISEASE OF THE RESPIRATORY TRACT

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CD30 is a protein first described as a surface marker on Hodgkin's lymphoma cells. Recently CD30 has been demonstrated on Th2-type T lymphocytes (produce IL-4, 5, 6, 10 and 13), which have a pro-inflammatory cytokine profile, but is not found on Th1-type T lymphocytes (produce IL-2 and IFN-gamma). Its ligand, CD30L, has also been described, CD30-CD30L interaction has been shown to aid the development of T lymphocyte clones into a Th2 rather than a Th1 phenotype. Th2-type cytokines are inextricably linked to the aetiology of inflammatory airway disease.

Firstly we investigated serum CD30 levels in various patient groups. We have demonstrated significant differences in serum CD30 levels in the following groups, atopic asthmatics (mean = 149 iu/L, n = 62), non-atopic asthmatics (mean = 107 iu/L n = 13) and atopic rhinitis/dermatitis (mean = 90 iu/L n = 36) and normal controls (mean = 14 iu/L, n = 9).

Secondly we cultured peripheral blood mononuclear cells from allergic individuals and normals. When these cultures were stimulated with house dust mite antigen (Der p 1) and IL-2 or Der p 1 with both IL-2 and IL-4, surface expression of CD30 on T lymphocytes could be demonstrated using fluorescent staining and flow cytometric analysis. after 9 days culture in the allergic individuals but not in normals. The presence of IL-4 in the culture increased the degree of surface CD30 expression.

These results are important as they show that allergic individuals have an expandable population of memory T lymphocytes which respond to allergen by expressing CD30 and developing Th-2 phenotype. Most work on CD30 and Th-2 cytokines has hitherto been carried out an T cell clones. We have developed a relatively simple in vitro system of looking at T lymphocyte response to allergen which will allow the testing of novel therapeutic interventions with a view to modulating the immune response in allergic disease. Our work also suggests that even non-allergic patients with inflammatory airway disease may have increased Th2 activity, which has not been shown previously.
patient was treated symptomatically and is presently stable.

Conclusion: Scimitar syndrome, with its wide spectrum of abnormalities should be considered when reviewing plain chest x-ray in patients with recurrent right lower lobe respiratory tract infection.

(P.29) DECREASED RESPONSIVENESS OF NEUTROPHIL ADHESION MOLECULES IN CYSTIC FIBROSIS (CF)

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Recent studies indicate that the ability of circulating neutrophils to regulate surface levels of adhesion molecules may be altered in disease situations. The aim of this study was to determine if changes in neutrophil responsiveness accompanies chronic inflammation in CF. Neutrophils in blood samples from 17 CF patients and 13 age-matched control subjects were analysed by flow cytometry for expression of L-selectin and Mac-1 (CD11b) following stimulation by interleukin-8 (IL-8) and fMLP. As expected, both IL-8 and fMLP provoked a decrease in surface levels of L-selectin and an increase in CD11b levels. However, the magnitude of these changes was significantly lower in CF patients than in control subjects (Table). These results suggest that chronic exposure to inflammatory stimuli in vivo may alter neutrophil responsiveness in CF.

Stim Control CF
% Change L-Selectin
IL-8 -46.5 ± 4.7 -29.0 ± 4.9
fMLP -79.4 ± 5.6 -55.3 ± 7.9
% Change CD11b
IL-8 195.5 ± 31.2 122.5 ± 26.3
fMLP 320.4 ± 51.3 221.5 ± 38.6

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PHARMACOLOGY

(P.30) DRUG PRESCRIBING IN A LONG-STAY UNIT

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Given the emphasis on rational prescribing, we reviewed drug use in a 208 bedded long-stay unit. Prescribing patterns were analysed on an appointed day thereby obtaining a “snapshot” of prescribing practices.

One hundred and ninety four long-stay residents, with a mean age of 78, were on 1188 drugs, the maximum number of drugs per patient was 12, the minimum 1 and the average 6.1. Sixty percent of prescriptions fell within one of the following therapeutic categories: central nervous system (CNS) preparations (321 prescriptions), analgesics (145), gastrointestinal preparations (139) and cardiovascular preparations (125). There were 19 prescriptions for respiratory drugs and only 36 prescriptions were for antibiotics. The most commonly prescribed CNS preparations were anti-psychotics (127), benzodiazepines (113), anti-depressants (30). 43% of all analgesics prescribed (63) were NSAIDs. The most commonly prescribed H2 blocker was cimetidine (33), Nuseals Aspirin (43), digoxin (35) and captopril (24) were the most commonly prescribed cardiovascular drugs. 25% of drugs were issued on an as required basis, i.e. “PRN”. The most commonly prescribed PRN therapeutic classes were analgesics (100 prescriptions) followed by gastrointestinal (74) and CNS preparations (68).

These results contrast with prescribing patterns in hospitals and general practice and may provide an insight into the challenges and realities of management in long-stay units.

Supported by the Health Research Board.

(P.31) EVALUATION OF PHYSICIAN/CLINICAL PHARMACY INTERACTION IN A MEDICAL UNIT

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Evaluation of physician requests to hospital based clinical pharmacist for (1) Drug Information, (2) Possible Adverse Drug Reaction (ADR) was undertaken over a two year period from Jan ’94 to Dec ’95 (Admissions - 1,667, OPD Attendances - 5,908). Overall 55 requests were made.

(1) Drug Information: Advice/information on new drugs, formulation, dosage, safety consideration prior to drug prescribing was given in 23 cases.

(2) Suspected ADR: A total of 32 suspected adverse drug reactions were investigated. In 4 cases, no ADR link was established, after extensive literature/data base search. ADR’s were confirmed in 28 cases of which 11 were reported to N.D.A.B.

Regular on-going interaction between physicians and clinical pharmacy allowed critical analysis of new drugs and heightened awareness of potential adverse drug reactions in current clinical practice.

(P.32) ARE HOSPITAL PHARMACISTS BETTER THAN HOSPITAL DOCTORS OR NURSES AT IDENTIFYING COMMONLY PRESCRIBED DRUGS?

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We previously demonstrated that commonly prescribed medications are not easily identified by patients, doctors or nurses in the hospital setting[1,2]. We then investigated the ability of hospital pharmacists, 33 in all, to identify the same 12 commonly prescribed branded and generic drugs. Correct identification as follows:- bendroflumethiazide K (32/33), cimetidine (33/33), diazepam 5mg (31/33), diazepam 5mg generic (30/33), digoxin (24/33), ferrous sulphate (14/33), frusemide (16/33), mefenamic acid (33/33), paracetamol (27/33), prednisolone (11/33), temezepam (33/33), theophylline (25/33). Pharmacists had 78% correct answers compared with 62% for nurses and 42% correct for doctors.

The pharmacists had no difficulty recognising drugs with brand names written on them e.g. cimetidine, but like nurses and doctors had difficulty identifying the plain white tablets e.g. prednisolone. Generic drugs were less well recognised. A number stated that they were unwilling to definitively identify medication with no clear marking. Pharmacists were also asked to list the top 5 prescribed drugs, 10 got 1/5 correct and 23 got
0/5 correct. In contrast 36 out of 80 doctors got 1/5 correct, 25 got 2 right and only 4 got 3 right.

We conclude that hospital pharmacists are generally better than doctors or nurses at identifying commonly prescribed drugs but their knowledge of the top 5 prescribed drugs is not as good as that of doctors. All professionals need assistant in this important task.

References
1. McCormack, P. et al. Br. J. Clin. Pharmac. 1991; 31, 608P.
2. Hall, M. et al. Br. J. Clin. Pharmac 1992; 34, 406P.

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(P.33) GENERAL PRACTICE PRESCRIBING OF METHADONE IN THE EASTERN HEALTH BOARD
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It is has been advocated that funding for the prescribing of methadone in general practice should be provided separate from the indicative drugs budgeting scheme on the assumption that this may act as a disincentive to G.P.s to take on care of drug addicts.

The objective was to analyse the current level and cost of methadone prescribing in 550 general practices in the Eastern Health Board over a six month period.

There was a review of methadone prescriptions for GMS patients from Jan. to Jun. 1995.

1,087 persons received prescriptions. 3,945 scripts were issued. The age-specific prescribing rate for the total population was 6/10,000 (males 10/10,000, females 3/10,000). Males aged 25-34 years had the highest age specific rates (44/100,000). The cost of methadone prescriptions amounted to £73,605 for the six months.

There was a trend towards an increase in the number of G.P.s who prescribed methadone over the period. Only four of the 70 G.P.s (5.7%) who prescribed methadone issued in excess of 50 scripts for the period studied.

For a small number of G.P.s methadone prescribing is a significant cost item on their budget. In the light of this, government policy should be reviewed with a view to excluding methadone from the Indicative Drug Budgeting Scheme.

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(P.35) ETHNIC DIFFERENCES IN SERUM CHOLINESTERASE ACTIVITY
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There is increasing evidence that some of the wide variation in the response to medicines has a genetic origin which may be expressed on a racial basis. To further study inter-ethnic differences in pharmacology we compared the activity of an enzyme responsible for the breakdown of endogenous substances and drugs - serum cholinesterase (pseudocholinesterase), dibucaine and fluoride numbers - in 200 Irish and 200 Iranian healthy subjects. Irish subjects had significantly higher serum cholinesterase activity (7.28 ± 0.14 vs 5.22 ± 0.09 u/ml, mean ± SEM, p < 0.01). The % inhibition of enzyme activity by dibucaine (82.19 ± 0.68 vs 69.29 ± 0.68) and by fluoride (79.90 ± 0.46 vs 70.13 ± 0.62) was reduced (p < 0.01) in Iranian subjects suggesting reduced activity or more Iranians with inherited variants of cholinesterase. One Iranian subject with very low activity (dibucaine number below 20, atypical) had a history of apnea. These data indicate that the frequency of atypical and heterozygote genes for cholinesterase activity leading to prolonged apnea with succinylcholine (suxamethonium) is much higher in Iranian than Irish populations. This study emphasises the importance of ethnic pharmacology.

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(P.36) HOSPITAL PRESCRIBING: A DECADE OF CHANGE
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Drug prescribing data may reflect changes in therapy and disease pattern. We reviewed current drug use among patients (n = 578) in a Dublin teaching hospital in “snapshot” fashion on a designated day, and compared it with that obtained in 1985.

In 1985, patients received an average of 7.8 different drugs each, with 41% on 5 or more and 3% on none. By 1995, the average was 6.8 (range 1 - 19), with 62% on 5 or more. The percentage of patients receiving heparin fell from 42% to 13%, due mainly to a reduction in use on the medical side. The proportion of patients prescribed hypnotics fell from 55% to 37%, while SSRI’s are now the most used anti-depressants. Antibiotic choice changed from amp/amoxicillin to co-amoxiclav and the cephalosporins. Diuretics remained the most frequently used cardiovascular agents, accounting for 4% of all drugs used and prescribed for around one quarter of patients. Digoxin use remained constant, and by 1995, 20% of patients were on anti-platelet doses of aspirin. At least four different agents were in use in each of calcium antagonist, beta blocker and ACE inhibitor classes.

Some of these changes in therapy reflect therapeutic advances, changes in disease management, greater choice of therapy and amendment of less than desirable therapeutic practices. On the other hand, some may reflect fashion or pharmaceutical promotion, rather than change as a consequence of evidence-based practice.

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(P.37) REACTIVE HYPERAEMIA IN THE FOREARM IS NOT MEDIATED BY NITRIC OXIDE
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Studies of in vivo endothelial function in humans have usually involved intraarterial cannulation and the subsequent administration of substances that stimulate the endothelium to produce nitric oxide (NO). Such techniques are invasive and potentially hazardous. An alternative non-invasive method would be of benefit.

Animal studies have indicated that reactive dilation of vascular beds may be at least partially endothelium dependent.
This study aimed to determine whether reactive hyperaemia in the human forearm was an endothelial dependent process with the potential to be used as a non-invasive method of stimulating the endothelium.

Ten volunteers underwent brachial artery cannulation and randomly received either placebo or N-monomethyl-L-arginine (L-NMMA) (8µmol/min), an NO synthase inhibitor, for 10 minutes. Following this reactive hyperaemia was induced by the inflation of an arm cuff to 200 mmHg for 5 minutes and the response to this was measured by strain-gauge plethysmography. When flows had returned to baseline the process was repeated with the remaining substance. Results were analysed by repeated measures ANOVA.

L-NMMA resulted in significant reduction of basal forearm blood flow (p<0.01). There was no significant difference in reactive hyperaemia with either L-NMMA or placebo.

In conclusion, NO does not contribute to reactive hyperaemia in the human forearm.

(P.38) PARENTERAL MANAGEMENT OF HIV DISEASE IN THE COMMUNITY
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Home-based infusion therapy has been widely recognised as the optimum for treatment of disease states that require daily intravenous therapy from a patient-care aspect. Conditions necessitating intravenous therapies in HIV disease include: CMV retinitis, intractable cryptosporidial diarrhoea, azole-resistant candidosis, nutritional support with total parenteral nutrition, chemotherapy for AIDS-related malignancies and palliative care in the terminal phase of the disease. The need for such therapies is increasing as patient survival improves.

In 1993, the home-infusion service was set up in recognition of the need to treat patients, requiring intravenous therapy, in the home environment. This has been brought about by the development of small, light-weight pumps suitable for ambulatory use, the development of a service for aseptic compounding and the availability of permanent in-dwelling venous catheters. We describe the impact of this service on our patient cohort.

To date, sixty-five HIV positive patients have received parenteral therapy at home. Patients' age, sex, risk group, CDC stage, CD4 count, indication for therapy, complication rate and response to treatment are described.

The provision of this service has reduced the number and length of patient admissions with associated improvement of quality of life. In addition, it recognises that patients prefer to be treated in the home environment aided by a co-ordinated multidisciplinary approach.

(P.39) BLOOD ALCOHOL AND PSYCHOMOTOR PERFORMANCE IN YOUNG ADULTS – TWO WILL DO IS NOT TRUE
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Since blood alcohol levels over 80 mg/100 ml are now illegal for vehicle drivers we have investigated if the commonly held “safe” limit of two drinks will bring the young adult over the legal limit and if this amount of alcohol will affect their psychomotor skills.

Following informed consent 33 healthy volunteers, non-habitual drinkers on no medication (16 male, 17 female), with a median age of 24 (range 20-27) years participated and refrained from alcohol for at least 2 days. Each drank within 15 minutes two standard drinks (35.5 ml each) of 37.5% vodka (2.7 units of alcohol) plus 60 ml of orange juice at about 90 minutes after a standard mid-day meal. Their psychomotor performance was estimated by the number connecting technique at 45 minutes after alcohol consumption and they were also asked to rate their feelings (which included alertness, clear-headedness, competence and attentiveness) using a visual analogue scale of 1 to 10. Blood samples at one and two hours later were collected from the antecubital vein and analysed on the same day for alcohol content using enzymatic methods. Mean (± SEM) blood concentrations of alcohol at 1 and 2 hours respectively were 25.39 ± 6.19 and 21.62 ± 4.58 mg/l00 ml in males and 36.43 ± 11.89 and 38.66 ± 3.43 mg/l00 ml in females. Values were significantly higher in females.

Blood concentrations in females were also higher (p < 0.01) than in males when expressed per Kg body weight. While the blood alcohol in both the genders was considerably lower than the current legal limit in Ireland their psychomotor skills as estimated from their task completion time and their answers to questionnaires were indicative of an impaired CNS function. Thus while 2 drinks may keep many subjects below the legal limit, there is considerable inter-individual variation with females showing higher concentrations and both genders have evidence of impaired performance at these lower levels.

(P.40) A NEW TIME-DOMAIN PARAMETER TO DESCRIBE HEART RATE VARIABILITY (HRV) IN MAN
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A non-linear approach was used to develop an HRV parameter, robust to both data non-stationary and missing data points. Unlike the standard chaos approach, using higher dimensional embeddings and time-delays, we employed a one-dimensional correlation integral plot. The parameter thus obtained, allows an estimate of the spatial spreading of the attractor (SSA) or spatial variation of RR intervals along a straight line. Heart rate data from 18 volunteers (22:00 to 06:00 hr), after oral placebo or propranolol 80 mg, investigated the ability to detect drug effect.
Conclusion. The SSA (Mean ± S.E.M.) parameter, by allowing the data to be selectively de-correlated from long-range variations, was superior to standard methods for the detection of drug effect.

(P.41) THE EFFECT OF HORMONE REPLACEMENT THERAPY ON VITAMIN E STATUS IN POST MENOPAUSAL WOMEN

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Vitamin E (α-tocopherol) is the most important dietary antioxidant in lipid and cell membranes and its intake reversely relates to the incidence of coronary heart disease and certain cancers. Estrogen regenerates oxidized tocopherol radical in vitro but such interaction has not been investigated in post-menopausal women receiving estrogen containing hormone replacement therapy (HRT) although estrogen containing oral contraceptive may reduce plasma vitamin E level.

We studied 21 healthy post-menopausal women (aged 46 - 56) ammenorheic for at least one year. Fifteen subjects took a combination of Harmogen Provera therapy and 6 acted as a control group. Blood samples were taken from all subject at baseline and after 4 weeks.

In the HRT group, serum FSH levels were greatly reduced (86.46 ± 25.27 vs 68.67 ± 11.59 IU/l, p < 0.04, mean ± SD, after HRT) with an increased serum oestradiol level (< 20 - 28.68 vs 603.67 ± 343.56 pmol/l, p < 0.0001). No change occurred in the control group. Vitamin E status, measured either as plasma or red cell α-tocopherol respectively showed no change in both groups (HRT group 24.68 ± 5.42 vs 27.17 ± 3.39, 23.79 ± 5.19 vs 24.93 ± 4.37 μmol/l, p > 0.05).

We conclude that in post-menopausal women, 4 weeks estrogen containing HRT did not alter vitamin E concentrations in vivo.

References
1. Mukai, K. et al. Biochemimica et Biophysica Acta 1990; 1035: 348-352. 2. Ciavatti, M. et al. Free Radic. Biol. Med. 1991; 10: 325-338.

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ENDOCRINOLOGY

(P.42) BENEFITS OF NEWER BONE MARKERS OVER ROUTINE BIOCHEMISTRY IN PRIMARY HYPERPARATHYROIDISM

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We assessed the clinical benefit of the newer markers of bone formation: osteocalcin (Oc), procollagen 1 carboxyterminal peptide (PICP), bone alkaline phosphatase (BALP), and bone resorption: carboxyterminal telopeptide of type 1 collagen (ICTP) and urinary deoxypyrindinoline crosslinks (DPD) over traditional assays such as total alkaline phosphatase (TALP) and urinary hydroxyproline (OH/Pr) in 23 patients with primary hyperparathyroidism (PHPT). Patients were sampled basally, then at 2, 6, 24, 48 and 72 hours post surgery and again at 1.5, 3, 6 and 12 months post op. The mean basal PICP level was 89±26 ug/l (normal: 38-202) this increased to a peak at 48 h (168±74 ug/l), then declined to normal at 6 weeks (116±56 ug/l). Mean basal urinary DPD levels were raised at 8.6±1.2 nM/mM Cr. (normal n=0-6.0), they had normalised by 6 months to 5.9±1.4 nM/mM Cr. Mean BALP levels were always normal. Although normal the yearly mean Oc level was significantly lower than the basal value. Mean ICTP, OH/Pr and TALP levels were always normal. Therefore bone turnover in PHPT is best assessed by the newer markers PICP and DPD.

GERONTOLOGY

(P.43) ARE WINTER INFECTIONS RESPONSIBLE FOR SEASONAL CHANGES IN FIBRINOGEN LEVELS IN ELDERLY PEOPLE?

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We have previously described seasonal variation in fibrinogen with higher levels in winter. As fibrinogen is an acute phase reactant, the winter rise may be a response to seasonal infections. The present study investigates this hypothesis by examining seasonality in fibrinogen and markers associated with infection: white cell count (WCC), interleu kin-6 (IL-6), Human Herpes Virus 6 (HHV6) and Herpes Simplex Virus (HSV) antibodies. Monthly blood samples from healthy volunteers aged 75 and over were measured for fibrinogen, WCC, IL-6, HSV and HHV6 reactivation over a 1 year time period. A rhymetric method was used to examine the data for seasonality. Statistical significance was measured using the F-statistic. A highly significant seasonal variation (SV), peaking in mid-February, was found for fibrinogen (n=24; SV=0.629 g/l; F=76.14; p<0.01). No significant seasonal variation was present for measures of WCC (n=24; SV=0.209 e9/l; F=1.94); HHV6 (n=24; SV=0.065 au; F=0.55; p>0.05), HSV (n=7; SV=6.055 au; F=2.04; p=0.05) or IL-6 (n=7; SV=1.235 pg/ml; F=0.55; p>0.05). The present investigation does not support the hypothesis that seasonal variation in fibrinogen is a direct effect of the acute phase response, initiated by a seasonal variation in level of infection. The explanation for the seasonal changes in fibrinogen remains unknown.

(P.45) PLASMA HOMOCYSTEINE AND SERUM ANTIOXIDANT LEVELS IN THE ELDERLY

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Increased plasma homocysteine and reduced plasma antioxidants are risk factors in the development of vascular disease. Design: 131 subjects drawn from elderly people living in the community (Median age 85 yr, range 60-102 yr; 81 male).

Total plasma homocysteine, vitamin C, gamma tocopherol, retinol and beta carotene were measured by high pressure liquid chromatography.

Homocysteine levels in elderly males [median (range) = 12.35 μM (4-18.1), n=24] were significantly higher than in
elderly females [8.45 uM (4.8-24.8), n=30]. These values were also higher than in a younger (30-49 years) male cohort [mean = 7.85 uM, n= 610]. No correlations to vitamin concentrations were found, nor was there a correlation to age within the elderly cohort. Within the elderly females, a significant negative correlation with age was found in vitamin C, gamma tocopherol and beta carotene (p<0.05). However a significant increase in retinol was noted. A very strong correlation between vitamin C and gamma tocopherol levels was noted in the elderly population sample (p<0.001 after multiple regression).

Conclusion. Homocysteine levels in the elderly are higher than in samples of a younger population. A gender difference is maintained in the elderly.

(P.46) EXTENDED CARE PLACEMENTS: THE GENERAL HOSPITAL EXPERIENCE
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The provision of extended care forms one part of a spectrum of health care for older people. In the Eastern Health Board area all patients over the age of 65 must be assessed by the multidisciplinary geriatric team prior to placement. We report on the experience of the total number of referrals for assessment for extended care to one department of geriatric medicine in a 268 bed teaching hospital.

Ninety-eight patients listed for extended care in 1994. The mean number of days between listing for long term care and placement was 49 ± 45 days (range 3 to 206). Almost one quarter of patients died while in hospital awaiting long term care: this underlines the frailty of patients who are admitted to hospital and request long term care. Two patients were transferred to other institutions and 10 patients were able to get home. Of the remaining patients 35 (63%) were placed in statutory or voluntary long term care accommodation and only 37% were eligible (usually financially but in some cases due to significant disability) for nursing home care using the terms of the 1993 Nursing Home Act.

Patients who are listed for long term care through a general hospital are in general very frail, they tend to have a very extended length of stay and the provisions of the Nursing Home Act only apply to a minority. These findings underline the need for provision of adequate statutory and voluntary extended-care places within the Eastern Health Board area.

(P.47) FOLSTEIN OR CAPE: WHICH PREDICTS BEHAVIOURAL DYSFUNCTION?
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There are over 40 screening assessments for cognitive function and choosing the most appropriate may be difficult. Increasingly the importance of behavioural dysfunction is recognised. Can any of the cognitive assessments help to predict behavioural dysfunction? We compared and contrasted the Folstein mini mental state examination (MMSE) and the cognitive assessment schedule (CAS) of the Clifton assessment procedures for the elderly (CAPE) and compared them with the behavioural rating scale (BRS) of the CAPE.

The study was carried out on a total of 21 referrals to the occupational therapy departments by geriatricians in the Meath Hospital and St. James’s Hospital. All subjects were over 65 and medically stable. The time scale involved was May - July 1995. The MMSE and the CAS were administered within the one sitting and each was timed. BRS was rated the same day by either a staff or family member.

The average time to complete the MMSE (416 ± 124 s) was longer than the CAS (342 ± 171 s) but this was not statistically significant. The MMSE and CAS were significantly correlated (r = 8208, p < 0.0001): The CAS was significantly correlated with the behaviour scale (r = 0.551, p < 0.01) whereas the MMSE was not. These results suggest that equivalent assessments of cognitive function may be made with the MMSE or CAS, but a low CAS score will be a better prediction of behavioural dysfunction.

(P.49) UNEXPLAINED DYSPHAGIA ASSOCIATED WITH PROLONGED INTENSIVE CARE UNIT STAY
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A spectrum of neurological and myopathological changes are associated with patients in intensive care units. We observed several patients post discharge from ICU who presented with unexplained dysphagia which we suspected may be associated with the neurological complications of sepsis. The particular complication of dysphagia as a neurological manifestation of sepsis has not been documented. Our descriptive study presents a series of three patients with persistent dysphagia which may represent a similar phenomenon.

We selected patients for the study ranging from 75-87 years of age and on the basis of medical history including ICU stay, sepsis, and intubation. All patients presented with dysphagia as observed on videofluoroscopy. We studied the video findings in-depth in order to ascertain if similar swallow patterns were present in these patients and if this could be correlated with their medical history.

Each of the three patients presented with similar dysphagia signs. The oral phase of the swallow was moderately atypical but the pharyngeal phase was significantly atypical. It was felt that intubation alone was not the sole causative factor of this dysphagia.

The polyneuropathy associated with sepsis in ICU may explain the atypical swallow patterns observed in these patients. The severity of the persistent dysphagia can cause serious respiratory and medical consequences. There is a need for further investigation of this phenomenon to identify patients who are at risk.

(P.50) BEHAVIOURAL DISTURBANCES IN OLDER MEDICAL PATIENTS
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Little attention has been paid to the prevalence and phenomenology of behavioural disturbances among medical patients despite awareness of the high prevalence of cognitive
impairment in this patient population. We screened 79 consecutive admissions to a department of acute geriatric medicine. Patients were evaluated over a 2 week period using a modified version of the brief agitation rating scale. Medication use, cognitive function and impact on nursing time were also measured.

The prevalence of behavioural disturbance in this population was 19/79 (24%). The most frequent behavioural abnormalities were restlessness (12), complaining (12) and screaming (6). The most common underlying disorders were dementia, stroke disease, personality disorder and paranoid psychosis. The behavioural disturbance was only documented in the medical notes in 7 patients (37%) and in only 5 cases was a psychiatric consultation sought. These findings demonstrate that behavioural disturbances are not only common but also under-documented in elderly medical patients and there is a need for training in the detection and management of behavioural symptoms in this patient group.

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RHEUMATOLOGY & REHABILITATION

(P.51) ACUTE SHORTENING TECHNIQUE AS TREATMENT IN LOWER LIMB TRAUMA

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In lower limb trauma where there is severe compound fracture, the successful treatment of this depends on adequate bone and soft tissue debridement. As a result, subsequent bone defects can lead to instability and often require large amounts of bone grafts, and major soft tissue reconstruction is required to obtain skin cover. Large soft defects can be reduced by primary bone resection and shortening of the limb. This will improve the chance of bone healing if performed in the presence of an external fixator, then lengthening at a site away from the traumatised area can gradually restore limb length.

Two cases are presented to demonstrate the effect of compression / distraction techniques on soft tissue and bone injuries in these difficult situations.

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(P.52) A COMPARISON OF TWO NOMENCLATURE SYSTEMS FOR PRIMARY SYSTEMIC VASCULITIS

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Recently, two sets of criteria have been proposed for the nomenclature of primary vasculitides, the 1990 American College of Rheumatology (ACR) classification criteria and the 1992 Chapel Hill Consensus conference (CHC) definitions. The aim of this study was to determine the concordance of these two systems in a cohort of patients with primary systemic vasculitis.

Patients with systemic vasculitis were recruited who had a biopsy proven diagnosis or, who had typical clinical features associated with a positive antineutrophil cytoplasmic antibody (ANCA). The case notes were reviewed and patients were classified according to both sets of criteria.

Twenty-six patients were recruited, 21 of whom had a positive biopsy. Applying the 1990 ACR criteria, the diagnoses were, Wegener’s granulomatosis -WG (15), Churg Strauss syndrome -CSS (4), polyarteritis nodosa -PAN (2) and unclassified (5). Using the CHC definitions, the diagnoses were WG (5), microscopic polyangiitis -MPA (10), PAN (1) and undefined (10). There was concordance in only 5 patients (all WG).

There is significant discordance between these two criteria sets. Since the ACR criteria does not recognise MPA, they tend to overdiagnose WG. In addition, the CHC criteria cannot be applied without a biopsy and therefore surrogate features which predict the underlying histology are required to allow more practical application of the CHC definitions.

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(P.54) SALIVARY SMEARS – A SIMPLE DIAGNOSTIC TEST FOR SJÖGREN’S SYNDROME

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The objective was to determine the value of examination of dried freshly produced saliva, under light microscopy, in patients with xerostomia related to secondary Sjögren syndrome.

Ten patients with known connective tissue disease or Rheumatoid arthritis attending rheumatology clinic were enrolled into the study, all with symptomatic xerostomia and dry eyes. All had an abnormal Schirmer’s test. Five normal patients were enrolled, all of whom were without clinical evidence of rheumatological disease. Control patients were enrolled who had no clinical evidence of rheumatological disease. A salivary sample was collected and examined by light microscopy. Serum was also examined for the presence of anti-Ro/La, rheumatoid factor, and anti-nuclear factor.

All ten patients demonstrated ‘reindeer horn’ type ferning of saliva, a pattern of shorter thicker clubbed branches of crystallised mucus, in contrast to the normal ferning pattern of the healthy subjects.

Conclusion: We have shown in this preliminary report that light salivary microscopy is a simple test easily performed in an outpatient setting which could be a useful diagnostic procedure in Sjögren syndrome.

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(P.55) IMPROVEMENT IN PULMONARY HYPERTENSION WITH KETANSERIN

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Primary pulmonary hypertension (PPH) typically affects young individuals, and has a high morbidity and mortality. Secondary pulmonary hypertension complicating connective tissue diseases likewise carries a poor prognosis. We evaluated the acute and chronic effects of ketanserin, a selective serotonin type-2 receptor antagonist in 2 patients with pulmonary hypertension.

In the acute study ketanserin was administered as a peripheral venous infusion during right heart catheterisation. Following encouraging results during catheterisation oral administration of ketanserin 160mg daily in divided doses was instituted.

In patient 1, a 30 year old female with probable PPH, serial
cardiac catheterisations over a 1 year period showed a significant, sustained reduction in both mean pulmonary artery pressure from 49 mmHg at baseline to 24 mmHg at 1 year (normal 10-20 mmHg) and pulmonary vascular resistance 1118 units at baseline to 288 units at 1 year (normal <200 units).

In patient 2, a 61 year old female with limited scleroderma (CREST) echocardiography after 1 month’s oral ketanserin showed a reduction in estimated peak right ventricular systolic pressure from 60 mmHg at baseline to 13 mmHg (normal range 15-30 mmHg).

The acute and long term response to ketanserin with improvement in pulmonary haemodynamics in these patients suggests that if a beneficial effect is detected during catheterisation long term oral therapy may be worthwhile.

OBSTETRICS & GYNAECOLOGY

(P.57) EVALUATION OF THE PERINATAL DAY CENTRE AT THE COOMBE WOMEN’S HOSPITAL

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The purpose of this study was to evaluate patient satisfaction with antenatal care provided in the Perinatal Day Centre (PNDC). A self administered questionnaire was administered to 61 consecutive patients.

The main indications for referral were suspected small-for-dates (34%), non-proteinuric hypertension (23%), glucose tolerance testing (15%), reduced fetal movements (10%) and post-term evaluation (7.5%); 3% were nulliparae.

Thirty-two percent of patients were reviewed in the PNDC on the day of referral; the rest within 7 days. Twenty eight percent of patients lived more than 10 miles from the hospital and 48% spent more than 30 minutes in travelling there. Eighty five percent of patients scored their level of satisfaction with the service provided in the PNDC as > 7 out of 10; only 6.5% would have preferred admission; 42% said that they would prefer to visit the PNDC 5 times per week to avoid admission. The main area of dissatisfaction related to the waiting time for review prior to discharge, with 69.5% of patients waiting over 3 hours.

Patients attending the PNDC report a high level of satisfaction; changes to reduce the visit duration have been introduced.

(P.58) DOES SCREENING OF FOLLICLE STIMULATING HORMONE HELP TO PREDICT FOLLICULAR DEVELOPMENT?

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An attempt to determine the relative value of routine screening of serum follicle stimulating hormone (FSH) at day 3 cycle in predicting the ovarian response to gonadotrophins stimulation in in vitro fertilisation (IVF), and to improve the outcomes.

In an open, descriptive cohort study, cycle day 3 FSH levels measured prospectively in 422 consecutive women in their first two IVF cycles (n= 565). The results were grouped for analysis by banded values for FSH into group A, B and C; where FSH levels were low (< 7.9 iu/l); normal though above average (≥8 - <10 iu/l) and moderate high (≥10 - <15 iu/l) respectively. Gonadotrophins for ovarian stimulation were commencing initially at 225 iu for group A & B and at 450 iu for group C.

IVF performance was poor in most aspects (total follicles, oocytes & embryos transferred) in group B comparing with group A or C; the cumulative ongoing pregnancy rate (PR) over 2 IVF cycles in group B; was 15% comparing with 27.6% in group A (p < 0.05) However there was no significant difference in PR in group C (20%) comparing with other two groups.

Cycle day 3 FSH screening is predictive of follicular development in IVF. High initial dose of gonadotropins help to improve the pregnancy rate in the presence of moderate high level of FSH.

(P.59) THE CHANGE OF TAKING-UP THE ESSENTIAL PRE-CONCEPTUAL MEASURES BEFORE COMMENCING AN IN VITRO FERTILISATION PROGRAMME

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To examine the change of taking-up the essential pre-conceptual measurements; Rubella immune status, cervical cytology and prophylactic folic acid intake; following specific advice and publicity through 3 general public meetings with new patients prior to in vitro fertilization (IVF) programme.

In 1994 we studied 281 new couples for IVF for the presence of some specific pre-conceptual data (group A). In this study we follow-up the same intake in another 229 new women interviewed to commence IVF programme from January 1995 till September 1995 (group B).

In group (B) the taking-up measurements were dramatically improved. However, 30% and 18% still did not have Rubella immunity test and cervical cytology performed; compared to 54% and 36% in group (A) respectively (P<0.001). While folic acid intake was sustained at >90% in both groups.

Following specific advice the rate of taking-up of pre-conceptual measurements prior commencing IVF programme was improved. There is a future need for continuous enhancement of the publicity and advice regarding the importance of preconceptual measurements.

(P.60) ESTABLISHMENT OF AN INTRACYTOPLASMIC SPERM INJECTION (ICSI) PROGRAMME FOR THE TREATMENT OF MALE FACTOR AND IDIOPATHIC INFERTILITY

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The development of intracytoplasmic sperm injection (ICSI) for the treatment of severe male infertility[1] involves the direct injection of a single sperm into the oocyte and is a specialized technique presently available in few centres throughout the world.
The aim of this study was to introduce ICSI to Ireland for treatment of specific cases of male factor infertility. Following an introductory proving period using the bovine model, thirty-eight couples with infertility attributed to the male were selected for an ICSI attempt. Ovulation induction, oocyte retrieval and luteal management were as described for conventional IVF. The average age of patients selected for ICSI were 34.5 ± 3.7 years and 36.4 ± 4.6 years for the female and male respectively, with an average duration of infertility of 4.8 ± 2.6 years.

Table 1. Overall outcome following 38 ICSI cases.

| Per cycle started | Number of cycles started | 38 |
|-------------------|--------------------------|----|
| Number of oocyte retrievals (%) | 34 (89%) |
| Embryo transfers (%) | 26 (72%) |
| Positive hCG (%) | 7 (18%) |
| Viable pregnancies ultrasound (%) | 7 (18%) |
| Implantation rate (%) | 9/60 (14%) |

Preliminary results from the 38 cases studied demonstrated that fertilization and embryo transfer was obtained in 72% of cases and pregnancy obtained in 7/26 (25%) of those achieving a transfer giving an implantation rate of 14%.

References
1. Palermo, G., Joris, H., Devroey, P., Van Steirteghem, A. C. (1992). Fertilization and embryo transfer following intracytoplasmic injection of single spermatozoon into an oocyte. Lancet 1992; 340, 310: 17-18.
2. Harrison, R. F., Barry-Kinsella, C., Kondaveeti, U., Gordon, A. C., Hannon, K., Drudy, L., Hennelly, B., Keogh, I., Nargund, G., Verso, J. Irish Med. J. 1992; 85: 2, 63-65.

(P.61) REVIEW OF RED CELL TRANSFUSION IN GYNAECOLOGICAL SURGERY
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The aim was to review all red cell transfusions in gynaecological surgery in 1994. A retrospective review of Blood Bank Records and individual charts was carried out. 4611 patients underwent gynaecological surgery; 97 (21%) were cross matched and 60 (1.3%) were transfused, 184 units were transfused. There was no single unit transfusions. The mean number of units transfused per patient was 3. This accounted for 33% of all units transfused this year. 92% of patients were undergoing elective surgery. The overall cross match/transfusion ratio was 2.

Intraoperative difficulty was recorded in 56% of cases. 64% of patients were transfused perioperatively and 36% postoperatively. The percentage of patients requiring blood transfusions in the the main individual operation categories was as follows:

- Radical surgery: 57%; total abdominal hysterectomy and salpingo-oophorectomy, 17%; vaginal hysterectomy and repair, 16%; subtotal abdominal hysterectomy, 30%; vaginal hysterectomy alone 12.5%; and total abdominal hysterectomy alone 5%.

- Adverse reactions to transfusions were seen in 5% of patients.

Conclusion: The majority of patients transfused were undergoing elective surgery. Vaginal hysterectomy was associated with greater blood loss than abdominal hysterectomy. Only half of all units cross matched were transfused.

(P.62) A CASE OF SUBACUTE CEREBELLAR DEGENERATION SECONDARY TO OVARIAN CARCINOMA
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A 64 year old woman presented with a three day history of paraesthesia in her lower limbs and difficulty walking. Neurological examination revealed sensory loss in her limbs and truncal ataxia. Romberg's sign was positive. Pelvic examination revealed a large pelvic mass that was distinct from the uterus.

Routine blood investigations were normal. CSF culture, CT brain and serum electrophoresis were negative. Anti-purkinje cell antibodies were not present. CA-125 levels were elevated at 159 micrograms/litre.

Laparotomy revealed a 20 cm left ovarian tumour. A total abdominal hysterectomy, bilateral salpingo-oophorectomy and omentectomy was performed. Histology revealed a poorly differentiated clear cell adenocarcinoma of the left ovary. The capsule was intact and peritoneal washings were negative. She made a good postoperative recovery. She received six courses of carboplatin without ill effect. Her neurological symptoms resolved.

Subacute cerebellar degeneration can occur as a paraneoplastic disorder in ovarian carcinoma. The mechanism by which cancer can cause neurological disorders is not fully understood. Paraneoplastic cerebellar degeneration occurs with or without the presence of Purkinje cell antibodies.

(P.63) CONVENTIONAL DILATATION AND CURETTAGE VERSUS ENDOMETRIAL PIPELLE BIOPSY
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Dilatation and curettage (D+C) is the most common operation performed in the U.K. The liberal use of D+C has been criticised.

The objective of this study was to evaluate the use of outpatient endometrial pipelle biopsy and determine its safety in terms of detecting abnormalities. Complications and financial costs were also evaluated.

Data was reviewed from an active gynaecological unit from February 1993 to January 1995, using theatre and outpatient records.

A total of 303 D+Cs and 104 endometrial pipelle biopsies were performed in this period. 9 malignancies were detected by D+C and 1 by pipelle biopsy. A total of 24 and 3 benign abnormalities were detected by each method respectively. There was a higher complication rate in the D+C group but the failure rate was higher in the endometrial pipelle biopsy group. The monetary savings over this period is estimated at E20,307. There were no missed malignancies to our knowledge over the 8 year period since endometrial pipelle biopsy was introduced to this hospital.

Our study indicates that outpatient endometrial pipelle biopsy appears to be safe, efficacious and economical.
**Ultrasound and its Correlation with Clinical Findings in Gynaecology**

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While ultrasound findings may sometimes be in conflict with clinical examination, it is the case that there are instances when ultrasound findings have, following subsequent laparotomy, been found to be wholly incorrect. It is therefore not surprising that there remain some gynaecologists who view ultrasound with scepticism, preferring to rely solely on their clinical findings. There have been few studies that directly compare clinical, ultrasound and surgical findings in the detection of pelvic masses.

The objective of the study was firstly to directly compare the reliability of clinical and ultrasound examination findings in the detection of pelvic masses proven by subsequent laparotomy and secondly to determine the accuracy of ultrasound in detecting malignancy.

This was as a retrospective review of 86 women who underwent a laparotomy because of a pelvic mass between January 1993 to February 1995. Information was obtained from theatre and patient records. Real time abdominal ultrasound was used. Findings at laparotomy were correlated with clinical and ultrasound findings.

The sensitivity and specificity of ultrasound in detecting a uterine mass was 94% and 99% respectively. This contrasts sharply with clinical examination (sensitivity = 74% and specificity = 94%). Similar findings were obtained when ultrasound was compared to clinical examination in detecting ovarian masses. Ultrasound is capable of predicting benign disease with reasonable confidence but the prediction of malignancy is less reliable.

In conclusion, ultrasound is more sensitive and specific in detecting pelvic masses compared to clinical examination. The scepticism that some gynaecologists harbour about this investigative tool is unwarranted.

**Pregnancy-induced Osteoporosis: Need to Increase Calcium and Vitamin D Intake**

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Osteoporosis occurring during pregnancy or lactation is a rare event despite the homeostatic demands of the foetus for calcium. We investigated the case of a 24 year old woman who, a rare event despite the homeostatic demands of the foetus for calcium. We investigated the case of a 24 year old woman who, during pregnancy, developed severe back pain due to a vertebral compression fracture. Bone mineral density (BMD) was measured by dual-energy X-ray absorptiometry. Calcium metabolism and bone turnover were studied.

There was a severe reduction in BMD in the spine (Z-score = -4.8) and femoral neck (Z-score = -3.6); but, serial measurements showed no further reduction in BMD. Indices of calcium metabolism and bone turnover were normal.

Pregnancy-induced osteoporosis is a severe but self-limited disorder in calcium homeostasis of unknown aetiology. Women with low BMD prior to pregnancy may be at increased risk. In view of increased demand, supplemental calcium and vitamin D should be considered during pregnancy and lactation.

**Pregnancy-induced Osteoporosis: Need to Increase Calcium and Vitamin D Intake**

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The aim of this study was to assess the clinical status on admission and the critical care management of children presenting with meningococcal infection. This was a retrospective study of the charts of 46 consecutive admissions.

Mean age was 3.43 years (±3.46). The average duration of symptoms prior to admission was 20.4 hours (±11.09). On admission, 17.4% were hypotensive, 45.6% had clinical signs of haemodynamic instability and 54.8% of cases that had a Wood gas analysis on admission had a metabolic acidosis (Bases excess < -5.0). The mortality rate was 10.9%. 80% of deaths were hypotensive on admission and all had a metabolic acidosis. Of the 41 survivors 9.7% were hypotensive on admission, 39% had clinical signs of cardiovascular compromise, 78% were admitted to the high dependency unit, 25% required invasive pressure monitoring and 7.3% were ventilated and received inotropic support.

In this study children presenting with meningococcal infection have a high incidence of cardiovascular instability. Successful management is dependent on early presentation and initiation of therapy and on aggressive intensive care monitoring and support of the cardiovascular and vital organ systems.

Reference

1. Mercier, J. C., Beaufils, F., Hartman, J. F., Atzema, D. Haemodynamic patterns of meningococcal shock in children Critical Care Medicine 1988; 16: 27-33.

**The Crying Pattern of Preterm Infants**

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The normal crying curve and incidence of colic for term infants are well known. We studied prospectively the crying pattern and the incidence of colic in preterm infants to determine if prematurity influenced these behaviours.

The subjects were consecutive preterm infants admitted to the Cork neonatal units for two and a half months from July 1995. A continuous 24 hour diary was completed on each infant by the neonatal nurses, when the babies were on full oral feeding and no longer required intensive care. The parents completed the diaries after discharge. Colic was defined according to Wessel’s rule of threes. Two unwell babies were excluded. The duration of follow up was from 2 to 16 weeks.

Fifty infants were recruited and 45 completed the study (4 lost to follow up and one withdrawn due to sepsis). Mean range gestational age was 31 (26-36) weeks and birthweight was 1.52 (0.64-2.4) kg. The mean (range) age of crying onset was x(y-z) weeks; crying peak was x(y-z) weeks and crying offset was x(y-z) weeks. One baby developed colic in the period of follow up.

Conclusions: The incidence of Wessel’s colic was less than expected in these preterm babies. The crying pattern according to chronological age was different from that described in term babies. In general preterm babies had a delayed onset of crying, but the pattern became similar to term babies when allowance was made for gestational age. The findings suggest that the crying patterns of early infancy have a developmental basis.
A SIBLING CONTROLLED STUDY OF COGNITIVE, EMOTIONAL AND BEHAVIOURAL SEQUELAE TO REYE'S SYNDROME

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We re-evaluated 18 children who had had RS (1979-86), with their closest-age siblings using the Wechsler Scales, Coopersmith Self Esteem Inventory and Achenback Child Behaviour Checklist (ACBC) (Duffy J. et al 1991). The RS patients' means were consistently lower than that of their sibs. However, comparison of mean raw data, using "T-tests", yielded significant differences only in the ACBC scores, in that RS children exhibited significantly more problem behaviours than their sibs (p=0.033). After categorisation of IQ data, further comparisons between the groups (using X²), found RS patients were significantly more likely to score "below average" in tests of Verbal IQ compared to their sibs (p=0.04). Age of onset and clinical stage were also found to be more important predictors of outcome. Children less than 1 year of age at onset of RS had significantly lower IQ scores on all measures of cognitive ability (p=0.003) and more problem behaviours (p=0.01) than children over 1 year of age. No significant differences were found in comparison with sibs. Clinical Stage to which RS progressed affected only Verbal IQ scores. Children in whom consciousness had been impaired had significantly lower IQ scores than both their sibs and RS children in whom consciousness was less impaired (p=0.02). In conclusion outcome remains cautiously positive, with 13/18 RS children attending mainstream schools or in employment without apparent difficulties.

HYPERNATRAEMIC DEHYDRATION AND BREASTFEEDING POLICY: ARE NINE WHO/UNICEF STEPS SUFFICIENT?

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A national breastfeeding policy was introduced by the Department of Health in 1994. Factors identified for promotion of breastfeeding were based on the WHO/UNICEF "Ten Steps for Successful Breastfeeding". We present clinical cases which suggest that one step may need to be modified.

The charts of breastfed babies admitted to the special care baby unit were reviewed for one year following the introduction of the national breastfeeding policy to this hospital.

Thirteen term breastfed babies were admitted because of fever and dehydration. None of the babies had water or bottle feed supplements. Ten of the thirteen mothers were primigravida. Eleven babies were admitted in the six months following the introduction of an exclusive breastfeeding policy. The nursing staff were then alerted to the risk of dehydration, but two further babies of mums committed to exclusive breastfeeding were admitted in the subsequent six months. Routine biochemistry, haematology and a limited septic screen was performed in all babies. Three of the thirteen babies had lumbar punctures. The mean (range) weight loss on admission was 9.5 (4.1-16)%. The mean (range) plasma sodium level was 147.6 (138-156) mEq/l and the mean (range) urea was 6.5 (2.1-13.4) mEq/l. There was no growth from the cultures of the blood, urine, CSF and swabs. All the babies were given intravenous fluids and parenteral antibiotics for 48 hours. The outcome was satisfactory in all babies and breastfeeding was reestablished in eleven of the thirteen babies.

Conclusions: The common factor to these babies was inadequate fluid intake prior to admission associated with strict adherence to the policy, and avoidance of all supplements including water. We conclude that the WHO/UNICEF step 6 "not to give food or drink other than breastmilk unless medically indicated" is too restrictive in the immediate postpartum period.

PREVALENCE AND FREQUENCY OF HEADACHE IN SCHOOL CHILDREN

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The prevalence and frequency of headache in 2745 schoolchildren aged 4 to 19 years old from randomly selected schools in Dublin, Wicklow and Kildare was assessed by questionnaire.

42.5% of children reported headache in the previous 12 months 44.8% of girls and 40.5% of boys reported headache (P < 0.0001).

0.6% of children reported daily headache
5.9% of children reported weekly headache
9.4% of children reported monthly headache
22.5% of children reported headache less often than monthly

The percentage of children with headache at each frequency, other than daily, increased with increasing age. In girls headache showed a marked rise at ages 14, 15 and 16 years.

Reported prevalence of headache in the past year in 5 to 15 year old Aberdeen children was 66% and 48% was recorded for Swedish children aged 8, 11, 13 and 17 years old. This study is the first community based prevalence study of headache in Irish schoolchildren.

DYSPHAGIA IN CHILDREN WITH NEURODEVELOPMENTAL HANDICAP

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Our aim was to test the hypothesis that there is no correlation between the type of feeding & swallowing disorder the child has with the neurological diagnosis or the radiological findings. A further purpose was to develop a classification of the feeding & swallowing disorders which would guide us towards a management plan. A retrospective analysis of the data collected between the years 1988-94 from the feeding & swallowing clinic at Booth Hall Children’s Hospital was done. 73 children were included in our study. Ages ranged from 4 months to 17 yrs. All the children were assessed by the members of the feeding & swallowing team and had videofluoroscopic assessment by the same radiologist. Neurological signs, speech therapy assessments & videofluoroscopy findings were compared between children with spastic quadripleasis & those without. Significant differences were noted. A clinical classification was devised using cluster analysis. We conclude that there is no causal relationship between the neurological diagnosis & the type of dysphagia. There are three distinct groups of children who require different strategies of clinical management.
PUBLIC HEALTH MEDICINE

(P.73) USE OF OPTICAL SCANNING TECHNOLOGY IN THE SURVEILLANCE OF SURGICAL SITE INFECTIONS
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Surveillance commenced in January 1995 to continuously monitor the incidence of surgical site infections (SSI). Employing modern optical scanning technology (Formic for Windows version 2.0, Formic Limited, London) a questionnaire was designed, which required minimal completion time. The questionnaire includes relevant data based on the American National Nosocomial Infections Surveillance System for SSI including the SSI risk index.

Surveillance commences at the time of surgery and continues until the patient’s discharge. Optical scanning technology allows rapid reading of surveillance questionnaires thereby bypassing the bottleneck of manual data entry. By October 1995, details of 2,156 procedures had been recorded. The crude SSI rate for these patients was 2.7%. The patient risk index used demonstrated that there were increased chances of developing SSI in certain patient groups. Seventy-nine per cent of SSI had presented by the 10th post-operative day. The length of stay increased by an average of 4 days in patients developing SSI.

Regular feedback to individual surgeons, theatre and ward staff maintains awareness and highlights possible problems. We recommend optical scanning technology to all those engaged in surveillance work. This system would be especially useful were data collected is transported from outlying hospitals to a central receiving centre for collation and analysis.

(P.76) FRANCIS CRUMPE MD, RED TIDE AND TETANUS
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In 1872 Francis Crumpe published a paper in which he described the therapeutic effect of poisonous mussels (PSP) on a case of tetanus. He obtained the mussels from Tralee Ship Canal on the occasion of its infrequent emptying, and entertained the idea of using them in tetanus after treating a young girl with PSP who recovered after 24 hours. Prior to the use of PSP he described it’s paralytic effect in two cockrels who both recovered. In concluding his successful use of PSP he speculated as to the clinical nature and role of the toxin Tralee Ship Canal was opened in 1846. The water was relatively stagnant and would have contained plenty of nutrients. As such it would have been an ideal habitat for toxic algae which may have been brought across the Atlantic as spores in bilge water. The emptying of the canal may well have been done at times of algal blooming. This is the first Irish Report of PSP and a most remarkable use of saxitoxin (?) in the treatment of tetanus, antedating the current management by seventy years.

References.
1. Crumpe, F. Observation on the Musculus Venosus in tetanus. Dub J Med. Sci. 1872; 54: 257-62
2. Andersen, D. M. Red Tides Scientific American 1994; 271: 52-58.

(P.77) SMOKING IN IRISH MEDICAL JOURNALS: A CONTENT ANALYSIS 1960-94
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This study was carried out to quantify the published research on smoking in Irish medical journals; to ascertain the type of research carried out; and to identify the authors of that research. Five Irish medical journals published between 1960-94 were studied (The Irish Journal of Medical Science, The Journal of the Irish Medical Association/The Irish Medical Journal, The Journal of the Irish Colleges of Physicians and Surgeons and Forum. During the 35 years under study, 50 papers explicitly dealing with smoking were published. Only 2 papers appeared in Forum. There was a decline in published papers in the eighties with a resurgence in the early nineties. Of the 50 papers, a majority were observational and ten were editorials. Only one paper dealt with smoking cessation, and one with preventive work. General practitioners were poorly represented as authors. One doctor (Prof. R. Mulcahy) published at least one paper on smoking in each quinquennium since 1960. This study underlines the relative insignificance of smoking as a topic for research in Ireland. A major sea change in attitude will be required if the government’s targets for smoking cessation are to be realised, particularly if they are to be achieved by relying on the medical profession.

(P.78) DOCTORS KNOWLEDGE OF COST OF RADIOLOGICAL INVESTIGATIONS
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Radiology represents a major cost centre within a hospital. Lack of awareness of cost amongst doctors may result in the inappropriate requesting of radiological services. This study assesses doctors knowledge of the cost to a tertiary referral hospital of commonly performed radiological procedures and investigations.

Doctors were asked to estimate the cost of 9 items namely - Chest X-ray, Arch Aortogram, Ultrasound Abdo., Lumbosacral Spine, Barium Enema, CT Brain, CT Abdo., Ultrasound Abdomen, I.V.P. and Percutaneous Gastrostomy tube insertion under radiological screening.

60 Doctors in St. Vincent’s Hospital were surveyed. Doctors as a group overestimated the cost of all 9 individual tests, by margins ranging from 10% (I.V.P. & Gastrostomy insertion) to 100% (CT Brain/CT Abdo.)

The total cost to the hospital of all 9 items was £650. Consultants overestimated this total cost by 107%, followed by Registrars, Interns and S.H.O’s who overestimated the total cost by margins of 51%, 43% and 12% respectively.

Conclusion: Doctors tend to overestimate what radiological procedures and investigations cost a public hospital, often by quite wide margins. Thus, any excessive requesting of radiology services by doctors is not due to a lack of awareness of their true cost to the hospital.

(P.79) PREMATURE MORTALITY IN SMALL AREAS
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The objective was to identify the main disease groups contributing to premature mortality in Dublin; in each Community Care Area (CCA); and in each of the District Electoral Divisions.
The findings suggest that tHcy is an independent risk factor for CHD with no threshold level.

levels of homocysteine (geometric mean 13.5 (12.6 - 14.3)μmol/L vs 11.9 (11.3 - 12.6)μmol/L; p = 0.005. There was a graded increase in the relative risk (odds ratio; OR) of CHD in the 2nd, 3rd and 4th quartile of tHcy (OR 1.4, 1.9, 2.2; trend p = 0.006) relative to the first quartile. Adjustment for age, town, social class, body mass index, smoking, physical activity, alcohol intake, hypertensive status, serum cholesterol and serum creatinine did not attenuate this association. (OR 2.1, 2.3, 2.7; trend p = 0.04). The findings suggest that tHcy is an independent risk factor for CHD with no threshold level.

By emphasising deaths in younger individuals YPLL is a valuable tool for planning and monitoring local health promotion initiatives.

**Reference**

1. MRC Vitamin Study Research Group. Prevention of neural tube defects: results of the Medical Council Research vitamin study Lancet 1991; 338: 131-7.
RHEUMATOLOGY

(P.83) MORE EXPERIENCE WITH USING THE PINS AND RUBBER BANDS TRACTION SYSTEM (SUZUKI) FOR MANAGEMENT OF THE INTRA-ARTICULAR PHALANGEAL FRACTURES

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Unstable intra-articular fractures with or without dislocation of the phalangeal joints often lead to joint stiffness and loss of function.

Nine patients with comminuted intra-articular phalangeal fractures were treated in our unit by dynamic external fixator using "Pins and Rubber Bands Traction System". The mean age was 32.3 years, and the follow-up average was 4.6 months.

Five patients had full and good range of motion in the involved joints. Three patients had poor results, and one patient underwent open reduction one week following the original procedure.

The technique and our results are discussed. This dynamic frame is compact, comfortable for the patient, easy to apply and allows early mobilisation. Careful selection of patients and close follow-up in the first few weeks are needed.

GENERAL PRACTICE

(P.84) STORAGE AND HANDLING OF VACCINES BY GENERAL PRACTITIONERS

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This study examines how GP's store and handle vaccines. All 144 GP's in a health board region were invited to take part. GP's were interviewed in their practice premises about how they deal with vaccines. Fridges were examined and temperature recorded post interview. Oral polio was taken from 20 randomly selected fridges for potency testing. Cold chain monitors and freeze watch indicators were used to monitor batches of vaccine stored.

Of the 144 GP's, 142(98.6%) agreed to participate, 140 used 111 fridges to store vaccine, 2 store vaccine at room temperature. Of the 111 fridges, 6 (5.4%) had the power supply safeguarded, 9 (8.1%) had thermometers, 36 (32.4%) had vaccine only stored therein. During defrosting, vaccine was adequately protected in 22 (19.8%). Of the 138 GP's who use multi-dose vaccine vials, 133 (97.2%) keep them for further use at the end of a day/session, 3 store them at room temperature. 42 (37.8%) fridges had indicators used to monitor batches of vaccine stored.

This study indicates that vaccine potency could be seriously compromised due to breaks in the cold-chain and suggests the need for guidelines to be drawn up, implemented and monitored to ensure the integrity of immunisation schemes.

PSYCHIATRY

(P.86) GENDER AFFECTS OBSTETRIC COMPLICATIONS IN SCHIZOPHRENIA AND MANIA

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The purpose of this study is to examine the relative importance of obstetric complications (OC’s) in the aetiology of schizophrenia and mania.

Using the Dublin Psychiatric Case Register, birth records of 635 patients with an ICD-9 diagnosis of schizophrenia or mania were obtained. These records were evaluated for obstetric complications using two scales, the Lewis, Owen and Murray scale (LOM) and the Parnas scale. The mothers of those going on to develop schizophrenia did not differ from those going on to mania in regards maternal age, parity, social class, or period of pregnancy. However, males who developed schizophrenia when compared to males developing mania, experienced significantly more OC’s when rated by the LOM scale and more frequent OC’s on the Parnas scale of greater severity. No significant differences were found between females with schizophrenia and those with mania.

References
1. Lewis, S. W., Owen, M. J., Murray, R. M. Obstetric complications and schizophrenia: methodology and mechanisms. In: Schultz, S. C., Tamminga, C. A. eds. Schizophrenia: Scientific progress. New York: Oxford University Press, 1989.
2. Parnas, J., Schulzinger, F., Teasdall, T. W. et al. Perinatal complications and clinical outcome within the schizophrenia spectrum. British Journal of Psychiatry 1982; 140: 416-420.
**FUNCTIONING IN FIRST EPISODE PSYCHOSIS**

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The aim was to evaluate the diagnosis, symptomatology and level of functioning of patients presenting with a first episode of psychosis to a catchment area service and a private psychiatric hospital. All patients presenting with a first episode of psychosis were assessed using the SCID-P, the Positive and Negative Syndrome Scale (PANSS) and the Global Assessment of Functioning scale (GAF).

Fifty-eight patients (34 male, 24 female) ranging in age from 15 to 65 years (Mean ± SD = 28.4 ± 10.8) were included in the study. The mean total PANSS score was 84.8 (SD ± 21.6) and was strongly correlated with the GAF score (p < 0.001) but independent of age (p = 0.16). Males had a significantly lower GAF score compared to females (p = 0.04) but there was no gender difference in the total PANSS score (p = 0.20).

Twenty-five patients (43%) had a lifetime prevalence of drug abuse or dependence but only 12 patients (21%) had signs of drug abuse or dependence in the month prior to presentation. Level of functioning was strongly influenced by the severity of psychopathology. Substance abuse is common in individuals presenting with a first episode of psychosis.

**THE CLOSURE OF AN INSTITUTION-PROFILE OF PATIENTS REMAINING**

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Psychiatry has moved from custodial care towards care in the community. Adequate reprovision will have to be made in order to discharge the remaining continuously hospitalized patients. The objectives of this study were to describe an entire long-stay hospital population, to examine the differences between the old and new long stay groups within this population and to evaluate the needs for community residential and day care facilities in order for hospital closure to take place. The study group consisted of the total long-stay population of St. Davnet’s Hospital, Monaghan. The patients were assessed using the Community Placement Questionnaire (CPQ).

One hundred and twenty four patients were included in the study. Fifty-six were female and 89% were single. The mean age of the total group was 68.7 years. The majority suffered from schizophrenia. The assessment revealed a globally disabled group with multiple handicaps. The new long-stay group were disabled as the old long-stay group. The patients were characterised into four groups with regard to placement recommendations. These were a specialist unit for chronically disturbed geriatrics, a geriatric unit, a high support hostel and a medium support hostel.

The remaining population of this hospital were highly dependent with multiple handicaps but would live in community with adequate support. There is little difference between the needs of the old long-stay and those of the new long-stay.

**FREQUENCY OF HLA A9 (A23/A24) IN FAMILIAL SCHIZOPHRENICS AND CONTROLS**

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Failure of the immune system to identify self peptides is likely to lead to the development of an autoimmune reaction. Susceptibility to autoimmunity is strongly influenced by genes clustered in the HLA region (chromosome 6p) particularly class I (A, B and C) and class II (D, Q and P). It has been suggested that there is an autoimmune component in the aetiology of schizophrenia. Of many conflicting reports from case/control studies using HLA antigens the most consistent finding has been an increased frequency of HLA-A9 (now split into A23/A24). Additionally, a susceptibility locus for schizophrenia has been reported near the HLA locus. To attempt to confirm the HLA A9 hypothesis, we have genotyped a preliminary sample of 63 familial schizophrenic probands and 77 unrelated controls at the HLA-A region, using a PCR-SSOP technique. The frequency of HLA-A24 (the major component of A9) in patients and controls respectively was 12.5% vs 15.5%. These findings do not support the hypothesis. Some of the discrepancy may be due to unspecified cross-reactions produced by commercial antisera used in the microlymphocytotoxicity method of previous studies. However it is also possible that the HLA association with schizophrenia may reflect linkage disequilibrium with unidentified gene(s) within the HLA region which is less strong in the Irish population.
(P.91) DOPAMINE D3 MS1 GENOTYPES IN FAMILIAL SCHIZOPHRENICS AND CONTROLS

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Schizophrenia is a common mental disorder affecting about 1% of the general population with a devastating disturbance of mind and personality. Family, twin and adoption studies have demonstrated that the disease is largely genetic with a polygenic mode of transmission. Dopamine receptors have been implicated in the aetiology of the disease. As yet 5 dopamine genes have been identified (D1-D5). In particular the D3 receptor is expressed in the limbic regions of the brain, implicated in the control of emotions. Association studies of a D3 polymorphism (Glycine to Serine substitution at position 9) with schizophrenia have produced conflicting findings, many of which, however, have demonstrated a significant excess of homozygosity, or excess of the 1-1 genotype at this polymorphism. In this study, 200 familial schizophrenics and 239 Irish unrelated controls were genotyped. The result show a small increase in the frequency of the 1-1 genotype which did not attain statistical significance (patients, 41.5% vs. controls, 38.5%). Homozygosity (alleles 1-1 and 2-2) was also slightly increased in the patients (patients, 55.5% vs. controls, 48.9%). The small increase in the frequency of the 1-1 genotype and of homozygosity in the patients is in keeping with earlier findings but suggests that the effect, if any, of D3 sequence variation in the development of the disease is small.

(P.94) CAN GENERAL PRACTITIONERS PRESCRIBE PSYCHOTROPIC MEDICATIONS? THE PATIENTS' VIEWS

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Lack of information about general practitioners' (GP's) ability to prescribe psychotropic medication may affect patients' compliance. In this study, 73 out of 75 patients attending a psychiatry out-patient clinic completed a questionnaire which documented how many had run out of medication, the steps taken if they had and the role each patient thought their GP played in their treatment. 82% indicated that their GP knew what their current medication was but only 46% thought that their GP could provide them with a prescription if they did not have one from the clinic. This figure was similar in those who had (21%) and had not (79%) run out of medication in the past. On running out of medication, 42% of patients waited until their next appointment, 29% attended their GP and the remainder either contacted the department or went to a chemist. In conclusion, many patients do not appreciate the entitlement of their GP's to prescribe psychotropics for them.

(P.92) PARENTAL SOCIAL CLASS IN PATIENTS WITH SCHIZOPHRENIA AND MANIA

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Literature regarding whether or not the social class distribution of patients with psychiatric illness may differ from the general population remains controversial. We sought to clarify this by examining social class at the time of birth, to see whether patients with serious psychiatric illnesses (schizophrenia and mania) differ from the general population.

Paternal occupation of 450 schizophrenic patients, and 77 manic patients, from the Dublin Psychiatric Case Register, were obtained from birth registration details and categorised according to Central Statistics Office criteria. The same-sex previous live birth was used as a matched control.

There was no difference between the social class of patients with schizophrenia or mania (p=0.32). Neither patients with schizophrenia (p=0.31) nor mania (p=0.153) differed from controls in social class distribution. Paternal social class was found to be related to amount of time spent in hospital (p=0.001, mean=439.62), and educational age (p<0.001, mean=15.01) and "age at onset of the illness" (p=0.03, mean=31.59).

These results suggest that social class of origin may not be related to the development of either schizophrenia or mania. However, social class of origin may be relevant in terms of presentation of schizophrenia for treatment.

(P.95) EXECUTIVE FUNCTION AND NEGATIVE SYMPTOMS IN CHRONIC SCHIZOPHRENIA

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Cognitive function is widely recognised to be impaired in schizophrenia but there is an ongoing debate as to whether this impairment is generalised or localised, progressive or static, similar in both sexes, or related to symptoms. Using the Positive and Negative Syndrome Scale (PANSS) we measured psychopathology in 48 chronic in-patients (27M, 21F; mean age 68.0±12.7) who satisfied Feighner criteria for schizophrenia. Subsequent to this, we assessed their global cognitive function using the Mini-Mental State Examination (MMSE) and their frontal cognitive function using a new instrument, the Executive Interview (EXIT).

Poor performance on the EXIT was associated strongly with increasing severity of negative (r=-0.74, p<0.001) but not positive (r=-0.09, NS) symptoms, in both males (r=-0.73, p<0.001) and females (r=-0.76, p<0.001). Overall EXIT performance declined modestly with increasing age (r=-0.32, p=0.05) but this phenomenon was confined to females (r=-0.64, p=0.01; males: r=-0.13, NS). MMSE performance was also associated with negative symptoms (r=-0.67, p<0.001) but decreased more prominently with age (r=-0.59, p<0.001) and showed no gender difference.

Frontal dysfunction in schizophrenia appears to be intimately related to negative symptoms over the course of severe chronic illness, and may reflect among males a more static trait deficit than is accessed by the MMSE.

This study was supported by the Stanley Foundation.
There were 14 males and 10 females in the responding group.

While determinants of the course of schizophrenia are unclear, emerging evidence suggests that the longer psychosis proceeds unchecked before initiation of anti-psychotic therapy, the poorer may be long-term outcome. We have reported that, among older in-patients, increasing duration of initially untreated psychosis in the pre-neuroleptic era was associated with a deterioration to a state of muteness (after controlling for intervening variables). The current survivors of this population have now been examined more extensively using the Positive and Negative Syndrome Scale (PANSS), the Mini-Mental State Examination (MMSE) and the Executive Interview (EXIT).

Responses were received from 28 (93%) of the 30 patients.

A questionnaire comprising 10 questions was circulated to patients who are selected and who agree to participate in the Royal College examinations play an important role. As psychiatrists and exam organisers, we should be aware of the potentially stressful experience which this might present.

The purpose of our study was to elicit attitudes to the exam, and also knowledge of the examination procedure.

A questionnaire comprising 10 questions was circulated to 30 patients who had participated in the Royal College examinations.

Responses were received from 28 (93%) of the 30 patients. There were 14 males and 10 females in the responding group. None of the patients had previously participated in the examinations. All of the respondents (n=28) felt that the examinations.

We discuss the case of a fourteen year old boy who presented with bilateral ptosis present since birth, microcephaly and pigmentary retinopathy(10). He was found to have mild facial and proximal limb weakness. Creatinine kinase and LDH were raised.

Muscle biopsy showed ragged red fibres consistent with a mitochondrial myopathy(1). Electron microscopy showed abnormal mitochondria.

The term mitochondrial myopathy describes a diverse range of clinical disease(13) and this is discussed.

References
1. McKechnie, N. M., King, M., Lee, W. R. Retinal pathology in Kearns Sayre Syndrome. Br. J. Ophthalmol. 1985; 69: 63-75.
2. Johns, D. R. Mitochondrial DNA and disease. NEJM 1995; 10: 638-644.
3. Hammans, S. R., Morgan-Hughes, J. A. Mitochondrial myopathies: Clinical features, investigation, treatment and genetic counselling. In: Shapira, A. V. H., Di Mauro, S., ed. Mitochondrial disorders in Neurology. Oxford: Butterworth Heinemann, 1994.
(P.100) PHENYTOIN INDUCED LYMPHADENOPATHY (A CASE STUDY OF THE PHENYTOIN HYPERSENSITIVITY SYNDROME)

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We describe the case of a 37 year old woman who developed an adenopathy while on phenytoin for new onset complex partial seizures.

She developed a vasculitic skin rash with pruritis and oedema associated adenopathy, low grade fever and mouth ulcers.

Lab tests showed leucocytosis, eosinophilia and abnormal liver function. Skin biopsy indicated an inflammatory picture without vasculitis. CT thorax confirmed axillary and para-aortic adenopathy. Lymph node biopsy confirmed a reactive lymphadenopathy.

References
1. Harris, D. W. S., Ostlere, L., Buckley, C., Whittaker, S., Swiny, P., Rustin, M. H. A. Phenytoin induced pseudolymphoma. A report of a case and review of the literature. Br. J. Derm. 1992; 127: 403-406.
2. Rapp, R. P., Norton, J. A., Young, B., Tibb, P. A. Cutaneous reactions in head injured patients receiving phenytoin for seizure prophylaxis. Neurosurgery 1983; 13: 272-5.
3. Gam, R. A., Neal, J. A., Connell, F. G. Hydantoin induced pseudopseudolymphoma. Ann Intern. Med. 1968; 69: 557-68.

(P.101) PUDENDAL NERVE AND BOWEL CONTROL

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The aim of this study was to assess the characteristics of patients referred for pudendal nerve studies over a one year period.

31 consecutive patients were asked a standard questionnaire and nerve studies were performed as described by Kiff and Swash and Swash and Snook.

Of the 31 patients, only 3 were male. The age range was from 21 to 79 (mean 50).

10 presented with constipation and 19 with faecal incontinence. Two had both symptoms.

Bladder incontinence was presented in 10 of 31 patients. Of these, faecal incontinence was the cardinal symptom in 8 patients, constipation in 2. 12 patients were nulliparous. Of the remaining 17, 14 had a history of complicated births involving forceps (7), caesarean section (4), post partum haemorrhage (1), breech without forceps (2).

14 patients had pelvic surgery and one had major trauma. 22 of 31 patients had bilaterally delayed pudendal nerve terminal motor latency (PNTML). 7 of 31 people had ulaterally delayed PNTML. 2 were right sided, 5 were left sided. 2 had normal PNTML.

The range of measurements was 1.8 - 9.2 ms with a mean of 3.65 ms.

In conclusion, delayed PNTML was seen in 11 of 12 patients with constipation and 19 of 20 with faecal incontinence. Pelvic surgery and a complicated obstetric history were significant. Urological symptoms were also a common association.

References
1. Kiff, E. S., Swash, M. Slowed conduction in the pudental nerves in idiopathic (neurogenic) faecal incontinence. Br. J. Surg. 1984; 71: 615-616.
2. Laurberg, S., Swash, M., Henry, M. M. Delayed external sphincter repair for obstetric tear. B. J. Surg. 1988; 75: 786-788.

(P.102) THE AUDITORY PAIRED CLICK PARADIGM IN ALZHEIMER’S DISEASE

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The P50 component of the middle latency auditory evoked potential is attenuated in response to the second of paired clicks in a normal population. In schizophrenia, this attenuation is minimal. In Alzheimer’s Disease (AD), the results have varied between centres depending on the frequency of the stimuli and the interclick interval. We studied 10 AD patients, 10 elderly controls (EC) and 10 young controls (YC) using a paradigm of 32 sets of paired clicks.

| Click 1 (Conditioning) | AD patients | EC patients | YC patients |
|------------------------|-------------|-------------|-------------|
| P50 latency            | 55.6 msec   | 59.28 msec  | 55.81 msec  |
| P50 amplitude          | 6.18 μV     | 3.30 μV     | 4.02 μV     |
| Click 2 (Testing)      |             |             |             |
| P50 latency            | 54.37 msec  | 58.05 msec  | 61.26 msec  |
| P50 amplitude          | 4.55 μV     | 2.59 μV     | 2.87 μV     |
| C/T Ratio              | 0.9         | 0.77        | 0.81        |

In contrast to previous studies, our study demonstrates significantly larger absolute P50 generation and recovery amplitudes in AD patients compared to elderly controls and young controls.

(P.104) LIPOPROTEIN (a) AND ITS POTENTIAL AS A SCREENING TEST FOR INTRACRANIAL ANEURYSMS

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The purpose of study was to establish a simple screening
test to identify asymptomatic intracranial aneurysms (ICAs). An association between atherosclerosis and ICAs is recognised. Elevated serum lipoprotein (a) [Lp(a)] is an independent risk factor for atherogenesis. We aimed to assess the degree of correlation between serum Lp(a) and the occurrence of sporadic ruptured aneurysms and familial asymptomatic aneurysms.

Lp(a) levels were measured in (a) 50 patients with ICAs and 42 normal controls, (b) 25 first degree relatives of patients with familial subarachnoid haemorrhage (SAH). ICAs were detected by cerebral angiography.

Patients with sporadic ICAs had significantly elevated Lp(a) levels when compared with matched controls. Mean level was 20.1 mg/dl in patients and 10.8 mg/dl in controls. In the familial studies, 10 out of 11 subjects with asymptomatic ICAs had elevated Lp(a) levels. One young female with elevated Lp(a) had a pre-aneurysm dilatation at operation. Six out of 14 subjects without ICAs had elevated Lp(a) levels; four of these were in the second or third decade of life and may yet develop aneurysms.

Conclusions: Lp(a) has potential as a biological marker for ICAs. Follow-up studies are required on angiographically negative subjects. We have begun a genetic case-control study to establish if particular apoprotein (a) gene polymorphisms can be correlated with the occurrence of ICAs.

(P.106) POST MASTECTOMY BREAST RECONSTRUCTION - OUR EXPERIENCE IN SHEFFIELD
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Post mastectomy breast reconstruction has undergone several changes in the recent years. Attitudes have changed towards the problem from both the patient and the reconstructive surgeon, as aesthetic outcome receives a greater emphasis than previously. There is a shift towards using autologous tissue as a means of reconstruction; these new technically difficult procedures entail a longer learning.

Centralization of this type of reconstruction in highly specialized centres only will serve the patient better.

We share our experience of post mastectomy breast reconstruction spread out over the past five years. Seventy-eight consecutive cases of breast reconstruction are included in the study.

Different techniques of breast reconstruction were used with a recent switch to Transverse Rectus Abdominis Myocutaneous (TRAM) flap; we feel that TRAM flap is the gold standard of breast reconstruction as far as the ultimate cosmetic result is concerned. Ours is only a moderate sized study compared to some published, yet it is representative of the experience of most of the plastic surgery units in the British Isles.

(P.105) ANTINEURONAL ANTIBODIES: A REVIEW OF ONE YEAR'S TESTS
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Clinically significant paraneoplastic neurological disorders are rare, most are associated with small cell Lung, female genital tract and breast carcinoma. The malignancy is often silent and the neurological manifestations vary from encephalomyelitis, cerebellar degeneration, sensory neuropathy to neuromuscular block. Prognosis is usually poor. Pathogenesis is thought to be related to cross reaction with neurons of antibody produced to tumour antigens. Detection of these antineuronal antibodies in serum has assisted diagnosis of paraneoplastic encephalomyelitis in which ANTI-HU antibodies are present and cerebellar degeneration, in which ANTI-YO are found. In our lab, we used avidin-biotin-complex immunocytochemistry to detect ANTI-HU (cortical neuron antibodies) and ANTI-YO (Purkinje cell antibodies) in patients' sera. Tests were performed on human frontal cortex and cerebellum, at 1 in 500 and 1 in 4,000 dilutions, with positive and negative controls. Of 68 sera, 6 were positive. Two patients had repeat positives; in one, antibody titre rose in the second sample. Subsequent patient review showed 3 positives (2 patients) had identifiable carcinoma with paraneoplastic CNS signs, 2 had no identifiable malignancy but had no other cause of their CNS disorder and are being followed up; details of one patient were unavailable. These results are similar to other centres.

(P107) INDUCTION OF A HEAT SHOCK RESPONSE PROTECTS TUMOUR CELLS FROM MONOCYTE MEDIATED LYSIS
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The proliferation of tumour cells despite the presence of tumouricidal mediators could be due induction of a heat shock response, a universal cellular defence mechanism in host cells and possibly tumour cells. Protection may be mediated either by increasing intracellular levels or surface expression of heat shock proteins (HSP).
The aim was to assess the effect of heat shock induction on tumour cell protection against host effector cells. The heat shock response was induced in SW707 colorectal cells by either sodium
arsenite (0-320μM for 6hr) or by hyperthermia (42°C for 20 min). Monocyte (Mø)-mediated cytotoxicity or flow cytometry to evaluate surface expression of HSP60 and HSP70 were assessed.

Cytotoxicity showed a significant decrease in all treated groups (p<0.002) when compared to the control value. There was also a significant decrease in all groups (p<0.001) when compared to the 42°C value. No significant alteration in surface expression of either HSP60 or HSP70 was seen.

Conclusion: Heat shocking tumour cells significantly protects them from Mø-mediated tumour cell lysis. Since the flow cytometric data indicate that there is no concomitant increase in surface expression of HSP60 and HSP70 on the tumour cell following heat shock, it can be inferred that induction of intracellular HSP levels are responsible for the protective effect on the tumour cells.

(P.108) QUALITY OF LIFE (QOL) ASSESSMENT IN ADVANCED CANCER
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A 4 week QOL study in 157 consecutive advanced cancer patients was undertaken to compare the subjective 28 question Fact-G with simple subjective global tools (visual analog, categorical scales: VAS, CAS), objective tools (Spitzer QLI and ECOG performance status) and verbal patient description. We anticipated the high drop out rate enrolling 157 to achieve 87 complete study patients for statistical purposes. The study sample appeared representative of the advanced cancer population in the USA. Generally QOL was satisfactory despite the severity of illness. There were significant differences in all measures between those who described QOL in verbal terms as positive and negative, particularly CAS, VAS, and QLI (p<0.0001). There were significant intercorrelations between QLI and PS (observer rated), CAS and PS (subject rated) respectively (p<0.00001). Taking patient description as the gold standard, simple, global QOL measures e.g. VAS or CAS are as effective as multidimensional ones (FACT-G and QLI).

(P.109) THE SYMPTOMS OF ADVANCED CANCER IN 1,000 PATIENTS
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A prospective analysis of symptoms in 1,000 patients on initial referral to the Palliative Care Service of the Cleveland Clinic was made using the Paradox relational database. The median number of symptoms per patient was 11 (range 1-27). The 10 most frequent symptoms were pain 82%, easy fatigue 67%, weakness 64%, anorexia 64%, >10% weight loss 60%, lack of energy 59%, dry mouth 55%, constipation 51%, dyspnea 51% and early satiety 50%. Patients 65 years and under had more pain, sleep problems, depression, anxiety, vomiting and headache (all p<0.01). The prevalence of early satiety, nausea, vomiting and anxiety were greater in females; dysphagia and hoarseness in males. Patients with >25% weight loss had more GI symptoms; of these females had more nausea, early satiety; males had more dysphagia. Survival from diagnosis was greater for females <65 years (female median 18 months, male median 13 months, p<0.0016). Anorexia was associated with reduced survival since diagnosis in the total population and in males. Anorexia and dysphagia were associated with reduced survival from referral. Advanced cancer patients were polysymptomatic. Symptom prevalence differed with age, gender and cancer site. The pattern of GI symptoms was related to gender and severe weight loss. Specific symptoms were associated with reduced survival. There was a gender difference in survival favoring females.

(P.110) THE ANTI-TUMOUR EFFICACY OF TAURINE AND RECOMBINANT INTERLEUKIN-2 IN VIVO
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The administration of recombinant interleukin-2 (rIL-2) is limited by the induction of increased microvascular permeability. The in vivo antineoplastic effects of taurine in combination with rIL-2 were investigated and its impact on the associated vascular leak was examined. Lung metastases were established in mice via tail vein injection. Ten days after injection mice were randomized into treatment groups. On day 18 the mice were sacrificed; lungs were removed, weighed and metastases counted. Treatment of tumour-bearing mice with rIL-2 alone resulted in a significant reduction in tumour nodule incidence compared to a control group, while the group receiving rIL-2 + taurine showed an even further reduction in the incidence of lung nodules. Animals receiving rIL-2 showed a significant increase in mean wet lung weight compared to control lung weight, while mean wet lung weight of the rIL-2 + taurine group was significantly less than that of the rIL-2 group and comparable to control values. Animals receiving rIL-2 + taurine in vivo demonstrated significantly enhanced splenocyte-mediated antimelanoma activity ex vivo compared to animals receiving rIL-2 alone. Thus taurine may have an important role in modulating both metastatic growth and the associated toxicity of rIL-2 immunotherapy.

(P.111) A MOLECULAR AND IMMUNOHISTOCHEMICAL STUDY OF THE P53 TUMOUR SUPPRESSOR GENE IN COLON CANCER
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The prognostic significance of abnormalities in the p53 tumour suppressor gene and in the expression of its protein in colorectal carcinoma may be influenced by the method of analysis used. We studied p53 abnormalities in 66 patients with colorectal cancer followed for more than 10 years. Single-strand conformation polymorphism analysis (SSCP) was used to detect alterations in exons 5-8 of the p53 gene. Paraffin sections were examined immunohistochemically for p53 overexpression with
the monoclonal antibody DO-7 (Dako) both with and without microwave antigen retrieval.

Abnormalities of the p53 gene were found in 41% of cases by SSCP analysis but were unrelated to age, sex, tumour size or differentiation. Outcome was unrelated to SSCP abnormalities (p=0.19). Overexpression of p53 protein was seen in 47% of cases by immunohistochemistry without microwave antigen retrieval and in 52% of cases with microwaving. Poor long-term survival was related to immunohistochemical expression of p53 protein either with (p=0.03) or without (p=0.02) microwave antigen retrieval.

These results suggest that immunohistochemical detection of the p53 protein product may be more useful than SSCP analysis of the encoding p53 gene in identifying those at high risk of colorectal cancer recurrence and death.

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(P.112) SUPPRESSOR MACROPHAGES: A NOVEL COMPONENT OF THELYMPHORETICULAR INFILTRATE OF BREAST TUMOURS

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The anti-tumour activity of tumour infiltrating lymphocytes (TILs) is known to be poor and therapeutic manipulation of these cells has met with little success. Suppressor macrophages (SMo) influence T cell cytotoxicity and proliferation. We hypothesized that SMo are a component of the lymphoreticular infiltrate and that these cells may be related to lymphocyte numbers within the tumour. TGF-b may influence macrophage phenotype.

Colorctal and breast tumours were obtained within an hour of resection. Tumours were dissociaggregated with collagenase and DNase for three hours. Antibodies was used to identify SMo (RFD1 and RFD7) and T cell subsets (CD4 and CD8) by flow cytometry on the resulting cell suspension. Pre-op blood was collected from patients and TGF-b levels determined by ELISA.

**Results:**

- **Smo%**
- **Tcells%**
- **CD4%**
- **CD8%**
- **TGF-b (ng/ml)**

**Breast-malign.**
- Pre-op: 14.6±3 19.2±4 5.4±2 13.8±5 95.2±1.1
- 48 hrs: 4.4±2* 5.6±1 4.4±1 1.2±1 49.9±1.3

**Colon-malign.**
- Pre-op: 5.3±1 37.1±28 22.7±15 14.4±12 56.1±26
- 48 hrs: 4.9±1 6.4±1 3.9±1 2.5±1 31.1±7

Mean±S.E.M; *=p<0.003; *=p<0.005

Conclusions: We have shown for the first time that SMo, defined by the antibodies RFD1 and RFD7, are present within breast tumours. We have also shown that the balance of T cell subsets is different in these tumours and may be related to SMo content. Circulating TGF-b levels are increased in breast cancer and associated with greater SMo numbers. This was not found to be the case in colorectal cancers. These results imply the existence of a fundamental difference in the make-up of the lymphoreticular infiltrate between these cancers.

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(P.113) ARM VOLUME CHANGES FOLLOWING AXILLARY CLEARANCE FOR BREAST CANCER

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Swelling of the upper limb is an uncommon but well recognised complication of breast cancer treatment. In severe cases, patients have limited arm function and feel disfigured. In a pilot study, the incidence of arm swelling following complete axillary clearance in the immediate post-operative period and at long term follow-up was investigated. Arm volume measurements were performed using an opto-electronic volumeter (Bosl Medizintechnik, Hamburg). Both ipsilateral and contralateral arm volumes were assessed. The expected volume of the ipsilateral arm volume was calculated using the formula: 

\[
\text{Pre-op} = 48 \text{ hrs}  
\text{5 days}  
\text{>3 months}  
\]

Arm Volume (%) 0.99±0.55 1.30±0.79 0.69±0.26 5.45±1.06 (Mean % change in arm volume ± SEM)

There was no significant change in arm volume in the immediate post operative period. Clinically detectable arm swelling was found on 3 patients who had undergone axillary clearance at least 3 months previously but none had any impairment of arm function.

We conclude that axillary clearance can be performed safely and that arm swelling is an uncommon complication. A larger study is planned to investigate factors such as the influence of pectoralis minor division, duration of the operation and the number of axillary nodes retrieved on upper limb volume.

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(P.114) EPIDERMAL GROWTH FACTOR LEVELS IN THE SALIVA OF PATIENTS WITH SKIN AND/OR GUT DISEASE

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Epidermal growth factor (EGF) is a potent mitogen and has been shown to accelerate healing of epithelial damage both in the skin and the gut. In the skin EGF is not produced locally as the requisite mRNA is not present but EGF receptors are present on the surface of basal keratinocytes. EGF is produced in various sites in the GI tract including the submucosal salivary glands. We have hypothesised that as there is up-regulation of salivary EGF production in some enteropathies a similar situation may occur in disorders of the skin with an associated enteropathy. Using a sensitive radio-immunoassay, EGF activity was estimated in stimulated saliva from 87 patients with various skin disorders, 49 patients with gastrointestinal disease, 8 patients with mixed dermatological and gut disease and 41 normal healthy volunteer controls. Elevated EGF activity was found in the following groups of patients: skin cancers, psoriasis, acne, oesophagitis and ulcerative colitis. The hypothesis of up-regulation of salivary EGF production in skin associated enteropathy was rejected but the discovery of elevated EGF activity in skin cancers and psoriasis may have aetiological and therapeutic implications.
eczematous reaction to ultraviolet radiation and sometimes damage to bile ducts. The pathogenesis of CAD may be auto-immune in origin with a heightened cutaneous immune response to ultraviolet light. The coexistence of CAD and PBC is a new association which has not previously been documented and may not be fortuitous given the similar pathogenesis of both diseases.

(P.115) MALIGNANT FIBROUS HISTIOCYTOMA
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The malignant fibrous histiocytoma (MFH) is considered an uncommon malignancy. Its potential for invasion, metastasis and death of patient has been reported in literature. It can be confused with other tumours including fibrosarcoma. Salient histologic features include cells of both the fibrocytic and histiocytic series.

MFH with its high recurrence rate and lethal potential merits an aggressive evaluation and treatment.

We present unusual case of recurrent MFH treated in our unit with an open question as to what qualifies to be adequate primary surgical excision.

(P.116) MERKEL CELL CARCINOMA: THE ROLE OF PRIMARY TREATMENT WITH RADIOTHERAPY
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The recommended management of localised Merkel Cell Carcinoma has been wide surgical excision, combined with adjuvant radiotherapy in selected cases. The risk of recurrent regional disease is reported to be between 30% and 45%.

A 70 year old woman with Merkel Cell tumour on the cheek is presented; this patient was treated exclusively with radiotherapy to a total dose of 50 Gy over 18 days. The tumour regressed rapidly during the treatment, and there were no signs of local or regional recurrence. The patient is still alive and free of disease for 45 months.

(P.117) CHRONIC ACTINIC DERMATITIS ASSOCIATED WITH PRIMARY BILIARY CIRRHOSIS
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Chronic Actinic Dermatitis (CAD) is a rare photosensitive disorder which primarily affects elderly men resulting in an eczematous reaction to ultraviolet-radiation and sometimes visible light. The pathogenesis has been attributed to an autoimmune process, possibly in response to a photoallergen which has yet not been identified.

We report a 71 year old female patient who developed CAD four years after being diagnosed with primary biliary cirrhosis (PBC). Abnormal monochromator irradiation tests were detected with narrow band UBV, UVA and in addition visible light wavelengths. Photoprovocation tests induced florid vesicular eczema and multiple patch and photo-patch tests were positive, findings typical of CAD. Immunoglobulin G was elevated at 2290 mg/dL and liver histology was typical of PBC with an elevated anti-mitochondrial antibody. Routine biochemical and immunological tests were normal and porphyrin screen was negative.

Azathioprine 50 mg/day induced remission of CAD. PBC is an auto-immune disorder where cell-mediated immunity is impaired, suggesting that sensitized T lymphocytes may cause damage to bile ducts. The pathogenesis of CAD may be auto-immune and multiple patch and photo-patch tests were positive, four years after being diagnosed with primary biliary cirrhosis an auto-immune disorder where cell-mediated immunity is impaired, suggesting that sensitized T lymphocytes may cause immunological tests were normal and porphyrin screen was negative.

(P.118) PHYSIOLOGICAL SKIN CHANGES IN PREGNANCY
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Skin appendages undergo physiologically induced alterations during the gravid state. An altered endocrine status with the advent of a new endocrine organ occurring induces physical adaptations as the placenta produces its own hormones.

Changes range from pigmented alterations which can be either generalized or localized with the occurrence of a linea nigra to vascular and haematologic changes. Cutaneous benign tumours have been documented especially during the end of the second trimester.

Appendageal changes affecting the hair with second trimester hirsutism and post partum telogen effluvium together with nail changes (Beau's lines, onycholysis and subungual keratosis) have been described. Glandular adaptations show a generalized increased activity affecting the entire body with exception of the palms. Mucous membrane involvement can result in pregnancy gingivitis and granuloma gravidarum.

The occurrence of pruritis gravidarum, dermatoctraphism and non-pitting oedema have their usual onset at the beginning of the third trimester and clear spontaneously post partum. Pregnancy provides a varied and intriguing spectrum of physiological skin changes important to the patient and her physicians.

(P.119) CUTANEOUS POLYARTERITIS NODOSA WITH JOINT INVOLVEMENT
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We present two cases of Cutaneous Polyarteritis Nodosa (PAN) associated with seronegative arthritis: The first patient, a 50 year old male presented in 1993 complaining of a 7 year history of pain, stiffness and swelling affecting his right ankle. He also noted intermittent tender nodules on the dorsum of his foot and over his ankle over the preceding three years. The second patient, a 51 year old male, presented in 1994 complaining of a 5 month history of tender nodules on his shins, and pain and swelling of his right ankle. Skin biopsies of the nodules in both cases showed medium vessel vasculitis consistent with polyarteritis nodosa. Neither patient had any symptoms or signs to suggest systemic involvement. The only abnormality on laboratory investigations for vasculitis was elevated ESR. X-Rays showed periosteal elevation and new bone formation in case 1, and were normal in case 2. Bone scan demonstrated increased uptake at the talo-navicular joint in case 1 and at the right ankle in case 2. Synovial biopsy and MRI confirmed the presence of an inflammatory arthropathy in patient 1. Joint involvement has been a prominent feature throughout the course in both cases requiring aggressive treatment with
cyclophosphamide and systemic corticosteroids in case 1.

Cutaneous PAN is a localised cutaneous vascular disorder with a benign chronic relapsing course. In one review, 12 of 23 patients had arthralgias but an association with arthritis has not been emphasized in the literature to date. We conclude that this condition may present as a seronegative arthropathy in which the joint symptoms may be the most prominent feature and aggressive immunosuppressive therapy may be required for control.

Reference

1. Diaz-Perez, Jose L. Winkelmann, R. K. Cutaneous Periarteritis Nodosa. Arch. Dermatol. 1974; 110: 407-414.

(P.120) DERMATOLOGICAL COMPLICATIONS OF CARDIAC TRANSPANTATION

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Cardiac transplantation patients have an increased risk of skin disease. In our centre, 119 heart transplants were performed with a 5 year survival of 75%. Eighty three patients are now alive and 39 have required dermatological assessment.

The mean age of patient was 48.3 years, (range 11-64 years); 99 males, 20 females. Skin infections were diagnosed in 13 of 39 patients. Drug side effects, including sebaceous hyperplasia and steroid acne, were common. In the patients who developed skin cancer, mean time from transplant to development of lesions was 3.1 years. Eleven of 36 patients had 32 non melanoma skin cancers (NMSC), 28 squamous cell carcinomas (SCC), 4 basal cell carcinomas (BCC), giving SCC/BCC ratio of 7:1. Three of 11 patients had multiple skin cancers, one had 12 tumours. Nine of 39 patients had actinic keratoses, two thirds of whom had SCCs. Nineteen of 39 patients had viral warts, two of whom had SCCs. Viral warts, premalignant and malignant lesions were located on sun exposed sites.

Skin complications of cardiac transplantation though mild were very common. The observed incidence of NMSC in age matched cardiac transplant recipients, appears much higher than the expected incidence of 171.38 per 100,000 population (National tumour registry 1994). Regular dermatological assessment of cardiac transplant patients is necessary to detect skin disease and early skin cancer.

(P.121) RENAL TRANSPLANT RECIPIENTS, SUNLIGHT, WARTS AND SKIN CANCER - A CLINICAL STUDY

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The increased incidence of warts and skin cancer in renal transplant recipients (RTR) is well known. The oncogenic potential of unusual Human Papilloma Virus (HPV) types has been postulated from warts and in both premalignant and non-melanoma skin cancer (NMSC). The possible etiological role of sun exposure in facilitating the development of HPV associated skin disorders is also suggested.

A clinical study to assess the risk factors for development of these lesions in 50 RTR attending the dermatology service. Age and sex matched haemodialysis patients were similarly examined as controls.

40 male and 10 female patients with a mean duration of transplant of 10.6 years, range 1 to 25 years. A total of 191 NMSC (range 1 to 57), 175 SCC and 16 BCC, ratio 10.9:1, were excised from 26 RTR of which over 95% had viral warts, most commonly occurring on exposed sites and always preceded the development of neoplastic lesions. Both were associated with mean duration from transplantation, 4 years for warts and 10.8 for skin cancer and not the type of immunosuppressive treatment. None of the control patients had similar findings. Conclusions: The close clinical association of viral wart lesions and development of skin cancer in these patients suggests a close relationship to immunosuppression, in addition to exposure to ultraviolet radiation.

This study highlights the high rate of NMSC in RTR. These patients justify early and regular skin assessments soon after transplantation with advice on sun protection.

(P.122) MONOCHROMATOR LIGHT TESTING AS AN AID TO DERMATOLOGICAL DIAGNOSIS

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Sensitivity to ultraviolet (UV) light may be established by exposure to broad band UVA and UVB radiation. The minimal erythema dose (MED) can be determined at individual wavelengths using a monochromator. UV action spectra of photosensitive disorders may thus be constructed. We examine the value of this process in distinguishing two clinically similar photosensitive disorders.

The radiation from a xenon arc is separated into component wavelengths using the monochromator. Each wavelength is focused on unaffected skin, on the patient’s back. The patient is exposed to a range of doses of W radiation. The MED is determined for a series of wavelengths from 300 to 400 nm.

Chronic actinic dermatitis (CAD) and drug induced photosensitivity are photosensitive disorders which may have similar clinical history and presentation. Ten CAD and 14 drug induced photosensitivity patients were tested. UVA photosensitivity was seen in 71% of the latter group. The remaining 29% had normal MLTs as the implicated drug had been discontinued prior to testing. CAD patients were sensitive to both WA and WB radiation. Forty-three percent of these patients were also sensitive to visible light (400 to 800 nm).

Monochromator light test (MLT) results show that UVA photosensitivity dissociated from WB photosensitivity is indicative of a drug induced light sensitive disorder. Sensitivity to both WA and WB however indicates a diagnosis of CAD. MLTs can therefore distinguish between clinically similar photosensitive disorders.

IMMUNOLOGY

(P123) PLATELETS ARE ACTIVATED IN MYELOPROLIFERATIVE DISORDERS (MPD) BUT ACTIVATION FAILS TO PREDICT THROMBOSIS

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Patients with MPD have an increased incidence of both
thrombosis and haemorrhage suggesting a pivotal role for; platelets in these conditions. This study aimed to examine platelet activation antigen expression in stable patients with MPD and to examine the predictive value of these antigens prospectively.

52 patients with MPD had P selectin and GP53 measured using a refined minimally manipulative flow cytometric technique. Expression of P selectin -median 5.1% (inter quartile range 2.1-10.9), control 2.0% (1.3-4.0) and GP53 -median 4.0% (1.8-5.7), control -2.1% (1.0-2.9), were significantly elevated p<0.01. Patients were followed for a median of 26 months. 15% experienced thrombosis and 6% bleeding during follow up. At entry to the study 48% of patients had previously experienced thrombosis, median disease duration 8 deaths, 3 of which were caused by thrombotic events in which the MPD was a major risk factor.

Increased expression of P selectin or GP53 expression failed to predict thrombosis or bleeding in this study. Nor was any significant retrospective relationship demonstrated. However, previous thrombotic events were strongly associated with future events (p<0.05). This association was independent of disease, duration, age and medication. Not surprisingly disease duration was also correlated with thrombotic/bleeding events.

(P.126) CYTOKINE AND DEXAMETHASONE REGULATION OF TAURINE TRANSPORT INTO CaCO2 CELLS
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Taurine levels fall in gut mucosal cells during critical illness. However, taurine transport into human intestinal cells is poorly understood. The aim was to establish the efficiency of taurine uptake by enterocytes, and to examine uptake under stressful conditions.

To investigate efficiency of taurine uptake, confluent Caco-2 cells were incubated for time points up to 10h. In a second study, cells were incubated for 9h with medium containing dexamethasone and / or cytokines. Media for both studies was supplemented with [3H]-taurine. Radioactivity was related to mg/ml protein to calculate rate of taurine uptake for each time point.

Study 1: Uptake exhibited a steady linear response which approached saturation at 7h. Maximal uptake occurred at 9h after which the rate levelled off. Study 2: Dexamethasone alone reduced taurine uptake by 75.4% (p<0.001) and in combination with TNF-α and IFN γ it decreased transport by 66.3%. (p<0.001). LPS alone impaired uptake by 56% (p<0.001).

Conclusion: We have established the time course over which taurine transport reaches its maximum rate in Caco-2 cells, and that corticosteroids and cytokines significantly impair uptake of taurine in these cells.

(P.127) AGE RELATED CHANGES IN PROINFLAMMATORY CYTOKINE PRODUCTION
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Elderly individuals have an increased risk of infection suggesting that immune responsiveness is altered with age. Changes in the level of proinflammatory cytokine production may be an important indication of any such age related change.

Using flow cytometry we examined intracellular TNFα, IL-18 and IL-6 in PBMCs from normal healthy volunteers of different ages ranging from 22 up to 85 yr (n=28). TNF and IL6 levels from PMA stimulated CD3 positive cells (T cells) were shown, using this technique, to increase in an age dependent manner (P<0.05). No IL-18 was detected in any T cell sample.

No significant differences were observed between the different age groups for TNFα, IL-18 or IL-6 in CD14+ cells (monocytes). The age related changes detected by flow cytometry have been confirmed using conventional ELISAs. This novel method of proinflammatory cytokine detection has detected increased TNF and IL6 levels in T cells from elderly healthy volunteers which may help explain some of the exaggerated inflammatory responses seen in elderly patients.

(P.128) FLOW CYTOMETRIC DETECTION OF INTRACELLULAR PROINFLAMMATORY CYTOKINES
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Detection of proinflammatory cytokines by conventional ELISA or bioassay is problematic due to the presence of naturally occurring biological inhibitors. Flow cytometry allows the simultaneous detection of both intra and extracellular antigens thus intracellular cytokine levels can be quantified while cell surface markers allow cell type identification. A range of monoclonal antibodies were examined for TNFα, IL-18 and IL-6 using saponin permeabilisation of T cells (CD3), monocytes (CD14) and epithelial cells (Ber-Ep4). T cells and monocytes were grown in culture, up to 72 hr with or without PMA activation, and intracellular cytokine levels were shown to increase with time, with the stimulated samples producing more cytokine than the spontaneous samples (P<0.05). ELISAs performed on these same samples (n=24) correlated well with the flow cytometric results (r=0.52).

TNFα, IL-18 and IL-6 are detectable in monocytes while only TNFα and IL-6 have been detected in T cells and epithelial cells using this methodology. This novel technique will allow us to identify the cytokine producing cell while also avoiding the influence of the extracellular milieu, thus being useful for a number of research and diagnostic applications.

GASTROENTEROLOGY

(P.130) HEPATITIS A, B, C, D & E SEROPREVALENCE IN THE UNITED ARAB EMIRATES (UAE)
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All the viral Hepatitis are said to be common in the Middle East. Hepatitis A virus (HAV) seroprevalence is said to be 100% in the adult population of Gulf countries. Hepatitis B, C and D seroprevalence are taken from blood banks data which are biased by selection criteria and the background of blood donors. Very little is known about HEV in the UAE.
The aim was to investigate the seroprevalence of HAV, HBV, HCV, HDV & HEV in the UAE.

We prospectively recruited volunteers drawn from all the UAE, socioeconomic classes and from different age groups in both sexes. Each donated 10ml of venous blood and using an indirect enzyme immunosassay were tested for total Ig to HAV, HBsAg using monocolonal antibody to HBsAg; for HCV antibodies using recombinant antigens HC-34, HC-43, C-100 and NS-5, (3rd generations); for total Ig to HDV and for total Ig to HEV. Positive samples were retested in duplicate for confirmation.

Results:

| Results       | Total No. | +VE Serum | %    |
|---------------|-----------|-----------|------|
| HAV           | 1583      | 1227      | 77.5 |
| HBV           | 1447      | 30        | 2.1  |
| HCV           | 1447      | 11        | 0.8  |
| HDV           | 30        | 0         | 0    |
| HEV           | 1447      | 77        | 5.3  |

This large sero-epidemiological study clearly shows that HAV is decreasing in the UAE. HBV is low but significant, HCV is similar to Southern European countries, HEV is lower than expected and HDV does not exist in HBsAg carriers in the UAE.

(P.132) MODULATION OF ULCERATIVE COLITIS BY TAURINE

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Reactive oxygen and nitrogen species produced by inflammatory cells plays a role in tissue injury and inflammation. Taurine, a B-amino acid present in high concentrations in mucosa. Animals supplemented with taurine demonstrated attenuated MPO activity (p=0.001). Administration of Taurine did not lead to a reduction in Nitric oxide production. Thus, Taurine appears to have a beneficial role in reducing the severity of disease. A reduction in MPO and respiratory burst may be beneficial in reducing tissue damage.

(P.134) INTERFERON-RIBAVIRIN COMBINATION THERAPY FOR CHRONIC HEPATITIS C, 18 YEARS POST INOCULATION

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In 1977 anti-D serum contaminated by Hepatitis C was given to women subsequently identified by a national screening programme which revealed 438 to be positive for RNA of Hepatitis C, type lb. 94 were referred to this centre for evaluation. 10 had moderate activity by modified Knodell index, mean 8 (±1.4), bridging fibrosis and a mean ALT of 77 (42-176). Six months dual therapy was administered. Two patients withdrew due to depression (2) and hyperthyroidism (1). One patient did not respond. Seven responded with normalisation of ALT and negative PCR. Eight patients showed improved histology (KAI 4 ± 1.5), fibrosis was unchanged. Adverse reactions in the treated group included marrow suppression (1) and thyrotoxicosis (1). At six months follow up four remain in remission with normal ALT negative PCR, three have relapsed, (PCR positive, mean ALT 87(50-150). We conclude that despite adverse prognostic indicators in this homogenous group with chronic hepatitis C, lb and long disease duration, dual therapy with interferon and ribavirin achieved results comparable to prolonged high dose interferon in patients with more favourable initial prognoses.

(P.135) ERADICATION OF H.PYLORI WITH A 5 DAY COURSE OF AZITHROMYCIN

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The aim of the study is to evaluate a 5 day course of Azithromycin in combination with Omeprazole in eradication of H.pylori.

Twenty-four patients with proved H.pylori infection and peptic ulcer disease were treated with Omeprazole 40 mg daily for 2 months plus Azithromycin 500 mg daily for 5 days. H.pylori was diagnosed on the basis of CLO test and histology. This was done at the beginning and 3 months after the treatment. Eradication was defined as negative CLO test as well as negative histology.

Out of 24 patients, 2 patients were lost to follow-up. Only 21 patients were analysed. Sixteen patients responded to treatment and had successful eradication as well as healing of their ulcers. These included 8 patients with gastric ulcers (79.95%), 4 patients with duodenal ulcers, 2 patients with gastric and duodenal ulcers and 3 patients with non-ulcer dyspepsia. Five patients did not respond including 2 with non-ulcerative dyspepsia. 2 duodenal ulcers and 1 gastric ulcer. However their ulcers have healed and symptoms relieved and they were treated with other H.pylori eradication regimes.

Conclusion. In this small study we have shown that Azithromycin 5 mg once daily for 5 days is an alternative safe effective and well tolerated monotherapy for eradication of H.Pylori.

(P.137) AUTOIMMUNITY IN ANTI-D ASSOCIATED HEPATITIS C VIRUS INFECTION

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It has been suggested that Hepatitis C Virus (HCV) infection is associated with a high prevalence of autoimmune disease, but that this risk may be diminished in patients who received a low viral load at initial infection.

The aim was to determine the prevalence of symptoms, signs and markers of autoimmune disease in a group of women...
infected with HCV contaminated Anti-D immunoglobulin. 50 patients, mean age 44.3 years (range 32 - 65 yrs) were examined. 7 patients (14%) were rheumatoid factor positive. ANA was positive in 6 patients (12%) but titres were 1/10 in 4/6. Thyroid globulin antibodies were found in 3 patients (6%) with 1 also being TM positive. 2 further patients were positive for thyroid microsomal ab. Prevalence of APA, ARA, SM were 4%, 2% and 2% respectively. One patient had cryoglobulins detected while antibodies against mitochondria and LKM-1 were not found only one patient of 50 was symptomatic. These levels of antibodies are no greater than levels in the general population and similar to other groups infected with HCV contaminated Anti-D. These results further support the hypothesis that either low viral inoculum or long duration of infection may in some way result in a low level of autoimmunity.

(P.138) LACK OF EVIDENCE OF IgA DEFICIENCY IN HEPATITIS C VIRUS INFECTION
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A previous study (Ilan et al, Arch Int. Med., 1993; 3: 1588-1592) suggested that IgA deficiency disposes towards Hepatitis C Virus (HCV) infection in some patients. It has also been suggested that IgA deficiency may occur as a result of the viral infection as a secondary event.

The aim was to determine the prevalence of selective and partial IgA deficiency in patients with HCV infection using a radio-immunodiffusion technique. Serum IgG and IgM levels were also examined.

Immunoglobulin levels were measured in 67 patients, 59 women and 8 men, mean age 45.3 years (range 29 - 72 years) infected with blood between 1977 and 1990. None of the patients were found to have selective or partial IgA deficiency. Mean IgA = 2.59 g/l (range 0.86 g/l - 5.19 g/l). Furthermore no patient exhibited deficiency of IgG or IgM.

Conclusion: No evidence of IgA or other immunoglobulin deficiency exists among this group of patients with HCV infection. While it may be possible that IgA levels decrease following infection, no evidence exists that this phenomenon persists in the long term.

(P.140) MUTATION SCREENING OF THE hMSH2 GENE IN THE IRISH HNPCC POPULATION
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Hereditary non-polyposis colorectal cancer (HNPPC) is the most common form of hereditary colon cancer and accounts for up to 10% of the overall cancer incidence. The disease is inherited in an autosomal dominant manner and is characterised by predominantly right-sided tumours.

HNPPC is caused by mutations in one of four mismatch repair genes. These genes are homologues of the bacterial mismatch repair system and their function is to detect and correct defects in DNA. The hMSH2 gene is reported to account for up to 60% of cases, hMLH1, hPMS1 and hPMS2 account for 30%, 5% and 5% of cases respectively.

We have collected eighteen Irish HNPCC families which satisfy the Amsterdam criteria for the disease. We have screened the entire hMSH2 gene in eight of these families. A combination of Single Strand Conformational analysis (SSCP) followed by dideoxy sequencing was used to detect defects in the DNA. Sequence analysis revealed the presence of a novel polymorphism in exon 5 in one family and a possible splice site mutation in the remaining ten families, using a novel mutation detection technique.

(P.141) GLIADIN ANTIBODIES AND HYPOSPLENISM IN COELIAC DISEASE: EFFECT OF DIETARY COMPLIANCE
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Serial IgA gliadin antibody (IgAGA) studies are used as a surrogate for repeated small intestinal biopsy to monitor dietary compliance in treated coeliac patients. We have correlated IgAGA levels with indices of hyposplenism (platelets and erythrocyte "pits") to determine if either index can be used to monitor adherence to a gluten free diet. The study population of 129 biopsy proven coeliacs was stratified according to dietary status into 114 gluten free diet (groups A) and 15 normal diet (group B). The IgA gliadin antibody titres were significantly lower in Group A than Group B (44.5 : 126 units p = 0.007). In Group A gliadin antibody titres showed a statistically significant correlation with both platelet (p = 0.039) and pits count (p = 0.04); in Group B gliadin antibody titres correlated with platelet counts only (p = 0.003). Those on a gluten free diet were further subdivided according to reported degree of adherence to the diet (strict diet - SGFD, lax diet - LGFD). Significantly higher gliadin antibody titres were found in LGFD than SGFD (103.6 ; 27.9 p = 0.003), but the platelet and pit counts were similar in the two groups.

IgAGA is superior to platelet or pit counts in monitoring dietary compliance in coeliac disease.

(P.142) VALIDATION OF A NEW COMMERCIAL ENDOMYSIAL ANTIBODY DETECTION SLIDE
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IgA endomysial antibodies (IgAEA) are said to be more specific and sensitive indicators of coeliac disease than IgA gliadin antibodies (IgAGA). Initially the IgAEA substrate was monkey oesophagus and more recently umbilical cord. A new commercial product has become available using primate smooth muscle (Accu Track - Diagnostic Slides). We have undertaken a preliminary study to compare the performance of this IgAEA assay and IgAGA Elisa in treated and untreated coeliacs, coeliac relatives and controls.

The study population consisted of 127 biopsy-proven coeliacs who were stratified according to "reported" dietary status into 89 good gluten free diet (group A), 24 poor gluten free diet (group B) 14 normal diet (group C) and 10 unaffected coeliac relatives (group D) and 5 controls (group E). Elevated IgAGA (>25 units) were found in the following groups: A 37%, B 46%, C 50%, D 20%. IgAEA were positive in A 27%, B 33%, C 50%.
With respect to IgAGA positivity, there were 11 false positive IgAEA A 18%, B 12.5%, C 14% and 23 false negative - A 8%, B 8%, C 14%, D 20%.

In this preliminary study in untreated coeliac patients the performance of the IgAEA test was on a par with the IgAGA assay.

(P.143) AETIOLOGY AND OUTCOME OF ACUTE UPPER GUT HAEMORRHAGE IN THE ELDERLY
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We investigated upper gut bleeding in patients aged 75 years and over. A proforma addressing demography, drug therapy, clinical status, timing of endoscopy / surgery, and outcome was used. 109 consecutive patients (median age 80 years, range 75-92) were studied over 6 months. 106 (97%) underwent gastroscopy with a 97% diagnostic yield. 32 patients had severe oesophagitis, 2 had oesophageal malignancy, 29 had gastric ulcers - 5 of which are malignant and 23 had duodenal ulcers. Ucerogenetic drugs were implicated in 52 patients. 38 patients were referred for surgery, 8 operated upon with one postoperative death. 51 had haemoglobins of 10g/dl or less. All malignant lesions were inoperable. The overall mortality was 6% reducing to 2% if neoplasia were excluded. Co-morbidity influenced mortality, 92 patients were discharged with a median hospital stay of 15 days. Information on cause of bleeding greatly influenced management.

The prognosis of gut haemorrhage in the very old need not be so poor. A few require surgery but the majority respond to active medical resuscitation which is a key factor in determining outcome. We advocate low threshold for endoscopy, judicious use of ulceregens and adherence to guidelines on management of upper gut haemorrhage.

(P.145) PCR NEGATIVE HEPATITIS PATIENTS HAVE MINIMAL INFLAMMATION AND FIBROSIS
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Of 1013 RIBA positive anti-D associated chronic hepatitis C patients, 438 were PCR positive but had surprisingly mild disease. The disease status of the PCR negative patients was hitherto uncertain and is the subject of this study. 20/72 RIBA positive patients referred to this centre were biopsied because of elevated ALT (4) or florid symptoms which dated from inoculation (16).

Results

| RIBA BANDS | Histological Activity Index * |
|------------|-------------------------------|
| 1          | 5.1,0,1                       |
| 2          | 3.2,5(F), 2(F), 0.4(F), 2,1,2  |
| 3          | 0.2,1,2                       |
| 4          | 2,2,3                         |

No bile duct damage, lymphoid follicles or aggregates was observed. 3/20 had mild periportal fibrosis (F), 2 of these had steatohepatitis with obesity (1) and impaired glucose tolerance (1) suggesting dual pathology. We conclude that RIBA positive, PCR negative patients have minimal disease activity. Elevated ALT and fibrosis may be associated with a non-alcohol steatohepatitis and these processes may be synergistic. Finally, number and type of RIBA bands is not a predictor of inflammatory activity.

*Desmet 1994. Ishak 1995

(P.147) A CORRELATION OF HAPLOTYPE WITH PHENOTYPIC EXPRESSION IN IRISH HAEMOCHROMATOSIS PATIENTS
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Haemochromatosis (HH), a common recessively inherited disorder of iron metabolism is closely linked to the HLA-A locus on chromosome 6. Linkage studies have demonstrated a close association between (HH) and the HLA alleles, A3 and B7 ("ancestral haplotype"). Heterogeneity at the molecular level may account for the variance in clinical phenotypic expression. The aim was to evaluate phenotypic expression of HH in the presence/absence of the A3-B7 ancestral haplotype. 32 probands (26M:6F) from unrelated Irish families were investigated. Phenotypic variability was assessed with regard to 1) age; 2) % trans.sat.; 3) serum ferritin; 4) liver bx iron grade; 5) body iron stores and 6) symptomatology. Three males were homozygous for A3B7, 15 were heterozygous for A3B7 and 2 were non-A3B7. Symptomatology, trans. sat., serum ferritin and liver bx grade were not influenced by homozygosity or heterozygosity for A3B7. Conclusion: There were no significant differences in phenotypic expression on comparison of the three haplotype groups. No predominant genotype appears to be responsible for phenotypic severity in Irish families indicating the possibility of multiple mutagenicity of the HH gene.

(P.148) CLINICAL AND BIOCHEMICAL EXPRESSION OF THE GENETIC ABNORMALITY IN HAEMOCHROMATOSIS
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The association between the HLA locus and Haemochromatosis (HH) has allowed early identification of affected siblings. It is unclear what proportion of subjects who are predicted to be homozygous or heterozygous for the disease by HLA typing develop the disease. Studies correlating clinical features with HLA type in families from Ireland - a putative source of this Celtic trait have not been described.

The aim was to correlate clinical, biochemical and pathologic features of HH with HLA typing in 67 first degree relatives of 12 probands.

Initial analyses identified 12 homozygous (HH), 40 heterozygous (Hn) and 15 normal (nn) individuals. However, 11/40 Hn individuals had stainable iron on liver biopsy, confirming HH. Further HLA analysis revealed 7 homozygous x heterozygous matings and identification of all disease haplotypes within each pedigree allowed final classification of 30 HH, 25 Hn and 12 nn individuals.
Conclusion: This study demonstrates the importance of HLA typing in the clinical management of families with HH. Furthermore, in multiply affected families the incidence of homozygous x heterozygous matings is high indicating the high degree of “pseudodominance” in the Irish population.

(P.149) NITRIC OXIDE MEDIATES HEPATOCYTE INJURY

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The degree of acute hepatic failure after severe trauma and sepsis is related to the extent of hepatocyte (HC) damage and cell death resulting from either necrosis or apoptosis. We have previously demonstrated that TNF-α and LPS can directly lead to HC necrosis, but not apoptosis. Recent, studies have shown that reactive oxygen intermediates (ROI) and nitric oxide (NO) are capable of inducing apoptosis in eukariotic cells. However, it is unclear whether ROI or NO are involved in HC cell death. The aims of this study were to evaluate the role of NO and ROI in HC cell death (apoptosis vs necrosis). HCs were isolated from Sprague-Dawley rats, and cultured with the NO donor, sodium nitroprusside (SNP) or the ROI generation system, hypoxanthine-xanthine oxidase (HX-XOD) and H2O2. The effect of LPS, TNF-α, and IFN-γ alone or in combination with different antioxidants and the NO synthase inhibitor, N-methyl arginine (NMA) on HCs was also assessed. SNP caused a dose-dependent increase in HC apoptosis. ROI generated by HX-XOD and H2O2 did not induce HC apoptosis, but when combined with antioxidants resulted in increased HC NO production and apoptosis. This effect was attenuated by NMA. SNP also induced HC damage and HC necrosis. Moreover, TNF-α-mediated HC damage and necrosis could be further reduced by the combination of antioxidants and NMA. These results indicate that ROI preferentially induce HC necrosis, but not apoptosis. Induction of NO resulted in both HC apoptosis as well as HC necrosis, which suggest that overproduction of NO may be detrimental during the SIRS.

(P.150) A NUTRITIONAL PROFILE OF 50 DIETETIC REFERRALS FROM AN ACUTE GERIATRIC UNIT

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Many older people are nutritionally compromised. There is clear evidence that: nutrition intervention reduces morbidity and mortality in older patients.

To identify the spectrum of nutritional abnormalities referred for dietetic intervention and the problems associated with nutritional assessment, 50 elderly patients were alphanumerically selected from files of the Department of Nutrition and Dietetics.

The most common dietetic interventions were: use of supplements 60%; high protein high calorie diet 46%; nasogastric feeding 26%; reduction fat 8%; iron/thiamine assessment 6%; high fibre diet 6%; diabetic diet 4%; nutrition swallow programme 2%; lipid lowering diet 2%. Some 60% referred required nutritional supplements, but the profile of intervention was not uniform. Mean albumin was 34.3g/l. Mean weight was 57.8kg. Poor cognitive status greatly increased the requirement for dietetic consultation time. Lack of dietetic resources results in inadequate monitoring of these patients following discharge. This study highlights the need for a dedicated clinical nutrition service, for medical services for older people.

References:
1. Sullivan, D. H., Walls, R. C. J. Am. Geriatr. Soc. 1994; 42: 471-477.
2. Larson, J., Unosson, M., Ek, A. C. et al. Clinical Nutrition 1990; 9: 179-184.

(P.151) UN-METABOLISED FOLIC ACID IN SERA OF SUBJECTS CONSUMING FORTIFIED FOODS

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Periconceptual consumption of folic acid has been shown to decrease the incidence of neural tube defects. The preventative strategy of universal food fortification with folic acid presents the possible risk of masking the diagnosis of cobalamin deficiency in pernicious anaemia. In addition, the ultimate long-term effect of universal exposure of adult or foetal cells to a synthetic substance, ie. folic acid, is unknown. In this study, the threshold oral dose of folic acid in a number of foods above which metabolically-unaltered vitamin appeared in serum post-prandially was determined in a young and elderly population by microbiological assay of serum pre-fractionated by HPLC. Subjects on a five-day regime of fortified cereal and bread along with their normal unfortified diet were shown to have a threshold level of 400μg/d, above which unaltered folic acid appeared in the serum. Individuals given folic acid in either isotonc saline, milk or white bread exhibited a threshold level of 200μg per serving. From patterns of food consumption in Ireland, even moderate levels of fortification are likely to lead to some population groups being exposed to excessive amounts of un-altered folic acid in serum.

(P.152) OXIDATIVE STRESS IN CYSTIC FIBROSIS

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An increase in oxidative stress in cystic fibrosis patients has been suggested. Activated neutrophils in the presence of chronic lung inflammation in addition to increased activity of the electron transport chain in CF may increase free radical generation. Antioxidant protection against free radical attack is likely to be compromised as a result of deficiencies in fat soluble antioxidants vitamins. In the present study stimulated thiobarbituric acid reacting substances (TBARS) were measured to determine the ability of plasma to withstand lipid peroxidation. Copper was used to initiate the breakdown of lipids to lipid hydroperoxides and eventually to aldehydes, mainly malondialdehyde (MDA). Pooled CF plasma and pooled control plasma were incubated for 0, 30, 60, 90, 140 and 200 min. MDA complexes with thiobarbituric acid which absorbs at approximately 535 nm. There is a lag phase where antioxidants
in the plasma or tissue protect against lipid peroxidation, then a log phase where the protective effect is overcome and finally the reaction reaches a plateau when lipid peroxidation is complete. Absorbance at 532 nm was measured in all samples and zero order and first derivative spectra were obtained. The lag phase appears to be longer in the pooled CF plasma compared with controls. Plasma α-tocopherol levels were within the normal range in both groups, indicating an alternative protective effect in CF.

(P.153) THE RESPONSE OF PLASMA HOMOCYSTEINE TO INCREASED METHIONINE SUPPLEMENTATION

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Mild hyperhomocysteinæmia is an established risk factor for heart disease. A source of homocysteine in humans is the essential amino acid methionine found in protein of animal origin. In an 8-week study weekly fasting plasma homocysteine levels were examined in a group of healthy male subjects (n=6) under normal dietary conditions (weeks 1 to 4) and in response to graded increased methionine intakes (weeks 5, 6, 7). Nutrient intakes, including methionine, were calculated from 4x3-day food records.

Under normal dietary conditions weekly mean plasma homocysteine levels were not significantly different (ANOVA) from each other ranging from 6.82±1.77 to 9.42±2.73 μmol/l. Doubling daily methionine intakes (supplementing with 25mg/kg/d) did not result in a significant increase in plasma homocysteine (8.56±3.68 μmol/l), however, significant increases were achieved when diets were supplemented with methionine at levels of 50 and 75mg/kg/d resulting in mean plasma homocysteine levels of 13.37±5.9 and 18.05±11.08, respectively.

Mean plasma homocysteine levels returned to baseline (8.76±3.42 μmol/l) 10 days post supplementation.

We conclude that supplementary methionine results in a significant increase in plasma homocysteine only when levels of five times the normal dietary intake are reached.

ENDOCRINOLOGY

(P.154) QUANTITATION OF LIPOPROTEIN LIPASE (LPL) mRNA EXPRESSION DURING HUMAN MONOCYTE MATURATION

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This study is evaluating the use of a synthetic construct which encompasses primer binding sites for LPL and a variety of cytokine and other transcripts, to quantify LPL expression in cultured human monocyte-derived macrophages. Following isolation of total RNA at various times during cell culture, its reverse transcription (RT) using random hexamer primers generates first strand cDNA and specific amplification of LPL cDNA targets by polymerase chain reaction (PCR), generates products identifiable on gel electrophoresis. Quantitation of message is obtained by incorporating the pAW108 construct in the RT assay in varying quantities as an internal standard with known amounts of monocyte-macrophage RNA (lμg). PCR amplification of this construct yields size distinguishable products from that produced by the monocyte-macrophage LPL cDNA transcript. PCR conditions for the assay have been optimised at 29 cycles of denaturation (limin@94°C), annealing (1.5min@55°C) and extension (limin@72°C). LPL mRNA has been detected in cultured monocytes and macrophages throughout their differentiation. Also increased expression of monocyte LPL mRNA has been observed following 15 hr incubations with chylomicrons (30μg/6x10⁶ mononuclear cells/ml) when compared with controls. Interestingly, little or no lipase mRNA was detectable in circulating monocytes using identical PCR conditions to preparations of mRNA from the day 4 and day 8 cultured cells. This methodology will now permit investigation of the factors controlling LPL expression in cultured human mononuclear cells.

(P.155) REGRESSION OF VASCULAR PLAQUE WITH GROWTH HORMONE

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Replacement growth hormone (GH) therapy in adult hypopituitarism is attracting increasing interest. In 1992 Markussis¹ detected premature atherosclerosis by ultrasonography in the untreated patient. We have shown plaque regression with patients on replacement GH (Norditropin) in a 4-month trial. 11 females and 9 males were recruited, mean age 49.6 years. At each timepoint plaque characteristics were measured by Duplex Ultrasound. 6 patients showed a large reduction in plaque size (mean 21%) after four months treatment (p value < 0.001). Similarly, highly significant values in Cholesterol, HDL and LDL and Apo A1 are achieved.

Mean

|                | Chol | HDL | LDL | Apo A1 |
|----------------|------|-----|-----|--------|
| pretreatment   | 6.54 | 1.23| 5.04| 119    |
| posttreatment  | 5.64⁺| 1.24⁺| 3.79⁺| 109⁺   |

⁺Parameters achieve a high degree of statistical significance (p< 0.001).

The significant reductions achieved in plaque characteristics in six patients studied who showed plaque formation correlates with other parameters traditionally accepted as reducing cardiovascular risk.

Reference

1. Markussis, V., Beshyah, S. A., Fisher, C., Sharp, P., Nicolaides, A. N., Johnston, D. G. Detection of premature atherosclerosis by high resolution ultrasonography in symptom free hypopituitary adults. Lancet, 1992; 340 (8829): 1188-92.
(P.158) INCREASED PRESSOR RESPONSE TO 
NORADRENALINE INFUSION IN PITUITARY 
DEPENDENT CUSHING’S SYNDROME

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Hypertension is found in approximately 70% of patients with 
Cushing’s syndrome, but the mechanism is poorly understood.
Previous studies in our unit have examined levels of 
exchangeable sodium, plasma renin and angiotensin II and 
cardiac sensitivity to phenylephrine. One previous study has 
demonstrated enhanced pressor responsiveness to noradrenaline 
in a group of patients with Cushing’s syndrome due to adrenal 
adenoma.

We have investigated the blood pressure response to 
noradrenaline in 7 patients with pituitary dependent Cushing’s 
syndrome and in 7 controls matched for age, sex and BMI. 
Noradrenaline was infused for 10 minute intervals at five 
different concentrations between 0.01 and 0.18 mcg.kg.min⁻¹ 
Multiple systolic and diastolic readings were recorded and the 
infusion was stopped if the systolic pressure became ≥ 200 
mmHg, diastolic ≥ 110 mmHg or the systolic pressure rose ≥ 35 
mmHg.

Baseline blood pressure in the patients with Cushing’s disease 
(CD) was 140/88 + 6/3 compared with 122/83 + 6/6 mmHg in 
the normal controls (NC). In 6 of the 7 patients with Cushing’s 
disease, the test had to be stopped before completion of the 
protocol, whereas this was necessary in only one control subject. 
The change in blood pressure from baseline to the blood pressure 
value recorded either at the time the test was stopped or at the 
peak blood pressure reading during equivalent noradrenaline 
infusions was compared between the matched pairs. The mean 
change in diastolic pressure was 22 + 5 mmHg in CD compared 
with 7 + 2 in NC (P<0.05). There was no statistically significant 
difference in either systolic pressure (28 ± 5 vs 26 ± 5 mmHg) 
or mean arterial pressure (23 ± 5 vs 14 ± 3 mmHg). These results 
demonstrate an increased diastolic pressor response to 
noradrenaline in Cushing’s disease. Increased pressor sensitivity 
to noradrenaline may contribute to the elevated blood pressure 
seen in Cushing’s disease.

(P.159) IRISH KINDRED WITH MULTIPLE ENDOCRINE 
NEOPLASIA 2A: RET PROTO-ONCOGENE MUTATION

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Multiple Endocrine Neoplasia type 2A (MEN2A) is an 
inherited disease comprising medullary thyroid cancer (MTC), 
primary hyperparathyroidism and phaeochromocytoma. Since 
1994 mutations have been identified in the RET protooncogene 
on chromosome 10 permitting DNA analysis of carrier status.

The proband, a 43 year-old mother of 8 children, presented 
in 1976 with full expression of MEN2A. Biochemical screening 
over the next 19 years only identified MTC in a 13 year old 
daughter that was confirmed by thyroid surgery.

DNA analysis identified a T2548C transition in the RET gene 
in the daughter. This is a common mutation in MEN2A that 
results in a substitution of cysteine by arginine at codon 634.
Carrier status was found in 1 of the 7 remaining children.

Given the certainty of DNA analysis the approach the 
MEN2A has altered such that carriers can be subjected to 
intensive screening and normal offspring need no further 
attention.

(P.160) PLASMA HOMOCYSTEINE IN INSULIN 
DEPENDENT (TYPE 1) DIABETES MELLITUS AND 
CONTROL SUBJECTS. EFFECT OF GENDER, AGE AND 
POSTURE

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Increased plasma homocysteine (tHcy) is an independent risk 
factor for premature vascular disease. Patients with insulin-
dependent diabetes have an increased prevalence of 
cardiovascular disease. Accordingly, we measured plasma tHcy 
concentration in 119 such patients (15-59y), randomly selected, 
and in 51 control subjects.

In controls, tHcy was higher in males than in females (supine: 
geometric mean (95% CI): 8.3 (7.2,9.6) v 5.9 (5.1,7.0) µmol/L, 
P<0.001), as previously described, but there was no gender 
difference in patients. Male patients, without microvascular 
complications, had lower tHcy than controls (supine: 6.5 (5.4, 
7.8) v 8.3 (7.2,9.6) µmol/L, p<0.05), but values in female 
patients without complications were similar to those of female 
controls. tHcy significantly correlated with age in diabetics but 
not in controls. tHcy increased in patients with increased severity 
of microvascular complications, partly due to the effect of age. 
tHcy was higher when standing than when supine in both 
controls (8.0 (7.0,9.1) v 7.1 (6.4,8.0)µLmol/L, p<0.05) and 
patients (6.9 (6.5,7.4) v 6.4 (6.0,6.9)µmol/L, p<0.02).

The absence of gender difference, the association between 
tHcy and age, and higher levels with increasing microvascular 
complications suggest tHcy could be of pathogenic significance 
in IDDM patients, despite unexpectedly low levels in male 
patients without complications. Differences between supine and 
eree samples may be due to haemodilution of albumin-bonded 
tHcy in the latter.

(P.161) TREATMENT OF HYPERTHYROIDISM WITH 
STANDARD DOSE/DOSES OF RADIO-ACTIVE IODINE 
IN THE WEST OF IRELAND

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A review of the treatment outcome of thyrotoxicosis with 
standard dose/doses of radio-active iodine (SDRAI) in 67 
consecutive patients presented to the Endocrinology Department, 
UCHG, from December 1992-December 1993 was analysed. The 
mean pre-treatment levels of free thyroxine (FT4) was correlated 
with the treatment outcome. There was statistically significant 
difference in the pre-treatment FT4 between responders and non-
responders to the first dose RAI (p = 0.001). Response with 
tHcy, from December 1992-December 1993 was analysed. The 
mean pre-treatment levels of free thyroxine (FT4) was correlated 
with the treatment outcome. There was statistically significant 
difference in the pre-treatment FT4 between responders and non-
responders to the first dose RAI (p = 0.001). Response with 

responded to the second and third doses of RAI respectively giving a total response rate of 92.5% and 97% respectively. Interestingly, 2/67 (2.99%) patients failed to respond even to the fourth dose of RAI. In total, 4/67 (5.97%) patients with TVD toxicity (3 females and 1 male). Two responded to the first dose (one with hypothyroidism and the other with euthyroidism). The remaining 2 required a second dose, which produced the same results. No statistically significant difference in the response rate between TVD toxicity and T4 toxicity (P = 0.9) was observed.

(P.162) CHARACTERISTICS OF 1,051 CURRENT IDDM ATTENDERS TO A DIABETES CENTRE DRAWN FROM A HOMOGENOUS N. EUROPoNEAN POPULATION

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Inherent in the St. Vincent Declaration targets is the need for continuous data collection and audit. We present preliminary information from the Mater database, the first prospective audit of patients from a homogenous Irish population.

1,051 IDDMs (527M:524F) were identified with the following characteristics (mean ± SD), age 37.3 ± 14.4 years, duration of DM 185 ± 11.2 years, BMI 24.4 ± 3.0 (males) and 24.2 ± 4.0 kg/m² (females), HbA1c 8.6 ± 1.97% (n<6.2%). No male:females differences existed in the above nor in microvascular complication rate 10.1% (predominantly peripheral vascular disease and ischaemic heart disease).

However, males were more likely to be current smokers (34% vs 27%, p = 0.01). Hypertension rates (17.2M vs 15.4F%, cholesterol > 6.5 mmol/l (6.2M vs 9.8F% were similar but more males had cholesterol < 5.2 mmol/l (64.8M vs 53.8F%, p < 0.01).

Clinical nephropathy was present in 11.4% of males vs 8.7% in females (p<0.05). 11.9% had clinical peripheral neuropathy. Retinopathy will be described elsewhere. 10.4% of females and 23.2% of males had a history of hyperthyroidism and 2.5% of females vs 1.4% of males had hypothyroidism. 7.8% had history of psychiatric disease. Conclusion Although not a population

(P.163) PREDICTORS OF CORONARY ARTERY DISEASE AND ITS SEVERITY IN PATIENTS WITH DIABETES MELLITUS

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Patients with diabetes mellitus (DM) are at a higher risk of developing vascular complications, including coronary artery disease (CAD). We performed a detailed analysis of predictors of CAD and its severity in patients with DM and chest pain.

19 patients in total Single vessel CAD (SVD) in 4, double vessel (DVD) in 5, and triple vessel (TYD) in 5 on cine contrast angiography Clinical, biochemical and dobutamine stress echocardiographic findings are tabulated below for patients with angiographically proven coronary artery disease.

| Characteristics          | Number | Percentage |
|--------------------------|--------|------------|
| Mean age (years)         | 59.6   | 9/5        |
| Typical angina yes/no    |        |            |
| Duration of DM (years)   |        |            |
| Mean HbA1c               |        |            |
| Type DM                  |        |            |
| Insulin dependent        | 5      |            |
| Oral hypoglycaemics      | 7      |            |
| Diet controlled          | 2      |            |
| Smoking history          | 6 (43) |            |
| Hypercholesterolaemia    | 4 (29) |            |
| Hypertension             | 8 (43) |            |
| Family history CAD       | 6 (43) |            |
| Angiopathy (PVD, CVA etc)| 3 (21) |            |
| Retinopathy              | 5 (35) |            |
| Proteinuria              | 5 (36) |            |
| DSE Positive for CAD     | 11 (79)|            |

Patients with TVD had a longer duration of DM (19.4 years) and were more likely to have retinopathy (100%). The sensitivity of DSE was excellent for severe disease.

Conclusion: Duration of DM, retinopathy, and a positive DSE were the best predictors of severe CAD in a diabetic population with chest pain.

(P.164) IMPAIRED RESPONSIVENESS TO ENDOTHELIN-1 IN INSULIN-DEPENDENT DIABETES MELLITUS (IDDM)

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The haemodynamic hypothesis for the pathogenesis of diabetic microangiopathy argues that an initial increase in microvascular flow leads to sclerosis and disturbed microvascular autoregulation. We have recently demonstrated impairment of vasocostrictor responses to endothelin-1, a potent endothelium-derived constrictor substance, in NIDDM and have suggested that this could contribute to the initiation of microangiopathy. The purpose of this study was to determine whether responsiveness to endothelin-1 is also impaired in IDDM. Non-specific vascular smooth muscle contraction was assessed using high dose serotonin. Eleven patients with IDDM and 11 control subjects underwent forearm blood flow (FFB) measurement by venous occlusion plethysmography in response to local infusions of endothelin-1 (5 pmol/min for 60 minutes) and serotonin (30 µg/min for 2 minutes). Control subjects showed slow onset vasoconstriction in response to endothelin-1 reaching maximum at 35 minutes (p<0.01). The diabetic group did not respond to endothelin-1. Group differences were significant (p=0.02). The two groups showed similar vasoconstriction in response to serotonin. In conclusion, vasoconstriction in response to endothelin-1 is impaired in IDDM. Non-specific vascular smooth muscle contraction is preserved. Impaired vascular responsiveness to endothelin-1 is a possible common mechanism for the pathogenesis of microangiopathy in IDDM and NIDDM.

(P.165) TOTAL AND IONISED CALCIUM IN THE INTENSIVE CARE UNIT

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We measured total corrected (Tca) and standardised ionised calcium (Ica) in a population of 76 intensive care (ICU) patients.
(with a mean age of 57±22 years, 59% male) to determine the prevalence of abnormalities in circulating calcium and its possible determinants. Severity of illness was measured by the APACHE II score (acute physiological and chronic health evaluation). For comparison of Ica we examined 20 subjects undergoing arterial gas samples which proved to be normal and 40 non-critically ill hypoxic patients. Ica was measured on arterial gas samples and corrected for pH.

84% of ICU patients had a Total Ca (unadjusted) of <2.2 mmol/l. After adjustment for serum albumin, 55% of ICU patients had a Total Ca <2.2 mmol/l. 30% of ICU patients had a serum phosphate of <0.8 mmol/l. Ica in controls was 1.44 ± 0.017 mmol/l and 1.38 ± 0.015 mmol/l in hypoxic non ICU patients (NS). Ica in ICU was lower: 1.34 ± 0.016 (<0.003). Tca and Ica were not significantly related. Tca and Ica did not significantly differ between patients who died and who survived in the ICU, and they were not related to APACHE II score. In conclusion, both Tca and Ica are frequently low in ICU patients but do not predict APACHE II score or death.

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**INFECTION DISEASE / GU MEDICINE**

(P.167) NEEDLESTICK INJURIES AND HIV ANTIBODY TESTING IN THE VIRUS REFERENCE LABORATORY 1992-1995

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From July 1987 to June 1995 there was a 16-fold increase in the annual number of specimens submitted to the virus reference laboratory because of a perceived risk of contracting HIV through a needlestick injury, blood splash, human bite, or through occupational exposure. Needlestick-associated specimens also comprise an increasing proportion of 'at-risk' specimens, rising from 0.9% in the year July 1987-June 1988 to 9.4% in the year July 1994-June 1995.

Between July 1992 and June 1995 a total of 1787 patients had specimens submitted for HIV antibody testing after a perceived exposure to HIV. Of these only 209 patients had more than 1 specimen taken. Although the time of putative exposure is rarely available, the median interval between 1st and 2nd post-exposure specimens for these 209 patients is 3 months with 136/209 (65%) lying between 1 to 6 months.

If the risk of HIV infection from a needlestick injury is assessed as sufficient to warrant serological investigation, the timing and number of blood samples are important. A negative report from a single early specimen may not indicate an absence of infection. A baseline specimen and follow-up specimens at 6 weeks, 3 months and at a minimum of 6 months post-exposure are recommended. Appropriate serology for other viral infections (hepatitis B and hepatitis C) should also be considered.

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(P.168) USING THE INTERNET AND THE WORLD WIDE WEB TO COMBAT INFECTIOUS DISEASE

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The Internet and the World Wide Web are potentially significant channels of communication to both national users of the virology service provided by the Virus Reference Laboratory and the international virology community. World Wide Web Pages are being developed by the WHO, the CDC in the US, Senti-Web in France, and by the CDSC in England and Wales as a means of rapidly disseminating information on new and resurgent infectious diseases.

The Virus Reference Laboratory launched its Web home page in early 1995. This initially referenced the Web versions of Virus Alert, the Virus Reference Laboratory Bulletin. Additional Web pages outlining the services provided by the VRL were added later in the year. The VRL Web home page also references international Web pages of virology and associated interests.

The VRL Web Home Page has had 4512 external accesses between April and December 1995. These accesses originate from all over the world.

Ireland: 16%  
U.K.: 15%  
Europe: 21%  
N. America: 39%  
Rest of the world: 10%

An encouraging feature is the level of accesses to the electronic editions of 'Virus Alert'. These total over 50% of homepage hits.

The VRL is continuing to develop its Web pages to encourage local users to avail of its services.

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(P.169) HEPATITIS A IGM TESTING IN THE VIRUS REFERENCE LABORATORY 1992-1995

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From July 1992 to December 1994 the number of hepatitis A infections indicated by the presence of anti-hepatitis A immunoglobulin M detected by the virus reference laboratory fell from over 50 cases per month to less than 15 cases per month. Over the same period the total number of hepatitis A IgM tests carried out by the Virus Reference Laboratory nearly trebled from approximately 300 per month to over 800 per month.

Since the beginning of 1995 a significant sustained increase in the numbers of hepatitis A cases has occurred. The number of cases in 1995 was 229 against 121 in 1994. This reverses the continuous fall observed over previous years. The reason for this increase remains unidentified at present. This increase has occurred following a dramatic increase in the total number of hepatitis A IgM tests carried out by the VRL since February/March 1994. The increase in the number of tests carried out since this time is primarily attributable to increased hepatitis testing following receipt of hepatitis C-contaminated Rhesus anti-D immunoglobulin.

Analysis of the age profiles of the positive patients and of all the referrals indicates that 95.5% of positive results were found in patients aged 50 yr or less whilst 31% of all HAV IgM tests were performed on individuals aged 51 yr or greater.

This raises the question whether greater selectivity should be employed when requesting Hepatitis A tests.

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(P.170) VARIATION IN DRUG COMPLIANCE RATES IN HIV POSITIVE PATIENTS

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One hundred percent drug compliance is rarely achieved, especially in patients on long term multi drug regimens. Previous
studies report compliance rates ranging from 30 to 50% in HIV negative patients. There has been no comprehensive study of compliance in HIV positive patients. Accurate measurements of compliance are not easy; easy measurements of compliance are not accurate!.

To determine the compliance rate in HIV positive patients attending St. James Hospital, Dublin, one hundred consecutive patients attending the service were interviewed (homosexual 46, IVDU 45, heterosexual 9). The questionnaire was divided into three sections. Firstly, a medical review was completed by the clinician who included demographic data, CD4 count, CDC staging, Karnofsky index and prescribed medication. Secondly, the pharmacy detailed the medication dispensed to each patient. The third section comprised a patient interview to determine adherence to, and understanding of prescribed drug therapy.

We report an overall compliance rate of 61%. This was unevenly distributed between the two main patient groups (89% in homosexuals, 24% in IVDU). The following factors were found to influence compliance: number of medications, CDC stage, Karnofsky index, dysphagia, educational and socio-economic factors. We also found that poor patient understanding of the prescribed therapy significantly affected compliance.

Reference

Haynes, R B Patient compliance then and now Patient Educ Couns 1987, 10, 103-105

(P.171) HIV TESTING AND CONCOMITANT STD INFECTION

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The aim was to determine the incidence of STDs in patients presenting for HIV testing at the Department of Genito-Urinary Medicine, Saint James's Hospital.

A retrospective analysis of all patient notes who presented for HIV testing between July '94 and December '94 was undertaken. According to clinical policy all patients had been screened for the following STDs: Neisseria gonorrhoea, Chlamydia trachomatis Trachomonas vaginalis, Candida, Human papilloma virus, Herpes simplex virus Syphilis and Hepatitis B. In addition intravenous drug users (IVDUs) were also screened for Hepatitis C. All patients underwent pre test counselling. Sex, age, risk groups and diagnoses were noted.

504 patients presented for HIV testing, of whom 66% were male, 34% female, with an average age of 28.5 years. Of the total, 8% were, or had previously been IVDUs. Of the total 46 IVDUs, 37 were heterosexual males and 2 were bisexual and 4 were females. 10.2% of the male patients were homosexual and 4 4% bisexual.

There were 15 positive HIV tests (3% of total); 14 males and 1 female. In this group there were 5 patients with hepatitis C, all of whom were IVDUs. No other STDs were detected.

In the HIV negative group Hepatitis C was diagnosed in 20, Hepatitis B in 4, Anogenital warts in 58, Herpes genitalis in 10, Syphilis in 3, N. gonorrhoea in 9, T. Vaginalis in 1, C. trachomatis in 12, G. vaginalis in 5 and Candidiasis in 47.

This study confirms the importance of STD screening in all patients requesting a HIV test. Of the total testing for HIV, 30% had a concurrent STD diagnosis. Although no STDs were identified in the HIV positive group this may be more a reflection on the makeup of the Irish HIV positive population, the majority being IVDUs, rather than a difference in the mode of sexual transmission. Of the 15 HIV positive patients, 7 were IVDUs: Other reasons may include the time difference, years in some cases, between risk exposure and the time of HIV testing.

(P.172) ROLE OF PCR & SEROLOGY IN THE DIAGNOSIS OF TOXOPLASMOSIS IN AIDS PATIENTS

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Toxoplasmosis is the most common opportunistic infection of the central nervous system in AIDS patients. In clinical practice the diagnosis depends on clinical, radiographic and serological findings coupled to clinical response to therapy. Brain biopsy is not routinely performed.

In this retrospective review, we describe our experience with diagnosing toxoplasmosis. We examined the clinical demographics and presentation, radiographic findings, response to therapy and patient outcome.

(a) Role of polymerase chain reaction (PCR) in detecting toxoplasma gondii from blood and CSF samples

(b) The usefulness of serology in diagnosing acute infection. All cases diagnosed as toxoplasmosis based on the above criteria were reviewed. PCR to detect toxoplasma gondii DNA used primers to the B1 gene giving a 223bp amplification product Serological tests used were Sabin-Feldmen DYE test and latex agglutination.

There were 25 cases diagnosed (17 M, 8F, CD4 0-300; CDC IV 19). 3 patients unknown to be HIV positive presented with cerebral toxoplasmosis. 22 patients were not receiving continuous systemic prophylaxis against PCP. Diagnostic value of T gondii PCR in blood and CSF showed a sensitivity of 20%, specificity of 100%, PPV was 100% and NPV was 40%. Determination of Ig subtype was of limited value 25% (6) of patients were seronegative of whom 50% (3) had histologically proven disease. 2 of these latter 3 cases were PCR negative. The DYE test was of poor predictive value.

This review confirms the need to combine all parameters in making a diagnosis of toxoplasmosis in immunocompromised hosts.

(P.173) EVALUATION OF THE ABBOTT IMx HIV-1/HIV-2 3rd GENERATION PLUS ASSAY FOR THE DETECTION OF ANTIBODY TO HIV-1 AND HIV-2 INCLUDING SUBTYPE O IN HUMAN SERUM AND PLASMA

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The Abbott IMx HIV-1/HIV-2 3rd generation plus assay was developed, rapid and fully automated microparticle enzyme immunoassay Abbott IMx HIV-1/HIV-2 3rd generation plus assay for the detection of antibody to HIV-1 and HIV-2 including subtype O in human serum or plasma was evaluated.

The assay was evaluated by testing specimens from blood donors, diagnostic populations and hospitalized patients, HIV seroconversion panels confirmed HIV-positive specimens, and potentially interfering specimens.

The Abbott IMx HIV-1/HIV-2 3rd generation plus assay showed an overall apparent specificity of 99.97% (lower limit
of 95% CI 99.84%) in the tested blood donor populations (n=3471). This comparable to the specificity found for the Abbott IMx HIV-1/HIV-2 3rd generation plus EIA (99.93%) and the AxSYM HIV-1/HIV-2 Assay (99.90%).

The apparent sensitivity of the Abbott IMx HIV-1/HIV-2 3rd generation plus assay is at least equivalent to that of the Abbott IMx HIV-1/HIV-2 3rd generation plus EIA and the AxSYM HIV-1/HIV-2 Assay. Of 21 HIV-1 seroconversion panels tested, the Abbott IMx HIV-1/HIV-2 3rd generation plus assay detected seroconversion earlier on up to 6 panels, depending on the comparison assay. Among 785 specimens from asymptomatic and symptomatic HIV patients, the Abbott IMx HIV-1/HIV-2 3rd generation plus assay detected 100 (785) including 7 specimens characterized as HIV-1 Subtype O.

The Abbott IMx HIV-1/HIV-2 3rd generation plus assay is an extremely sensitive and highly specific assay for the early detection of antibody to HIV-1/HIV-2 and shows at least an equivalent performance to the Abbott IMx HIV-1/HIV-2 3rd generation plus EIA and the AxSYM HIV-1/HIV-2 assay. The fully automated IMx instrument system offers ease of use and rapid results on a widely accepted and reliable platform.

(P.174) ANTI-STREPTOKINASE ANTIBODIES IN THE GENERAL POPULATION

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Streptokinase (SK), a 47kD protein produced by Group C b hemolytic streptococci, is a widely used thrombolytic agent. Anti-SK antibodies arise either as a result of therapeutic administration of SK or following natural infection with streptococci. Although the clinical significance of anti-SK antibodies is not clear, there is evidence that some anti-SK antibodies arising from natural infections can interfere with SK activity in vitro, resulting in thrombolytic failure. To facilitate further investigations of these antibodies, we have developed and validated a highly sensitive functional assay, which measures SK neutralisation activity of serum independently of other circulating inhibitory factors in the sample, and a rapid and convenient enzymeimmunoassay for the detection of anti-SK antibodies. Analysis of over 200 random serum samples from the local blood bank with the enzymeimmunoassay showed the prevalence of anti-SK antibodies to be approximately 13%. All the positive samples and an equal number of the negative samples randomly selected were analysed by the functional assay. The agreement between the results of the two assays was excellent indicating that our enzymeimmunoassay was a conventional method for detection of anti-SK antibodies which could neutralise SK activity in vitro.

(P.175) SENSITIVE AND RAPID DETECTION OF M. TUBERCULOSIS IN SPUTUM USING PCR

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The timely identification of M. tuberculosis infection is important for patient management with regard to anti-tuberculosis drug therapy, isolation precautions and prophylaxis. Conventional methods of detection such as microscopy and culture either lack sensitivity and specificity or are time-consuming. In this study we investigated the use of a PCR based diagnostic assay for the detection of M. tuberculosis in sputum samples. This assay has been developed by BioResearch Ireland (BRI) and Raggio Italgene. Sputum samples were lysed and PCR amplified using an M. tuberculosis complex-specific primers. The results obtained using the BRI/CT-TRAK™ technology were initially compared to the Amplicor system (Hoffman La Roche). Both probe detection methods represent fast and reliable methods for the detection of M. tuberculosis in clinical samples. This test is designed to eliminate the possibility of obtaining false negatives.

(P.176) STRONGYLOIDES STERCORALIS INFECTION IN IRELAND; REPORT OF TWO CASES AND REVIEW

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Strongyloides stercoralis infection in humans is endemic in the tropics. As travel is becoming more common, it will be seen more frequently. Two cases of this infection in Irish people are described.

Case I. A 21 year old women had travelled and worked in poor rural areas of Mexico for one month, three years before presentation. Two and a half years later she developed abdominal discomfort, anorexia and sore throat. Myalgia, arthralgia and a transient skin rash began to appear in the next month. Eosinophilia, mild anaemia and raised liver blood tests were noted. ELISA test for strongyloides was positive but parasites were not seen in the faeces. Ivermectin was given and the patient feels better.

Case II. A 31 year old nurse had arthralgia, fatigue and some weight loss for 18 months. On two occasions in the last four years, she had been travelling extensively in S.E. Asia for a total of four months. She was admitted to hospital because of acute fever and loin pain. A urinary tract infection was diagnosed. Absolute eosinophil count was raised 0.63x10^9/l. ESR was 17mm/hr. Strongyloides ELISA was positive and treatment administered as above.

Strongyloides is the most important nematode in the returned tropical traveller. It can multiply and persist within the body for long periods of time and it can cause hyperinfection syndrome, a protean fulminating infection of bowel, lungs, blood stream and brain, in those who are immunocompromised. Diagnosis can be difficult by stool microscopy. Thiabendazole has side effects but ivermectin is safe and effective.

(P.177) CLOSTRIDIUM DIFFICILE ASSOCIATED DIARRHOEA IN HIV POSITIVE PATIENTS

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Studies have suggested that the incidence of C. difficile associated diarrhoea (CDAD) in HIV positive patients is 3-4.1 per 100 hospital admissions. More severe symptoms have
been documented in this patient group. Between January and June 1995, there was an outbreak of C. difficile-associated diarrhoea (CDAD) at St. James's Hospital. The aims of this study were to determine the incidence and outcome of CDAD in HIV positive and negative patients. We prospectively reviewed all patients with diarrhoea, a positive C. difficile cytotoxin assay, and in whom no other infectious cause for diarrhoea was identified. Demographic data, history of diarrhoeal episodes, risk factors and outcome were recorded.

The incidence of CDAD in HIV negative patients was 1.2 per 100 hospital admissions, compared to 1 per 100 admissions in HIV positive patients. The average number of courses of antibiotics received, in HIV negative patients prior to the onset of symptoms was 2.3, and 76% of this group were exposed to third generation cephalosporins. HIV positive patients received an average of 3.4 courses of antibiotics and no patients received third generation cephalosporins. There were no deaths due to CDAD in HIV positive patients however 4 HIV negative patients died from severe pseudomembranous colitis.

In conclusion we documented a unexpectedly low incidence and complication rate of CDAD in HIV positive patients. This is surprising considering their multiple hospital admissions and exposure to antimicrobial and chemotherapeutic agents. This may be explained by the fact that all HIV positive patients in St. James's Hospital are nursed in a special unit. Heightened infection control awareness due to the underlying diagnosis may reduce risk of nosocomial acquisition of C. difficile due to cross infection.

(P.178) DEMOGRAPHIC CHANGES IN HIV POSITIVE TESTS IN IRELAND 1987 - 1995

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The number of new positive HIV specimens detected at the virus reference laboratory has risen from a cumulative total of 638 in July of 1987 to 1597 in September of 1995. We examined our data to determine the proportional make up of these positives. We further examined our data in order to show the further category which includes blood donors, haemophiliacs, IVDA made up 49% of the total positive HIV specimens. Positive specimens from homosexual individuals rose from 10.9% of total positives in August 1987 to 20.6% in September 1995. There were no recorded positive specimens from heterosexual exposure in August 1987 but in September 1995 8.9% of positive specimens recorded heterosexual exposure. A further category which includes blood donors, haemophiliacs, transplant patients and organ donors made up 25% of total positives in August 1987 and in September 1995 made up 22.4% of total positives. We further examined our data in order to show how these changes occurred by ascertaining how many new positive patients have been discovered per year in each of the main risk groups. See table.

| Year | Ivda | Hom | Het |
|------|------|-----|-----|
| 1987 | 56   | 18  | 0   |
| 1988 | 55   | 17  | 8   |
| 1989 | 59   | 13  | 6   |
| 1990 | 50   | 17  | 6   |
| 1991 | 49   | 14  | 6   |
| 1992 | 47   | 14  | 6   |
| 1993 | 46   | 13  | 6   |
| 1994 | 46   | 13  | 6   |
| 1995 | 46   | 13  | 6   |

We conclude that IVDA made up a smaller proportion of newly diagnosed cases of HIV infection in 1995 than they did in 1987. Conversely a history of homosexual or heterosexual exposure is more frequent in newly diagnosed HIV infection in 1995 than in 1987.

MICROBIOLOGY

(P.179) DEVELOPMENT OF IMMUNOASSAYS FOR THE DETECTION OF PARVOVIRUS B19 IgG AND PARVOVIRUS B19 IgM

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With the growing awareness of Parvovirus B19 the need for an efficient immunodiagnostic test for the detection of antiviral antibodies is becoming increasingly important. Previous immunoassay development has been hampered by lack of sufficiently pure viral antigens. We have developed two immunoassays based on recombinant viral antigen for the detection of both IgM and IgG antibodies. The IgM immunoassay is of the Mu-capture format whereas the IgG immunoassay relies on the capture of anti-Parvovirus B19 IgG by immobilised viral antigen. Both immunoassays can be completed within 2.5 hr. Assay evaluation showed sensitivity of 100% and specificity of 95% for both IgG and IgM detection when compared against Parvovirus B19 IFA. Intraassay and interassay reproducibility were also examined and were found to be in the range 2-10% and 5-15%, respectively. Both immunoassays are sufficiently reliable and robust to facilitate routine use as Parvovirus B19 screening immunoassays.

(P.180) ECHOVIRUS TYPE 22 AND SUDDEN DEATH AMONG INFANTS

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In the United Kingdom echovirus type 22 (Echo-22) is regularly isolated, with nearly 200 reports annually to the Central Public Health Laboratory. Reports increased during 1986-1988 and overall it is the second most commonly reported echovirus in the U.K. Echo-22 epidemiology is different to that of other enteroviruses; over 90% of patients with Echo-22 isolated are less than 2 years of age Echo-22 shows distinctive and unique cytopathogenic features in tissue culture, and based on sequence analyses, it seems to belong to a separate subgroup of picornaviruses.

Echo-22 has been associated with respiratory symptoms in premature infants, myocarditis and severe encephalitis. In 1989 an outbreak of acute flaccid paralysis associated with echo-22 was described in Jamaica in six patients, four of whom died.

We describe three cases of sudden death in infants associated with echovirus type 22 infection:

Case 1: S D. born 20/7/94; birth asphyxia and death at two days of age; Echo-22 isolated on 22/11/94 from spleen.

Case 2: S N born 1/1/94; sudden death on 21/9/94; Echo-22 isolated on 26/11/94 from lymph node.

Case 3: L B born 8/11/95, sudden death on 10/11/95, Echo-22 isolated on 13/11/95 from post-mortem nasopharyngeal aspirate.

(P.181) UNTREATED URINARY TRACT INFECTIONS

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This study assessed the antibiotic sensitivity of organisms causing urinary tract infections (UTI) among genito-urinary
medicine (GUM) clinic attenders in order to determine whether it is worthwhile giving tetracycline for dipstick (nitrite) positivity, even in the absence of clinical features of UTI.

We looked retrospectively at 100 laboratory confirmed UTI's diagnosed among GUM clinic attenders over a period of eight months. We assessed antibiotic sensitivities of the organisms involved, and determined how many dipstick positive urines which were left untreated turned out to be real UTI's.

86% of UTI's were due to coliforms and 66% of these were sensitive to tetracycline. 4% of UTI's were due to staphylococcus saprophyticus, 3% due to beta haemolytic streptococcus group B, 2% due to enterococcus, 2% due to proteus species and 2% due to coagulase negative staphylococci. 25% of nephur positive urines were left untreated. 32% of these were nitrite positive. Failure to treat a positive urine dipstick which turned out to be a UTI necessitated a further clinic visit for adequate treatment.

Nitrile positive urines should be treated as a UTI, even in the absence of clinical features of UTI, either with trimethoprim or tetracycline. The number of untreated UTI's and unnecessary extra visits to GUM clinics would have been reduced with the use of judicious antibiotic therapy for nitrite positive urines.

(P.182) CLONAL SPREAD OF VANCOMYCIN-RESISTANT ENTEROCOCCUS FAECIUM AMONG CANCER PATIENTS

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Strains of enterococci resistant vancomycin have been reported with increasing frequency. In 1995, we investigated an increase in the frequency of vancomycin-resistant Enterococcus faecium (VREF) among patients in the haematology/oncology unit using pulse-field gel electrophoresis (PFGE) to genotype these isolates and to assist in establishing the source of these VREF. Eighteen clinical isolates of VREF from blood, urine, sputum and faeces and two environmental isolates were collected from separate patients between March and July 1995. Minimum inhibitory concentrations (MICs) to several antibiotics including tetracycline and vancomycin were determined by agar dilution. PFGE were performed following Smal restriction endonuclease digestion. Antimicrobial susceptibility testing revealed high level resistance to vancomycin and teicoplanin; MICs >128 mg/L and >32 mg/L respectively. This antibiogram is consistent with a van A phenotype. PFGE of all 20 isolates revealed identical patterns indicating clonal spread of VREF. Subsequent implementation of infection control measures reduced the frequency of VREF isolation. PFGE proved useful in demonstrating clonal spread of VREF and in emphasizing the need for infection control measures.

(P.183) AN AUDIT OF 520 EPISODES OF BACTERAEMIA IN A DUBLIN TEACHING HOSPITAL

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A prospective audit of bacteraemia in our 600 bed teaching hospital was carried out from February 1991 to March 1993. Clinical and microbiological data were collected on 520 episodes of bacteraemia in 78 patients. Of these 230 (42%) were hospital acquired and 200 (38%) community acquired.

Urinary tract and respiratory tract sources were implicated in 30% and 14% of community acquired episodes, making E. coli and S. pneumoniae the commonest community acquired isolates (41% and 16% respectively). Other Gram negative bacilli accounted for 13% and S. aureus for 11%.

Coagulase negative staphylococci were the commonest hospital acquired isolate (24%) followed by S. aureus (22%), E. coli (15%) and Enterococcus spp. (10%). Enterobacter spp. were the second commonest Gram negative isolate (5%). Central venous cannulae were implicated in 43% of hospital acquired cases. Urinary tract infections accounted for 20%. 63% of which were catheter related. Invasive diagnostic procedures (angiography, prostate and liver biopsies, sinography) were implicated in 10 episodes.

Gentamicin resistance was found in 9% of hospital acquired aerobic Gram negative bacilli and MRSA accounted for 13% of hospital acquired S. aureus. These figures are higher than expected but may be explained by outbreak of MRSA and gentamicin resistant Enterobacter spp. which occurred during the study period.

(P.184) HAEMAGGLUTINATION STUDIES ON MORAXELLA CATARRHALIS

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The past several years have seen a significant increase in the recognition of Moraxella (Branhamella) catarrhalis as a respiratory pathogen(1). The pathogenic mechanisms employed by the organism are largely unknown, but adherence may play a role(1).

In our investigation the haemagglutinating activity of 40 isolates of M. catarrhalis was determined by a microtitre method. No isolate agglutinated horse, chick or sheep red blood cells (RBC). Seventeen isolates agglutinated human RBC, while 7 of these 17 isolates also agglutinated rabbit red blood cells. Haemagglutination of human and rabbit red blood cells was inhibited by porcine mucin. Galactose inhibited the haemagglutinating activity of the 7 isolates which agglutinate both human and rabbit RBC and yet had no effect on the haemagglutinating activity of the isolates which haemagglutinate human RBC alone.

Electron microscopy studies of the bacteria demonstrated a diffuse outer fibrillar layer on the surface of haemagglutinating positive isolates, this layer was subsequently removed following trypsin treatment, as was the haemagglutinating activity. A 200 kDa trypsin sensitive protein appears to be associated with haemagglutinating properties.

References
1. Catlin, B. W. Branhamella catarrhalis: an organism gaining respect as a pathogen. Clin. Microbiol. Rev. 1990; 3: 293-320.
2. Mbaki, N., Rikitomi, N., Nagatake, T., Matsumoto, K. Correlation between Branhamella catarrhalis adherence to oropharyngeal cells and seasonal incidence of lower respiratory tract infections. Tohoku J. Exp. Med. 1987; 153: 111-121.
(P.185) A SURVEY OF THE PERIOD PREVALENCE OF METHICILLIN RESISTANT STAPHYLOCOCCUS AUREUS (MRSA) IN IRELAND

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MRSA is an increasingly important cause of morbidity, and is spreading from large hospitals to smaller community-based facilities and nursing homes. The objective of this study was to obtain an indication of the size of the MRSA problem in Ireland prior to introducing national MRSA control guidelines.

A survey of all microbiology laboratories in Ireland was carried out over two weeks in Spring 1995. For patients from whom MRSA was isolated during the study period standard demographic and clinical data were requested and period prevalence/1000 discharges was calculated.

All 45 microbiology laboratories surveyed responded. MRSA was isolated from 448 patients during the 2 week period. The period prevalence of MRSA/1,000 discharges was 16.5. Males aged 65+ had the highest rate of infection (50/1000 discharges). Half of all isolates were from patients in surgical or medical wards, but 4% were from community-based sources e.g. GP’s, nursing homes, hospices. Thirty-two percent of MRSA patients were infected rather than colonised.

MRSA is clearly a substantial problem in Ireland. While it is largely a hospital problem at present, the increasing trend for day procedures and shorter stays means that infection will increase in the community. A survey in a university hospital in the USA revealed 41% of MRSA cases to be community-acquired.

(P.186) THE PREVALENCE OF CHLAMYDIA AND MYCOPLASMA IN CHILDREN WITH RECURRENT ACUTE TONSILLITIS

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Tonsil core specimens were cultured for bacteria including Mycoplasma, Chlamydia and Ureaplasma urealyticum in 70 children undergoing tonsillectomy for recurrent acute tonsillitis. Serology for Chlamydia and Mycoplasma pneumoniae was obtained in 55 of the children. The polymerase chain reaction (PCR) was used to investigate the presence of Chlamydia pneumoniae in core tonsil tissue. Ureaplasma urealyticum was cultured in three children (4.3%) and Mycoplasma salivarium obtained in 55 of the children. The polymerase chain reaction demonstrated past infection with C. pneumoniae in 18% and with M. pneumoniae in 16% of children with recurrent tonsillitis. However C. pneumoniae and M. hominis do not play a significant role in childhood recurrent tonsillitis.

(P.187) HIGH LEVEL GENTAMICIN RESISTANCE IN E. HIRAE

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Multiply resistant enterococci are increasingly common causes of serious infection in hospitalized patients. High level gentamicin resistance (MIC > 1000 mgA) in enterococci further compromises the therapy of such infections.

We have identified seven clinical isolates of Enterococcus hirae demonstrating high-level gentamicin resistance (HLGR: MIC > 1000 mg/l). To our knowledge this is the first report of HLGR for this enterococcus species. Plasmid analysis has demonstrated the presence of a single, large plasmid in all seven isolates, as well as several smaller plasmids in some of the isolates. Filter mating experiments have revealed that in all seven cases, HLGR was transferred to a laboratory recipient E. faecalis JH-22 by conjugation. Plasmid analysis of transconjugant strains confirmed transfer of the large plasmid in all cases. Based on restriction enzyme profiles, two distinct conjugative plasmids were identified for the E. hirae isolates investigated. At present we are using Southern blot techniques with oligonucleotide probes designed to hybridise to the HLGR determinant found in other species of Enterococcus. The results will confirm whether or not the same resistance determinant is responsible for the dissemination of HLGR in the genus Enterococcus.

(P.189) GENTAMICIN SERUM ASSAYS: AN AUDIT

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Aminoglycosides remain commonly used in the treatment of severe Gram negative infection and have conventionally been given on a twice or thrice daily basis. Single daily dosing offers advantages with respect to less nephrotoxicity, better bactericidal activity, convenience, nursing time, cost and should avoid subtherapeutic dosing which has a significant impact on outcome. We reviewed serum gentamicin assays from January to December 1995 to assess potential toxicity and subtherapeutic dosing in patients who received once daily gentamicin and those who received multiple daily dosing. 4346 assays were performed in the study period. 520 of those were random assays and not included. There was a trend towards significantly less potentially toxic levels in the once daily group compared to the multiple daily group (p<0.1). Once daily dosing produced significantly less subtherapeutic dosing (p<0.001). Over 98% of peak assays in the once daily group were in the recommended range. We conclude that current practice of multiple daily dosing of gentamicin leads to significant underdosing and more potentially toxic trough levels. Measurement of trough assays only in patients who are treated with once daily aminoglycosides is sufficient and will have considerable cost savings.
(P.190) RSV SUBGROUP PREDOMINANCE IN IRELAND OVER SEVEN YEARS
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Respiratory, syncytial virus (RS virus) is a major respiratory pathogen of infants less than 1 year old. It occurs in annual epidemics during the winter and early spring in temperate climates. During RS virus epidemics a significant number of infants less than 6 months old are hospitalised with symptoms of bronchiolitis and pneumonia.

RS virus exists in two antigenically distinct subgroups, A and B, which are known to cocirculate in the same community during the same RS virus season. There is much debate regarding the virulence of one strain over the other.

Using a panel of monoclonal antibodies specifically directed against the two RS virus strains, 167 RS virus isolates from specimens sent to the Virus Reference Laboratory, University College Dublin, over seven consecutive RS virus seasons (1987-1994) were typed and the RS virus subgroup predominance monitored. Subgroup A was the most predominant of the RS virus isolates accounting for 67.7% of the total and was found to be the predominant RS virus strain in six out of the seven RS virus seasons studied. Subgroup B predominated in a season in which the number of RS virus detections peaked much later than normal.

(P.191) IDENTIFICATION AND SENSITIVITY TESTING OF CANDIDA Sp. ISOLATED FROM PATIENTS IN THE INTENSIVE CARE UNIT
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Treatment of fungal infections in patients in intensive care unit (ICU) is usually empiric. The aim of this study was to identify Candida species isolated from I.C.U. patients and to test their susceptibility to antifungal agents to enable more directed therapy.

Forty Candida sp. from 23 patients in I.C.U. were isolated from the following sites, blood culture (5), central venous catheter (7), chest drain fluid (5), wounds (8), catheter urine (8), bronchial lavage (3), sputum (4). Strains were identified by standard procedures. Minimum inhibitory concentrations of amphotericin B, 5-flucytosine and fluconazole were obtained against the two RS virus strains, 167 RS virus isolates from specimens sent to the Virus Reference Laboratory, University College Dublin, over seven consecutive RS virus seasons (1987-1994) were typed and the RS virus subgroup predominance monitored. Subgroup A was the most predominant of the RS virus isolates accounting for 67.7% of the total and was found to be the predominant RS virus strain in six out of the seven RS virus seasons studied. Subgroup B predominated in a season in which the number of RS virus detections peaked much later than normal.

(P.192) GANGLION INFILTRATING THE ULNAR ARTERIAL WALL - AN UNUSUAL CASE
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Ganglion is probably the commonest tumour encountered in the hand and the wrist. It often arises from tendon sheath or lining of a joint capsule. The treatment can be surgical or nonsurgical, the latter includes aspiration with or without injection of steroids. Surgical treatment of ganglion can pose a difficult situation to deal with. It requires hand surgeon to deal with one such problem.

We present a 46 year old man with tender mass in the hypothenar eminence. During surgical exploration it was obvious that the ganglion was infiltrating the wall of the ulnar artery, and the histology proved this later.

The clinical features, management and the outcome of this unusual case are discussed.

(P.193) ACUTE ISCHAEMIC PRECONDITIONING INCREASES MUSCLE FLAP SURVIVAL
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Ischaemic preconditioning (IPC) of the myocardium with repeated brief periods of ischaemia and reperfusion (I-R) prior to prolonged ischaemia significantly reduces subsequent infarction. Following IPC two "windows of opportunity" (early and late) exist during which prolonged ischaemia can occur with reduced myocardial infarction. We investigated if IPC of skeletal muscle prior to flap creation improved subsequent flap survival and perfusion in either early or late windows.

The latissimus dorsi muscles (LDM) of Sprague-Dawley rats were used.

Group 1: (control, n=12). The LDM was elevated as a thoracodorsally based island flap.
Group 2: (early IPC, n=8). The LDM was preconditioned with two 30 minute episodes of normothermic global ischaemia with intervening 10 minute episodes of reperfusion prior to elevation.
Group 3: (late IPC, n=8). The LDM was elevated 24 hours after IPC ischaemia was created by occlusion of the thoracodorsal artery and vein and the intercostal perforators having previously isolated the muscle on these vessels. Muscle perfusion was assessed by a laser Doppler perfusion imager. One week after flap elevation the percentage of muscle necrosis was measured by computer-assisted planimetry.
IPC significantly reduced muscle flap necrosis (Table) in both early and late windows. Muscle flap perfusion was similar in all groups.

| Table 1: Percentage of muscle flap necrosis and % decrease in muscle flap perfusion post elevation. Results expressed as mean ± SEM *= p < 0.05 |
|---------------------------------------------|-----------------|
| Group 1 (control)                         | 35 ± 2          |
| Group 2 (early IPC)                       | 15 ± 1          |
| Group 3 (late IPC)                        | 20 ± 3          |

(50)
systemic infection, mostly pneumonia or gastroenteritis; anti-lymphocyte markers and HIV P24 antigen. Death was due to factor, CNS pathology was a late feature of the disease and anti-
demonstrate a histological and serological picture suggesting
autoantibody titre.

demonstrate poor correlation between histological features and
overall more severe disease on liver histology. Both groups
usually possible with liver histology and serology. Some women
the values are much higher in AIH. Similarly AIH patients show
elevated liver enzymes, positive ANF and ASM autoantibodies,
the grading and staging system of Ishak et al (1995).

of patients. Liver biopsies from all women were compared using
mitochondrial (AMA) antibodies are compared for both groups
by the ischaemia of flap creation during both the early and late
windows. Therefore IPC may have clinical application in the
prevention of muscle flap necrosis.

Conclusion: IPC of skeletal muscle prior to flap creation
significantly reduces subsequent muscle flap necrosis caused
by the ischaemia of flap creation during both the early and late

(P.194) A COMPARATIVE STUDY OF CHRONIC HEPATITIS C AND AUTOIMMUNE HEPATITIS: BIOCHEMISTRY SEROLOGY, HISTOLOGY
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This study compares the biochemical, serological and histopathological findings in 20 women with chronic hepatitis C virus (HCV) infection with 20 age-matched women with established autoimmune hepatitis (AIH). There is increasing evidence of autoimmunity in HCV liver pathology. Because of different treatment regimens for HCV (d-interferon) and AIH (steroids, immunosuppression), clear distinction between the two diseases is desirable.

Liver enzymes (ALT, AST, Alkaline phosphatase), anti-nuclear factor (ANF), anti-smooth muscle (ASM) and anti-mitochondrial (AMA) antibodies are compared for both groups of patients. Liver biopsies from all women were compared using the grading and staging system of Ishak et al (1995).

The results show that while some women in both groups show elevated liver enzymes, positive ANF and ASM autoantibodies, the values are much higher in AIH. Similarly AIH patients show overall more severe disease on liver histology. Both groups demonstrate poor correlation between histological features and autoantibody titre.

We conclude that distinction between HCV and AIH is usually possible with liver histology and serology. Some women with chronic HCV and positive autoantibodies however; demonstrate a histological and serological picture suggesting that chronic HCV may be mediated by an immunopathogenic mechanism.

(P.195) ABSENCE OF HIV ENCEPHALITIS IN THE BRAINS OF 11 ROMANIAN CHILDREN WITH AIDS
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Paediatric AIDS represents only 5% of cases worldwide. In most published series parental IV drug use was the main risk factor, CNS pathology was a late feature of the disease and anti-retroviral treatment had been given. We studied eleven brains from Romanian children with probable postnatal HIV infection using standard neuropathological stains and immunostains for lymphocyte markers and HIV P24 antigen. Death was due to systemic infection, mostly pneumonia or gastroenteritis; anti-retroviral treatment had not been given. Three cases showed terminal changes only. 5 showed lymphocytic meningitis and 4 of these also had perivascular lymphocytic inflammation (CD3 positive) in the subependymal regions, brainstem and choroid plexus. Two brains showed purulent meningitis and one case had central pontine myelinolysis probably related to profound metabolic disturbance. Basal ganglia mineralization, HIV encephalitis (HIVE) or HIV leucoencephalopathy (HIVL) were not present. These findings differ considerably from those described in US cases, in whom the majority have evidence of HIV within the CNS. Relatively early death from systemic infection may account for the lack of HIVE/HIVL in these cases. The lymphocytic meningitis and perivascular inflammation may represent an immuno-allergic reaction, previously reported as “early” changes, regarded as important in inducing vascular damage which allows subsequent entry of HIV into the brain.

(P.196) THE SIGNIFICANCE OF APOPTOSIS IN CHRONIC HCV LIVER DISEASE
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The aim of this study is to assess apoptosis in areas of interface hepatitis and spotty necrosis in Hepatitis C Virus (HCV) infected liver biopsies, and to correlate the degree of apoptosis with severity of histological activity.

25 liver biopsies were randomly selected from a group of Type lb HCV positive women. These patients were diagnosed by Recombinant Immunoblot Assay (RIBA) test and the presence of HCV RNA was confirmed using the polymerase chain reaction (PCR). Apoptosis was demonstrated in the biopsies by the Oncor ApopTag in-situ hybridisation technique. The average number of apoptotic hepatocytes per portal tract, and within the parenchyma per 10X objective, was determined. The modified Histological Activity Index (H.A.I.) was used to score each biopsy.

Comparison of the results shows that increasing numbers of apoptotic hepatocytes are consistently associated with increasing scores for interface hepatitis and spotty necrosis.

It is concluded that apoptosis occurs in HCV infected livers and that it correlates with increasing histological activity indicating a significant role for apoptosis in the pathogenesis of HCV liver disease.

(P.197) THE p53 AND bcl-2 GENES IN POST-TRANSPLANT LYMPHOPROLIFERATIVE DISEASE
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We studied the role of the p53 and bcl-2 genes in the pathogenesis of post-transplant lymphoproliferative disease (PTL). Ten cases were examined by immunohistochemical and molecular methods. Immunohistochemistry was performed using standard and antigen retrieval methods, with the p53 DO-7 and the bcl-2 oncprotein clone 124 antibodies. DNA was extracted from paraffin blocks and subjected to PCR, and single-strand conformation polymorphism (SSCP) analysis searching for mutated p53 genes. Samples showing any evidence of aberrant migrations were further analysed by direct sequencing. PCR was also used to detect bcl-2 gene rearrangements.

| % MUSCLE NECROSIS | % DECREASE IN PERFUSION |
|-------------------|------------------------|
| Group 1. 23 ± 4*  | 24 ± 7                 |
| Group 2. 15 ± 2*  | 24 ± 6                 |
| Group 3. 11 ± 5*  | 36 ± 4                 |

% DECREASE IN PERFUSION
Immunohistochemistry for bcl-2 oncoprotein without antigen retrieval gave negative results, but with antigen retrieval, showed positive staining in 6 out of 8 cases. No bcl-2 rearrangements were detected by PCR. The combination of SSCP and sequencing confirmed only wild type DNA in all cases. p53 immunohistochemistry by standard methods revealed positive staining in only one out of nine samples analysed. When the antigen retrieval method was employed for this antibody, positive staining was seen in > 10% of tumour cells in four further cases.

Our results suggest that p53 does not play major role in PTLD. Bcl-2 overexpression but not rearrangement may contribute to the development of PTLD.

(P.198) DNA VIRUSES IN TRANSPLANT ARTERIOPATHY

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Transplant arteriopathy (TA) is the major cause of death in cardiac allograft recipients. The pathogenesis is unclear. We have previously shown a plasma cell predominance in the infiltrate of TA, leading us to hypothesise a role for Epstein-Barr virus (EBV) infection in its pathogenesis. An association between cytomegalovirus (CMV) and TA has previously been suggested. The aim of the study was to investigate the role of Epstein-Barr virus (EBV) and cytomegalovirus (CMV) in the pathogenesis of TA.

We performed PCR for CMV and EBV DNA and protein (LMP) in seven cases of TA, involving cardiac allografts. Restriction mapping was used to confirm that PCR products were either CMV or EBV DNA respectively.

CMV DNA was found in four cases. EBV DNA was found in six of the seven cases and EBV LMP staining was present in six cases. EBV was detected in all cases by either PCR or IHC.

Our results suggest that EBV infection may play a pathogenic role in transplant arteriopathy. The evidence for a similar role for CMV is less strong.

(P.199) AUTOSOMAL DOMINANT HEREDITARY SPASTIC PARAPLEGIA IS NOT LINKED TO THE HSP LOCUS ON CHROMOSOME 2

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Hereditary spastic paraplegia (HSP) is a neurodegenerative disorder characterised by progressive spasticity, primarily of the lower limbs. It can be inherited in an autosomal dominant (AD), autosomal recessive or X-linked manner. We have identified a large Irish family (family A) affected with AD HSP that cosegregates with dementia. Three loci have previously been identified that are linked to AD HSP in families of different ethnic origin. The locus on chromosome 2 is reported to be the major HSP locus. The aim of the present study was to examine family A for linkage to the chromosome 2 HSP locus.

DNA has been extracted from blood taken from all 45 co-operating family members for genotyping. Polymorphic microsatellite markers from chromosome region 2p24-21 have been amplified by PCR, electrophoresed on a denaturing polyacrylamide gel and detected by silver staining. Linkage analysis was carried out using the LINKAGE series of programs.

Linkage analysis excluded the HSP gene from the chromosome 2p locus. The most significant marker was D2S367, with a LOD score of -2.12 for recombination fraction 0.19, thereby excluding approximately 19cM either side of this marker. Negative LOD scores were also obtained for the other markers chosen (D2S391, D2S392, D2S352, D2S174) excluding 20cM, 8cM, 4cM and 8cM respectively.

The current study has therefore successfully excluded linkage of AD HSP in family A to the major locus on chromosome 2p. Further studies are underway to exclude linkage of HSP in this family from other candidate loci, prior to carrying out a genome wide search. The presence of dementia in this family in association with HSP suggests that a new and as yet unidentified gene is responsible.

(P.201) HOMOZYGOSITY MAPPING INDICATES CONGENITAL HEREDITARY ENDOTHELIAL DYSTROPHY (CHED) IS NOT LINKED TO AN IDENTIFIED CONEAL DYSTROPHY LOCUS

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CHED is a corneal endothelial dystrophy characterised by diffuse bilateral corneal opacities resulting in impaired vision. Both autosomal dominant and autosomal recessive modes of inheritance have been described. Another endothelial dystrophy, posterior polymorphous dystrophy (PPMD) has been linked to 20q11.

We have used homozygosity mapping to analyse a pedigree with autosomal recessive CHED for linkage to 20q11. All affected individuals are offspring of consanguinous matings. Homozygosity mapping is based on the principle that these offspring would be homozygous for genetic markers near the disease gene. Homozygous regions would be random between different offspring of these matings, except at the disease locus shared by affected offspring.

DNA was extracted from blood taken from 22 family members, 14 of which have CHED. Allele frequencies were determined in pooled DNA from affected individuals. Pooled DNA from unaffected individuals was used as a control. At the disease locus, a shift in allele frequencies towards a single homozygous allele would be observed in the affected DNA pool. Pooled DNA was genotyped by PCR for 3 polymorphic microsatellite markers in the region of 20q11. PCR products were separated on a polyacrylamide gel and visualised by silver staining. Similar allele frequencies were observed at these loci in both DNA pools demonstrating independent assortment of alleles. In addition, affected and unaffected family members were individually genotyped at these loci and no significant loss of heterogeneity in the affected individuals at these loci was observed. These data indicate exclusion of linkage of the CHED gene to 20q11.
(P.202) GENOME-WIDE SEARCH FOR NOVEL GENE SEQUENCES IN BREAST CARCINOMA USING REPRESENTATIONAL DIFFERENCE ANALYSTS

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We employed a technique called Representational Difference Analysis to search for previously undescribed translocations or deletions which may be involved in breast carcinogenesis.

DNA was isolated from both invasive ductal carcinoma of the breast and normal tissue from the same patient. Following restriction enzyme digestion and ligation of oligonucleotide linkers, PCR was carried out on both tumour and normal DNA using oligonucleotide specific primers to obtain a representation of each genome (Amplicons). Digestion with the same restriction enzyme removed the original linkers, and a second set of oligonucleotides were ligated to normal amplicons only. The tumour derived amplicons were subtractively hybridised to the normal and subsequent PCR was used to isolate fragments unique to the normal DNA (Difference Products). This was possible since oligonucleotides were ligated to normal DNA only. Following a series of further subtractive hybridisations and subsequent amplifications, purified difference product was obtained. Difference products in the size range 500-1500 bp were obtained.

Following further rounds of subtractive hybridisation and amplification, purified difference product will be sequenced and characterised by comparison with known gene sequences. The chromosomal location of the affected gene will be established by in-situ hybridisation and somatic cell hybridisation, using the difference product as probe.

(P.203) AN HEREDITARY SPASTIC PARAPARESIS IS NOT LINKED TO SPINOCEREBELLAR ATAXIA LOCI

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Hereditary spastic paraparesis (HSP) is a variably expressed neurodegenerative disorder which exhibits clinical and genetic heterogeneity. HSP can be inherited in an autosomal dominant (AD), autosomal recessive (AR) or X-linked manner. AD-HSP has been linked to a number of loci. D6S274 gave maximum exclusion of 13cM on either side of the SCA-II locus with a LOD of -2.08 at a recombination fraction of 0.13. Other markers examined also outruled linkage to these loci.

We conclude that the gene for AD-HSP is unlinked to the major SCA loci.

(P.204) NO EVIDENCE OF DECREASED BONE FORMATION IN TOTAL, PROTEIN S DEFICIENT PATIENTS

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Protein S is secreted by osteoblasts and case reports of reduced bone mineral density in patients with total protein S deficiency have lead to the hypothesis that this inherited disorder is associated with generalised osteoblast dysfunction predisposing to osteoporosis. We have assessed bone formation in 8 patients (2 male and 6 female) with total protein S deficiency and 4 controls (2 male and 2 female) using two recently available sensitive markers; serum osteocalcin (Oc) and serum procollagen 1 carboxyterminal peptide (PICP), both secreted by the osteoblast. The mean total protein S level amongst the patients was 40 ± 12% (ref range 62-135%), mean Oc was 14.2 g/ml (ref range 5.2-59 g/ml) and the mean PICP was 81.5 ± 15 ugA (ref range 38-02 ugA/l). In the control group, mean Oc was 12.6 ± 5 g/ml and the PICP was 124 ± 37 ug/l. There was no statistical difference between both groups using either marker.

In conclusion bone formation as assessed by serum osteocalcin and PICP appears to be normal in patients with total protein S deficiency.

Reference
Pan et al. Thrombosis Research 1990: 58, 221.

(P.205) SIGNIFICANCE OF LOW SERUM VITAMIN B12

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Serum Vitamin B12 is frequently measured in the investigation of anaemia, and in screening neurological and other disorders. Frequently, patients are found with low serum vitamin B12 level with a normal Hb and without clinical abnormalities relevant to vitamin B12 deficiency. This study was carried out to determine the significance of a low serum vitamin B12 level. 959 vitamin B12 measurements were carried out over an 8 month period using a chemiluminescence method (Abbott IMX).

Clinical data was obtained retrospectively. Of the 959 samples 81 (8.4%) representing 65 patients had a low serum vitamin B12 level (>180 pg/ml) with a mean of 152 pg/ml (39-179). Data was available on 44 patients. 20 (45%) had a Hb below the normal range with median serum vitamin B12 level of 158 pg/ml (75-184). 19 (45%) had a normal Hb, MCV and MCHC with a median serum vitamin B12 of 152 pg/ml (52-210), and 5 had a normal Hb with an abnormal MCV or MCH. LFT’s, autoantibodies, Schillings test and bone marrow examination data will be presented.

In conclusion in patients with a low serum vitamin B12 level, there was no significant difference in the B12 levels in those patients with a normal or a low Hb concentration. It would appear that serum vitamin B12 is a poor discriminatory test but that changing the normal range may not help in screening. Low serum vitamin B12 on its own may not appear to provide adequate grounds for lifelong replacement therapy.
(P.206) EPIDEMIOLOGY AND SURVIVAL RATES FOR ALL 324 LYMPHOMA PATIENTS REGISTERED IN CORK AND KERRY OVER THE EIGHT YEAR PERIOD 1983/1990

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An indepth review of all 324 lymphoma (ICD-O code 196) patients registered by the Southern Tumour Registry during the eight year period 1983/1990. Annual age adjusted rates of 7.6 and 5.4 per 100,000 were seen for males and females respectively. These levels indicate a lifetime (up to 75 yr) risk of 1 in 133 for males and 1 in 172 for females. As expected the overall incidence of Hodgkin’s was lower with one third of male and one quarter of female lymphoma cases affected by the disease. A distinct age specific pattern is evident depending on lesion type. Marked variation in incidence levels were noted throughout the study region. An extremely varied pattern is evident in the survival rates for lymphoma patients. The Cork and Kerry rates for malignant lymphoma are relatively low when compared with international levels.

References
1. Cancer, The Irish Experience. M. J. Crowley
2. Muir, C., Warehouse, J., Mack, T., Powell, J., Whelan, S. Cancer incidence in Five Continents volume VI. IARC Scientific Publications No.88. Lyon: International Agency for Research on Cancer, 1987.